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(54) Title: METHODS FOR IMPROVING THE EFFICACY AND EXPANSION OF IMMUNE CELLS

(57) Abstract: The invention provides methods of making immune effector cells (e.g., T cells, NK cells) that can be engineered to express a chimeric antigen receptor (CAR), compositions and reaction mixtures comprising the same, and methods of treatment using the same.

METHODS FOR IMPROVING THE EFFICACY AND EXPANSION OF IMMUNE CELLS

RELATED APPLICATIONS

This application claims priority to U.S. Serial No. 62/195,056 filed July 21, 2015, the contents of which are incorporated herein by reference in their entireties.

SEQUENCE LISTING

The instant application contains a Sequence Listing which has been submitted electronically in ASCII format and is hereby incorporated by reference in its entirety. Said ASCII copy, created on July 18, 2016, is named N2067-7081WO_SL.txt and is 2,053,055 bytes in size.

BACKGROUND OF THE INVENTION

Until about a decade ago, T cell activation *in vitro* was carried out primarily with the use of mitogenic lectins, such as phytohemagglutinin (PHA) and concanavalin A (Con A). These mitogenic molecules bind to glycoproteins on the cell surface. To achieve T cell receptor (TCR) complex-specific stimulation, antibodies specific to surface molecules, including CD2, CD3, CD28 and CD45 have been used. These antibodies provided the required co-stimulatory signal to trigger complete activation and proliferation of T cells in culture (Frauwirth and Thompson *J Clin Invest* (2002) Feb;109(3):295-9). The field has progressed to immobilizing these antibodies to accessory cells, beads or a solid surface for robust expansion of T lymphocytes (Trickett and Kwan *J Immunol Methods* (2003) Apr 1;275(1-2):251-5).

However, limitations with existing protocols for activation and expansion of T cells still remain. An exemplary listing of these limitations includes the following. For example, existing protocols rely on the presence of functional TCRs on the surface of T cells. This limits the activation of T cells to those cells with a functional TCR. Primary T lymphocytes are a heterogeneous pool of cells that could include T cells without a functional TCR, thus limiting the T cells populations that can be activated. Production, procurement and use of antibodies to cell surface molecules, such as CD2, CD3, CD28 and CD45, can be expensive and dependent on the availability of such antibodies. Additionally, since complete T cell activation may require two different antibodies (primary stimulant such as anti-CD3, and a secondary

stimulant, such as anti-CD28), the cost is further increased. Furthermore, since CD3/CD28 stimuli are typically left in culture for long time durations, the TCRs are being engaged for prolonged, repeated stimulations. Prolonged high levels of TCR stimulation can provide robust activation signal to naïve T cells with concurrent activation-induced cell death (AICD) of memory T cells (Collette Y, *et al. Blood* (1998) Aug 15;92(4):1350-63; Kerstan A and Hünig T *J Immunol* (2004) Feb 1;172(3):1341-5; Noel, PJ *et al. J Immunol.* 1996 Jul 15;157(2):636-42).

Accordingly, the need exists to improve the *in vitro* expansion and activation of immune cells, e.g., immune effector cells.

SUMMARY OF THE INVENTION

The present disclosure pertains, at least in part, to methods for improving the expansion and/or activation (e.g., *in vitro* expansion and/or activation) of immune cells (e.g., immune effector cells). Some embodiments described herein provide for expansion and/or activation of immune cells by transiently expressing a Chimeric Antigen Receptor (CAR) molecule. Said CAR-expressing immune cells can be activated via a ligand of the CAR molecule, e.g., a ligand of the CAR antigen binding domain (e.g., a cognate antigen molecule or an anti-idiotypic antibody molecule). In embodiments, the methods disclosed herein allow for expansion of immune cells, without requiring the presence of a functional T cell receptor, and/or without substantially altering the phenotype of the immune cell. For example, immune effector cells including anergized T cells, hematopoietic stem cells, NK cells, and B-cells can be expanded using the methods described herein. Furthermore, immune cells can be expanded without substantially altering their undifferentiated phenotype and/or without prolonged, repeated stimulation of the T-cell receptor. In certain embodiments, the methods described herein allow for superior proliferation and cell number yield, compared to conventional TCR-stimulated expansion. Thus, the improved methods and compositions (e.g., modified immune cell populations, reaction mixtures) disclosed herein can provide a significant benefit for cellular therapy, e.g., immunotherapy.

Accordingly, in one aspect, the invention features a method of expanding and/or activating a population of immune cells, e.g., immune effector cells. The method includes introducing a CAR molecule (e.g., a nucleic acid encoding a CAR molecule) into the immune cell population, under conditions suitable for expression (e.g., transient expression) of the CAR

molecule (e.g., thereby producing a "first CAR-expressing cell population," or a "transient CAR-expressing cell population" as referred to herein). In certain embodiments, the CAR molecule comprises an antigen binding domain (e.g., an antigen binding domain of an antibody molecule). The method includes contacting the first or transient CAR-expressing cell population with a ligand of the CAR molecule, e.g., a ligand of the CAR antigen binding domain (e.g., a cognate antigen molecule (e.g., a recombinant antigen) or an anti-idiotypic antibody molecule), under conditions such that immune cell expansion and/or activation occurs, thereby producing an "expanded and/or activated immune cell population." In embodiments, the ligand of the CAR molecule is present in/on (e.g., immobilized or attached to) a substrate, e.g., a non-naturally occurring substrate. The method can further include culturing the population of immune cells in the presence of the ligand of the CAR molecule.

In a related aspect, the invention features a method of expanding and/or activating a population of immune cells, e.g., immune effector cells. The method includes providing a first CAR-expressing cell population, or a transient CAR-expressing cell population as described herein, and contacting said CAR-expressing cell population with a ligand of the CAR molecule, e.g., a ligand of the CAR antigen binding domain (e.g., a cognate antigen molecule (e.g., a recombinant antigen) or an anti-idiotypic antibody molecule), under conditions such that immune cell expansion and/or activation occurs, thereby producing an "expanded and/or activated immune cell population." In embodiments, the ligand of the CAR molecule is present in/on (e.g., immobilized or attached to) a substrate, e.g., a non-naturally occurring substrate. The method can further include culturing the population of immune cells in the presence of the ligand of the CAR molecule.

In an embodiment, the transiently expressed CAR is produced by transiently introducing a nucleic acid (e.g., an RNA or DNA) encoding a CAR into the cell, under conditions that allow for production of the CAR.

In an embodiment, the transiently expressed CAR is produced by using a sortase. For example, the sortase may be used to couple an extracellular domain (e.g., comprising an antigen-binding domain and a sortase recognition motif) to a sortase acceptor member (e.g., comprising a sortase acceptor motif, a transmembrane domain, and optionally an intracellular signaling domain or a switch domain). In an embodiment, the transiently expressed CAR comprises a sortase transfer signature, e.g., that resulted from the coupling of a sortase

recognition motif to a sortase acceptor motif. In an embodiment, the sortase, the CAR, or the sortase acceptor member is as described in PCT/CN2014/090503 filed November 6, 2014, or PCT/CN2014/082600 filed July 21, 2014, each of which is herein incorporated by reference in its entirety.

The aforesaid methods can be carried our *in vitro*, *ex vivo* or *in vivo*.

In some embodiments, the population of immune cells used in the methods described herein is acquired, e.g., obtained, from a blood sample from a subject (e.g., a cancer patient). In one embodiment, the population of immune cells is obtained by apheresis.

In some embodiments, the immune cell population includes immune effector cells, e.g., as described herein. Exemplary immune effector cells include T cells, e.g., alpha/beta T cells and gamma/delta T cells, B cells, natural killer (NK) cells, natural killer T (NKT) cells, mast cells, myeloid-derived phagocytes, or a combination thereof.

In certain embodiments, the immune cell population includes primary T cells or subsets of lymphocytes, including, for example, anergized T cells, naïve T cells, T-regulatory cells, Th-17 cells, stem T cells, or a combination thereof.

In some embodiments, the immune cell population includes peripheral blood mononucleated cells (PBMCs), or cord blood cells, or a combination thereof.

In one embodiment, the immune cell population includes cells that express a low level of, or do not have, a T cell receptor (e.g., a functional T cell receptor). In another embodiment, the immune cell population includes cells that have non-functional or substantially impaired T cell receptors.

In one embodiment, the nucleic acid encoding the CAR molecule (e.g., the first CAR molecule) is an RNA molecule, e.g., an *in vitro* transcribed (IVT) RNA. In one embodiment, a CAR encoding RNA construct as described herein is introduced into the immune cell population by transfection or electroporation. In one embodiment, the CAR molecule is expressed transiently (e.g., the CAR molecule does not, or does not substantially, integrate into the cellular genome). In one embodiment, the CAR molecule is expressed in the immune cell for a finite period of time or number of cell replications, e.g., less than 50 days (e.g., less than 40, 30, 25, 20, 15, 10, 5 or fewer days).

In one embodiment, the CAR molecule is transiently expressed on the immune cell surface and is internalized post a single ligand (e.g., antigen) stimulation. In embodiments, the immune cell does not receive repeated ligand (e.g., antigen) stimulation.

In other embodiments, the strength of the immune cell stimulation is customized to a desired level, e.g., by adjusting one or both of: the CAR-surface density, or the affinity of the CAR antigen binding domain to the ligand, e.g., the antigen. For example, increasing the CAR-surface density on the immune cell, or increasing the affinity of the CAR binding domain to the ligand (e.g., antigen) may increase the strength of the immune cell stimulation.

In other embodiments, the nucleic acid encoding the CAR molecule (e.g., the first CAR molecule) is a DNA vector or an RNA vector. In one embodiment, the vector is selected from the group consisting of a DNA, an RNA, a plasmid, a lentivirus vector, adenoviral vector, or a retrovirus vector. In one embodiment, the vector is a lentivirus. In one embodiment, the nucleic acid is stably integrated into the cellular genome.

In embodiments, the encoded CAR molecule is as described herein, e.g., a tumor antigen-binding CAR (e.g., CD19 CAR) as described herein.

In another embodiment, the ligand of the CAR molecule is a cancer associated antigen, e.g., a cancer associated antigen recognized by a CAR molecule as described herein, e.g., a CD19 CAR.

In some embodiments, the substrate is a non-cellular substrate. The non-cellular substrate can be a solid support chosen from, e.g., a plate (e.g., a microtiter plate), a membrane (e.g., a nitrocellulose membrane), a matrix, a chip or a bead. In embodiments, the ligand of the CAR molecule is present in the substrate (e.g., on the substrate surface). The ligand can be immobilized, attached, or associated covalently or non-covalently (e.g., cross-linked) to the substrate. In one embodiment, the ligand is attached (e.g., covalently attached) to a bead. In the aforesaid embodiments, the immune cell population can be expanded *in vitro* or *ex vivo*.

In other embodiments, the substrate is a cell, e.g., a cell expressing the ligand, e.g., a cell expressing the cognate antigen on its surface. In one embodiment, the cognate antigen is heterologous to the cell, e.g., is a recombinant antigen expressed on the cell surface. In another embodiment, the cognate antigen is endogenously expressed on a cell, e.g., a tumor cell. In the aforesaid embodiments, the immune effector cell population can be expanded *in vitro*, *ex vivo*

or *in vivo*. In one embodiment, T cells are expanded *in vivo*, *e.g.*, by lymph node injection, or by injection of the tumor-infiltrating lymphocytes (TIL) into a tumor.

In one embodiment, the CAR-expressing immune cells are cultured in the presence of the ligand of the CAR molecule for a predetermined period (e.g., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 18, 21, 22, 23 or 24 hours) or (e.g., 1, 5, 10, 15, 20, 25, 30, 35, 40, 45 or 50 days). In one embodiment, the CAR-expressing cells are cultured for a period of 4 to 9 days. In one embodiment, the CAR-expressing cells are cultured for a period of 8 days or less, e.g., 7, 6 or 5 days.

In some embodiment, the CAR-expressing immune cell population shows at least 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12 or higher population doublings. In one embodiment, the CAR-expressing immune cell population shows a total of 8-10, or about 9 population doublings.

In one embodiment, the CAR-expressing immune cell population expands to a total of 200-, 300-, 400-, 450-, 500-, 550-, 600-, 650-fold or higher expansion per cell. In one embodiment, the CAR-expressing immune cell population are expanded about 500-fold. In one embodiment, an average cell multiplies to over 400-600, or about 500 cells. In some embodiments, the cell expansion is measured by a method described herein, such as flow cytometry. In one embodiment, the cell expansion is measured at about 5, 10, 15, 20, 25, 30, 35, 40, 45, or 50 days after stimulation with the ligand, e.g., the cognate antigen. In one embodiment, the cell expansion is measured between 10 and 25 days after stimulation with the ligand. In one embodiment, the expansion is measured 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 days after stimulation with the ligand.

In one embodiment, the expansion and/or activation of the immune cell population using the methods described herein does not substantially stimulate the TCRs on the immune cell. In embodiments, the methods described herein lead to less rapid differentiation of the immune cells and/or promotes "younger" T cell phenotypes in culture. In some embodiments, the expanded and/or activated immune cell population includes immune effector cell having a less differentiated phenotype, e.g., a younger cell, e.g., a young T cell. In some embodiments, a younger T cell may be a naïve T cell (T_N), a memory stem cell (T_{SCM}), a central memory T cell (T_{CM}), or a combination thereof.

In certain embodiments, the methods disclosed herein further include contacting the expanded and/or activated immune cell population with a nucleic acid encoding a second CAR

molecule, e.g., a vector comprising a nucleic acid encoding a second CAR, thereby producing a second CAR-expressing cell population.

In one embodiment, the nucleic acid encoding the second CAR molecule is selected from the group consisting of a DNA, an RNA, a plasmid, a lentivirus vector, adenoviral vector, or a retrovirus vector. In one embodiment, the nucleic acid encoding the second CAR molecule vector is a lentivirus.

In other embodiments, the nucleic acid encoding a second CAR molecule is an IVT RNA.

In some embodiment, the first and second CAR molecules are directed to the same antigen, e.g., the same tumor cell antigen. In one embodiment, the first and second CAR molecules are the same CAR molecule. In such embodiments, the immune cell population expressing (e.g., transiently expressing) the first CAR is expanded and/or activated *in vitro* or *ex vivo*, e.g., by contacting said immune cell population with the tumor cell antigen or an anti-idiotypic antibody against the CAR binding antibody molecule (e.g., a CD19-antigen or anti-CD19 idiotypic antibody immobilized onto a non-cellular or cellular substrate as described herein). Alternatively, or in combination, the immune cell population expressing (e.g., stably expressing) the second CAR is expanded and/or activated *in vivo*, e.g. by contacting an endogenous tumor cell antigen (e.g., CD19). In one embodiment, the second CAR-expressing immune cell is administered to a subject, e.g., as part of a therapeutic protocol.

In other embodiments, first and second CAR molecules are directed to different antigens, e.g., different tumor cell antigens. In one embodiment, the first and second CAR molecules are different CAR molecules (e.g., a first and second CAR molecule). In such embodiments, the immune cell population expressing (e.g., transiently expressing) the first CAR is expanded and/or activated *in vitro* or *ex vivo*, e.g., by contacting said immune cell population with a first tumor cell antigen or a first anti-idiotypic antibody against the antigen binding domain of the CAR (e.g., a mesothelin antigen or an anti-idiotypic antibody against the mesothelin-binding domain of the CAR molecule immobilized onto a non-cellular or cellular substrate as described herein). Alternatively, or in combination, the immune cell population expressing (e.g., stably expressing) the second CAR is expanded and/or activated *in vivo*, e.g. by contacting an endogenous second tumor cell antigen (e.g., CD19). In one embodiment, the

second CAR-expressing immune cell is administered to a subject, e.g., as part of a therapeutic protocol.

In one embodiment, the first and second CAR is chosen from a ROR1 CAR, a CD19 CAR, a CD20 CAR, a CD22 CAR, a CD123 CAR, a CD10 CAR, a CD34 CAR, a FLT-3 CAR, a CD79b CAR, a CD179b CAR, a mesothelin CAR or a CD79a CAR, e.g., a CAR as described herein. In one embodiment, the first and second CARs are the same. In other embodiments, the first and second CARs are different. Any combination of first and second CAR can be used in the methods disclosed herein.

In certain embodiments, the methods further comprise storing the expanded and/or activated immune cell population after the appropriate expansion period. In one embodiment, the expanded and/or activated immune cell population is cryopreserved according to a method described herein. In one embodiment, the expanded and/or activated immune cell population is cryopreserved in an appropriate media, e.g., an infusible media, e.g., as described herein.

In another aspect, the invention features a method of treating a disorder or condition (e.g., a disorder or condition as described herein), in a subject. The method includes administering to the subject an expanded and/or activated immune cell population made according to one or more of the methods described herein. In embodiments, the method includes acquiring (e.g., obtaining) the expanded and/or activated immune cell population. The expanded and/or activated immune cell population can be obtained from a suitable storage condition, e.g., cryopreservation.

In some embodiments, the immune cell population includes immune effector cells, e.g., a described herein. Exemplary immune effector cells include T cells, e.g., alpha/beta T cells and gamma/delta T cells, B cells, natural killer (NK) cells, natural killer T (NKT) cells, mast cells, hematopoetic stem cells (HSC), myeloic-derived phagocytes, or a combination thereof.

In certain embodiments, the immune cell population includes primary T cells or subsets of lymphocytes, including, for example, anergized T cells; naïve T cells; T-regulatory cells; Th-17 cells; stem T cells, or a combination thereof.

In some embodiments, the immune cell population includes peripheral blood mononucleated cells (PBMCs), or cord blood cells, or a combination thereof.

In yet another aspect the invention features a method of treating, or providing anti-tumor immunity to, a subject having a cancer. The method includes administering to the subject an effective amount of an immune effector cell population (e.g., an expanded and/or activated immune cell population as described herein) that expresses a CAR molecule (e.g., a first and/or second CAR molecule as described herein), alone or in combination with an additional therapy, e.g., a second therapy as described herein.

In some embodiments, the treatment method includes acquiring (e.g., obtaining) the expanded and/or activated immune cell population using one or more of the methods described herein. For example, the expanded and/or activated immune cell population may have been previously obtained by introducing a first CAR molecule (e.g., a nucleic acid molecule encoding the first CAR molecule as described herein, e.g., an IVT RNA encoding the first CAR) under conditions suitable for expression (e.g., transient expression) of the CAR molecule; and contacting said CAR-expressing cell population with a ligand of the CAR molecule, e.g., a ligand of the CAR antigen binding domain (e.g., a cognate antigen molecule (e.g., a recombinant antigen) or an anti-idiotypic antibody molecule), under conditions such that immune cell expansion and/or activation occurs. In embodiments, the ligand of the CAR molecule is present in/on (e.g., immobilized or attached to) a substrate, e.g., a non-naturally occurring substrate, as described herein. The expanded and/or activated immune cell population can be stored under suitable conditions, e.g., cryopreservation, as described herein.

In certain embodiments, the treatment methods disclosed herein further include acquiring (e.g., obtaining) a second CAR-expressing cell population, e.g. a second CAR-expressing cell population as described herein. For example, the expanded and/or activated immune cell population may have been previously contacted with a nucleic acid encoding the second CAR molecule, e.g., a vector comprising a nucleic acid encoding a second CAR. In one embodiment, the nucleic acid encoding the second CAR molecule is selected from the group consisting of a DNA, a RNA, a plasmid, a lentivirus vector, adenoviral vector, or a retrovirus vector. In one embodiment, the nucleic acid encoding the second CAR molecule vector is a lentivirus.

In some embodiment, the first and second CAR molecules are directed to the same antigen molecule, e.g., the same cancer associated antigen. In one embodiment, the first and second CAR molecules are the same CAR molecule. In such embodiments, the immune cell

population expressing (e.g., transiently expressing) the first CAR was previously expanded and/or activated *in vitro* or *ex vivo*, e.g., by contacting said immune cell population with the cancer associated antigen or an anti-idiotypic antibody against the CAR binding antibody molecule (e.g., a CD19-antigen or anti-CD19 idiotypic antibody immobilized onto a non-cellular or cellular substrate as described herein). In one embodiment, the second CAR-expressing immune cell is administered to a subject, e.g., as part of a therapeutic protocol.

In other embodiments, first and second CAR molecules are directed to different antigens, e.g., different cancer associated antigens. In one embodiment, the first and second CAR molecules are different CAR molecules (e.g., a first and second CAR molecules). In such embodiments, the immune cell population expressing (e.g., transiently expressing) the first CAR was previously expanded and/or activated *in vitro* or *ex vivo*, e.g., by contacting said immune cell population with a first cancer associated antigen or a first anti- idiotypic antibody against the antigen binding domain of the CAR molecule (e.g., an antigen or an anti-idiotypic antibody against the binding domain of the CAR molecule immobilized onto a non-cellular or cellular substrate as described herein). In one embodiment, the second CAR-expressing immune cell is administered to a subject, e.g., as part of a therapeutic protocol.

In one embodiment, the first and second CAR molecules are each chosen independently from a ROR1 CAR, a CD19 CAR, a CD20 CAR, a CD22 CAR, a CD123 CAR, a CD10 CAR, a CD34 CAR, a FLT-3 CAR, a CD79b CAR, a CD179b CAR, a mesothelin CAR or a CD79a CAR, e.g., a CAR as described herein. In one embodiment, the first and second CARs are the same. In other embodiments, the first and second CARs are different. Any combination of first and second CAR can be used in the methods disclosed herein.

In one exemplary embodiment, the first CAR is directed to mesothelin and the mesothelin CAR-expressing cell is contacted with a mesothelin antigen or anti-idiotypic antibody against the mesothelin-antigen binding domain of the CAR; and the second CAR is directed to CD19 (e.g., a CD19 CAR disclosed herein). In another exemplary embodiment, the first CAR is directed to CD19 and the CD19 CAR-expressing cell is contacted with a CD19 antigen or anti- idiotypic antibody against the CD19-antigen binding domain of the CAR; and the second CAR is directed to mesothelin (e.g., a mesothelin CAR disclosed herein).

In some embodiments, the immune cell population used in the aforesaid therapeutic methods includes immune effector cells, e.g., a described herein. Exemplary immune effector

cells include T cells, e.g., alpha/beta T cells and gamma/delta T cells, B cells, natural killer (NK) cells, natural killer T (NKT) cells, mast cells, hematopoetic stem cells (HSC), myeloic-derived phagocytes, or a combination thereof.

In yet another aspect, the invention features an immune cell preparation or reaction mixture, e.g., comprising a population of immune effector cells (e.g., comprising a first and/or second CAR molecule or a nucleic acid encoding a first and/or second CAR molecule), e.g., made according to the methods described herein. In certain embodiments, the first and second CAR molecules are expressed simultaneously (e.g., completely or partially overlapping expression), or are expressed sequentially.

Additional features or embodiments of any of the aforesaid methods, preparations, and reaction mixtures include one or more of the following:

Immune Cell Expansion and/or Activation

In certain embodiments, methods disclosed herein include expanding and/or activating a population of immune cells, e.g., immune effector cells. The method includes acquiring a population of immune cells and contacting the cells with a nucleic acid encoding a CAR molecule, under conditions suitable for expression (e.g., transient expression) of the CAR molecule, wherein the CAR molecule binds to a ligand, e.g., a cognate antigen molecule (e.g., a recombinant antigen) or an anti-idiotype antibody against the antigen-binding domain of the CAR molecule; and culturing the population of immune cells in the presence of the cognate antigen molecule or the anti- idiotype antibody.

In one embodiment, the population of immune effector cells are autologous to the subject who the cells will be administered to for treatment. In one embodiment, the population of immune effector cells are allogeneic to the subject who the cells will be administered to for treatment.

In one embodiment, the population of immune effector cells are T cells isolated from peripheral blood lymphocytes. In an embodiment, the population of T cells are obtained by lysing the red blood cells and/or by depleting the monocytes. In an embodiment, the population of T cells is isolated from peripheral lymphocytes using, e.g., a method described herein. In one embodiment, the T cells comprise $CD4^+$ T cells. In another embodiment, the T

cells comprise $CD8^+$ T cells. In another embodiment, the T cells comprise regulatory T cells. In a further embodiment, the T cells comprise naïve T-cells. In one embodiment, the immune effector cells comprise hematopoietic stem cells (e.g., cord blood cells). In another embodiment, the immune effector cells comprise B cells. In a further embodiment, the immune effector cells comprise NK cells. In another embodiment, the immune effector cells comprise NKT cells. In another embodiment, the immune effector cells comprise Th-17 cells.

In one embodiment, the immune effector cells have a reduced level of T cell receptors or do not have T cell receptors. In another embodiment, the immune effector cells have non-functional or substantially impaired T cell receptors.

In one embodiment, the population of immune effector cells can be obtained from a blood sample from a subject, e.g., obtained by apheresis. In one embodiment, the immune effector cells collected by apheresis are washed to remove the plasma fraction and, optionally, the cells are provided in an appropriate buffer or media for subsequent processing steps. In one embodiment, the cells are washed with a buffer such as, e.g., phosphate buffered saline (PBS). In an embodiment, the cells are washed in a wash solution that lacks one or more divalent cation such as calcium and magnesium. In one embodiment, the immune effector cells are washed in a buffer that has substantially no divalent cations.

In one embodiment, the method comprises generating a population of RNA-engineered cells transiently expressing exogenous RNA from the population of immune effector cells. The method comprises introducing an in vitro transcribed RNA or synthetic RNA into a cell from the population, where the RNA comprises a nucleic acid encoding a CAR, e.g., a CAR described herein, e.g., a CD19 CAR described herein.

In one embodiment the RNA is introduced into the immune effector cells by a method described herein (e.g., electroporation). In one embodiment, at least at least 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96 %, 97%, 98%, 99% or 100% of the immune effector cells express the CAR mRNA.

In another embodiment, at least at least at least 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96 %, 97%, 98%, 99% or 100% of the immune effector cells express the CAR on their cell surface.

In one embodiment, the immune effector cells are expanded and/or activated by culturing the immune effector cells in the presence of a ligand, e.g., a cognate antigen molecule or an anti-idiotype antibody. In one embodiment, the immune effector cells are contacted with

the cognate antigen molecule or anti-idiotype antibody at least, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 28, 32, 36, 36, or 48 hours after the RNA is introduced into the immune effector cells. In one embodiment, the immune effector cells are contacted with the cognate antigen molecule or an anti-idiotype antibody less than 24, 15, 12, 10, or 8 hours after RNA is introduced into the immune effector cells.

In one embodiment, the ligand is a molecule that binds to and/or activates the CAR, e.g., on the cell surface of the population of immune effector cells expressing (e.g., transiently expressing) a CAR (e.g., a CAR described herein, e.g., a CD19 CAR described herein). In one embodiment, the cognate antigen molecule is the cognate antigen of the CAR. In one embodiment, the cognate antigen molecule is a recombinant antigen recognized by the antigen binding portion of the CAR. In one embodiment the cognate antigen molecule is a cancer associated antigen, e.g., a cancer associated antigen described herein, e.g., CD19. In one embodiment, the ligand is an anti-idiotype antibody (e.g., it is an antibody molecule that binds to the antigen binding domain of the CAR) e.g., an anti-CD19 idiotype antibody.

In one embodiment, the ligand is attached to a substrate. In one embodiment, the substrate is a solid support. In one embodiment, the substrate is selected from microtiter plates (e.g., ELISA plates); membranes (e.g., nitrocellulose membranes, PVDF membranes, nylon membranes, acetate derivatives, and combinations thereof); fiber matrix, Sepharose matrix, sugar matrix; plastic chips; glass chips; or any type of bead (e.g., Luminex beads, Dynabeads, magnetic beads, flow-cytometry beads, and combinations thereof). In one embodiment, the substrate is an ELISA plate. In another embodiment, the substrate is a bead, e.g., Dynabeads.

In one embodiment, the CAR expressing immune effector cells are contacted with the ligand-, e.g., antigen-, coated beads at a ratio of 1:100, 1:50, 1:40, 1:30, 1:20, 1:10, 1:9, 1:8, 1:7, 1:6, 1:5, 1:4, 1:3, 1:2, 1:1, 2:1, 3:1, 4:1, 5:1, 6:1, 7:1, 8:1, 9:1, 10:1, or 15:1 beads per immune effector cell. In one embodiment, the CAR expressing immune effector cells are contacted with antigen coated beads at a ratio of 3:1 beads per immune effector cell.

In one embodiment, the immune effector cells are further expanded in an appropriate media (e.g., media described herein) that may, optionally, contain one or more factors for proliferation and/or viability, including serum (e.g., fetal bovine or human serum), interleukin-2 (IL-2), insulin, IFN-γ, IL-4, IL-7, GM-CSF, IL-10, IL-12, IL-15, IL-21, TGFβ, and TNF-α or any other additives for the growth of cells. In one embodiment, the cells are expanded in the

presence IL-15 and/or IL-7 (e.g., IL-15 and IL-7). In one embodiment, the immune effector cells are expanded in the presence of IL-2.

In one embodiment, immune effector cells transduced with a nucleic acid encoding a CAR, e.g., a CAR described herein, e.g., a CD19 CAR described herein, are expanded in culture for a period of several hours (e.g., about 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 18, 21 hours) to about 40 days (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39 or 40 days). In one embodiment, the cells are expanded for a period of 4 to 9 days. In one embodiment, the cells are expanded for a period of 8 days or less, e.g., 7, 6 ,5, 4, or 3 days.

Potency of the immune effector cells can be defined, e.g., by various T cell functions, e.g. proliferation, target cell killing, cytokine production, activation, migration, or combinations thereof. In one embodiment, the immune effector cells, e.g., a CD19 CAR cell described herein, expanded for 5 days show at least one, two, three or four fold increase in cells doublings upon antigen stimulation as compared to the same cells expanded in culture for 9 days under the same culture conditions. In one embodiment, the immune effector cells, e.g., the cells expressing a CD19 CAR described herein, are expanded in culture for 5 days, and the resulting cells exhibit higher proinflammatory cytokine production, e.g., IFN-γ and/or GM-CSF levels, as compared to the same cells expanded in culture for 9 days under the same culture conditions. In one embodiment, the immune effector cells, e.g., a CD19 CAR cell described herein, expanded for 5 days show at least a one, two, three, four, five, ten fold or more increase in pg/ml of proinflammatory cytokine production, e.g., IFN-γ and/or GM-CSF levels, as compared to the same cells expanded in culture for 9 days under the same culture conditions.

In one embodiment, the immune effector cells are expanded at least a 200-fold (e.g., 200-fold, 250-fold, 300-fold, 350-fold, 400-fold, 450-fold, 500-fold, 550-fold, or 650-fold) increase in cells, e.g., as measured by a method described herein such as flow cytometry. In one embodiment, the cells are expanded about 500 fold.

In one embodiment, the cell expansion is measured at about 5, 10, 15, 20, 25, 30, 35, 40, 45, or 50 days after stimulation with the ligand, e.g., the cognate antigen molecule. In one embodiment, the cell expansion is measured between 10 and 25 days after stimulation with the ligand, e.g., the cognate antigen molecule. In one embodiment, the expansion is measured 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 days after stimulation with the ligand, e.g., the cognate antigen molecule.

In one embodiment, the immune effector cells are cryopreserved after the appropriate expansion period. In one embodiment, the cells are cryopreserved according to a method described herein. In one embodiment, the expanded cells are cryopreserved in an appropriate media, e.g., an infusible media, e.g., as described herein.

In one embodiment the method includes contacting the immune effector cells with a nucleic acid encoding a first CAR (e.g., an *in vitro* transcribed RNA) under conditions suitable for transient expression of the first CAR, wherein the first CAR targets a cognate antigen molecule, and expanding the population of immune effector cells by culturing the first CAR expressing immune effector cells in the presence of the cognate antigen molecule, and further contacting the cells with a vector comprising a nucleic acid encoding a second CAR. In one embodiment, the vector is selected from the group consisting of a DNA, a RNA, a plasmid, a lentivirus vector, adenoviral vector, or a retrovirus vector. In one embodiment, the cell from the population of immune effector cells, is transduced with a vector once, e.g., within one day after population of immune effector cells are obtained from a blood sample from a subject, e.g., obtained by apheresis.

In one embodiment, the first CAR targets a cognate antigen molecule and the second CAR targets the same cognate antigen molecule. In one embodiment, the first CAR targets a cognate antigen molecule and the second CAR a different cognate antigen molecule. In one embodiment, the first CAR targets a cancer associated antigen described herein and the second CAR targets the same cancer associated antigen described herein. In one embodiment, the first CAR that targets a cancer associated antigen described herein and the second CAR targets a different cancer associated antigen described herein. In one embodiment, the first CAR is a ROR1 CAR, a CD19 CAR, a CD20 CAR, a CD22 CAR, a CD123 CAR, a CD10 CAR, a CD34 CAR, a FLT-3 CAR, a CD79b CAR, a CD179b CAR, a mesothelin CAR or a CD79a CAR described herein and the second nucleic acid encodes a ROR1 CAR, a CD19 CAR, a CD20 CAR, a CD22 CAR, a CD123 CAR, a CD10 CAR, a CD34 CAR, a FLT-3 CAR, a CD79b CAR, a CD179b CAR, a mesothelin CAR or a CD79a CAR described herein.

In another aspect, the disclosure features a reaction mixture comprising a population of immune effector cells wherein a plurality of the cells of the population in the reaction mixture comprise a nucleic acid molecule, e.g., in vitro transcribed RNA or synthetic RNA, that

comprises a CAR encoding sequence, e.g., a CD19 CAR encoding sequence, e.g., as described herein.

In one embodiment, at least at least 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96 %, 97%, 98%, 99% or 100% of the immune effector cells express the CAR mRNA.

In another embodiment, at least at least at least 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96 %, 97%, 98%, 99% or 100% of the immune effector cells express the CAR on their cell surface.

In one embodiment, the reaction mixture can further comprise a ligand as described herein (e.g., a cognate antigen molecule or an anti-idiotype antibody). In one embodiment, the ligand is a molecule that binds to and/or activates the CAR on the cell surface of the population of immune effector cells expressing, e.g. transiently expressing, a CAR, e.g., a CAR described herein, e.g., a CD19 CAR described herein. In one embodiment, the ligand is the cognate antigen of the CAR. In one embodiment the cognate antigen is a cancer associated antigen, e.g., a cancer associated antigen described herein, e.g., CD19. In another embodiment the ligand is an anti- idiotype antibody, e.g., an anti-CD19 idiotype antibody.

In one embodiment, the ligand, e.g., the cognate antigen molecule or the anti-idiotype antibody, is attached to a substrate. In one embodiment, the substrate is a solid support. In one embodiment, the substrate is selected from microtiter plates (e.g., ELISA plates); membranes (e.g., nitrocellulose membranes, PVDF membranes, nylon membranes, acetate derivatives, and combinations thereof); fiber matrix, Sepharose matrix, sugar matrix; plastic chips; glass chips; or any type of bead (e.g., Luminex beads, magnetic beads (e.g., Dynabeads), flow-cytometry beads, and combinations thereof). In one embodiment, the substrate is an ELISA plate. In another embodiment, the substrate is magnetic beads, e.g., Dynabeads.

In one embodiment, the CAR expressing immune effector cells and the ligand (e.g., antigen) coated beads are present in a ratio of 1:100, 1:50, 1:40, 1:30, 1:20, 1:10, 1:9, 1:8, 1:7, 1:6, 1:5, 1:4, 1:3, 1:2, 1:1, 2:1, 3:1, 4:1, 5:1, 6:1, 7:1, 8:1, 9:1, 10:1, or 15:1 beads per immune effector cell. In one embodiment, the CAR expressing immune effector cells and the ligand (e.g., antigen) coated beads are present in a ratio of 3:1 beads per immune effector cell.

In one embodiment, the reaction mixture further comprises one or more factors for enhancing proliferation and/or viability, including serum (e.g., fetal bovine or human serum), e.g., one, two, three, four, five or more of: interleukin-2 (IL-2), insulin, IFN-γ, IL-4, IL-7, GM-CSF, IL-10, IL-12, IL-15, IL-21, TGFβ, and TNF-α or any other additives for the growth of cells. In one embodiment, the reaction mixture further comprises IL-15 and/or IL-7. In one embodiment, the cells are expanded in the presence of IL-2.

In one embodiment, a plurality of the cells of the population in the reaction mixture comprise one or both of a nucleic acid encoding a first CAR molecule and a nucleic acid encoding a second CAR molecule, e.g., a CAR described herein.

In one embodiment, the nucleic acid encoding the first CAR is an *in vitro* transcribed RNA as described herein.

In one embodiment, the nucleic acid encoding the second CAR is a vector selected from the group consisting of a DNA, a RNA, a plasmid, a lentivirus vector, adenoviral vector, or a retrovirus vector.

In one embodiment, the first CAR targets a cognate antigen molecule and the second CAR targets the same cognate antigen molecule.

In one embodiment, the first CAR targets a cognate antigen molecule and the second CAR a different cognate antigen molecule.

In one embodiment, the first CAR targets a cancer associated antigen described herein and the second CAR targets the same cancer associated antigen described herein.

In one embodiment, the first CAR targets a cancer associated antigen described herein and the second CAR targets a different cancer associated antigen described herein.

In one embodiment, the first CAR is chosen from a ROR1 CAR, a CD19 CAR, a CD20 CAR, a CD22 CAR, a CD123 CAR, a CD10 CAR, a CD34 CAR, a FLT-3 CAR, a CD79b CAR, a CD179b CAR, a mesothelin CAR or a CD79a CAR described herein; and the second nucleic acid encodes a ROR1 CAR, a CD19 CAR, a CD20 CAR, a CD22 CAR, a CD123 CAR, a CD10 CAR, a CD34 CAR, a FLT-3 CAR, a CD79b CAR, a CD179b CAR, a mesothelin CAR or a CD79a CAR described herein.

In one embodiment, the reaction mixture further comprises a cryoprotectant or stabilizer such as, e.g., a saccharide, an oligosaccharide, a polysaccharide and a polyol (e.g., trehalose,

mannitol, sorbitol, lactose, sucrose, glucose and dextran), salts and crown ethers. In one embodiment, the cryoprotectant is dextran.

Additional features and embodiments of the methods are described herein in the section entitled "Further Embodiments of the Methods, preparations, and reaction mixtures"

CAR Molecules

In accordance with the methods, preparations, and reaction mixtures described herein, an immune effector cell, e.g., obtained by a method described herein, can be engineered to contain a CAR molecule (also referred to herein as "CAR") that targets one or more cancer associated antigens. In some embodiments, the tumor antigen is a tumor antigen described in International Application WO2015/142675, filed March 13, 2015, which is herein incorporated by reference in its entirety.

In some embodiments, the cancer associated antigen (tumor antigen) is chosen from one or more of: CD19; CD123; CD22; CD30; CD171; CS-1 (also referred to as CD2 subset 1, CRACC, SLAMF7, CD319, and 19A24); C-type lectin-like molecule-1 (CLL-1 or CLECL1); CD33; epidermal growth factor receptor variant III (EGFRvIII); ganglioside G2 (GD2); ganglioside GD3 (aNeu5Ac(2-8)aNeu5Ac(2-3)bDGalp(1-4)bDGlcp(1-1)Cer); TNF receptor family member B cell maturation (BCMA); Tn antigen ((Tn Ag) or (GalNAcα-Ser/Thr)); prostate-specific membrane antigen (PSMA); Receptor tyrosine kinase-like orphan receptor 1 (ROR1); Fms-Like Tyrosine Kinase 3 (FLT3); Tumor-associated glycoprotein 72 (TAG72); CD38; CD44v6; Carcinoembryonic antigen (CEA); Epithelial cell adhesion molecule (EPCAM); B7H3 (CD276); KIT (CD117); Interleukin-13 receptor subunit alpha-2 (IL-13Ra2 or CD213A2); Mesothelin; Interleukin 11 receptor alpha (IL-11Ra); prostate stem cell antigen (PSCA); Protease Serine 21 (Testisin or PRSS21); vascular endothelial growth factor receptor 2 (VEGFR2); Lewis(Y) antigen; CD24; Platelet-derived growth factor receptor beta (PDGFR-beta); Stage-specific embryonic antigen-4 (SSEA-4); CD20; Folate receptor alpha; Receptor tyrosine-protein kinase ERBB2 (Her2/neu); Mucin 1, cell surface associated (MUC1); epidermal growth factor receptor (EGFR); neural cell adhesion molecule (NCAM); Prostase; prostatic acid phosphatase (PAP); elongation factor 2 mutated (ELF2M); Ephrin B2; fibroblast activation protein alpha (FAP); insulin-like growth factor 1 receptor (IGF-I receptor), carbonic anhydrase IX (CAIX); Proteasome (Prosome, Macropain) Subunit, Beta Type, 9 (LMP2); glycoprotein 100 (gp100); oncogene fusion protein consisting of breakpoint cluster region

(BCR) and Abelson murine leukemia viral oncogene homolog 1 (Abl) (bcr-abl); tyrosinase; ephrin type-A receptor 2 (EphA2); Fucosyl GM1; sialyl Lewis adhesion molecule (sLe); ganglioside GM3 (aNeu5Ac(2-3)bDGalp(1-4)bDGlcp(1-1)Cer); transglutaminase 5 (TGS5); high molecular weight-melanoma-associated antigen (HMWMAA); o-acetyl-GD2 ganglioside (OAcGD2); Folate receptor beta; tumor endothelial marker 1 (TEM1/CD248); tumor endothelial marker 7-related (TEM7R); claudin 6 (CLDN6); thyroid stimulating hormone receptor (TSHR); G protein-coupled receptor class C group 5, member D (GPRC5D); chromosome X open reading frame 61 (CXORF61); CD97; CD179a; anaplastic lymphoma kinase (ALK); Polysialic acid; placenta-specific 1 (PLAC1); hexasaccharide portion of globoH glycoceramide (GloboH); mammary gland differentiation antigen (NY-BR-1); uroplakin 2 (UPK2); Hepatitis A virus cellular receptor 1 (HAVCR1); adrenoceptor beta 3 (ADRB3); pannexin 3 (PANX3); G protein-coupled receptor 20 (GPR20); lymphocyte antigen 6 complex, locus K 9 (LY6K); Olfactory receptor 51E2 (OR51E2); TCR Gamma Alternate Reading Frame Protein (TARP); Wilms tumor protein (WT1); Cancer/testis antigen 1 (NY-ESO-1); Cancer/testis antigen 2 (LAGE-1a); Melanoma-associated antigen 1 (MAGE-A1); ETS translocation-variant gene 6, located on chromosome 12p (ETV6-AML); sperm protein 17 (SPA17); X Antigen Family, Member 1A (XAGE1); angiopoietin-binding cell surface receptor 2 (Tie 2); melanoma cancer testis antigen-1 (MAD-CT-1); melanoma cancer testis antigen-2 (MAD-CT-2); Fos-related antigen 1; tumor protein p53 (p53); p53 mutant; prostein; surviving; telomerase; prostate carcinoma tumor antigen-1 (PCTA-1 or Galectin 8), melanoma antigen recognized by T cells 1 (MelanA or MART1); Rat sarcoma (Ras) mutant; human Telomerase reverse transcriptase (hTERT); sarcoma translocation breakpoints; melanoma inhibitor of apoptosis (ML-IAP); ERG (transmembrane protease, serine 2 (TMPRSS2) ETS fusion gene); N-Acetyl glucosaminyl-transferase V (NA17); paired box protein Pax-3 (PAX3); Androgen receptor; Cyclin B1; v-myc avian myelocytomatosis viral oncogene neuroblastoma derived homolog (MYCN); Ras Homolog Family Member C (RhoC); Tyrosinase-related protein 2 (TRP-2); Cytochrome P450 1B1 (CYP1B1); CCCTC-Binding Factor (Zinc Finger Protein)-Like (BORIS or Brother of the Regulator of Imprinted Sites), Squamous Cell Carcinoma Antigen Recognized By T Cells 3 (SART3); Paired box protein Pax-5 (PAX5); proacrosin binding protein sp32 (OY-TES1); lymphocyte-specific protein tyrosine kinase (LCK); A kinase anchor protein 4 (AKAP-4); synovial sarcoma, X breakpoint 2 (SSX2); Receptor for Advanced Glycation Endproducts (RAGE-1); renal ubiquitous 1 (RU1); renal ubiquitous 2 (RU2);

legumain; human papilloma virus E6 (HPV E6); human papilloma virus E7 (HPV E7); intestinal carboxyl esterase; heat shock protein 70-2 mutated (mut hsp70-2); CD79a; CD79b; CD72; Leukocyte-associated immunoglobulin-like receptor 1 (LAIR1); Fc fragment of IgA receptor (FCAR or CD89); Leukocyte immunoglobulin-like receptor subfamily A member 2 (LILRA2); CD300 molecule-like family member f (CD300LF); C-type lectin domain family 12 member A (CLEC12A); bone marrow stromal cell antigen 2 (BST2); EGF-like module-containing mucin-like hormone receptor-like 2 (EMR2); lymphocyte antigen 75 (LY75); Glypican-3 (GPC3); Fc receptor-like 5 (FCRL5); and immunoglobulin lambda-like polypeptide 1 (IGLL1).

In one embodiment, the cancer associated antigen targeted by the CAR molecule is CD19, e.g., a CD19 CAR described herein (e.g., CTL019). In one embodiment, the CD19 CAR comprises the amino acid, or has the nucleotide sequence shown in **Table 4**.

In some embodiments, the antigen binding domain of the CAR molecule comprises an antibody, an antibody fragment, an scFv, a Fv, a Fab, a (Fab')2, a single domain antibody (SDAB), a VH or VL domain, or a camelid VHH domain.

In some embodiments, the transmembrane domain of the CAR molecule comprises a transmembrane domain chosen from the transmembrane domain of an alpha, beta or zeta chain of a T-cell receptor, CD28, CD3 epsilon, CD45, CD4, CD5, CD8, CD9, CD16, CD22, CD33, CD37, CD64, CD80, CD86, CD134, CD137, CD154, KIRDS2, OX40, CD2, CD27, LFA-1 (CD11a, CD18), ICOS (CD278), 4-1BB (CD137), GITR, CD40, BAFFR, HVEM (LIGHTR), SLAMF7, NKp80 (KLRF1), CD160, CD19, IL2R beta, IL2R gamma, IL7R α, ITGA1, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CD11d, ITGAE, CD103, ITGAL, CD11a, LFA-1, ITGAM, CD11b, ITGAX, CD11c, ITGB1, CD29, ITGB2, CD18, LFA-1, ITGB7, TNFR2, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRTAM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100 (SEMA4D), SLAMF6 (NTB-A, Ly108), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, PAG/Cbp, NKp44, NKp30, NKp46, NKG2D, and/or NKG2C.

In certain embodiments, the transmembrane domain of the CAR molecule comprises an amino acid sequence of a CD8 transmembrane domain having at least one, two or three modifications but not more than 20, 10 or 5 modifications of an amino acid sequence of SEQ ID NO: 6, or a sequence with 95-99% identity to an amino acid sequence of SEQ ID NO: 6. In one embodiment, the transmembrane domain comprises the sequence of SEQ ID NO: 6.

In other embodiments, nucleic acid sequence encoding the CD8 transmembrane domain comprises the sequence of SEQ ID NO: 17, or a sequence with 95-99% identity thereof.

In certain embodiments, the antigen binding domain is connected to the transmembrane domain by a hinge region. In one embodiment, the hinge region comprises the amino acid sequence of a CD8 hinge, e.g., SEQ ID NO: 2; or the amino acid sequence of an IgG4 hinge, e.g., SEQ ID NO: 36, or a sequence with 95-99% identity to SEQ ID NO:2 or 36. In other embodiments, the nucleic acid sequence encoding the hinge region comprises a sequence of SEQ ID NO: 13 or SEQ ID NO: 37, corresponding to a CD8 hinge or an IgG4 hinge, respectively, or a sequence with 95-99% identity to SEQ ID NO:13 or 37.

In other embodiments, the CAR comprises an intracellular signaling domain, e.g., a primary signaling domain and/or a costimulatory signaling domain. In some embodiments, the intracellular signaling domain comprises a primary signaling domain. In some embodiments, the intracellular signaling domain comprises a costimulatory signaling domain. In some embodiments, the intracellular signaling domain comprises a primary signaling domain and a costimulatory signaling domain.

In certain embodiments, the primary signaling domain comprises a functional signaling domain of a protein selected from the group consisting of CD3 zeta, CD3 gamma, CD3 delta, CD3 epsilon, common FcR gamma (FCER1G), FcR beta (Fc Epsilon R1b), CD79a, CD79b, Fc gamma RIIa, DAP10, and DAP12.

In one embodiment, the primary signaling domain of the CAR molecule comprises a functional signaling domain of CD3 zeta. The CD3 zeta primary signaling domain can comprise an amino acid sequence having at least one, two or three modifications but not more than 20, 10 or 5 modifications of an amino acid sequence of SEQ ID NO: 9 or SEQ ID NO: 10, or a sequence with 95-99% identity to an amino acid sequence of SEQ ID NO:9 or SEQ ID NO: 10. In some embodiments, the primary signaling domain comprises a sequence of SEQ ID NO:9 or SEQ ID NO: 10. In other embodiments, the nucleic acid sequence encoding the primary signaling domain comprises a sequence of SEQ ID NO:20 or SEQ ID NO: 21, or a sequence with 95-99% identity thereof.

In some embodiments, the intracellular signaling domain of the CAR molecule comprises a costimulatory signaling domain. For example, the intracellular signaling domain can comprise a primary signaling domain and a costimulatory signaling domain. In some embodiments, the costimulatory signaling domain comprises a functional signaling domain of a

protein chosen from one or more of CD27, CD28, 4-1BB (CD137), OX40, CD30, CD40, PD-1, ICOS, lymphocyte function-associated antigen-1 (LFA-1), CD2, CD7, LIGHT, NKG2C, B7-H3, a ligand that specifically binds with CD83, CDS, ICAM-1, GITR, BAFFR, HVEM (LIGHTR), SLAMF7, NKp80 (KLRF1), CD160, CD19, CD4, CD8alpha, CD8beta, IL2R beta, IL2R gamma, IL7R alpha, ITGA4, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CD11d, ITGAE, CD103, ITGAL, CD11a, LFA-1, ITGAM, CD11b, ITGAX, CD11c, ITGB1, CD29, ITGB2, CD18, LFA-1, ITGB7, TNFR2, TRANCE/RANKL, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRTAM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100 (SEMA4D), CD69, SLAMF6 (NTB-A, Ly108), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, LAT, GADS, SLP-76, PAG/Cbp, NKp44, NKp30, NKp46, or NKG2D.

In some embodiments, a population of immune effector cells, *e.g.*, T cells, comprise a mixture of cells containing CAR molecules having two or more intracellular signaling domains. In embodiments, the population of immune effector cells comprise one or more CAR-comprising a CD28 signaling domain and a 4-1BB signaling domain. For example, a first immune effector cell comprises a CAR molecule comprising a CD28 signaling domain, and a second immune effector cell comprises a CAR molecule comprising a 4-1BB signaling domain. Expression of CAR molecules comprising a CD28 signaling domain and/or a 4-1BB signaling domain can be transient or stable.

In certain embodiments, the costimulatory signaling domain of the CAR molecule comprises an amino acid sequence having at least one, two or three modifications but not more than 20, 10 or 5 modifications of an amino acid sequence of SEQ ID NO:7 or SEQ ID NO: 16, or a sequence with 95-99% identity to an amino acid sequence of SEQ ID NO:7 or SEQ ID NO: 16. In one embodiment, the costimulatory signaling domain comprises a sequence of SEQ ID NO: 7 or SEQ ID NO: 16. In other embodiments, the nucleic acid sequence encoding the costimulatory signaling domain comprises a sequence of SEQ ID NO:18 or SEQ ID NO: 15, or a sequence with 95-99% identity thereof.

In other embodiments, the intracellular domain of the CAR molecule comprises the sequence of SEQ ID NO: 9 or SEQ ID NO: 10, and the sequence of SEQ ID NO: 7 or SEQ ID NO: 16, wherein the amino acid sequence(s) comprising the intracellular signaling domain are expressed in the same frame and as a single polypeptide chain.

In certain embodiments, the nucleic acid sequence encoding the intracellular signaling domain comprises a sequence of SEQ ID NO:18 or SEQ ID NO: 15, or a sequence with 95-99% identity thereof, and a sequence of SEQ ID NO:20 or SEQ ID NO:21, or a sequence with 95-99% identity thereof.

In some embodiments, the CAR further comprises a leader sequence. In one embodiment, the leader sequence comprises the sequence of SEQ ID NO: 1.

In certain embodiments, the antigen binding domain of the CAR molecule has a binding affinity KD of 10^{-4} M to 10^{-8} M.

In one embodiment, the antigen binding domain of the CAR molecule is an antigen binding domain described herein, e.g., an antigen binding domain described herein for a target provided above.

In some embodiments, the CAR comprises a ROR1 CAR, a CD19 CAR, a CD20 CAR, a CD22 CAR, a CD123 CAR, a CD10 CAR, a CD34 CAR, a FLT-3 CAR, a CD79b CAR, a CD179b CAR, a mesothelin CAR or a CD79a CAR described herein.

In some embodiments, the CAR comprises a CD19 CAR, e.g., a CD19 CAR described herein. In embodiments, the CD19 CAR comprises an antigen binding domain described herein, e.g., in Table 1 or 4.

In other embodiment, the antigen-binding portion of the CAR recognizes and binds to the extracellular domain of the the mesothelin protein. Exemplary mesothelin CAR sequences are found, for example, in International Publication No. WO 2013/040557 A2, which is incorporated by reference herein in its entirety.

Methods of treatment/Combination therapies

In another aspect the invention features a method of treating, or providing anti-tumor immunity to, a subject having a cancer. The method includes administering to the subject an effective amount of an immune effector cell population, wherein the immune effector cell population is, or was previously, expanded by contacting the immune effector cell population, with a nucleic acid encoding a CAR, under conditions suitable for transient expression of the CAR, wherein the CAR targets a cognate antigen molecule; and culturing the population of immune effector cells in the presence of a ligand, e.g., the cognate antigen molecule or an anti-idiotypic antibody molecule. In one embodiment, the nucleic acid is RNA, e.g., in vitro transcribed RNA. In another embodiment, the cognate antigen molecule is a cancer associated

antigen molecule. In one embodiment, the cognate antigen molecule or the anti-idiotypic antibody molecule is attached to a substrate, e.g., a bead.

In some embodiments, the method further includes administering to the subject an immune effector cell population comprising a second CAR (e.g., a vector comprising a nucleic acid encoding a second CAR), wherein the immune effector cell population is, or was previously, expanded as described herein. In one embodiment, the vector is selected from the group consisting of a DNA, a RNA, a plasmid, a lentivirus vector, adenoviral vector, or a retrovirus vector.

In one embodiment, the population of immune effector cells, is transduced with a vector once, e.g., within one day after population of immune effector cells are obtained from a blood sample from a subject, e.g., obtained by apheresis. In one embodiment, the first CAR targets a cognate antigen molecule and the second CAR targets the same cognate antigen molecule. In one embodiment, the first CAR targets a cognate antigen molecule and the second CAR a different cognate antigen molecule. In one embodiment, the first CAR targets a cancer associated antigen described herein and the second CAR targets the same cancer associated antigen described herein. In one embodiment, the first CAR that targets a cancer associated antigen described herein and the second CAR targets a different cancer associated antigen described herein.

In one embodiment, the first CAR is a ROR1 CAR, a CD19 CAR, a CD20 CAR, a CD22 CAR, a CD123 CAR, a CD10 CAR, a CD34 CAR, a FLT-3 CAR, a CD79b CAR, a CD179b CAR, a mesothelin CAR or a CD79a CAR described herein and the second nucleic acid encodes a ROR1 CAR, a CD19 CAR, a CD20 CAR, a CD22 CAR, a CD123 CAR, a CD10 CAR, a CD34 CAR, a FLT-3 CAR, a CD79b CAR, a CD179b CAR, a mesothelin CAR or a CD79a CAR described herein.

In accordance with methods of treating a disorder as described herein (e.g., a cancer) and providing anti-tumor immunity described herein, in some embodiments, the method comprises administering to a subject a CAR molecule, or a population of immune effector cells made by a method described herein. In some embodiment the population of immune effector cells is engineered to express a CAR molecule, e.g. a CAR described herein, e.g., a CD19 CAR described herein.

Also provided herein is a composition comprising an immune effector cell (*e.g.*, a population of immune effector cells made as described herein) that comprises a CAR molecule (e.g., a CAR molecule as described herein) for use in the treatment of a subject having a disease associated with expression of a tumor antigen, e.g., a disorder as described herein.

In one embodiment, the cancer is a hematological cancer such as, e.g., ALL or CLL. In one embodiment, the cancer, e.g., a hematological cancer described herein, such as, e.g., a leukemia (e.g., ALL or CLL) or a lymphoma (e.g., MCL, HL, or NHL).

In one embodiment, a disease associated with a tumor antigen, e.g., a tumor antigen described herein, e.g., CD19, is selected from a proliferative disease such as a cancer or malignancy or a precancerous condition such as a myelodysplasia, a myelodysplastic syndrome or a preleukemia, or is a non-cancer related indication associated with expression of a tumor antigen described herein. In one embodiment, the disease is a cancer described herein, e.g., a cancer described herein as being associated with a target described herein. In one embodiment, the hematologic cancer is leukemia. In one embodiment, the cancer is selected from the group consisting of one or more acute leukemias including but not limited to B-ALL, T-ALL, ALL; one or more chronic leukemias including but not limited to chronic myelogenous leukemia (CML), chronic lymphocytic leukemia (CLL); additional hematologic cancers or hematologic conditions including, but not limited to B cell prolymphocytic leukemia, blastic plasmacytoid dendritic cell neoplasm, Burkitt's lymphoma, diffuse large B cell lymphoma, follicular lymphoma, hairy cell leukemia, small cell- or a large cell-follicular lymphoma, malignant lymphoproliferative conditions, MALT lymphoma, mantle cell lymphoma, Marginal zone lymphoma, multiple myeloma, myelodysplasia and myelodysplastic syndrome, non-Hodgkin lymphoma, Hodgkin lymphoma, plasmablastic lymphoma, plasmacytoid dendritic cell neoplasm, Waldenstrom macroglobulinemia, and/or "preleukemia" (e.g., a diverse collection of hematological conditions united by ineffective production (or dysplasia) of myeloid blood cells). In certain embodiment, a disease associated with expression of a tumor antigen described herein includes, but is not limited to, atypical and/or non-classical cancers, malignancies, precancerous conditions or proliferative diseases expressing a tumor antigen as described herein; and any combination thereof.

In embodiments, the disease associated with expression of the tumor antigen is selected from the group consisting of a proliferative disease, a precancerous condition, a cancer, and a non-cancer related indication associated with expression of the tumor antigen.

In another embodiment, the disease associated with a tumor antigen described herein is a solid tumor. In embodiments, the cancer is chosen from colon cancer, rectal cancer, renal-cell carcinoma, liver cancer, non-small cell carcinoma of the lung, cancer of the small intestine, cancer of the esophagus, melanoma, bone cancer, pancreatic cancer, skin cancer, cancer of the head or neck, cutaneous or intraocular malignant melanoma, uterine cancer, ovarian cancer, rectal cancer, cancer of the anal region, stomach cancer, testicular cancer, uterine cancer, carcinoma of the fallopian tubes, carcinoma of the endometrium, carcinoma of the cervix, carcinoma of the vagina, carcinoma of the vulva, Hodgkin's Disease, non-Hodgkin's lymphoma, cancer of the endocrine system, cancer of the thyroid gland, cancer of the parathyroid gland, cancer of the adrenal gland, sarcoma of soft tissue, cancer of the urethra, cancer of the penis, solid tumors of childhood, cancer of the bladder, cancer of the kidney or ureter, carcinoma of the renal pelvis, neoplasm of the central nervous system (CNS), primary CNS lymphoma, tumor angiogenesis, spinal axis tumor, brain stem glioma, pituitary adenoma, Kaposi's sarcoma, epidermoid cancer, squamous cell cancer, T-cell lymphoma, environmentally induced cancers, combinations of said cancers, and metastatic lesions of said cancers.

In certain embodiments of any of the aforesaid methods or uses, the tumor antigen associated with the disease is chosen from one or more of: CD19, CD123, CD22, CD30, CD171, CS-1, CLL-1 (CLECL1), CD33, EGFRvIII , GD2, GD3, BCMA, Tn Ag, PSMA, ROR1, FLT3, TAG72, CD38, CD44v6, CEA, EPCAM, B7H3, KIT, IL-13Ra2, Mesothelin, IL-11Ra, PSCA, PRSS21, VEGFR2, LewisY, CD24, PDGFR-beta, SSEA-4, CD20, Folate receptor alpha, ERBB2 (Her2/neu), MUC1, EGFR, NCAM, Prostase, PAP, ELF2M, Ephrin B2, FAP, IGF-I receptor, CAIX, LMP2, gp100, bcr-abl, tyrosinase, EphA2, Fucosyl GM1, sLe, GM3, TGS5, HMWMAA, o-acetyl-GD2, Folate receptor beta, TEM1/CD248, TEM7R, CLDN6, TSHR, GPRC5D, CXORF61, CD97, CD179a, ALK, Polysialic acid, PLAC1, GloboH, NY-BR-1, UPK2, HAVCR1, ADRB3, PANX3, GPR20, LY6K, OR51E2, TARP, WT1, NY-ESO-1, LAGE-1a, MAGE-A1, MAGE A1, ETV6-AML, sperm protein 17, XAGE1, Tie 2, MAD-CT-1, MAD-CT-2, Fos-related antigen 1, p53, p53 mutant, prostein, survivin and

telomerase, PCTA-1/Galectin 8, MelanA/MART1, Ras mutant, hTERT, sarcoma translocation breakpoints, ML-IAP, ERG (TMPRSS2 ETS fusion gene), NA17, PAX3, Androgen receptor, Cyclin B1, MYCN, RhoC, TRP-2, CYP1B1, BORIS, SART3, PAX5, OY-TES1, LCK, AKAP-4, SSX2, RAGE-1, human telomerase reverse transcriptase, RU1, RU2, legumain, HPV E6, E7, intestinal carboxyl esterase, mut hsp70-2, CD79a, CD79b, CD72, LAIR1, FCAR, LILRA2, CD300LF, CLEC12A, BST2, EMR2, LY75, GPC3, FCRL5, and IGLL1.

In one embodiment, the population of cells are autologous to the subject administered the population. In one embodiment, the population of cells is allogeneic to the subject administered the population. In one embodiment, the subject is a human.

In one embodiment, the population of immune effector cells transduced with a nucleic acid encoding a CAR, e.g., a CAR described herein, e.g., a CD19 CAR described herein, are expanded, e.g., by a method described herein. In one embodiment, the cells are expanded for a period of 8 days or less, e.g., 7, 6 ,5, 4, or 3 days. In one embodiment, the cells, e.g., a CD19 CAR cell described herein, are expanded in culture for 5 days, and the resulting cells are more potent than the same cells expanded in culture for 9 days under the same culture conditions, e.g., as described herein.

In one embodiment, the subject is administered 10^4 to 10^6 immune effector cells per kg body weight of the subject. In one embodiment, the subject receives an initial administration of a population of immune effector cells (e.g., an initial administration of 10^4 to 10^6 immune effector cells per kg body weight of the subject, e.g., 10^4 to 10^5 immune effector cells per kg body weight of the subject), a plurality of which comprise the nucleic acid encoding a CAR, e.g., a CAR described herein, e.g., a CD19 CAR described herein, and one or more subsequent administrations of a population of immune effector cells (e.g., one or more subsequent administration of 10^4 to 10^6 immune effector cells per kg body weight of the subject, e.g., 10^4 to 10^5 immune effector cells per kg body weight of the subject), a plurality of which comprise a nucleic acid encoding a CAR, e.g., a CAR described herein, e.g., a CD19 CAR described herein. In one embodiment, the one or more subsequent administrations are administered less than 15 days, e.g., 14, 13, 12, 11, 10, 9, 8, 7, 6, 5, 4, 3, or 2 days after the previous administration, e.g., less than 4, 3, 2 days after the previous administration. In one embodiment, the subject receives a total of about 10^6 immune effector cells per kg body weight of the subject over the course of at least three administrations of a population of immune effector cells, e.g., the subject receives an initial dose of 1 x 10^5 immune effector cells, a

second administration of 3 x 10^5 immune effector cells, and a third administration of 6 x 10^5 immune effector cells, and, e.g., each administration is administered less than 4, 3, 2 days after the previous administration.

In certain embodiments, the methods or uses are carried out in combination with an agent that increases the efficacy of the immune effector cell, e.g., an agent as described herein.

For example, in one embodiment, the agent can be an agent, which inhibits an inhibitory molecule. Examples of inhibitory molecules include PD1, PD-L1, CTLA4, TIM3, CEACAM (e.g., CEACAM-1, CEACAM-3 and/or CEACAM-5), LAG3, VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4 and TGF beta. In one embodiment, the agent which inhibits an inhibitory molecule comprises a first polypeptide, e.g., an inhibitory molecule, associated with a second polypeptide that provides a positive signal to the cell, e.g., an intracellular signaling domain described herein. In one embodiment, the agent comprises a first polypeptide, e.g., of an inhibitory molecule such as PD1, PD-L1, CTLA4, TIM3, CEACAM (e.g., CEACAM-1, CEACAM-3 and/or CEACAM-5), LAG3, VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4 or TGF beta, or a fragment of any of these (e.g., at least a portion of the extracellular domain of any of these), and a second polypeptide which is an intracellular signaling domain described herein (e.g., comprising a costimulatory domain (e.g., 41BB, CD27 or CD28, e.g., as described herein) and/or a primary signaling domain (e.g., a CD3 zeta signaling domain described herein). In one embodiment, the agent comprises a first polypeptide of PD1 or a fragment thereof (e.g., at least a portion of the extracellular domain of PD1), and a second polypeptide of an intracellular signaling domain described herein (e.g., a CD28 signaling domain described herein and/or a CD3 zeta signaling domain described herein).

In one embodiment, the cells expressing a CAR molecule, e.g., a CAR molecule described herein, are administered in combination with an agent that ameliorates one or more side effect associated with administration of a cell expressing a CAR molecule, e.g., an agent described herein.

In one embodiment, a CAR molecule, e.g., a CAR molecule described herein, is administered in combination with a B-cell inhibitor. For example, a CD19 CAR-expressing cell is administered in combination with one or more additional B-cell inhibitors. In some embodiments, the B-cell inhibitor is a second CD19 inhibitor. In some embodiments, the B-cell inhibitor is an inhibitor of one or more of CD10, CD19, CD20, CD22, CD34, CD123, FLT-3, ROR1, CD79b, CD179b, or CD79a.

In some embodiments, the B-cell inhibitor is a small molecule inhibitor; a polypeptide, e.g., a soluble ligand, an antibody, or antigen-binding fragment thereof that binds to a B-cell antigen (e.g., one or more of CD10, CD19, CD20, CD22, CD34, CD123, FLT-3, ROR1, CD79b, CD179b, or CD79a); or an inhibitory nucleic acid (e.g., a double stranded RNA (dsRNA), small interfering RNA (siRNA), or short hairpin RNA (shRNA)). In other embodiments, the B-cell inhibitor is a cell that expresses a CAR (e.g., a CAR-expressing immune effector cell) that binds to a B-cell antigen (e.g., one or more of CD10, CD19, CD20, CD22, CD34, CD123, FLT-3, ROR1, CD79b, CD179b, or CD79a).

In one aspect, the CAR (e.g., a CD19 CAR, a mesothelin CAR, a ROR1 CAR, a CD20 CAR, a CD22 CAR, a CD123 CAR, a CD10 CAR, a CD34 CAR, a FLT-3 CAR, a CD79b CAR, a CD179b CAR, or a CD79a CAR) comprises an optional leader sequence (e.g., an optional leader sequence described herein), an extracellular antigen binding domain, a hinge (e.g., hinge described herein), a transmembrane domain (e.g., transmembrane domain described herein), and an intracellular stimulatory domain (e.g., intracellular stimulatory domain described herein). In one aspect an exemplary CAR construct comprises an optional leader sequence (e.g., a leader sequence described herein), an extracellular antigen binding domain, a hinge, a transmembrane domain, an intracellular costimulatory domain (e.g., an intracellular costimulatory domain described herein) and an intracellular stimulatory domain.

Subjects

In one embodiment, the subject, e.g., the subject from which immune cells are acquired and/or the subject treated, is a human, e.g., a cancer patient.

In certain embodiments, the subject has a disease associated with expression of a tumor- or cancer associated-antigen, e.g., a disease as described herein. In one embodiment, the subject has a cancer, e.g., a cancer as described herein.

In one embodiment, the subject has a cancer that is chosen from a hematological cancer, a solid tumor, or a metastatic lesion thereof. Exemplary cancers include, but are not limited to, B-cell acute lymphocytic leukemia (B-ALL), T-cell acute lymphocytic leukemia (T-ALL), acute lymphocytic leukemia (ALL), chronic myelogenous leukemia (CML), chronic lymphocytic leukemia (CLL), B cell promyelocytic leukemia, blastic plasmacytoid dendritic cell neoplasm, Burkitt's lymphoma, diffuse large B cell lymphoma, follicular lymphoma, hairy cell leukemia, small cell- or a large cell-follicular lymphoma, malignant lymphoproliferative

conditions, MALT lymphoma, mantle cell lymphoma (MCL), marginal zone lymphoma, multiple myeloma, myelodysplasia and myelodysplastic syndrome, non-Hodgkin's lymphoma (NHL), Hodgkin's lymphoma (HL), plasmablastic lymphoma, plasmacytoid dendritic cell neoplasm, and Waldenstrom macroglobulinemia. In one embodiment, the cancer is ALL. In another embodiment, the cancer is CLL.

In embodiments, the subject does not have a relapsed cancer. In other embodiments, the subject has a relapsed cancer.

In one embodiment, the immune cell (e.g., the population of immune effector cells) is acquired, e.g., obtained, from a subject having a haematological cancer, e.g., a leukemia, e.g., CLL, ALL, or a lymphoma, e.g., MCL, NHL, or HL.

Further Embodiments of the Methods, preparations, and reaction mixtures

In accordance with the methods of treating and/or making (e.g., expanding and/or activating), preparations, and reaction mixtures described herein, in embodiments, the method further comprises removing T regulatory cells, e.g., CD25+ T cells, from the immune cell population, e.g., to thereby provide a population of T regulatory-depleted cells, e.g., CD25+ depleted cells, that are suitable for expression of a CAR.

In one embodiment, the population of T regulatory-depleted cells contains less than 30%, 25%, 20%, 15%, 10%, 5%, 4%, 3%, 2%, 1% of CD25+ cells.

In one embodiment, the immune cell population includes cells of a subject having cancer, e.g., a subject having a CD25 expressing cancer such as, e.g., chronic lymphocytic leukemia (CLL). In one embodiment, the population of T regulatory-depleted cells contains less than 50%, 40%, 30%, 25%, 20%, 15%, 10%, 5%, 4%, 3%, 2%, 1% of CD25+ cells and less than 50%, 40%, 30%, 25%, 20%, 15%, 10%, 5%, 4%, 3%, 2%, 1% of tumor cells.

In one embodiment, the immune cell population is autologous to the subject who the cells will be administered to for treatment. In one embodiment, the population of immune effector cells are allogeneic to the subject who the cells will be administered for treatment.

In one embodiment, the T regulatory cells, e.g., CD25+ T cells, are removed from the population using an anti-CD25 antibody, or fragment thereof, or a CD25-binding ligand, e.g. IL-2. In one embodiment, the anti-CD25 antibody, or fragment thereof, or CD25-binding ligand is conjugated to a substrate, e.g., a bead, or is otherwise coated on a substrate, e.g., a

bead. In one embodiment, the anti-CD25 antibody, or fragment thereof, is conjugated to a substrate as described herein.

In one embodiment, the T regulatory cells, e.g., CD25+ T cells, are removed from the population using CD25 depletion reagent from Militenyi™. In one embodiment, the ratio of cells to CD25 depletion reagent is $1e^7$ cells to 20 uL, or $1e^7$ cells to15 uL, or $1e^7$ cells to 10 uL, or $1e^7$ cells to 5 uL, or $1e^7$ cells to 2.5 uL, or $1e^7$ cells to 1.25 uL.

In one embodiment, the population of T regulatory-depleted cells, e.g., CD25+ depleted cells, are suitable for expression of a CAR described herein, e.g., a CD19 CAR described herein. In one embodiment, the population of T regulatory-depleted cells contains less than 30%, 25%, 20%, 15%, 10%, 5%, 4%, 3%, 2%, 1% of the leukemia cells, e.g., CLL cells, ALL cells, or lymphoma cells, e.g., MCL cells, NHL cells, or HL cells. In one embodiment, the population of immune effector cells are obtained from a subject having CLL, and the population of T regulatory-depleted cells, e.g., CD25+ depleted cells, contains less than 30%, 25%, 20%, 15%, 10%, 5%, 4%, 3%, 2%, 1% of the leukemia cells, e.g., CLL cells and are suitable for expression of a CD19 CAR described herein. In one embodiment, the population of T regulatory-depleted cells contains less than 15%, 10%, 5%, 4%, 3%, 2%, 1% of CD25+ cells and less than 15%, 10%, 5%, 4%, 3%, 2%, 1% of tumor cells, e.g., CD25 expressing tumor cells, e.g., CLL cells. In one embodiment, the population of T regulatory-depleted cells contains less than 10%, 5%, 4%, 3%, 2%, 1% of CD25+ cells and less than 10%, 5%, 4%, 3%, 2%, 1% of tumor cells, e.g., CD25 expressing tumor cells, e.g., CLL cells.

In one embodiment, the method of making further comprises removing cells from the population which express a tumor antigen, e.g., a tumor antigen that does not comprise CD25, e.g., CD19, CD30, CD38, CD123, CD20, CD14 or CD11b, to thereby provide a population of T regulatory depleted, e.g., CD25+ depleted, and tumor antigen depleted cells that are suitable for expression of a CAR, e.g., a CAR described herein. In one embodiment, tumor antigen expressing cells are removed simultaneously with the T regulatory, e.g., CD25+ cells. For example, an anti-CD25 antibody, or fragment thereof, and an anti-tumor antigen antibody, or fragment thereof, can be attached to the same substrate, e.g., bead, which can be used to remove the cells or an anti-CD25 antibody, or fragment thereof, or the anti-tumor antigen antibody, or fragment thereof, can be attached to separate beads, a mixture of which can be used to remove the cells. In other embodiments, the removal of T regulatory cells, e.g., CD25+ cells, and the removal of the tumor antigen expressing cells is sequential, and can occur, e.g., in

either order. In one embodiment, the method of making further comprises removing cells from the population which express a check point inhibitor, e.g., a check point inhibitor described herein, e.g., one or more (e.g., one, two, or three) of: of PD1+ cells, LAG3+ cells, and TIM3+ cells, to thereby provide a population of T regulatory depleted, e.g., CD25+ depleted cells, and check point inhibitor depleted cells, e.g., PD1+, LAG3+ and/or TIM3+ depleted cells. In one embodiment, check point inhibitor expressing cells are removed simultaneously with the T regulatory, e.g., CD25+ cells. For example, an anti-CD25 antibody, or fragment thereof, and an anti-check point inhibitor antibody, or fragment thereof, can be attached to the same bead which can be used to remove the cells, or an anti-CD25 antibody, or fragment thereof, and the anti-check point inhibitor antibody, or fragment there, can be attached to separate beads, a mixture of which can be used to remove the cells. In other embodiments, the removal of T regulatory cells, e.g., CD25+ cells, and the removal of the check point inhibitor expressing cells is sequential, and can occur, e.g., in either order.

In one embodiment, the population of cells to be removed are neither the regulatory T cells or tumor cells, but cells that otherwise negatively affect the expansion and/or function of CART cells, e.g. cells expressing CD14, CD11b, CD33, CD15, or other markers expressed by potentially immune suppressive cells. In one embodiment, such cells are envisioned to be removed concurrently with regulatory T cells and/or tumor cells, or following said depletion, or in another order.

In one embodiment, the method further comprises removing cells from the population which express CD14, to thereby provide a population of T regulatory-depleted, e.g., CD25+ depleted cells, and CD14+ depleted cells. In one embodiment, CD14+ cells are removed simultaneously with the T regulatory, e.g., CD25+ cells. For example, an anti-CD25 antibody, or fragment thereof, and an anti-CD14 antibody, or fragment thereof, can be attached to the same bead which can be used to remove the cells; or an anti-CD25 antibody, or fragment thereof, and the anti-CD14 antibody, or fragment thereof, can be attached to separate beads, a mixture of which can be used to remove the cells. In other embodiments, the removal of T regulatory cells, e.g., CD25+ cells, and the removal of the CD14+ cells is sequential, and can occur, e.g., in either order.

In one embodiment, the population of immune effector cells provided have been selected based upon the expression of one or more markers, e.g., 1, 2, 3, 4, 5, 6, 7, or more of:

CD3, CD28, CD4, CD8, CD27, CD127, CD45RA, and CD45RO, e.g., the provided population of immune effector cells (e.g., T cells) are CD3+ and/or CD28+.

In one embodiment, the method further comprises obtaining a population of immune effector cells, e.g., T cells, enriched for the expression of one or more markers, e.g., 1, 2, 3, 4, 5, 6, 7, or more of: CD3, CD28, CD4, CD8, CD27, CD127, CD45RA, and CD45RO. In an embodiment, population of immune effector cells are enriched for CD3+ and/or CD28+ cells. For example, T cells isolated by incubation with anti-CD3/anti-CD28 conjugated beads are obtained. In one embodiment, the method further comprises selecting cells from the population of T regulatory- depleted cells, e.g., CD25+ depleted cells, which express one or more markers, e.g., 1, 2, 3, 4, 5, 6, 7, or more of: CD3, CD28, CD4, CD8, CD45RA, and CD45RO.

In one embodiment, the method further comprises activating the population of T regulatory depleted cells, e.g., CD25+ depleted cells, e.g., by a method described herein.

In one embodiment, the method of making further comprises transducing a cell from the population of T regulatory-depleted cells, e.g., the population of CD25+ depleted cells, with a vector comprising a nucleic acid encoding a CAR, e.g., a CAR described herein, e.g., a CD19 CAR described herein. In one embodiment, the vector is selected from the group consisting of a DNA, a RNA, a plasmid, a lentivirus vector, adenoviral vector, or a retrovirus vector. In one embodiment, the cell from the population of T regulatory-depleted cells, e.g., the population of CD25+ depleted cells, is transduced with a vector once, e.g., within one day after population of immune effector cells are obtained from a blood sample from a subject, e.g., obtained by apheresis.

In one embodiment, the method further comprises generating a population of RNA-engineered cells transiently expressing exogenous RNA from the population of T regulatory-depleted cells, e.g., the population of CD25+ depleted cells. The method comprises introducing an in vitro transcribed RNA or synthetic RNA into a cell from the population, where the RNA comprises a nucleic acid encoding a CAR, e.g., a CAR described herein, e.g., a CD19 CAR described herein.

In one embodiment, the cells are expanded in an appropriate media (e.g., media described herein) that may, optionally, contain one or more factor for proliferation and/or viability, including serum (e.g., fetal bovine or human serum), interleukin-2 (IL-2), insulin, IFN-γ, IL-4, IL-7, GM-CSF, IL-10, IL-12, IL-15, IL-21, TGFβ, and TNF-α or any other additives for the growth of cells.

In one embodiment, the cells are expanded in an appropriate media (e.g., media described herein) that includes one or more interleukins that result in at least a 200-fold (e.g., 200-fold, 250-fold, 300-fold, 350-fold) increase in cells over a 14 day expansion period, e.g., as measured by a method described herein such as flow cytometry. In one embodiment, the cells are expanded in the presence IL-15 and/or IL-7 (e.g., IL-15 and IL-7).

In one embodiment, the cells are cryopreserved after the appropriate expansion period. In one embodiment, the cells are cryopreserved according to a method described herein. In one embodiment, the expanded cells are cryopreserved in an appropriate media, e.g., an infusible media, e.g., as described herein.

In one embodiment, the method of making further comprises contacting the population of immune effector cells with a nucleic acid encoding a telomerase subunit, e.g., hTERT. In an embodiment, the nucleic acid is DNA or RNA.

In one embodiment, the method further comprises, prior to expansion, removing T regulatory cells, e.g., CD25+ T cells, from the population, to thereby provide a population of T regulatory-depleted cells, e.g., CD25+ depleted cells to be expanded. In one embodiment, the T regulatory cells, e.g., CD25+ cells, are removed by a method described herein.

In one embodiment, the method further comprises, prior to expansion, removing T regulatory cells, e.g., CD14+ cells, from the population, to thereby provide a population of CD14+ depleted cells to be expanded. In one embodiment, the T regulatory cells, e.g., CD14+ cells, are removed by a method described herein.

In one embodiment, the method further comprises contacting the population of immune effector cells with a nucleic acid encoding a telomerase subunit, e.g., hTERT. In an embodiment, the nucleic acid is DNA or RNA.

In embodiments, the method comprises contacting the population of immune effector cells with a nucleic acid encoding a CAR, and a nucleic acid encoding a telomerase subunit, e.g., hTERT, under conditions that allow for CAR and telomerase expression.

In an embodiment, the nucleic acid encoding the telomerase subunit is RNA. In another embodiment, the nucleic acid encoding the telomerase subunit is DNA. In an embodiment, the nucleic acid encoding the telomerase subunit comprises a promoter capable of driving expression of the telomerase subunit.

In embodiments, the method of making comprises contacting the population of immune effector cells with a nucleic acid encoding a CAR and an RNA encoding a telomerase subunit, e.g., hTERT, under conditions that allow for CAR and telomerase expression.

In an embodiment, the nucleic acid encoding the CAR and the RNA encoding the telomerase subunit are part of the same nucleic acid molecule. In an embodiment the nucleic acid encoding the CAR and the RNA encoding the telomerase subunit are part of separate nucleic acid molecules.

In an embodiment, the method comprises contacting the population of immune effector cells with a nucleic acid encoding the CAR and the RNA encoding the telomerase subunit at substantially the same time. In an embodiment, the method of making comprises contacting the population of immune effector cells with a nucleic acid encoding the CAR before contacting the population of immune effector cells with the RNA encoding the telomerase subunit. In an embodiment, the method comprises contacting the population of immune effector cells with a nucleic acid encoding the CAR after contacting the population of immune effector cells with the RNA encoding the telomerase subunit.

In an embodiment, the RNA encoding the telomerase subunit is mRNA. In an embodiment, the RNA encoding the telomerase subunit comprises a poly(A) tail. In an embodiment, the RNA encoding the telomerase subunit comprises a 5' cap structure.

In an embodiment, the method comprises transfecting the immune effector cells with the RNA encoding the telomerase subunit. In an embodiment, the method of making comprises transducing the immune effector cells with the RNA encoding the telomerase subunit. In an embodiment, the method of making comprises electroporating the immune effector cells with the RNA encoding the telomerase subunit, under conditions that allow for CAR and telomerase expression.

In embodiments, the method comprises providing a population of immune effector cells (e.g., T cells or NK cells) that express a CAR and/or comprise a nucleic acid encoding a CAR; and contacting the population of immune effector cells with a nucleic acid encoding a telomerase subunit, e.g., hTERT, under conditions that allow for hTERT expression.

In embodiments, the method comprises providing a population of immune effector cells (e.g., T cells or NK cells) that express a nucleic acid encoding a telomerase subunit, e.g., hTERT, and and contacting the population of immune effector cells with a nucleic acid encoding a CAR, under conditions that allow for CAR expression.

Immune Effector Cell Preparations

In some embodiments, an immune effector cell preparation (e.g., a reaction mixture, or a population of immune effector cells) described herein is made by a method described herein.

In embodiments, the population of immune effector cells has been selected based upon the expression of one or more markers, e.g., CCR7, CD62L, CD45RO, and CD95, e.g., the population of immune effector cells (e.g., T cells) are CCR7+ and CD62L+.

In embodiments, the naïve T cells are identified based upon an expression pattern of CCR7+, CD62L+, CD45RO–, CD95–, wherein the stem central memory T cells are identified based upon an expression pattern of CCR7+, CD62L+, CD45RO–, CD95+, and wherein the central memory T cells are identified based upon an expression pattern of CCR7+, CD62L+, CD45RO+, CD95+.

In embodiments, an immune effector cell preparation described herein comprises a nucleic acid encoding a CAR, e.g., a CAR as described herein.

In embodiments, an immune effector cell preparation described herein comprises a nucleic acid encoding an exogenous telomerase subunit, e.g., hTERT. In an embodiment, the nucleic acid encoding an exogenous telomerase subunit is RNA, e.g., mRNA.

In embodiments, an immune effector cell preparation described herein comprises a CAR, e.g., a CAR as described herein; and an exogenous telomerase subunit, e.g., hTERT. In an embodiment, the cell does not comprise DNA encoding the exogenous telomerase subunit. For instance, the cell may have been contacted with mRNA encoding the exogenous telomerase subunit.

In one embodiment, the immune effector cell preparation is a population of T regulatory-depleted cells containing less than 50%, 40%, 30%, 25%, 20%, 15%, 10%, 5%, 4%, 3%, 2%, 1% of CD25+ cells. In one embodiment, the immune effector cell preparation is a population of T regulatory-depleted cells containing less than 50%, 40%, 30%, 25%, 20%, 15%, 10%, 5%, 4%, 3%, 2%, 1% of CD25+ cells and less than 50%, 40%, 30%, 25%, 20%, 15%, 10%, 5%, 4%, 3%, 2%, 1% of CD25 expressing tumor cells, e.g., CLL cells. In one embodiment, the immune effector cell preparation contains less than 15%, 10%, 5%, 4%, 3%, 2%, 1% of CD25+ cells and less than 15%, 10%, 5%, 4%, 3%, 2%, 1% of tumor cells, e.g., CD25 expressing tumor cells, e.g., CLL cells. In one embodiment, the immune effector cell

preparation contains less than 10%, 5%, 4%, 3%, 2%, 1% of CD25+ cells and less than 10%, 5%, 4%, 3%, 2%, 1% of tumor cells, e.g., CD25 expressing tumor cells, e.g., CLL cells.

In one embodiment, the immune effector cell preparation is a population of T regulatory-depleted cells containing less than 50%, 40%, 30%, 25%, 20%, 15%, 10%, 5%, 4%, 3%, 2%, 1% of CD25+ cells and less than 50%, 40%, 30%, 25%, 20%, 15%, 10%, 5%, 4%, 3%, 2%, 1% of a checkpoint inhibitor expressing cells, e.g., a PD1+ cells, LAG3+ cells, or TIM3+ cells.

In one embodiment, the immune effector cell preparation is a population of T regulatory-depleted cells containing less than 50%, 40%, 30%, 25%, 20%, 15%, 10%, 5%, 4%, 3%, 2%, 1% of CD25+ cells and less than 50%, 40%, 30%, 25%, 20%, 15%, 10%, 5%, 4%, 3%, 2%, 1% of CD14+ cells.

In embodiments, the immune effector cell preparation described herein comprises a population of autologous immune effector cells, e.g., a plurality of which are transfected or transduced with a vector comprising a nucleic acid molecule encoding a CAR, e.g., a CAR described herein, e.g., a CD19 CAR described herein, wherein the immune effector cell preparation contains less than 50%, 40%, 30%, 25%, 20%, 15%, 10%, 5%, 4%, 3%, 2%, 1% of CD25+ cells and less than 50%, 40%, 30%, 25%, 20%, 15%, 10%, 5%, 4%, 3%, 2%, 1% of tumor cells, e.g., CLL cells. In one embodiment, the immune effector cell preparation contains less than 15%, 10%, 5%, 4%, 3%, 2%, 1% of CD25+ cells and less than 15%, 10%, 5%, 4%, 3%, 2%, 1% of tumor cells, e.g., CD25 expressing tumor cells, e.g., CLL cells. In one embodiment, the immune effector cell preparation contains less than 10%, 5%, 4%, 3%, 2%, 1% of CD25+ cells and less than 10%, 5%, 4%, 3%, 2%, 1% of tumor cells, e.g., CD25 expressing tumor cells, e.g., CLL cells.

In one embodiment, the reaction mixture can further comprise an agent that activates and/or expands to cells of the population, e.g., an agent that stimulates a CD3/TCR complex associated signal and/or a ligand that stimulates a costimulatory molecule on the surface of the cells, e.g., as described herein. In one embodiment, the agent is a bead conjugated with anti-CD3 antibody, or a fragment thereof, and/or anti-CD28 antibody, or a fragment thereof.

In embodiments, a reaction mixture described herein comprises a population of T regulatory-depleted cells containing less than 50%, 40%, 30%, 25%, 20%, 15%, 10%, 5%, 4%, 3%, 2%, 1% of CD25+ cells. In one embodiment, the reaction mixture comprises a population

of T regulatory-depleted cells containing less than 50%, 40%, 30%, 25%, 20%, 15%, 10%, 5%, 4%, 3%, 2%, 1% of CD25+ cells and less than 50%, 40%, 30%, 25%, 20%, 15%, 10%, 5%, 4%, 3%, 2%, 1% of CD25 expressing tumor cells, e.g., CLL cells. In one embodiment, the population of cells contains less than 15%, 10%, 5%, 4%, 3%, 2%, 1% of CD25+ cells and less than 15%, 10%, 5%, 4%, 3%, 2%, 1% of tumor cells, e.g., CD25 expressing tumor cells, e.g., CLL cells. In one embodiment, the population of cells contains less than 10%, 5%, 4%, 3%, 2%, 1% of CD25+ cells and less than 10%, 5%, 4%, 3%, 2%, 1% of tumor cells, e.g., CD25 expressing tumor cells, e.g., CLL cells.

In one embodiment, the reaction mixture comprises a population of T regulatory-depleted cells containing less than 50%, 40%, 30%, 25%, 20%, 15%, 10%, 5%, 4%, 3%, 2%, 1% of CD25+ cells and less than 50%, 40%, 30%, 25%, 20%, 15%, 10%, 5%, 4%, 3%, 2%, 1% of a checkpoint inhibitor expressing cells, e.g., a PD1+ cells, LAG3+ cells, or TIM3+ cells. The reaction mixture may further comprise a buffer or other reagent, e.g., a PBS containing solution.

In one embodiment, the reaction mixture comprises a population of T regulatory-depleted cells containing less than 50%, 40%, 30%, 25%, 20%, 15%, 10%, 5%, 4%, 3%, 2%, 1% of CD25+ cells and less than 50%, 40%, 30%, 25%, 20%, 15%, 10%, 5%, 4%, 3%, 2%, 1% of CD14+ cells. The reaction mixture may further comprise a buffer or other reagent, e.g., a PBS containing solution.

In one embodiment, the reaction mixture further comprises one or more factor for proliferation and/or viability, including serum (e.g., fetal bovine or human serum), interleukin-2 (IL-2), insulin, IFN-γ, IL-4, IL-7, GM-CSF, IL-10, IL-12, IL-15, IL-21, TGFβ, and TNF-α or any other additives for the growth of cells. In one embodiment, the reaction mixture further comprises IL-15 and/or IL-7.

In one embodiment, a plurality of the cells of the population in the reaction mixture comprise a nucleic acid molecule, e.g., a nucleic acid molecule described herein, that comprises a CAR encoding sequence, e.g., a CD19 CAR encoding sequence, e.g., as described herein.

In one embodiment, a plurality of the cells of the population in the reaction mixture comprise a vector comprising a nucleic acid sequence encoding a CAR, e.g., a CAR described herein, e.g., a CD19 CAR described herein. In one embodiment, the vector is a vector described herein, e.g., a vector selected from the group consisting of a DNA, a RNA, a plasmid, a lentivirus vector, adenoviral vector, or a retrovirus vector.

In one embodiment, the reaction mixture further comprises a cryoprotectant or stabilizer such as, e.g., a saccharide, an oligosaccharide, a polysaccharide and a polyol (e.g., trehalose, mannitol, sorbitol, lactose, sucrose, glucose and dextran), salts and crown ethers. In one embodiment, the cryoprotectant is dextran.

In embodiments, the reaction mixture comprises a population of immune effector cells wherein a plurality of the cells of the population in the reaction mixture comprise a nucleic acid molecule, e.g., a nucleic acid molecule described herein, that comprises a CAR encoding sequence, e.g., a CD19 CAR encoding sequence, e.g., as described herein, and IL-7 and/or IL-15.

In one embodiment, a plurality of the cells of the population in the reaction mixture comprise a vector comprising a nucleic acid sequence encoding a CAR, e.g., a CAR described herein, e.g., a CD19 CAR described herein. In one embodiment, the vector is a vector described herein, e.g., a vector selected from the group consisting of a DNA, a RNA, a plasmid, a lentivirus vector, adenoviral vector, or a retrovirus vector.

Other features, objects, and advantages of the invention will be apparent from the description and drawings, and from the claims.

Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. Although methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present invention, suitable methods and materials are described below. All publications, patent applications, patents, and other references mentioned herein are incorporated by reference in their entirety. In addition, the materials, methods, and examples are illustrative only and not intended to be limiting.

BRIEF DESCRIPTION OF THE FIGURES

Figures 1A-1D show the differential effects of γ_c cytokines and IL-18 on CAR-T cell accumulation. **Figure 1A** is a schematic diagram of C4-27z CAR vector. **Figure 1B** is a graph showing the overall accumulation of CAR-T cells in response to various cytokines exposure. T cells were transduced and exposed to various exogenous cytokines with final concentrations of 10ng/mL from the next day (day 0). The numbers of CAR-T cells were calculated based on the number of T cells and the percentages of CAR expression. The curves are representative of 6

donors. *P <0.05, ***P <0.001. NC, no cytokine. **Figure 1C** is a histogram showing the proliferation of T cells in response to various cytokines. On day 7 after lentivirus transduction, T cells in NC group were labeled with CFSE (2.5μM), and then exposed to various cytokines. Seven days later, T cells were analyzed for CFSE dilution by flow cytometry. **Figure 1D** is a graph showing the viability of T cells 15 days after lentiviral transduction. T cells from various cytokine groups are stained with Annexin V and 7-AAD, and then analyzed for the proportions of viable cells (both Annexin V and 7-AAD negative). *P <0.05, **P <0.01 versus IL-2 group (n=6).

Figures 2A-2F shows the memory T cell subsets of CAR-T cells. **Figure 2A** shows CD95 expression in CD45RA+CD62L+ subpopulation of T cells before transduction and CAR-T cells 15 days after transduction. **Figures 2B** and **2C** are graphs showing the increase of memory stem T cell (Tscm) proportions in CD4+ (**Figure 2B**) and CD8+ T cells (**Figure 2C**) after lentiviral transduction. Tscm are defined as CD45RA+CD62L+CD95+CCR7+ T cell subsets. **Figure 2D** is a graph showing the correlation between the amount of naïve T (Tn, defined as CD45RA+CD62L+CD95- subpopulation) in T cells pre-transduction and the proportion of Tscm in CAR-T cells after transduction (n=6). Left bars represents the percentages of Tn in CD4+ and CD8+ T cells before transduction and right bars represents the percentages of Tscm in CD4+ and CD8+ CAR-T cells. *P <0.05, **P<0.01. **Figure 2E** is a graph showing Self-renew and differentiation of different subsets of CAR-T cells. FACS-sorted CAR+ Tscm, Tcm, Tem and Temra cells are cultured exposed to IL-2 (10ng/mL) for 3 days, then analyzed the phenotypes based on CD45RA and CD62L expression (n=3). **Figure 2F** is a histogram plot showing the proliferation of various subsets of CAR-T cells in response to IL-2. FACS-sorted CAR+ Tscm, Tcm, Tem and Temra cells were labeled with CFSE (2.5μM), and then cultured exposed to IL-2 (10ng/mL) for 3 days. Three days later, T cells were analyzed for CFSE dilution.

Figure 3A-3B show the correlation between CD45 RA expression and CFSE intensity. **Figure 3A** demonstrates that CD45RAexpression is inversely correlated with CFSE intensity. **Figure 3B** shows that for all cytokine groups (IL-2, IL-7, IL-15, IL-18 and IL-21), CD45RA+ T cells exhibited much lower CFSE levels than CD45RA dim and negative T cells indicating that CD45RA+ T cells had stronger proliferation activity than CD45RA- T cells.

Figure 4 shows the phenotypes of CAR-T cells resulting from exposure to different cytokines. **Figure 4** is a series of graphs showing the quantitation of CD45RA, CD62L, CCR7, CD27, CD28 and IL7Rα expression by FACS on the surface of CAR-T cells in indicated cytokine groups. The histograms represent mean value ± SEM of expression levels from 6 independent donors. *P <0.05, **P <0.01 versus IL-2 group.

Figures 5A-5D show the Functional analysis of CAR-T cells exposed to different cytokines. **Figure 5A**, **5B**, and **5C** are quantitative plots showing the percentages of cytokine-producing CAR-T cells in various cytokine groups (n=6) for production of IFNγ (**Figure 5A**), TNF-α (**Figure 5B**) and IL-2 (**Figure 5C**). Lentiviral transduced T cells are exposed to indicated cytokines for 14 days, and then co-cultured with SKOV3 cells for 5 hours before harvested for flow cytometry analysis. **Figure 5D** is a graph showing the antigen specific cytotoxic activity of CAR-T cells. Fourteen days after indicated cytokine exposure, the CAR-T cells were assessed for cytolytic ability by using a luciferase-based assay after 18-hour coculture with SKOV3 at the indicated E/T ratios. Untransduced T cells (UNT) served as negative effector controls. Data shown are mean value ± SEM of six independent cytolytic assays.

Figure 6A-6C: shows the phenotype and function of the CAR-T cells described above in Figure 5. **Figures 6A** and **6B** show that CD62L+ CAR-T cells (Tscm and Tcm) exhibited less cytokine production activity (**Figure 6A and 6B**) and weaker cytolytic capacity (**Figure 6C**) when compared with CD62L- CAR-T cells (Tem and Temra).

Figures 7A-7B show the expansion and phenotype of CAR-T cells exposed to antigen challenge. **Figure 7A** depicts two graphs showing the overall accumulation and viability of CAR-T previously exposed to indicated cytokines upon antigen challenge. The T cells exposed to indicated cytokines are harvested on day 15, and then co-cultured with SKOV3 at E/T ratios of 5:1 for 7 days. The expansions of CAR-T cells are calculated and the viability of T cells are evaluated on the seventh day. **Figure 7B** is two graphs showing the distribution of memory T subsets of CD4+ and CD8+ CAR-T cells in various cytokine groups. N.S., no statistical difference.

Figures 8A-8C show the antitumor activity of various CAR-T cells with previous cytokine exposure. **Figure 8A** Tumor growth curves of mice treated with various cytokine exposed C4-27z CAR-T cells, anti-CD19-27z CAR-T cells and untransduced T cells. The data

are presented as mean value ± SEM. The arrow indicates the time of T cell infusion. **Figure 8B** is a graph showing the quantitation of circulating human CD4+ and CD8+ T cell counts in mice peripheral blood 15 days after the first dose of CAR-T cell infusion. **Figure 8C** is a graph showing the quantitation of CAR expression on circulating human CD4+ and CD8+ T cells in mice blood.

Figure 9 is a series of FACS plots (top) showing the CD3 and CD19 populations and histograms (bottom) showing CD14 expression of cells from apheresis, cells selected with anti-CD3/CD28, cells depleted for CD25**,** and the CD25 enriched cells.

Figures 10A, 10B, and **10C** show the comparison of proliferation capacity between CD3/CD28 selected cells and CD25 depleted cells. **Figure 10A** is a graph showing the total cell number at the indicated days in culture. **Figure 10B** is a graph showing the quantified population doublings at each indicated day in culture**. Figure 10C** shows the percentage of viable cells at the indicated days in culture.

Figure 11 is a series of FACs plots showing the distribution of CD3 and CD19 in unmanipulated PBMCs and CD25-depleted PBMCs after culture with the indicated cytokine supplements, IL-7, IL-15, or IL-7 and IL-15.

Figure 12 are graphs showing expansion profile in population doublings (Figure 17A) and mean size (fL)(Figure 17B) of PBMCs that have been stimulated with anti-CD3 and CD28 beads, and left either unmanipulated (UTD) or transduced with a CD19 CAR (CD19.BBz), de-beaded, and then harvested at Day 5 and D9.

Figure 13 are graphs depicting cytotoxicity as a percent lysis of CD19 expressing K562 cells treated with PMBCs that have been stimulated with anti-CD3 and CD28 beads, and left either unmanipulated (UTD) or transduced with a CD19 CAR (CD19.BBz), de-beaded, and then harvested at Day 5 and D9.

Figure 14 are graphs depicting proliferation of PBMCs stimulated with anti-CD3 and CD28 beads (3x28 beads), wild type K562 cells, CD19 expressing K562 cells, ALL cells (Nalm6) or CLL cells (PI14). The PBMCs have been left either unmanipulated (UTD) or transduced with a CD19 CAR (CART19), de-beaded, and then harvested at Day 5 and D9.

Figure 15 is a schematic of an exemplary manufacturing scheme.

Figure 16 is a schematic of an exemplary manufacturing scheme.

Figure 17 are graphs depicting the level of cell proliferation of two different manufacturing batches of donor cells transfected with the CTL019 CAR, CHP959-115 and CHP959-121, expanded over a period of 0 to 9 days.

Figure 18 are graphs showing proinflammatory cytokine production, IFN-γ, GM-CSF, TNF-α and IL-4 of two different manufacturing batches of donor cells transfected with either CTL019 CAR, namely CHP959-115, or an ss1-mesoCAR, namely and CHP959-121, and expanded over a period of 0 to 9 days after apheresis.

Figure 19 are graphs depicting production levels IFN-γ, TNF-α, IL-6, IL-8, IL-2, IL-1β, GM-CSF and IL-4 in donor cells stimulated with anti-CAR19-idiotype antibody beads or control beads, transfected with CTL019 CAR and expanded for 5 to 9 days. No cytokine or low cytokine levels (<200 pg/ml) were detected with the control beads.

Figure 20 is a graph depicting cell killing based upon total lysates using a luciferase assay of Nalm6 (ALL) cells of PBMCs left either unmanipulated (UTD) or transduced with a CD19 CAR (CART19), de-beaded, and then harvested at Day 5 and D9. Various ratios of PMBCs to Nalm6 cells (effector (E):Target (T)) were cultured. As shown CART19 cells harvested at day 5 posses a better killing capacity.

Figure 21 is a graph depicting long term in vivo killing capacity of PBMCs left either unmanipulated (UTD) or transduced with a CD19 CAR (CART19), de-beaded, and then harvested at Day 5 and D9. The PBMCs were introduced into non-obese diabetic/severe combined immunodeficiency mice inoculated with Nalm6 cells.

Figures 22 is a schematic depiction of the use of mesothelin coated beads with mesothelin CARTs for cell expansion.

Figures 23 is a schematic depiction of the study design of Example 4.

Figures 24A and **24B** are graphs depicting population doublings (**Figure 24A**) and cell size (**Figure 24B**) of the cell types shown in **Figure 23**.

Figures 25A and**25B** are graphs depicting transduction efficiency after 5 days (**Figure 25A**) and 11 days (**Figure 25B**).

Figures 26A and **26B** show mesothelin CAR constructs and expression levels. Figure 26A is a schematic diagram of the different CAR constructs used in Example 4.

Figures 27A-27C shows expansion of peripheral blood T cells and cord blood CD8 T cells in culture through a mesothelin CAR stimulation. CD8 T cells are shown in **Figure 27A**. CD4 T cells are shown in **Figure 27B**. Cord blood CD8 T cells are shown in **Figure 27C**.

Figure 28 shows a schematic representation of a method for stimulation through a transiently expressed Chimeric Antigen Receptor (CAR) on the surface of T cells, by its cognate antigen.

Figure 29 is a schematic depiction of the use of CARs for cell expansion with beads coated with their cognate antigen.

Figures 30A and **30B** are graphs depicting population doublings (**Figure 30A**) and cell size (**Figure 30B**) of mesothelin CAR expressing cells after exposure to mesothelin coated beads.

Figures 31A-31C is a graph demonstrating expansion of peripheral blood T cells stimulated with mesothelin CAR (**Figure 31A**), or CD19 CAR (**Figure 31B**) and cord blood CD8 T cells stimulated with mesothelin CAR (**Figure 31C**) in culture.

Figures 32A-32C show CAR constructs and study design of example 6. **Figure 32A** is a schematic of the CAR constructs compared in Example 6. Both CARs contain a single-chain variable fragment of the FMC63 antibody that recognizes human CD19 or the SS1 scFv that binds human mesothelin. The transmembrane (TM) and intracellular domains are indicated. **Figure 32B** is a graph depicting flow cytometric analysis of cell surface expression of the CARs on day 1 after electroporation in comparison to a No-CAR electroporation only (Mock) control. The right panel shows the mean fluorescence intensities (MFIs) of the CARs detected with an anti-idiotype reagent. Data are representative of independent experiments verified with cells from over 25 individual healthy human donors. **Figure 32C** is a schematic of the study design. CD8+ T cells are electroporated with *in vitro* transcribed RNA. After the cells are allowed to rest overnight, the CAR expression is confirmed and the *in vitro* culture commences in the presence of cognate antigen-coated beads and cytokines.

Figures 33A-33E show BBz ICD provides a survival and proliferative advantage to CD8 T cells *in vitro*. **Figure 33A** shows CD69 levels measured on cell surface 24 hours after co-culture with cognate antigen. **Figure 33B** shows CD19 CAR T cell growth; CD4+ and CD8+ T cells were stimulated as in Figure 33A and as described in Example 6. Data are representative of at least ten different healthy donors. **Figure 33C** shows mesothelin CAR T cell growth of bulk CD8+ T cells (left) or naïve (CD45RO-CD62L+CD8+) T cells (right). CAR

T cells were stimulated using beads coated with mesothelin-Fc. **Figure 33D** shows representative plots (from at least six donors) of cell surface expression CCR7 and CD45RO on CAR T cells at specified time points during culture. Cells shown have been pre-gated for live CD3+CD8+ T cells. Numbers shown are percentages of cells detected in each gate. **Figure 33E** shows relative change of Tcm and Tem subsets in 28z and BBzCD19 CAR T cell culture at different time points. Absolute numbers of live cells were calculated for each population at the specified time points. The graphs show relative fold change of Tcm or Tem in BBz CAR T cells normalized to 28z CAR T cells. Data are plotted as mean ± SEM (****, $p < 0.0001$, **, $p =< 0.01$).

Figures 34A-34M show the effects of CAR signaling domain on cellular metabolism and preferential reliance on glycolysis or fatty acid oxidation by CAR T cells. As shown in Figures 34A-34D, BBz CAR T cells show elevated levels of oxygen consumption and spare respiratory capacity. **Figure 34A** shows the effects of antigen stimulation on mean cell volume after stimulation of CD19 CAR CD8+ T cells expressing 28z and BBz signaling domains with anti-idiotype. As shown in this figure, 28z and BBz CAR T cells have comparable mean cell sizes as measured on Days 0, 7 and 20. **Figure 34B** shows the oxygen consumption rates (OCRs) of 28z and BBz CAR T cells at baseline (after electroporation of CAR mRNA and before stimulation) on day 0 and after stimulation on days 7 and 21 in culture under basal conditions and in response to mitochondrial inhibitors, as specified in Example 6. Basal OCR levels (**Figure 34C**), basal OCR/ECAR ratio (**Figure 34D**), maximum respiratory levels (**Figure 34F**), and basal ECAR levels (**Figure 34G**) measured at Day 7 and Day 21 (revealing preferential elevation of OXPHOS in BBz CAR T cells). Data are representative of at least five independent experiments performed with cells from at least five healthy human donors plotted as mean ± SEM (*, $p < 0.05$). **Figure 34E** shows relative mRNA expression levels of genes involved in glycolytic metabolism and lipid oxidation assessed in 28z and BBz, CAR T cells. Plot represents data from at least three independent experiments with cells obtained from four independent donors (**, $p < 0.01$; *, $p < 0.05$). Data are represented as mean ± SEM. **Figures 34H-34J** show basal OCR levels measured for CAR T cells sorted for different memory phenotypes: central memory (CM; Figure 34H), naive (N; Figure 34I), and effector memory (EM; Figure 34J). Data are representative of at least three independent experiments performed with cells from at least three healthy human donors and plotted as mean ± SEM. **Figure 34K** shows basal ECAR levels measured for the three different sorted memory subsets. Data are

representative of at least three independent experiments performed with cells from at least three healthy human donors plotted as mean ± SEM (*, $p < 0.05$). **Figure 34L** shows the measurement of glucose uptake from extracellular media and lactate release into the media over a course of 48 hr. **Figure 34M** shows the percentage of labeled acetyl-CoA measured in T cells cultured with [$^{13}C_{16}$] palmitic acid to assess fatty acid uptake and breakdown.

Figures 35A-35C show that BBz CAR T cells show enhanced spare respiratory capacity (SRC). **Figure 35A** shows SRC measured as the ratio between the maximum OCR levels after treating cells with FCCP to the basal OCR levels at steady state while in culture. Data represents three independent donors tested (* $p < 0.05$). **Figure 35B** shows transmission electron microscopy of 28z and BBz CAR CD8+ T cells imaged at three different time point. Scale bars represent 2 μm. **Figure 35C** shows enumeration of the individual mitochondrion per cell. Data shown 20 individual randomly chosen cells (out of at least 75 cells analyzed per condition) represented as mean ± SEM (***, $p < 0.001$).

Figures 36A-36D show BBz CAR signaling imprints genetic alterations of T cell to enhance mitochondrial biogenesis. **Figure 36A** shows confocal images stained with Mitotracker (green), DAPI (blue) and a cell-membrane dye DiI (red). Scale bars represent 2μm. **Figure 36B** shows quantification of the percentage of cytoplasm occupied by mitochondria, measured as percentage of Mitotracker (green) within area enclosed the cell membrane (red). Data represented as mean ± SEM from at least three images each at specified time points with at least 15 independent cells scored per image. (****, $p < 0.0001$). **Figure 36C** shows relative mRNA expression of mitochondrial cytochrome c oxidase 1 (MT-CO1) and mitochondrial transcription factor A (TFAM) in BBz CAR T cells normalized to expression levels of 28z CAR T cells at specified time points. Data generated from at least three independent experiments with four independent donors (*, $p < 0.05$), represented as mean ± SEM. **Figure 36D** shows normalized mRNA expression levels of nuclear respiratory factor 1 (NRF1) and GA binding protein (NRF2) in BBz CAR T cells in comparison to 28z CAR T cells at specified time points. Data are generated from at least three independent experiments with four independent donors (*, $p < 0.05$) and represented as mean ± SEM.

Figure 37 shows expansion profiles of CD19-28z and CD19-BBz CAR T cells for two other independent donors. It is consistently observed that BBz CAR T cells continue to proliferate and survive longer in culture.

Figure 38 shows expansion profiles of mesothelin-specific CAR T cells for two other independent donors. It is consistently observed that BBz CAR T cells continue to proliferate and survive longer in culture.

Figure 39 shows the oxygen consumption rates (OCR) on 28z and BBz CAR T cells before stimulation (day 0) and on days 7 and 21 in culture, under basal conditions and in to the presence of mitochondrial inhibitors as specified in Example 6. Metabolic assays performed on mesothelin-specific CARs reveal higher oxygen consumption rates in BBz-CAR stimulated cells.

Figure 40 shows total population doublings between the two CAR constructs (CD19 CAR n=10, p**=<0.01, Mesothelin CAR n=6, p*=<0.05), as shown in Figures 37 and 38. CD19 or SS1 CAR T cells were stimulated with anti-idiotype antibody to the CD19 scFv or mesothelin-Fc immobilized on beads, respectively.

Figure 41 shows CAR and key cytokine receptor expression levels on cell surface post antigen exposure. The top panel shows the lack of any detectable CAR expression levels on the surface of T cells post engagement with anti-idiotype antibody to the CD19 scFv immobilized on beads. These plots represent the same cell populations which were assayed in Figure 32B that expressed CARs prior to antigenic stimulation. Bottom panel shows levels of cytokine receptors, IL-2Rα, IL-7Rα and IL-15Rα on cell surface as assayed by flow cytometry.

Figure 42 shows changes in mitochondrial content in 28z and BBz CAR T cells as measured on Day 21. Transmission electron microscopy of representative 28z and BBz CAR CD8+ T cells imaged at Day 21. Scale bars represent 2μm.

DETAILED DESCRIPTION

The methods described herein are based, at least in part, on the discovery that activation of a CAR expressed (e.g., transiently expressed) on an immune effector cell surface provides an effective means for expanding and/or activating a population of immune effector cells. As described herein, activation of a CAR on the surface of an immune effector cell by its cognate antigen or an anti-idiotypic antibody can result in cell expansion. In some embodiments, such cell expansion can be achieved without substantially altering the genotype or phenotype of the cell by transiently expressing the CAR (e.g., by *in vitro* transcribed RNA). The methods

described herein provide significant advantages over previously used methods for immune effector cell expansion.

In addition to being used to expand primary human T cells, methods described herein can be used in the expansion of specific subsets of T lymphocytes, including naïve cells, T-regulatory cell, Th-17 cells, anergized T cells, and stem cell T cells or cord blood cells. Without wishing to be bound by a particular theory, the method and compositions described herein provide an improvement over the conventional system, as repeated stimulations through the TCR can be lethal to antigen-inexperienced T cells. Single stimulation through transiently expressed surface receptor could avoid this issue. Furthermore, methods provided herein allow for T cells without disturbing the TCR for immunotherapy leading to less rapid differentiation and promoting "young" T cells in the culture. In other embodiments, the methods described herein enable high efficiency transduction using vectors, such as lentiviral vectors.

Advantageously, other cell types can be expanded that lack a T cell receptor or have T cell receptor with reduced function. For example, any type of hematopoietic stem cell can be expanded without alteration of their phenotype, and anergized T cells, TH17, NK, NKT and B cells can be expanded.

Viral-mediated gene transfer systems are being extensively used for pre-clinical and clinical immunotherapy studies. Current methods for viral-mediated gene transfer into T lymphocytes require activation of the cells, followed by addition of the viral vector. This activation is again traditionally accomplished by stimulating through the TCR. The methods of CAR-based stimulation described herein can be used to achieve high efficiency transduction with vectors such as lentiviral vectors. By stimulating through a transiently expressed CAR to achieve initial activation, the cells can be transduced with a lentiviral vector encoding the same or different CAR constructs.

In embodiments, the methods described herein provide for *in vitro* expansion of immune effector cells. In further embodiments, the methods described herein provide for *in vivo* expansion of T cells following lymph node injection or *in vivo* expansion of TILs following injection into a tumor.

Accordingly, in embodiments, the methods disclosed herein provide for methods of expanding a population of immune effector cells by contacting the population of immune

effector cells with a nucleic acid encoding a CAR, under conditions suitable for transient expression of the CAR, wherein the CAR targets a cognate antigen molecule; and culturing the population of immune effector cells in the presence of the cognate antigen molecule. In one embodiment, the nucleic acid is RNA, e.g., *in vitro* transcribed RNA. In another embodiment, the cognate antigen molecule is a cancer associated antigen molecule. In one embodiment, the cognate antigen molecule is attached to a substrate, e.g., a bead, and the immune effector cell population is expanded *in vitro*. In another embodiment, the cognate antigen is expressed on a cell, e.g., a tumor cell and the immune effector cell population is expanded *in vivo*. In another aspect the invention features a method of treating, or providing anti-tumor immunity to, a subject having a cancer, comprising administering to the subject an effective amount of an immune effector cell population, wherein the immune effector cell population is expanded by methods described herein.

Definitions

Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which the invention pertains.

The term "a" and "an" refers to one or to more than one (i.e., to at least one) of the grammatical object of the article. By way of example, "an element" means one element or more than one element.

The term "about" when referring to a measurable value such as an amount, a temporal duration, and the like, is meant to encompass variations of ±20% or in some instances ±10%, or in some instances ±5%, or in some instances ±1%, or in some instances ±0.1% from the specified value, as such variations are appropriate to perform the disclosed methods.

"Acquire" or "acquiring" as the terms are used herein, refer to obtaining possession of a physical entity (*e.g.*, a sample, a cell or cell population, a polypeptide, a nucleic acid, or a sequence), or a value, *e.g.*, a numerical value, by "directly acquiring" or "indirectly acquiring" the physical entity or value. In one embodiment, acquiring refers to obtaining or harvesting a cell or cell population (e.g., an immune effector cell or population as described herein). "Directly acquiring" means performing a process (*e.g.*, performing a synthetic or analytical or

purification method) to obtain the physical entity or value. "Indirectly acquiring" refers to receiving the physical entity or value from another party or source (*e.g.*, a third party laboratory that directly acquired the physical entity or value). Directly acquiring a physical entity includes performing a process that includes a physical change in a physical substance, *e.g.*, a starting material. Exemplary changes include making a physical entity from two or more starting materials, shearing or fragmenting a substance, separating or purifying a substance, combining two or more separate entities into a mixture, performing a chemical reaction that includes breaking or forming a covalent or non-covalent bond. Directly acquiring a value includes performing a process that includes a physical change in a sample or another substance, *e.g.*, performing an analytical process which includes a physical change in a substance, *e.g.*, a sample, analyte, or reagent (sometimes referred to herein as "physical analysis"), performing an analytical method, *e.g.*, a method which includes one or more of the following: separating or purifying a substance, *e.g.*, an analyte, or a fragment or other derivative thereof, from another substance; combining an analyte, or fragment or other derivative thereof, with another substance, *e.g.*, a buffer, solvent, or reactant; or changing the structure of an analyte, or a fragment or other derivative thereof, *e.g.*, by breaking or forming a covalent or non-covalent bond, between a first and a second atom of the analyte; or by changing the structure of a reagent, or a fragment or other derivative thereof, *e.g.*, by breaking or forming a covalent or non-covalent bond, between a first and a second atom of the reagent.

The term "bioequivalent" refers to an amount of an agent other than the reference compound (e.g., RAD001), required to produce an effect equivalent to the effect produced by the reference dose or reference amount of the reference compound (e.g., RAD001). In an embodiment the effect is the level of mTOR inhibition, e.g., as measured by P70 S6 kinase inhibition, e.g., as evaluated in an *in vivo* or *in vitro* assay, e.g., as measured by an assay described herein, e.g., the Boulay assay, or measurement of phosphorylated S6 levels by western blot. In an embodiment, the effect is alteration of the ratio of PD-1 positive/PD-1 negative T cells, as measured by cell sorting. In an embodiment a bioequivalent amount or dose of an mTOR inhibitor is the amount or dose that achieves the same level of P70 S6 kinase inhibition as does the reference dose or reference amount of a reference compound. In an embodiment, a bioequivalent amount or dose of an mTOR inhibitor is the amount or dose that achieves the same level of alteration in the ratio of PD-1 positive/PD-1 negative T cells as does the reference dose or reference amount of a reference compound.

The term "Chimeric Antigen Receptor" or alternatively a "CAR" refers to a set of polypeptides, typically two in the simplest embodiments, which when in an immune effector cell, provides the cell with specificity for a target cell, typically a cancer cell, and with intracellular signal generation. In some embodiments, a CAR comprises at least an extracellular antigen binding domain, a transmembrane domain and a cytoplasmic signaling domain (also referred to herein as "an intracellular signaling domain") comprising a functional signaling domain derived from a stimulatory molecule and/or costimulatory molecule as defined below. In some embodiments, the set of polypeptides are in the same polypeptide chain (e.g., comprise a chimeric fusion protein). In some embodiments, the set of polypeptides are not contiguous with each other, e.g., are in different polypeptide chains. In some embodiments, the set of polypeptides are not contiguous with each other, e.g., are in different polypeptide chains. In some embodiments, the set of polypeptides include a dimerization switch that, upon the presence of a dimerization molecule, can couple the polypeptides to one another, e.g., can couple an antigen binding domain to an intracellular signaling domain. In one aspect, the stimulatory molecule is the zeta chain associated with the T cell receptor complex. In one aspect, the cytoplasmic signaling domain comprises a primary signaling domain (e.g., a primary signaling domain of CD3-zeta). In one aspect, the cytoplasmic signaling domain further comprises one or more functional signaling domains derived from at least one costimulatory molecule as defined below. In one aspect, the costimulatory molecule of the CAR is chosen from the costimulatory molecules described herein, e.g., 4-1BB (i.e., CD137), CD27, ICOS, and/or CD28. In one aspect, the CAR comprises a chimeric fusion protein comprising an extracellular antigen binding domain, a transmembrane domain and an intracellular signaling domain comprising a functional signaling domain derived from a stimulatory molecule. In one aspect, the CAR comprises a chimeric fusion protein comprising an extracellular antigen binding domain, a transmembrane domain and an intracellular signaling domain comprising a functional signaling domain derived from a costimulatory molecule and a functional signaling domain derived from a stimulatory molecule. In one aspect, the CAR comprises a chimeric fusion protein comprising an extracellular antigen binding domain, a transmembrane domain and an intracellular signaling domain comprising two functional signaling domains derived from one or more costimulatory molecule(s) and a functional signaling domain derived from a stimulatory molecule. In one aspect, the CAR comprises a chimeric fusion protein comprising an extracellular antigen binding domain, a

transmembrane domain and an intracellular signaling domain comprising at least two functional signaling domains derived from one or more costimulatory molecule(s) and a functional signaling domain derived from a stimulatory molecule. In one aspect the CAR comprises an optional leader sequence at the amino-terminus (N-ter) of the CAR fusion protein. In one aspect, the CAR further comprises a leader sequence at the N-terminus of the extracellular antigen binding domain, wherein the leader sequence is optionally cleaved from the antigen binding domain (e.g., a scFv) during cellular processing and localization of the CAR to the cellular membrane.

"CAR molecule", depending on the context, refers to a CAR (e.g., a CAR polypeptide), a nucleic acid encoding a CAR, or both.

A CAR that comprises an antigen binding domain (e.g., a scFv, or TCR) that targets a specific tumor antigen X, such as those described herein, is also referred to as XCAR. For example, a CAR that comprises an antigen binding domain that targets CD19 is referred to as CD19CAR.

The term "signaling domain" refers to the functional portion of a protein which acts by transmitting information within the cell to regulate cellular activity via defined signaling pathways by generating second messengers or functioning as effectors by responding to such messengers.

The term "antibody," as used herein, refers to a protein, or polypeptide sequence derived from an immunoglobulin molecule which specifically binds with an antigen. Antibodies can be polyclonal or monoclonal, multiple or single chain, or intact immunoglobulins, and may be derived from natural sources or from recombinant sources. Antibodies can be tetramers of immunoglobulin molecules.

The term "antibody fragment" refers to at least one portion of an antibody, that retains the ability to specifically interact with (e.g., by binding, steric hindrance, stabilizing/destabilizing, spatial distribution) an epitope of an antigen. Examples of antibody fragments include, but are not limited to, Fab, Fab', $F(ab')_2$, Fv fragments, scFv antibody fragments, disulfide-linked Fvs (sdFv), a Fd fragment consisting of the VH and CH1 domains, linear antibodies, single domain antibodies such as sdAb (either VL or VH), camelid VHH domains, multi-specific antibodies formed from antibody fragments such as a bivalent fragment comprising two Fab fragments linked by a disulfide bridge at the hinge region, and an isolated CDR or other epitope binding fragments of an antibody. An antigen binding fragment can also

be incorporated into single domain antibodies, maxibodies, minibodies, nanobodies, intrabodies, diabodies, triabodies, tetrabodies, v-NAR and bis-scFv (see, e.g., Hollinger and Hudson, Nature Biotechnology 23:1126-1136, 2005). Antigen binding fragments can also be grafted into scaffolds based on polypeptides such as a fibronectin type III (Fn3)(see U.S. Patent No.: 6,703,199, which describes fibronectin polypeptide minibodies).

The term "inhibiton" or "inhibitor" includes a reduction in a certain parameter, e.g., an activity, of a given molecule, e.g., CD19, CD20, CD10, CD22, CD34, CD123, FLT-3, ROR1, CD79b, CD179b, mesothelin, or CD79a. For example, inhibition of an activity, e.g., an activity of CD20, CD10, CD19, CD22, CD34, CD123, FLT-3, ROR1, CD79b, CD179b, mesothelin, or CD79a, of at least 5%, 10%, 20%, 30%, 40%, or more is included by this term. Thus, inhibition need not be 100%. Activities for the inhibitors can be determined as described herein or by assays known in the art.

As used herein, the term "CD10" refers to an antigenic determinant known to be detectable on leukemia cells. The human and murine amino acid and nucleic acid sequences can be found in a public database, such as GenBank, UniProt and Swiss-Prot. For example, the amino acid sequences of human CD10 can be found at Accession Nos. NP_009218.2; NP_000893.2; NP_009219.2; NP_009220.2, and the mRNA sequences encoding them can be found at Accession Nos. NM_007287.2 (variant 1bis); NM_000902.3 (variant 1); NM_007288.2 (variant 2a); NM_007289.2 (variant 2b). In one aspect the antigen-binding portion of the CAR recognizes and binds an antigen within the extracellular domain of the CD10 protein. In one aspect, the CD10 protein is expressed on a cancer cell. As used herein, "CD10" includes proteins comprising mutations, e.g., point mutations, fragments, insertions, deletions and splice variants of full length wild-type CD10.

As used herein, the term "CD19" refers to the Cluster of Differentiation 19 protein, which is an antigenic determinant detectable on leukemia precursor cells. The human and murine amino acid and nucleic acid sequences can be found in a public database, such as GenBank, UniProt and Swiss-Prot. For example, the amino acid sequence of human CD19 can be found as UniProt/Swiss-Prot Accession No. P15391 and the nucleotide sequence encoding of the human CD19 can be found at Accession No. NM_001178098. As used herein, "CD19" includes proteins comprising mutations, e.g., point mutations, fragments, insertions, deletions and splice variants of full length wild-type CD19.

CD19 is expressed on most B lineage cancers, including, e.g., acute lymphoblastic

leukaemia, chronic lymphocyte leukaemia and non-Hodgkin lymphoma. Other cells with express CD19 are provided below in the definition of "disease associated with expression of CD19." It is also an early marker of B cell progenitors. See, e.g., Nicholson et al. Mol. Immun. 34 (16-17): 1157-1165 (1997). In one aspect the antigen-binding portion of the CART recognizes and binds an antigen within the extracellular domain of the CD19 protein. In one aspect, the CD19 protein is expressed on a cancer cell.

As used herein, the term "CD20" refers to an antigenic determinant known to be detectable on B cells. Human CD20 is also called membrane-spanning 4-domains, subfamily A, member 1 (MS4A1). The human and murine amino acid and nucleic acid sequences can be found in a public database, such as GenBank, UniProt and Swiss-Prot. For example, the amino acid sequence of human CD20 can be found at Accession Nos. NP_690605.1 and NP_068769.2, and the nucleotide sequence encoding transcript variants 1 and 3 of the human CD20 can be found at Accession No. NM_152866.2 and NM_021950.3, respectively. In one aspect the antigen-binding portion of the CAR recognizes and binds an antigen within the extracellular domain of the CD20 protein. In one aspect, the CD20 protein is expressed on a cancer cell. As used herein, "CD20" includes proteins comprising mutations, e.g., point mutations, fragments, insertions, deletions and splice variants of full length wild-type CD20.

As used herein, the terms "CD22," refers to an antigenic determinant known to be detectable on leukemia precursor cells. The human and murine amino acid and nucleic acid sequences can be found in a public database, such as GenBank, UniProt and Swiss-Prot. For example, the amino acid sequences of isoforms 1-5 human CD22 can be found at Accession Nos. NP 001762.2, NP 001172028.1, NP 001172029.1, NP 001172030.1, and NP 001265346.1, respectively, and the nucleotide sequence encoding variants 1-5 of the human CD22 can be found at Accession No. NM 001771.3, NM 001185099.1, NM 001185100.1, NM 001185101.1, and NM 001278417.1, respectively. In one aspect the antigen-binding portion of the CAR recognizes and binds an antigen within the extracellular domain of the CD22 protein. In one aspect, the CD22 protein is expressed on a cancer cell. As used herein, "CD22" includes proteins comprising mutations, e.g., point mutations, fragments, insertions, deletions and splice variants of full length wild-type CD22.

As used herein, the term "CD34" refers to an antigenic determinant known to be detectable on hematopoietic stem cells and some cancer cells. The human and murine amino acid and nucleic acid sequences can be found in a public database, such as GenBank, UniProt

and Swiss-Prot. For example, the amino acid sequences of human CD34 can be found at Accession Nos. NP_001020280.1 (isoform a precursor); NP_001764.1 (isoform b precursor), and the mRNA sequences encoding them can be found at Accession Nos. NM_001025109.1 (variant 1); NM_001773.2 (variant 2). In one aspect the antigen-binding portion of the CAR recognizes and binds an antigen within the extracellular domain of the CD34 protein. In one aspect, the CD34 protein is expressed on a cancer cell. As used herein, "CD34" includes proteins comprising mutations, e.g., point mutations, fragments, insertions, deletions and splice variants of full length wild-type CD34.

As used herein, the term "CD123" refers to an antigenic determinant known to be detectable on some malignant hematological cancer cells, e.g., leukemia cells. The human and murine amino acid and nucleic acid sequences can be found in a public database, such as GenBank, UniProt and Swiss-Prot. For example, the amino acid sequences of human CD123 can be found at Accession Nos. NP_002174.1 (isoform 1 precursor); NP_001254642.1 (isoform 2 precursor), and the mRNA sequences encoding them can be found at Accession Nos. NM_002183.3 (variant 1); NM_001267713.1 (variant 2). In one aspect the antigen-binding portion of the CAR recognizes and binds an antigen within the extracellular domain of the CD123 protein. In one aspect, the CD123 protein is expressed on a cancer cell. As used herein, "CD123" includes proteins comprising mutations, e.g., point mutations, fragments, insertions, deletions and splice variants of full length wild-type CD123.

As used herein, the term "CD79b" refers to an antigenic determinant known to be detectable on some malignant hematological cancer cells, e.g., leukemia cells. The human and murine amino acid and nucleic acid sequences can be found in a public database, such as GenBank, UniProt and Swiss-Prot. For example, the amino acid sequences of human CD79b can be found at Accession Nos. NP_000617.1 (isoform 1 precursor), NP_067613.1 (isoform 2 precursor), or NP_001035022.1 (isoform 3 precursor), and the mRNA sequences encoding them can be found at Accession Nos. NM_000626.2 (transcript variant 1), NM_021602.2 (transcript variant 2), or NM_001039933.1 (transcript variant 3). In one aspect the antigen-binding portion of the CAR recognizes and binds an antigen within the extracellular domain of the CD79b protein. In one aspect, the CD79b protein is expressed on a cancer cell. As used herein, "CD79b" includes proteins comprising mutations, e.g., point mutations, fragments, insertions, deletions and splice variants of full length wild-type CD79b.

As used herein, the term "CD79a" refers to an antigenic determinant known to be detectable on some malignant hematological cancer cells, e.g., leukemia cells. The human and murine amino acid and nucleic acid sequences can be found in a public database, such as GenBank, UniProt and Swiss-Prot. For example, the amino acid sequences of human CD79a can be found at Accession Nos. NP_001774.1 (isoform 1 precursor) or NP_067612.1 (isoform 2 precursor), and the mRNA sequences encoding them can be found at Accession Nos. NM_001783.3 (transcript variant 1) or NM_021601.3 (transcript variant 2). In one aspect, the antigen-binding portion of the CAR recognizes and binds an antigen within the extracellular domain of the CD79a protein. In one aspect, the CD79a protein is expressed on a cancer cell. As used herein, "CD79a" includes proteins comprising mutations, e.g., point mutations, fragments, insertions, deletions and splice variants of full length wild-type CD79a.

As used herein, the term "CD179b" refers to an antigenic determinant known to be detectable on some malignant hematological cancer cells, e.g., leukemia cells. The human and murine amino acid and nucleic acid sequences can be found in a public database, such as GenBank, UniProt and Swiss-Prot. For example, the amino acid sequences of human CD179b can be found at Accession Nos. NP_064455.1 (isoform a precursor) or NP_690594.1 (isoform b precursor), and the mRNA sequences encoding them can be found at Accession Nos. NM_020070.3 (transcript variant 1) or NM_152855.2 (transcript variant 2). In one aspect the antigen-binding portion of the CAR recognizes and binds an antigen within the extracellular domain of the CD179b protein. In one aspect, the CD179b protein is expressed on a cancer cell. As used herein, "CD179b" includes proteins comprising mutations, e.g., point mutations, fragments, insertions, deletions and splice variants of full length wild-type CD179b.

As used herein, the term "FLT-3" refers to an antigenic determinant known to be detectable on hematopoietic progenitor cells and some cancer cells, e.g., leukemia cells. The human and murine amino acid and nucleic acid sequences can be found in a public database, such as GenBank, UniProt and Swiss-Prot. For example, the amino acid sequences of human FLT-3 can be found at Accession Nos. NP_004110.2, and the mRNA sequences encoding them can be found at Accession Nos. NM_004119.2. In one aspect the antigen-binding portion of the CAR recognizes and binds an antigen within the extracellular domain of the FLT-3 protein. In one aspect, the FLT-3 protein is expressed on a cancer cell. As used herein, "FLT-3" includes proteins comprising mutations, e.g., point mutations, fragments, insertions, deletions and splice variants of full length wild-type FLT-3.

As used herein, the term "ROR1" refers to an antigenic determinant known to be detectable on leukemia precursor cells. The human and murine amino acid and nucleic acid sequences can be found in a public database, such as GenBank, UniProt and Swiss-Prot. For example, the amino acid sequences of isoforms 1and 2 precursors of human ROR1 can be found at Accession Nos. NP_005003.2 and NP_001077061.1, respectively, and the mRNA sequences encoding them can be found at Accession Nos. NM_005012.3 and NM_001083592.1, respectively. In one aspect the antigen-binding portion of the CAR recognizes and binds an antigen within the extracellular domain of the ROR1 protein. In one aspect, the ROR1 protein is expressed on a cancer cell. As used herein, "ROR1" includes proteins comprising mutations, e.g., point mutations, fragments, insertions, deletions and splice variants of full length wild-type ROR1.

As used herein, the term "mesothelin" refers to the 40-kDa protein, mesothelin, which is anchored at the cell membrane by a glycosylphosphatidyl inositol (GPI) linkage and an amino-terminal 31-kDa shed fragment, called megkaryocyte potentiating factor (MPF). Both fragments contain N-glycosylation sites. The term also refers to a soluble splice variant of the 40-kDa carboxyl-terminal fragment also called "soluble mesothelin/MPF-related". Preferably, the term refers to a human mesothelin of GenBank accession number AAH03512.1, and naturally cleaved portions thereof, e.g., as expressed on a cell membrane, e.g., a cancer cell membrane. As used herein, "mesothelin" includes proteins comprising mutations, e.g., point mutations, fragments, insertions, deletions and splice variants of full length wild-type mesothelin.

The term "scFv" refers to a fusion protein comprising at least one antibody fragment comprising a variable region of a light chain and at least one antibody fragment comprising a variable region of a heavy chain, wherein the light and heavy chain variable regions are contiguously linked, e.g., via a synthetic linker, e.g., a short flexible polypeptide linker, and capable of being expressed as a single chain polypeptide, and wherein the scFv retains the specificity of the intact antibody from which it is derived. Unless specified, as used herein an scFv may have the VL and VH variable regions in either order, e.g., with respect to the N-terminal and C-terminal ends of the polypeptide, the scFv may comprise VL-linker-VH or may comprise VH-linker-VL.

The portion of a CAR comprising an antibody or antibody fragment thereof may exist in a variety of forms where the antigen binding domain is expressed as part of a contiguous

polypeptide chain including, for example, a single domain antibody fragment (sdAb), a single chain antibody (scFv) and a humanized antibody (Harlow et al., 1999, In: Using Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory Press, NY; Harlow et al., 1989, In: Antibodies: A Laboratory Manual, Cold Spring Harbor, New York; Houston et al., 1988, Proc. Natl. Acad. Sci. USA 85:5879-5883; Bird et al., 1988, Science 242:423-426). In one embodiment, the antigen binding domain of a CAR comprises an antibody fragment. In a further embodiment, the CAR comprises an antibody fragment that comprises a scFv. As used herein, the term "binding domain" or "antibody molecule" refers to a protein, e.g., an immunoglobulin chain or fragment thereof, comprising at least one immunoglobulin variable domain sequence. The term "binding domain" or "antibody molecule" encompasses antibodies and antibody fragments. In an embodiment, an antibody molecule is a multispecific antibody molecule, e.g., it comprises a plurality of immunoglobulin variable domain sequences, wherein a first immunoglobulin variable domain sequence of the plurality has binding specificity for a first epitope and a second immunoglobulin variable domain sequence of the plurality has binding specificity for a second epitope. In an embodiment, a multispecific antibody molecule is a bispecific antibody molecule. A bispecific antibody has specificity for no more than two antigens. A bispecific antibody molecule is characterized by a first immunoglobulin variable domain sequence which has binding specificity for a first epitope and a second immunoglobulin variable domain sequence that has binding specificity for a second epitope.

The term "complementarity determining region" or "CDR," as used herein, refers to the sequences of amino acids within antibody variable regions which confer antigen specificity and binding affinity. For example, in general, there are three CDRs in each heavy chain variable region (e.g., HCDR1, HCDR2, and HCDR3) and three CDRs in each light chain variable region (LCDR1, LCDR2, and LCDR3). The precise amino acid sequence boundaries of a given CDR can be determined using any of a number of well-known schemes, including those described by Kabat et al. (1991), "Sequences of Proteins of Immunological Interest," 5th Ed. Public Health Service, National Institutes of Health, Bethesda, MD ("Kabat" numbering scheme), Al-Lazikani et al., (1997) JMB 273,927-948 ("Chothia" numbering scheme), or a combination thereof. Under the Kabat numbering scheme, in some embodiments, the CDR amino acid residues in the heavy chain variable domain (VH) are numbered 31-35 (HCDR1), 50-65 (HCDR2), and 95-102 (HCDR3); and the CDR amino acid residues in the light chain variable domain (VL) are numbered 24-34 (LCDR1), 50-56 (LCDR2), and 89-97 (LCDR3).

Under the Chothia numbering scheme, in some embodiments, the CDR amino acids in the VH are numbered 26-32 (HCDR1), 52-56 (HCDR2), and 95-102 (HCDR3); and the CDR amino acid residues in the VL are numbered 26-32 (LCDR1), 50-52 (LCDR2), and 91-96 (LCDR3). In a combined Kabat and Chothia numbering scheme, in some embodiments, the CDRs correspond to the amino acid residues that are part of a Kabat CDR, a Chothia CDR, or both. For instance, in some embodiments, the CDRs correspond to amino acid residues 26-35 (HCDR1), 50-65 (HCDR2), and 95-102 (HCDR3) in a VH, e.g., a mammalian VH, e.g., a human VH; and amino acid residues 24-34 (LCDR1), 50-56 (LCDR2), and 89-97 (LCDR3) in a VL, e.g., a mammalian VL, e.g., a human VL.

The portion of the CAR of the invention comprising an antibody or antibody fragment thereof may exist in a variety of forms where the antigen binding domain is expressed as part of a contiguous polypeptide chain including, for example, a single domain antibody fragment (sdAb), a single chain antibody (scFv), a humanized antibody, or bispecific antibody (Harlow et al., 1999, In: Using Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory Press, NY; Harlow et al., 1989, In: Antibodies: A Laboratory Manual, Cold Spring Harbor, New York; Houston et al., 1988, Proc. Natl. Acad. Sci. USA 85:5879-5883; Bird et al., 1988, Science 242:423-426). In one aspect, the antigen binding domain of a CAR composition of the invention comprises an antibody fragment. In a further aspect, the CAR comprises an antibody fragment that comprises a scFv.

The term "antibody heavy chain," refers to the larger of the two types of polypeptide chains present in antibody molecules in their naturally occurring conformations, and which normally determines the class to which the antibody belongs.

The term "antibody light chain," refers to the smaller of the two types of polypeptide chains present in antibody molecules in their naturally occurring conformations. Kappa (κ) and lambda (λ) light chains refer to the two major antibody light chain isotypes.

The term "recombinant antibody" refers to an antibody which is generated using recombinant DNA technology, such as, for example, an antibody expressed by a bacteriophage or yeast expression system. The term should also be construed to mean an antibody which has been generated by the synthesis of a DNA molecule encoding the antibody and which DNA molecule expresses an antibody protein, or an amino acid sequence specifying the antibody, wherein the DNA or amino acid sequence has been obtained using recombinant DNA or amino acid sequence technology which is available and well known in the art.

The term "antigen," "Ag," or "antigen molecule" refers to a molecule that provokes an immune response. This immune response may involve either antibody production, or the activation of specific immunologically-competent cells, or both. In some embodiments, an antigen is any macromolecule, including all proteins or peptides. In other embodiments, antigens are derived from recombinant or genomic DNA. Any DNA, which comprises nucleotide sequences or a partial nucleotide sequence encoding a protein that elicits an immune response therefore encodes an "antigen" as that term is used herein. An antigen need not be encoded solely by a full length nucleotide sequence of a gene. In embodiments, antigens include, but are not limited to, the use of partial nucleotide sequences of more than one gene and that these nucleotide sequences are arranged in various combinations to encode polypeptides that elicit the desired immune response. In an embodiment, an antigen need not be encoded by a "gene" at all. In one embodiment, an antigen can be generated synthesized or can be derived from a biological sample, or might be macromolecule besides a polypeptide. Such a biological sample can include, but is not limited to a tissue sample, a tumor sample, a cell or a fluid with other biological components. In embodiments, antigens include, for example, carbohydrates (e.g., monosaccharides, disaccharides, oligosaccharides, and polysaccharides).

The term "cognate antigen molecule" refers to any antigen described herein. In one embodiment, it refers to an antigen recognized, e.g., targeted, by a CAR molecule, e.g., any CAR described herein. In another embodiment, it refers to a cancer associated antigen described herein. In one embodiment, the cognate antigen molecule is a recombinant molecule.

The term "anti-idiotypic (or idiotype) antibody molecule" or "anti-antigen idiotypic (idiotype) antibody molecule" refers to an antibody molecule that binds to an antibody, e.g., the antigen-binding site or the variable region of an antibody. In one embodiment, the anti-idiotypic antibody molecule binds to an epitope of an antibody that is in contact with the antigen, e.g., an antigen as described herein (e.g., a cognate antigen molecule as described herein). In one embodiment, the anti-idiotypic antibody molecule binds to the CAR antigen binding domain, e.g., the portion of the CAR comprising an antibody or antibody fragment (e.g., the antigen binding portion of the CAR).

The term "ligand of a CAR molecule" as used herein refers to a molecule that binds to a CAR molecule or a portion of a CAR molecule. In one embodiment, a ligand binds to the CAR antigen binding domain, e.g., the portion of the CAR comprising an antibody or antibody fragment. In one embodiment, the ligand is an antigen molecule, e.g., a cognate antigen

molecule, e.g., as described herein. In another embodiment, the ligand is an anti-idiotypic antibody molecule, e.g., an anti-antigen (*e.g.*, CD19) idiotypic antibody molecule as described herein.

The term "autologous" refers to any material derived from the same individual to whom it is later to be re-introduced into the individual.

The term "allogeneic" refers to any material derived from a different animal of the same species as the individual to whom the material is introduced. Two or more individuals are said to be allogeneic to one another when the genes at one or more loci are not identical. In some aspects, allogeneic material from individuals of the same species may be sufficiently unlike genetically to interact antigenically

The term "xenogeneic" refers to any material derived from an animal of a different species.

The term "cancer" refers to a disease characterized by the uncontrolled growth of aberrant cells. Cancer cells can spread locally or through the bloodstream and lymphatic system to other parts of the body. Examples of various cancers are described herein and include but are not limited to, breast cancer, prostate cancer, ovarian cancer, cervical cancer, skin cancer, pancreatic cancer, colorectal cancer, renal cancer, liver cancer, brain cancer, lymphoma, leukemia, lung cancer and the like. The terms "tumor" and "cancer" are used interchangeably herein, e.g., both terms encompass solid and liquid, e.g., diffuse or circulating, tumors. As used herein, the term "cancer" or "tumor" includes premalignant, as well as malignant cancers and tumors.

"Derived from" as that term is used herein, indicates a relationship between a first and a second molecule. It generally refers to structural similarity between the first molecule and a second molecule and does not connotate or include a process or source limitation on a first molecule that is derived from a second molecule. For example, in the case of an intracellular signaling domain that is derived from a CD3zeta molecule, the intracellular signaling domain retains sufficient CD3zeta structure such that is has the required function, namely, the ability to generate a signal under the appropriate conditions. It does not connotate or include a limitation to a particular process of producing the intracellular signaling domain, e.g., it does not mean that, to provide the intracellular signaling domain, one must start with a CD3zeta sequence and delete unwanted sequence, or impose mutations, to arrive at the intracellular signaling domain.

The phrase "disease associated with expression of a tumor antigen" as described herein includes, but is not limited to, a disease associated with expression of a tumor antigen as described herein or condition associated with cells which express a tumor antigen as described herein including, e.g., proliferative diseases such as a cancer or malignancy or a precancerous condition such as a myelodysplasia, a myelodysplastic syndrome or a preleukemia; or a noncancer related indication associated with cells which express a tumor antigen as described herein. In one embodiment, a cancer associated with expression of a tumor antigen as described herein is a hematological cancer. In one embodiment, a cancer associated with expression of a tumor antigen as described herein is a solid cancer. Further diseases associated with expression of a tumor antigen as described herein include, but not limited to, e.g., atypical and/or non-classical cancers, malignancies, precancerous conditions or proliferative diseases associated with expression of a tumor antigen as described herein. Non-cancer related indications associated with expression of a tumor antigen as described herein include, but are not limited to, e.g., autoimmune disease, (e.g., lupus), inflammatory disorders (allergy and asthma) and transplantation. In some embodiments, the tumor antigen-expressing cells express, or at any time expressed, mRNA encoding the tumor antigen. In an embodiment, the tumor antigen-expressing cells produce the tumor antigen protein (e.g., wild-type or mutant), and the tumor antigen protein may be present at normal levels or reduced levels. In an embodiment, the tumor antigen -expressing cells produced detectable levels of a tumor antigen protein at one point, and subsequently produced substantially no detectable tumor antigen protein.

The phrase "disease associated with expression of CD19" includes, but is not limited to, a disease associated with a cells that expresses CD19 (e.g., wild-type or mutant CD19) or condition associated with a cell which expresses, or at any time expressed, CD19 (e.g., wild-type or mutant CD19) including, e.g., proliferative diseases such as a cancer or malignancy or a precancerous condition such as a myelodysplasia, a myelodysplastic syndrome or a preleukemia; or a noncancer related indication associated with cells which express CD19. For the avoidance of doubt, a disease associated with expression of CD19 may include a condition associated with a cell which does not presently express CD19, e.g., because CD19 expression has been downregulated, e.g., due to treatment with a molecule targeting CD19, e.g., a CD19 CAR, but which at one time expressed CD19. In one aspect, a cancer associated with expression of CD19 is a hematological cancer. In one aspect, the hematolical cancer is a leukemia or a lymphoma. In one aspect, a cancer associated with expression of CD19 includes

cancers and malignancies including, but not limited to, e.g., one or more acute leukemias including but not limited to, e.g., acute myeloid leukemia (AML), B-cell acute Lymphoid Leukemia (BALL), T-cell acute Lymphoid Leukemia (TALL), acute lymphoid leukemia (ALL); one or more chronic leukemias including but not limited to, e.g., chronic myelogenous leukemia (CML), Chronic Lymphoid Leukemia (CLL). Additional cancers or hematologic conditions associated with expression of CD19 comprise, but are not limited to, e.g., B cell prolymphocytic leukemia, blastic plasmacytoid dendritic cell neoplasm, Burkitt's lymphoma, diffuse large B cell lymphoma, Follicular lymphoma, Hairy cell leukemia, small cell- or a large cell-follicular lymphoma, malignant lymphoproliferative conditions, MALT lymphoma, mantle cell lymphoma (MCL), Marginal zone lymphoma, multiple myeloma, myelodysplasia and myelodysplastic syndrome, non-Hodgkin lymphoma, Hodgkin lymphoma, plasmablastic lymphoma, plasmacytoid dendritic cell neoplasm, Waldenstrom macroglobulinemia, myeloproliferative neoplasm; a histiocytic disorder (e.g., a mast cell disorder or a blastic plasmacytoid dendritic cell neoplasm); a mast cell disorder, e.g., systemic mastocytosis or mast cell leukemia; B-cell prolymphocytic leukemia, plasma cell myeloma, and "preleukemia" which are a diverse collection of hematological conditions united by ineffective production (or dysplasia) of myeloid blood cells, and the like.

Further diseases associated with expression of CD19 expression include, but not limited to, e.g., atypical and/or non-classical cancers, malignancies, precancerous conditions or proliferative diseases associated with expression of CD19. Non-cancer related indications associated with expression of CD19 include, but are not limited to, e.g., autoimmune disease, (e.g., lupus), inflammatory disorders (allergy and asthma) and transplantation. In some embodiments, the CD19-expressing cells express, or at any time expressed, CD19 mRNA. In an embodiment, the CD19-expressing cells produce a CD19 protein (e.g., wild-type or mutant), and the CD19 protein may be present at normal levels or reduced levels. In an embodiment, the CD19-expressing cells produced detectable levels of a CD19 protein at one point, and subsequently produced substantially no detectable CD19 protein.

In some embodiments, the tumor antigen-expressing cells express, or at any time expressed, mRNA encoding the tumor antigen. In an embodiment, the tumor antigen-expressing cells produce the tumor antigen protein (e.g., wild-type or mutant), and the tumor antigen protein may be present at normal levels or reduced levels. In an embodiment, the tumor antigen -expressing cells produced detectable levels of a tumor antigen protein at one

point, and subsequently produced substantially no detectable tumor antigen protein. In other embodiments, the disease is a CD19-negative cancer, e.g., a CD19-negative relapsed cancer. In some embodiments, the tumor antigen (e.g., CD19)-expressing cell expresses, or at any time expressed, mRNA encoding the tumor antigen. In an embodiment, the tumor antigen (e.g., CD19)-expressing cell produces the tumor antigen protein (e.g., wild-type or mutant), and the tumor antigen protein may be present at normal levels or reduced levels. In an embodiment, the tumor antigen (e.g., CD19)-expressing cell produced detectable levels of a tumor antigen protein at one point, and subsequently produced substantially no detectable tumor antigen protein.

The term "relapse" as used herein refers to reappearance of a disease (e.g., cancer) after an initial period of responsiveness, e.g., after prior treatment with a therapy, e.g., cancer therapy (e.g., complete response or partial response). The initial period of responsiveness may involve the level of cancer cells falling below a certain threshold, e.g., below 20%, 15%, 10%, 5%, 4%, 3%, 2%, or 1%. The reappearance may involve the level of cancer cells rising above a certain threshold, e.g., above 20%, 15%, 10%, 5%, 4%, 3%, 2%, or 1%. For example, e.g., in the context of B-ALL, the reappearance may involve, e.g., a reappearance of blasts in the blood, bone marrow (> 5%), or any extramedullary site, after a complete response. A complete response, in this context, may involve < 5% BM blast. More generally, in an embodiment, a response (e.g., complete response or partial response) can involve the absence of detectable MRD (minimal residual disease). In an embodiment, the initial period of responsiveness lasts at least 1, 2, 3, 4, 5, or 6 days; at least 1, 2, 3, or 4 weeks; at least 1, 2, 3, 4, 6, 8, 10, or 12 months; or at least 1, 2, 3, 4, or 5 years.

"Refractory" as used herein refers to a disease, e.g., cancer, that does not respond to a treatment. In embodiments, a refractory cancer can be resistant to a treatment before or at the beginning of the treatment. In other embodiments, the refractory cancer can become resistant during a treatment. A refractory cancer is also called a resistant cancer.

The term "conservative sequence modifications" refers to amino acid modifications that do not significantly affect or alter the binding characteristics of the antibody or antibody fragment containing the amino acid sequence. Such conservative modifications include amino acid substitutions, additions and deletions. Modifications can be introduced into an antibody or antibody fragment of the invention by standard techniques known in the art, such as site-directed mutagenesis and PCR-mediated mutagenesis. Conservative amino acid substitutions

are ones in which the amino acid residue is replaced with an amino acid residue having a similar side chain. Families of amino acid residues having similar side chains have been defined in the art. These families include amino acids with basic side chains (e.g., lysine, arginine, histidine), acidic side chains (e.g., aspartic acid, glutamic acid), uncharged polar side chains (e.g., glycine, asparagine, glutamine, serine, threonine, tyrosine, cysteine, tryptophan), nonpolar side chains (e.g., alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine), beta-branched side chains (e.g., threonine, valine, isoleucine) and aromatic side chains (e.g., tyrosine, phenylalanine, tryptophan, histidine). Thus, one or more amino acid residues within a CAR described herein can be replaced with other amino acid residues from the same side chain family and the altered CAR can be tested using the functional assays described herein.

The term "stimulation," refers to a primary response induced by binding of a stimulatory molecule (e.g., a TCR/CD3 complex or CAR) with its cognate ligand (e.g., antigen molecule), thereby mediating a signal transduction event, such as, but not limited to, signal transduction via the TCR/CD3 complex or signal transduction via the appropriate NK receptor or signaling domains of the CAR. Stimulation can mediate altered expression of certain molecules.

The term "stimulatory molecule," refers to a molecule expressed by an immune cell (e.g., T cell, NK cell, B cell) that provides the cytoplasmic signaling sequence(s) that regulate activation of the immune cell in a stimulatory way for at least some aspect of the immune cell signaling pathway. In one aspect, the signal is a primary signal that is initiated by, for instance, binding of a TCR/CD3 complex with an MHC molecule loaded with peptide, and which leads to mediation of a T cell response, including, but not limited to, proliferation, activation, differentiation, and the like. A primary cytoplasmic signaling sequence (also referred to as a "primary signaling domain") that acts in a stimulatory manner may contain a signaling motif which is known as immunoreceptor tyrosine-based activation motif or ITAM. Examples of an ITAM containing cytoplasmic signaling sequence that is of particular use in the invention includes, but is not limited to, those derived from CD3 zeta, common FcR gamma (FCER1G), Fc gamma RIIa,, FcR beta (Fc Epsilon R1b), CD3 gamma, CD3 delta , CD3 epsilon, , CD79a, CD79b, DAP10, and DAP12. In a specific CAR of the invention, the intracellular signaling domain in any one or more CARS of the invention comprises an intracellular signaling sequence, e.g., a primary signaling sequence of CD3-zeta. In a specific

CAR of the invention, the primary signaling sequence of CD3-zeta is the sequence provided as SEQ ID NO:9, or the equivalent residues from a non-human species, e.g., mouse, rodent, monkey, ape and the like. In a specific CAR of the invention, the primary signaling sequence of CD3-zeta is the sequence as provided in SEQ ID NO:10, or the equivalent residues from a non-human species, e.g., mouse, rodent, monkey, ape and the like.

The term "antigen presenting cell" or "APC" refers to an immune system cell such as an accessory cell (e.g., a B-cell, a dendritic cell, and the like) that displays a foreign antigen complexed with major histocompatibility complexes (MHC's) on its surface. T-cells may recognize these complexes using their T-cell receptors (TCRs). APCs process antigens and present them to T-cells.

An "intracellular signaling domain," as the term is used herein, refers to an intracellular portion of a molecule. The intracellular signaling domain can generate a signal that promotes an immune effector function of the CAR containing cell, e.g., a CART cell. Examples of immune effector function, e.g., in a CART cell, include cytolytic activity and helper activity, including the secretion of cytokines. In embodiments, the intracellular signaling domain is the portion of a protein which transduces the effector function signal and directs the cell to perform a specialized function. While the entire intracellular signaling domain can be employed, in many cases it is not necessary to use the entire chain. To the extent that a truncated portion of the intracellular signaling domain is used, such truncated portion may be used in place of the intact chain as long as it transduces the effector function signal. The term intracellular signaling domain is thus meant to include any truncated portion of the intracellular signaling domain sufficient to transduce the effector function signal.

In an embodiment, the intracellular signaling domain can comprise a primary intracellular signaling domain. Exemplary primary intracellular signaling domains include those derived from the molecules responsible for primary stimulation, or antigen dependent simulation. In an embodiment, the intracellular signaling domain can comprise a costimulatory intracellular domain. Exemplary costimulatory intracellular signaling domains include those derived from molecules responsible for costimulatory signals, or antigen independent stimulation. For example, in the case of a CART, a primary intracellular signaling domain can comprise a cytoplasmic sequence of a T cell receptor, and a costimulatory intracellular signaling domain can comprise cytoplasmic sequence from co-receptor or costimulatory molecule.

A primary intracellular signaling domain can comprise a signaling motif which is known as an immunoreceptor tyrosine-based activation motif or ITAM. Examples of ITAM containing primary cytoplasmic signaling sequences include, but are not limited to, those derived from CD3 zeta, FcR gamma, FcR beta, CD3 gamma, CD3 delta, CD3 epsilon, CD5, CD22, CD79a, CD79b, CD278 ("ICOS"), FcεRI, CD66d, CD32, DAP10 and DAP12.

The term "zeta" or alternatively "zeta chain", "CD3-zeta" or "TCR-zeta" is defined as the protein provided as GenBank Acc. No. BAG36664.1, or the equivalent residues from a non-human species, e.g., mouse, rodent, monkey, ape and the like, and a "zeta stimulatory domain" or alternatively a "CD3-zeta stimulatory domain" or a "TCR-zeta stimulatory domain" is defined as the amino acid residues from the cytoplasmic domain of the zeta chain that are sufficient to functionally transmit an initial signal necessary for T cell activation. In one aspect the cytoplasmic domain of zeta comprises residues 52 through 164 of GenBank Acc. No. BAG36664.1 or the equivalent residues from a non-human species, e.g., mouse, rodent, monkey, ape and the like, that are functional orthologs thereof. In one aspect, the "zeta stimulatory domain" or a "CD3-zeta stimulatory domain" is the sequence provided as SEQ ID NO:9 (mutant CD3 zeta). In one aspect, the "zeta stimulatory domain" or a "CD3-zeta stimulatory domain" is the sequence provided as SEQ ID NO:10 (wild-type human CD3 zeta).

The term "costimulatory molecule" refers to the cognate binding partner on a T cell that specifically binds with a costimulatory ligand, thereby mediating a costimulatory response by the T cell, such as, but not limited to, proliferation. Costimulatory molecules are cell surface molecules other than antigen receptors or their ligands that are required for an efficient immune response. Costimulatory molecules include, but are not limited to MHC class I molecule, TNF receptor proteins, Immunoglobulin-like proteins, cytokine receptors, integrins, signalling lymphocytic activation molecules (SLAM proteins), activating NK cell receptors, BTLA, a Toll ligand receptor, OX40, CD2, CD7, CD27, CD28, CD30, CD40, CDS, ICAM-1, LFA-1 (CD11a/CD18), 4-1BB (CD137), B7-H3, CDS, ICAM-1, ICOS (CD278), GITR, BAFFR, LIGHT, HVEM (LIGHTR), KIRDS2, SLAMF7, NKp80 (KLRF1), NKp44, NKp30, NKp46, CD19, CD4, CD8alpha, CD8beta, IL2R beta, IL2R gamma, IL7R alpha, ITGA4, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CD11d, ITGAE, CD103, ITGAL, CD11a, LFA-1, ITGAM, CD11b, ITGAX, CD11c, ITGB1, CD29, ITGB2, CD18, LFA-1, ITGB7, NKG2D, NKG2C, TNFR2, TRANCE/RANKL, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRTAM, Ly9 (CD229), CD160 (BY55),

PSGL1, CD100 (SEMA4D), CD69, SLAMF6 (NTB-A, Ly108), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, LAT, GADS, SLP-76, PAG/Cbp, CD19a, and a ligand that specifically binds with CD83.A costimulatory intracellular signaling domain refers to an intracellular portion of a costimulatory molecule. The intracellular signaling domain can comprise the entire intracellular portion, or the entire native intracellular signaling domain, of the molecule from which it is derived, or a functional fragment thereof.

The intracellular signaling domain can comprise the entire intracellular portion, or the entire native intracellular signaling domain, of the molecule from which it is derived, or a functional fragment thereof.

The term "4-1BB" refers to a member of the TNFR superfamily with an amino acid sequence provided as GenBank Acc. No. AAA62478.2, or the equivalent residues from a non-human species, e.g., mouse, rodent, monkey, ape and the like; and a "4-1BB costimulatory domain" is defined as amino acid residues 214-255 of GenBank Acc. No. AAA62478.2, or the equivalent residues from a non-human species, e.g., mouse, rodent, monkey, ape and the like. In one aspect, the "4-1BB costimulatory domain" is the sequence provided as SEQ ID NO:7 or the equivalent residues from a non-human species, e.g., mouse, rodent, monkey, ape and the like.

"Immune effector cell," as that term is used herein, refers to a cell that is involved in an immune response, e.g., in the promotion of an immune effector response. Examples of immune effector cells include T cells, e.g., alpha/beta T cells and gamma/delta T cells, B cells, natural killer (NK) cells, natural killer T (NKT) cells, mast cells, and myeloic-derived phagocytes.

"Immune effector function or immune effector response," as that term is used herein, refers to function or response, e.g., of an immune effector cell, that enhances or promotes an immune attack of a target cell. E.g., an immune effector function or response refers a property of a T or NK cell that promotes killing or the inhibition of growth or proliferation, of a target cell. In the case of a T cell, primary stimulation and co-stimulation are examples of immune effector function or response.

The term "effector function" refers to a specialized function of a cell. Effector function of a T cell, for example, may be cytolytic activity or helper activity including the secretion of cytokines.The term "encoding" refers to the inherent property of specific sequences of nucleotides in a polynucleotide, such as a gene, a cDNA, or an mRNA, to serve as templates for synthesis of other polymers and macromolecules in biological processes having either a

defined sequence of nucleotides (e.g., rRNA, tRNA and mRNA) or a defined sequence of amino acids and the biological properties resulting therefrom. Thus, a gene, cDNA, or RNA, encodes a protein if transcription and translation of mRNA corresponding to that gene produces the protein in a cell or other biological system. Both the coding strand, the nucleotide sequence of which is identical to the mRNA sequence and is usually provided in sequence listings, and the non-coding strand, used as the template for transcription of a gene or cDNA, can be referred to as encoding the protein or other product of that gene or cDNA.

Unless otherwise specified, a "nucleotide sequence encoding an amino acid sequence" includes all nucleotide sequences that are degenerate versions of each other and that encode the same amino acid sequence. The phrase nucleotide sequence that encodes a protein or a RNA may also include introns to the extent that the nucleotide sequence encoding the protein may in some version contain an intron(s).

The term "endogenous" refers to any material from or produced inside an organism, cell, tissue or system.

The term "exogenous" refers to any material introduced from or produced outside an organism, cell, tissue or system.

The term "expression" refers to the transcription and/or translation of a particular nucleotide sequence driven by a promoter.

The term "transfer vector" refers to a composition of matter which comprises an isolated nucleic acid and which can be used to deliver the isolated nucleic acid to the interior of a cell. Numerous vectors are known in the art including, but not limited to, linear polynucleotides, polynucleotides associated with ionic or amphiphilic compounds, plasmids, and viruses. Thus, the term "transfer vector" includes an autonomously replicating plasmid or a virus. The term should also be construed to further include non-plasmid and non-viral compounds which facilitate transfer of nucleic acid into cells, such as, for example, a polylysine compound, liposome, and the like. Examples of viral transfer vectors include, but are not limited to, adenoviral vectors, adeno-associated virus vectors, retroviral vectors, lentiviral vectors, and the like.

The term "expression vector" refers to a vector comprising a recombinant polynucleotide comprising expression control sequences operatively linked to a nucleotide sequence to be expressed. An expression vector comprises sufficient cis-acting elements for expression; other elements for expression can be supplied by the host cell or in an in vitro

expression system. Expression vectors include all those known in the art, including cosmids, plasmids (e.g., naked or contained in liposomes) and viruses (e.g., lentiviruses, retroviruses, adenoviruses, and adeno-associated viruses) that incorporate the recombinant polynucleotide.

The term "lentivirus" refers to a genus of the Retroviridae family. Lentiviruses are unique among the retroviruses in being able to infect non-dividing cells; they can deliver a significant amount of genetic information into the DNA of the host cell, so they are one of the most efficient methods of a gene delivery vector. HIV, SIV, and FIV are all examples of lentiviruses.

The term "lentiviral vector" refers to a vector derived from at least a portion of a lentivirus genome, including especially a self-inactivating lentiviral vector as provided in Milone et al., Mol. Ther. 17(8): 1453–1464 (2009). Other examples of lentivirus vectors that may be used in the clinic, include but are not limited to, e.g., the LENTIVECTOR® gene delivery technology from Oxford BioMedica, the LENTIMAX™ vector system from Lentigen and the like. Nonclinical types of lentiviral vectors are also available and would be known to one skilled in the art.

The term "homologous" or "identity" refers to the subunit sequence identity between two polymeric molecules, e.g., between two nucleic acid molecules, such as, two DNA molecules or two RNA molecules, or between two polypeptide molecules. When a subunit position in both of the two molecules is occupied by the same monomeric subunit; e.g., if a position in each of two DNA molecules is occupied by adenine, then they are homologous or identical at that position. The homology between two sequences is a direct function of the number of matching or homologous positions; e.g., if half (e.g., five positions in a polymer ten subunits in length) of the positions in two sequences are homologous, the two sequences are 50% homologous; if 90% of the positions (e.g., 9 of 10), are matched or homologous, the two sequences are 90% homologous.

"Humanized" forms of non-human (e.g., murine) antibodies are chimeric immunoglobulins, immunoglobulin chains or fragments thereof (such as Fv, Fab, Fab', F(ab')2 or other antigen-binding subsequences of antibodies) which contain minimal sequence derived from non-human immunoglobulin. For the most part, humanized antibodies and antibody fragments thereof are human immunoglobulins (recipient antibody or antibody fragment) in which residues from a complementary-determining region (CDR) of the recipient are replaced by residues from a CDR of a non-human species (donor antibody) such as mouse, rat or rabbit

having the desired specificity, affinity, and capacity. In some instances, Fv framework region (FR) residues of the human immunoglobulin are replaced by corresponding non-human residues. Furthermore, a humanized antibody/antibody fragment can comprise residues which are found neither in the recipient antibody nor in the imported CDR or framework sequences. These modifications can further refine and optimize antibody or antibody fragment performance. In general, the humanized antibody or antibody fragment thereof will comprise substantially all of at least one, and typically two, variable domains, in which all or substantially all of the CDR regions correspond to those of a non-human immunoglobulin and all or a significant portion of the FR regions are those of a human immunoglobulin sequence. The humanized antibody or antibody fragment can also comprise at least a portion of an immunoglobulin constant region (Fc), typically that of a human immunoglobulin. For further details, see Jones et al., Nature, 321: 522-525, 1986; Reichmann et al., Nature, 332: 323-329, 1988; Presta, Curr. Op. Struct. Biol., 2: 593-596, 1992.

"Fully human" refers to an immunoglobulin, such as an antibody or antibody fragment, where the whole molecule is of human origin or consists of an amino acid sequence identical to a human form of the antibody or immunoglobulin.

The term "isolated" means altered or removed from the natural state. For example, a nucleic acid or a peptide naturally present in a living animal is not "isolated," but the same nucleic acid or peptide partially or completely separated from the coexisting materials of its natural state is "isolated." An isolated nucleic acid or protein can exist in substantially purified form, or can exist in a non-native environment such as, for example, a host cell.

In the context of the present invention, the following abbreviations for the commonly occurring nucleic acid bases are used. "A" refers to adenosine, "C" refers to cytosine, "G" refers to guanosine, "T" refers to thymidine, and "U" refers to uridine.

The term "operably linked" or "transcriptional control" refers to functional linkage between a regulatory sequence and a heterologous nucleic acid sequence resulting in expression of the latter. For example, a first nucleic acid sequence is operably linked with a second nucleic acid sequence when the first nucleic acid sequence is placed in a functional relationship with the second nucleic acid sequence. For instance, a promoter is operably linked to a coding sequence if the promoter affects the transcription or expression of the coding sequence. Operably linked DNA sequences can be contiguous with each other and, e.g., where necessary to join two protein coding regions, are in the same reading frame.

The term "parenteral" administration of an immunogenic composition includes, e.g., subcutaneous (s.c.), intravenous (i.v.), intramuscular (i.m.), or intrasternal injection, intratumoral, or infusion techniques.

The term "nucleic acid" or "polynucleotide" refers to deoxyribonucleic acids (DNA) or ribonucleic acid (RNA), or a combination of a DNA or RNA thereof, and polymers thereof in either single- or double-stranded form. The term "nucleic acid" includes a gene, cDNA or an mRNA. In one embodiment, the nucleic acid molecule is synthetic (e.g., chemically synthesized) or recombinant. Unless specifically limited, the term encompasses nucleic acids containing analogues or derivatives of natural nucleotides that have similar binding properties as the reference nucleic acid and are metabolized in a manner similar to naturally occurring nucleotides. Unless otherwise indicated, a particular nucleic acid sequence also implicitly encompasses conservatively modified variants thereof (e.g., degenerate codon substitutions), alleles, orthologs, SNPs, and complementary sequences as well as the sequence explicitly indicated. Specifically, degenerate codon substitutions may be achieved by generating sequences in which the third position of one or more selected (or all) codons is substituted with mixed-base and/or deoxyinosine residues (Batzer et al., Nucleic Acid Res. 19:5081 (1991); Ohtsuka et al., J. Biol. Chem. 260:2605-2608 (1985); and Rossolini et al., Mol. Cell. Probes 8:91-98 (1994)).

The terms "peptide," "polypeptide," and "protein" are used interchangeably, and refer to a compound comprised of amino acid residues covalently linked by peptide bonds. A protein or peptide must contain at least two amino acids, and no limitation is placed on the maximum number of amino acids that can comprise a protein's or peptide's sequence. Polypeptides include any peptide or protein comprising two or more amino acids joined to each other by peptide bonds. As used herein, the term refers to both short chains, which also commonly are referred to in the art as peptides, oligopeptides and oligomers, for example, and to longer chains, which generally are referred to in the art as proteins, of which there are many types. "Polypeptides" include, for example, biologically active fragments, substantially homologous polypeptides, oligopeptides, homodimers, heterodimers, variants of polypeptides, modified polypeptides, derivatives, analogs, fusion proteins, among others. A polypeptide includes a natural peptide, a recombinant peptide, or a combination thereof.

The term "promoter" refers to a DNA sequence recognized by the synthetic machinery of the cell, or introduced synthetic machinery, required to initiate the specific transcription of a polynucleotide sequence.

The term "promoter/regulatory sequence" refers to a nucleic acid sequence which is required for expression of a gene product operably linked to the promoter/regulatory sequence. In some instances, this sequence may be the core promoter sequence and in other instances, this sequence may also include an enhancer sequence and other regulatory elements which are required for expression of the gene product. The promoter/regulatory sequence may, for example, be one which expresses the gene product in a tissue specific manner.

The term "constitutive" promoter refers to a nucleotide sequence which, when operably linked with a polynucleotide which encodes or specifies a gene product, causes the gene product to be produced in a cell under most or all physiological conditions of the cell.

The term "inducible" promoter refers to a nucleotide sequence which, when operably linked with a polynucleotide which encodes or specifies a gene product, causes the gene product to be produced in a cell substantially only when an inducer which corresponds to the promoter is present in the cell.

The term "tissue-specific" promoter refers to a nucleotide sequence which, when operably linked with a polynucleotide encodes or specified by a gene, causes the gene product to be produced in a cell substantially only if the cell is a cell of the tissue type corresponding to the promoter.

The terms "cancer associated antigen" or "tumor antigen" interchangeably refers to a molecule (typically protein, carbohydrate or lipid) that is preferentially expressed on the surface of a cancer cell, either entirely or as a fragment (e.g., MHC/peptide), in comparison to a normal cell, and which is useful for the preferential targeting of a pharmacological agent to the cancer cell. In some embodiments, a tumor antigen is a marker expressed by both normal cells and cancer cells, e.g., a lineage marker, e.g., CD19 on B cells. In some embodiments, a cancer-associated antigen is a cell surface molecule that is overexpressed in a cancer cell in comparison to a normal cell, for instance, 1-fold over expression, 2-fold overexpression, 3-fold overexpression or more in comparison to a normal cell. In some embodiments, a cancer-associated antigen is a cell surface molecule that is inappropriately synthesized in the cancer cell, for instance, a molecule that contains deletions, additions or mutations in comparison to the molecule expressed on a normal cell. In some embodiments, a cancer-associated antigen

will be expressed exclusively on the cell surface of a cancer cell, entirely or as a fragment (e.g., MHC/peptide), and not synthesized or expressed on the surface of a normal cell. In some embodiments, the CARs of the present invention includes CARs comprising an antigen binding domain (e.g., antibody or antibody fragment) that binds to a MHC presented peptide. Normally, peptides derived from endogenous proteins fill the pockets of Major histocompatibility complex (MHC) class I molecules, and are recognized by T cell receptors (TCRs) on CD8 + T lymphocytes. The MHC class I complexes are constitutively expressed by all nucleated cells. In cancer, virus-specific and/or tumor-specific peptide/MHC complexes represent a unique class of cell surface targets for immunotherapy. TCR-like antibodies targeting peptides derived from viral or tumor antigens in the context of human leukocyte antigen (HLA)-A1 or HLA-A2 have been described (see, e.g., Sastry et al., J Virol. 2011 85(5):1935-1942; Sergeeva et al., Blood, 2011 117(16):4262-4272; Verma et al., J Immunol 2010 184(4):2156-2165; Willemsen et al., Gene Ther 2001 8(21) :1601-1608 ; Dao et al., Sci Transl Med 2013 5(176) :176ra33 ; Tassev et al., Cancer Gene Ther 2012 19(2):84-100). For example, TCR-like antibody can be identified from screening a library, such as a human scFv phage displayed library.

The term "flexible polypeptide linker" or "linker" as used in the context of a scFv refers to a peptide linker that consists of amino acids such as glycine and/or serine residues used alone or in combination, to link variable heavy and variable light chain regions together. In one embodiment, the flexible polypeptide linker is a Gly/Ser linker and comprises the amino acid sequence $(Gly\text{-}Gly\text{-}Gly\text{-}Ser)_n$ (SEQ ID NO: 22), where n is a positive integer equal to or greater than 1. For example, n=1, n=2, n=3. n=4, n=5,n=6, n=7, n=8, n=9 and n=10. In one embodiment, the flexible polypeptide linkers include, but are not limited to, $(Gly_4\ Ser)_4$ (SEQ ID NO:27) or $(Gly_4\ Ser)_3$ (SEQ ID NO:28). In another embodiment, the linkers include multiple repeats of (Gly_2Ser), (GlySer) or (Gly_3Ser) (SEQ ID NO:29). Also included within the scope of the invention are linkers described in WO2012/138475, incorporated herein by reference).

As used herein, a 5' cap (also termed an RNA cap, an RNA 7-methylguanosine cap or an RNA m^7G cap) is a modified guanine nucleotide that has been added to the "front" or 5' end of a eukaryotic messenger RNA shortly after the start of transcription. The 5' cap consists of a terminal group which is linked to the first transcribed nucleotide. Its presence is critical for recognition by the ribosome and protection from RNases. Cap addition is coupled to transcription, and occurs co-transcriptionally, such that each influences the other. Shortly after

the start of transcription, the 5' end of the mRNA being synthesized is bound by a cap-synthesizing complex associated with RNA polymerase. This enzymatic complex catalyzes the chemical reactions that are required for mRNA capping. Synthesis proceeds as a multi-step biochemical reaction. The capping moiety can be modified to modulate functionality of mRNA such as its stability or efficiency of translation.

As used herein, "in vitro transcribed RNA" refers to RNA, e.g., mRNA, that has been synthesized in vitro. Generally, the in vitro transcribed RNA is generated from an in vitro transcription vector. The in vitro transcription vector comprises a template that is used to generate the in vitro transcribed RNA.

As used herein, a "poly(A)" is a series of adenosines attached by polyadenylation to the mRNA. In one embodiment of a construct for transient expression, the polyA is between 50 and 5000 (SEQ ID NO: 30), e.g., greater than 64, e.g., greater than 100, e.g., greater than 300 or 400 poly(A) sequences can be modified chemically or enzymatically to modulate mRNA functionality such as localization, stability or efficiency of translation.

As used herein, "polyadenylation" refers to the covalent linkage of a polyadenylyl moiety, or its modified variant, to a messenger RNA molecule. In eukaryotic organisms, most messenger RNA (mRNA) molecules are polyadenylated at the 3' end. The 3' poly(A) tail is a long sequence of adenine nucleotides (often several hundred) added to the pre-mRNA through the action of an enzyme, polyadenylate polymerase. In higher eukaryotes, the poly(A) tail is added onto transcripts that contain a specific sequence, the polyadenylation signal. The poly(A) tail and the protein bound to it aid in protecting mRNA from degradation by exonucleases. Polyadenylation is also important for transcription termination, export of the mRNA from the nucleus, and translation. Polyadenylation occurs in the nucleus immediately after transcription of DNA into RNA, but additionally can also occur later in the cytoplasm. After transcription has been terminated, the mRNA chain is cleaved through the action of an endonuclease complex associated with RNA polymerase. The cleavage site is usually characterized by the presence of the base sequence AAUAAA near the cleavage site. After the mRNA has been cleaved, adenosine residues are added to the free 3' end at the cleavage site.

As used herein, "transient" refers to expression of a non-integrated transgene for a period of hours, days or weeks, wherein the period of time of expression is less than the period of time for expression of the gene if integrated into the genome or contained within a stable plasmid replicon in the cell. In embodiments, a CAR molecule is transiently expressed in a

cell, e.g., host cell, for a finite period of time or number of cell replications, e.g., less than 50 days (e.g., less than 40, 30, 25, 20, 15, 10, 5, 4, 3, 2 or fewer days). In one embodiment, transient expression is effected using an in vitro transcribed RNA.

As used herein, "stable" refers to expression of a transgene that is for a longer period than transient expression. In embodiments, the transgene is integrated into the genome of a cell, e.g., a host cell, or contained within a stable plasmid replicon in the cell. In one embodiment, a transgene is integrated into the cell genome using a gene delivery vector, *e.g.*, a retroviral vector such as a lentivirus vector.

Apheresis is the process in which whole blood is removed from an individual, separated into select components, and the remainder returned to circulation. Generally, there are two methods for the separation of blood components, centrifugal and non-centrifugal. Leukapheresis results in the active selection and removal of the patient's white blood cells.

As used herein, the terms "treat", "treatment" and "treating" refer to the reduction or amelioration of the progression, severity and/or duration of a proliferative disorder, or the amelioration of one or more symptoms (e.g., one or more discernible symptoms) of a proliferative disorder resulting from the administration of one or more therapies (e.g., one or more therapeutic agents such as a CAR of the invention). In specific embodiments, the terms "treat", "treatment" and "treating" refer to the amelioration of at least one measurable physical parameter of a proliferative disorder, such as growth of a tumor, not necessarily discernible by the patient. In other embodiments the terms "treat", "treatment" and "treating" -refer to the inhibition of the progression of a proliferative disorder, either physically by, e.g., stabilization of a discernible symptom, physiologically by, e.g., stabilization of a physical parameter, or both. In other embodiments the terms "treat", "treatment" and "treating" refer to the reduction or stabilization of tumor size or cancerous cell count. Treatment need not be 100%, and in some embodiments a reduction or delay in at least one symptom of the disease or disorder by at least 50%, 60%, 70%, 80%, 90%, 95%, or 99% is sufficient to be considered within these terms.

The term "signal transduction pathway" refers to the biochemical relationship between a variety of signal transduction molecules that play a role in the transmission of a signal from one portion of a cell to another portion of a cell. The phrase "cell surface receptor" includes molecules and complexes of molecules capable of receiving a signal and transmitting signal across the membrane of a cell.

The term "subject" is intended to include living organisms in which an immune response can be elicited (e.g., mammals, e.g., humans). Examples of subjects include humans, monkeys, chimpanzees, dogs, cats, mice, rats, and transgenic species thereof. T cells can be obtained from a number of sources, including peripheral blood mononuclear cells, bone marrow, lymph node tissue, cord blood, thymus tissue, tissue from a site of infection, ascites, pleural effusion, spleen tissue, and tumors.

The term, a "substantially purified" cell refers to a cell that is essentially free of other cell types. A substantially purified cell also refers to a cell which has been separated from other cell types with which it is normally associated in its naturally occurring state. In some instances, a population of substantially purified cells refers to a homogenous population of cells. In other instances, this term refers simply to cell that have been separated from the cells with which they are naturally associated in their natural state. In some aspects, the cells are cultured in vitro. In other aspects, the cells are not cultured in vitro.

In the context of the present invention, "tumor antigen" or "hyperproliferative disorder antigen" or "antigen associated with a hyperproliferative disorder" refers to antigens that are common to specific hyperproliferative disorders. In certain embodiments, the tumor antigen is derived from a cancer including but not limited to primary or metastatic melanoma, thymoma, lymphoma, sarcoma, lung cancer, liver cancer, non-Hodgkin lymphoma, Hodgkin lymphoma, leukemias, uterine cancer, cervical cancer, bladder cancer, kidney cancer and adenocarcinomas such as breast cancer, prostate cancer, ovarian cancer, pancreatic cancer, and the like.

The term "transfected" or "transformed" or "transduced" refers to a process by which exogenous nucleic acid is transferred or introduced into the host cell. A "transfected" or "transformed" or "transduced" cell is one which has been transfected, transformed or transduced with exogenous nucleic acid. The cell includes the primary subject cell and its progeny.

The term "specifically binds," refers to an antibody, or a ligand, which recognizes and binds with a cognate binding partner protein present in a sample, but which antibody or ligand does not substantially recognize or bind other molecules in the sample.

Ranges: throughout this disclosure, various aspects of the invention can be presented in a range format. It should be understood that the description in range format is merely for convenience and brevity and should not be construed as an inflexible limitation on the scope of the invention. Accordingly, the description of a range should be considered to have specifically

disclosed all the possible subranges as well as individual numerical values within that range. For example, description of a range such as from 1 to 6 should be considered to have specifically disclosed subranges such as from 1 to 3, from 1 to 4, from 1 to 5, from 2 to 4, from 2 to 6, from 3 to 6 etc., as well as individual numbers within that range, for example, 1, 2, 2.7, 3, 4, 5, 5.3, and 6. As another example, a range such as 95-99% identity, includes something with 95%, 96%, 97%, 98% or 99% identity, and includes subranges such as 96-99%, 96-98%, 96-97%, 97-99%, 97-98% and 98-99% identity. This applies regardless of the breadth of the range.

Manufacturing and Methods of Making Immune Effector Cells

Provided herein are methods of manufacturing immune effector cells that can be engineered with a CAR, e.g., a CAR described herein, and reaction mixtures and compositions comprising such cells.

In one aspect, the disclosure features an immune effector cell (e.g., T cell, NK cell) engineered to express a CAR, wherein the engineered immune effector cell exhibits an antitumor property. An exemplaryantigen is a cancer associated antigen (i.e., tumor antigen) described herein. In one aspect, a cell is transformed with the CAR and the CAR is expressed on the cell surface. In some embodiments, the cell (e.g., T cell, NK cell) is transduced with a viral vector encoding a CAR. In some embodiments, the viral vector is a retroviral vector. In some embodiments, the viral vector is a lentiviral vector. In some such embodiments, the cell may stably express the CAR. In another embodiment, the cell (e.g., T cell, NK cell) is transfected with a nucleic acid, e.g., mRNA, cDNA, DNA, encoding a CAR. In some such embodiments, the cell may transiently express the CAR.

Furthermore, the present invention provides CART compositions and their use in medicaments or methods for treating, among other diseases, cancer or any malignancy or autoimmune diseases involving cells or tissues which express a tumor antigen as described herein.

In one aspect, the CAR of the invention can be used to eradicate a normal cell that express a tumor antigen as described herein, thereby applicable for use as a cellular conditioning therapy prior to cell transplantation.

Sources of Immune Effector Cells

In embodiments, prior to expansion and genetic modification or other modification, a source of cells, e.g., immune effector cells, e.g., a population of immune effector cells cells, can be acquired, e.g., obtained, from a subject. In one embodiment, the immune effector cells comprise T cells. In one embodiment, the T cells comprise CD4 T cells. In another embodiment, the T cells comprise CD8 T cells. In another embodiment, the T cells comprise regulatory T cells. In a further embodiment, the T cells comprise naïve T-cells. In one embodiment, the immune effector cells comprise hemapoetic stem cells (e.g., cord blood cells). In another embodiment, the immune effector cells comprise B cells. In a further embodiment, the immune effector cells comprise NK cells. In another embodiment, the immune effector cells comprise NKT cells. In another embodiment, the immune effector cells comprise Th-17 cells. In one embodiment, the immune effector cells do not have T cell receptors. In another embodiment, the immune effector cells have non-functional or substantially impaired T cell receptors.

In some embodiments, a cell population, e.g., a harvested cell population, comprises a T cell or population of T cells, e.g., at various stages of differentiation. Stages of T cell differentiation include naïve T cells, stem central memory T cells, central memory T cells, effector memory T cells, and terminal effector T cells, from least to most differentiated. After antigen exposure, naïve T cells proliferate and differentiate into memory T cells, e.g., stem central memory T cells and central memory T cells, which then differentiate into effector memory T cells. Upon receiving appropriate T cell receptor, costimulatory, and inflammatory signals, memory T cells further differentiate into terminal effector T cells. See, e.g., Restifo. Blood. 124.4(2014):476-77; and Joshi et al. J. Immunol. 180.3(2008):1309-15.

Naïve T cells (T_N) are characterized by the following expression pattern of cell surface markers: CCR7+, CD62L+, CD45RO–, CD95–. Stem central memory T cells (T_{SCM}) are characterized by the following expression pattern of cell surface markers: CCR7+, CD62L+, CD45RO–, CD95+. Central memory T cells (T_{CM}) are characterized by the following expression pattern of cell surface markers: CCR7+, CD62L+, CD45RO+, CD95+. Effector memory T cells (T_{EM}) are characterized by the following expression pattern of cell surface markers: CCR7–, CD62L–, CD45RO+, CD95+. Terminal effector T cells (T_{Eff}) are characterized by the following expression pattern of cell surface markers: CCR7–, CD62L–,

CD45RO–, CD95+. See, e.g., Gattinoni et al. Nat. Med. 17(2011):1290-7; and Flynn et al. Clin. Translat. Immunol. 3(2014):e20.

In embodiments, immune effector cells (e.g., a population of immune effector cells), e.g., T cells, are derived from (e.g., differentiated from) a stem cell, e.g., an embryonic stem cell or a pluripotent stem cell, e.g., an induced pluripotent stem cell (iPSC). In embodiments, the cells are autologous or allogeneic. In embodiments wherein the cells are allogeneic, the cells, e.g., derived from stem cells (e.g., iPSCs), are modified to reduce their alloreactivity. For example, the cells can be modified to reduce alloreactivity, e.g., by modifying (e.g., disrupting) their T cell receptor. In embodiments, a site specific nuclease can be used to disrupt the T cell receptor, e.g., after T-cell differentiation. In other examples, cells, e.g., T cells derived from iPSCs, can be generated from virus-specific T cells, which are less likely to cause graft-versus-host disease because of their recognition of a pathogen-derived antigen. In yet other examples, alloreactivity can be reduced, e.g., minimized, by generating iPSCs from common HLA haplotypes such that they are histocompatible with matched, unrelated recipient subjects. In yet other examples, alloreactivity can be reduced, e.g., minimized, by repressing HLA expression through genetic modification. For example, T cells derived from iPSCs can be processed as described in, e.g., Themeli *et al. Nat. Biotechnol.* 31.10(2013):928-35, incorporated herein by reference. In some examples, immune effector cells, e.g., T cells, derived from stem cells, can be processed/generated using methods described in WO2014/165707, incorporated herein by reference. Additional embodiments pertaining to allogeneic cells are described herein, e.g., in the "Allogeneic CAR Immune Effector Cells" section herein.

In certain aspects of the present disclosure, immune effector cells, e.g., T cells, can be obtained from a unit of blood collected from a subject using any number of techniques known to the skilled artisan, such as Ficoll™ separation. In one aspect, cells from the circulating blood of an individual are obtained by apheresis. The apheresis product typically contains lymphocytes, including T cells, monocytes, granulocytes, B cells, other nucleated white blood cells, red blood cells, and platelets. In one aspect, the cells collected by apheresis may be washed to remove the plasma fraction and, optionally, to place the cells in an appropriate buffer or media for subsequent processing steps. In one embodiment, the cells are washed with phosphate buffered saline (PBS). In an alternative embodiment, the wash solution lacks calcium and may lack magnesium or may lack many if not all divalent cations.

Initial activation steps in the absence of calcium can lead to magnified activation. As those of ordinary skill in the art would readily appreciate a washing step may be accomplished by methods known to those in the art, such as by using a semi-automated "flow-through" centrifuge (for example, the Cobe 2991 cell processor, the Baxter CytoMate, or the Haemonetics Cell Saver 5) according to the manufacturer's instructions. After washing, the cells may be resuspended in a variety of biocompatible buffers, such as, for example, Ca-free, Mg-free PBS, PlasmaLyte A, or other saline solution with or without buffer. Alternatively, the undesirable components of the apheresis sample may be removed and the cells directly resuspended in culture media.

In one aspect, T cells are isolated from peripheral blood lymphocytes by lysing the red blood cells and depleting the monocytes, for example, by centrifugation through a PERCOLL™ gradient or by counterflow centrifugal elutriation.

The methods described herein can include, e.g., selection of a specific subpopulation of immune effector cells, e.g., T cells, that are a T regulatory cell-depleted population, CD25+ depleted cells, using, e.g., a negative selection technique, e.g., described herein. In some embodiments, the population of T regulatory-depleted cells contains less than 30%, 25%, 20%, 15%, 10%, 5%, 4%, 3%, 2%, 1% of CD25+ cells.

In one embodiment, T regulatory cells, e.g., CD25+ T cells, are removed from the population using an anti-CD25 antibody, or fragment thereof, or a CD25-binding ligand, e.g. IL-2. In one embodiment, the anti-CD25 antibody, or fragment thereof, or CD25-binding ligand is conjugated to a substrate, e.g., a bead, or is otherwise coated on a substrate, e.g., a bead. In one embodiment, the anti-CD25 antibody, or fragment thereof, is conjugated to a substrate as described herein.

In one embodiment, the T regulatory cells, e.g., CD25+ T cells, are removed from the population using CD25 depleting reagent from Miltenyi™. In one embodiment, the ratio of cells to CD25 depletion reagent is $1e^7$ cells to 20 uL, or $1e^7$ cells to15 uL, or $1e^7$ cells to 10 uL, or $1e^7$ cells to 5 uL, or $1e^7$ cells to 2.5 uL, or $1e^7$ cells to 1.25 uL. In one embodiment, e.g., for T regulatory cells, e.g., CD25+ depletion, greater than 500 million cells/ml is used. In a further aspect, a concentration of cells of 600, 700, 800, or 900 million cells/ml is used.

In one embodiment, the population of immune effector cells to be depleted includes about 6 x 10^9 CD25+ T cells. In other aspects, the population of immune effector cells to be depleted include about 1 x 10^9 to 1x 10^{10} CD25+ T cell, and any integer value in between. In

one embodiment, the resulting population T regulatory-depleted cells has 2 x 10^9 T regulatory cells, e.g., CD25+ cells, or less (e.g., 1 x 10^9, 5 x 10^8, 1 x 10^8, 5 x 10^7, 1 x 10^7, or less CD25+ cells).

In one embodiment, the T regulatory cells, e.g., CD25+ cells, are removed from the population using the CliniMAC system with a depletion tubing set, such as, e.g., tubing 162-01. In one embodiment, the CliniMAC system is run on a depletion setting such as, e.g., DEPLETION2.1.

Without wishing to be bound by a particular theory, decreasing the level of negative regulators of immune cells (e.g., decreasing the number of unwanted immune cells, e.g., T_{REG} cells), in a subject prior to apheresis or during manufacturing of a CAR-expressing cell product significantly reduces the risk of subject relapse. For example, methods of depleting T_{REG} cells are known in the art. Methods of decreasing T_{REG} cells include, but are not limited to, cyclophosphamide, anti-GITR antibody (an anti-GITR antibody described herein), CD25-depletion, mTOR inhibitor, and combinations thereof.

In some embodiments, the manufacturing methods comprise reducing the number of (e.g., depleting) T_{REG} cells prior to manufacturing of the CAR-expressing cell. For example, manufacturing methods comprise contacting the sample, e.g., the apheresis sample, with an anti-GITR antibody and/or an anti-CD25 antibody (or fragment thereof, or a CD25-binding ligand), e.g., to deplete T_{REG} cells prior to manufacturing of the CAR-expressing cell (e.g., T cell, NK cell) product.

Without wishing to be bound by a particular theory, decreasing the level of negative regulators of immune cells (e.g., decreasing the number of unwanted immune cells, e.g., T_{REG} cells), in a subject prior to apheresis or during manufacturing of a CAR-expressing cell product can reduce the risk of a subject's relapse. In an embodiment, a subject is pre-treated with one or more therapies that reduce T_{REG} cells prior to collection of cells for CAR-expressing cell product manufacturing, thereby reducing the risk of subject relapse to CAR-expressing cell treatment. In an embodiment, methods of decreasing T_{REG} cells include, but are not limited to, administration to the subject of one or more of cyclophosphamide, anti-GITR antibody, CD25-depletion, or a combination thereof. In an embodiment, methods of decreasing T_{REG} cells include, but are not limited to, administration to the subject of one or more of cyclophosphamide, anti-GITR antibody, CD25-depletion, mTOR inhibitor, or a combination thereof. Administration of one or more of cyclophosphamide, anti-GITR antibody, CD25-

depletion, or a combination thereof, can occur before, during or after an infusion of the CAR-expressing cell product.

In some embodiments, the manufacturing methods comprise reducing the number of (e.g., depleting) T_{REG} cells prior to manufacturing of the CAR-expressing cell. For example, manufacturing methods comprise contacting the sample, e.g., the apheresis sample, with an anti-GITR antibody and/or an anti-CD25 antibody (or fragment thereof, or a CD25-binding ligand), e.g., to deplete T_{REG} cells prior to manufacturing of the CAR-expressing cell (e.g., T cell, NK cell) product. In an embodiment, a subject is pre-treated with cyclophosphamide prior to collection of cells for CAR-expressing cell product manufacturing, thereby reducing the risk of subject relapse to CAR-expressing cell treatment (e.g., CTL019 treatment). In an embodiment, a subject is pre-treated with an anti-GITR antibody prior to collection of cells for CAR-expressing cell (e.g., T cell or NK cell) product manufacturing, thereby reducing the risk of subject relapse to CAR-expressing cell treatment.

In an embodiment, the CAR-expressing cell (e.g., T cell, NK cell) manufacturing process is modified to deplete T_{REG} cells prior to manufacturing of the CAR-expressing cell (e.g., T cell, NK cell) product (e.g., a CTL019 product). In an embodiment, CD25-depletion is used to deplete TREG cells prior to manufacturing of the CAR-expressing cell (e.g., T cell, NK cell) product (e.g., a CTL019 product).

In one embodiment, the population of cells to be removed are neither the regulatory T cells or tumor cells, but cells that otherwise negatively affect the expansion and/or function of CART cells, e.g. cells expressing CD14, CD11b, CD33, CD15, or other markers expressed by potentially immune suppressive cells. In one embodiment, such cells are envisioned to be removed concurrently with regulatory T cells and/or tumor cells, or following said depletion, or in another order.

The methods described herein can include more than one selection step, e.g., more than one depletion step. Enrichment of a T cell population by negative selection can be accomplished, e.g., with a combination of antibodies directed to surface markers unique to the negatively selected cells. One method is cell sorting and/or selection via negative magnetic immunoadherence or flow cytometry that uses a cocktail of monoclonal antibodies directed to cell surface markers present on the cells negatively selected. For example, to enrich for CD4+ cells by negative selection, a monoclonal antibody cocktail can include antibodies to CD14, CD20, CD11b, CD16, HLA-DR, and CD8.

The methods described herein can further include removing cells from the population which express a tumor antigen, e.g., a tumor antigen that does not comprise CD25, e.g., CD19, CD30, CD38, CD123, CD20, CD14 or CD11b, to thereby provide a population of T regulatory-depleted, e.g., CD25+ depleted, and tumor antigen depleted cells that are suitable for expression of a CAR, e.g., a CAR described herein. In one embodiment, tumor antigen expressing cells are removed simultaneously with the T regulatory, e.g., CD25+ cells. For example, an anti-CD25 antibody, or fragment thereof, and an anti-tumor antigen antibody, or fragment thereof, can be attached to the same substrate, e.g., bead, which can be used to remove the cells or an anti-CD25 antibody, or fragment thereof, or the anti-tumor antigen antibody, or fragment thereof, can be attached to separate beads, a mixture of which can be used to remove the cells. In other embodiments, the removal of T regulatory cells, e.g., CD25+ cells, and the removal of the tumor antigen expressing cells is sequential, and can occur, e.g., in either order.

Also provided are methods that include removing cells from the population which express a check point inhibitor, e.g., a check point inhibitor described herein, e.g., one or more of PD1+ cells, LAG3+ cells, and TIM3+ cells, to thereby provide a population of T regulatory-depleted, e.g., CD25+ depleted cells, and check point inhibitor depleted cells, e.g., PD1+, LAG3+ and/or TIM3+ depleted cells. Exemplary check point inhibitors include PD1, PD-L1, PD-L2, CTLA4, TIM3, CEACAM (e.g., CEACAM-1, CEACAM-3 and/or CEACAM-5), LAG3, VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4, CD80, CD86, B7-H3 (CD276), B7-H4 (VTCN1), HVEM (TNFRSF14 or CD270), KIR, A2aR, MHC class I, MHC class II, GAL9, adenosine, and TGF (e.g., TGFbeta), e.g., as described herein. In one embodiment, check point inhibitor expressing cells are removed simultaneously with the T regulatory, e.g., CD25+ cells. For example, an anti-CD25 antibody, or fragment thereof, and an anti-check point inhibitor antibody, or fragment thereof, can be attached to the same bead which can be used to remove the cells, or an anti-CD25 antibody, or fragment thereof, and the anti-check point inhibitor antibody, or fragment there, can be attached to separate beads, a mixture of which can be used to remove the cells. In other embodiments, the removal of T regulatory cells, e.g., CD25+ cells, and the removal of the check point inhibitor expressing cells is sequential, and can occur, e.g., in either order.

Methods described herein can include a positive selection step. For example, T cells can isolated by incubation with anti-CD3/anti-CD28 (e.g., 3x28)-conjugated beads, such as

DYNABEADS® M-450 CD3/CD28 T, for a time period sufficient for positive selection of the desired T cells. In one embodiment, the time period is about 30 minutes. In a further embodiment, the time period ranges from 30 minutes to 36 hours or longer and all integer values there between. In a further embodiment, the time period is at least 1, 2, 3, 4, 5, or 6 hours. In yet another embodiment, the time period is 10 to 24 hours, e.g., 24 hours. Longer incubation times may be used to isolate T cells in any situation where there are few T cells as compared to other cell types, such in isolating tumor infiltrating lymphocytes (TIL) from tumor tissue or from immunocompromised individuals. Further, use of longer incubation times can increase the efficiency of capture of CD8+ T cells. Thus, by simply shortening or lengthening the time T cells are allowed to bind to the CD3/CD28 beads and/or by increasing or decreasing the ratio of beads to T cells (as described further herein), subpopulations of T cells can be preferentially selected for or against at culture initiation or at other time points during the process. Additionally, by increasing or decreasing the ratio of anti-CD3 and/or anti-CD28 antibodies on the beads or other surface, subpopulations of T cells can be preferentially selected for or against at culture initiation or at other desired time points.

In one embodiment, a T cell population can be selected that expresses one or more of IFN-γ, TNFα, IL-17A, IL-2, IL-3, IL-4, GM-CSF, IL-10, IL-13, granzyme B, and perforin, or other appropriate molecules, e.g., other cytokines. Methods for screening for cell expression can be determined, e.g., by the methods described in PCT Publication No.: WO 2013/126712.

For isolation of a desired population of cells by positive or negative selection, the concentration of cells and surface (e.g., particles such as beads) can be varied. In certain aspects, it may be desirable to significantly decrease the volume in which beads and cells are mixed together (e.g., increase the concentration of cells), to ensure maximum contact of cells and beads. For example, in one aspect, a concentration of 10 billion cells/ml, 9 billion/ml, 8 billion/ml, 7 billion/ml, 6 billion/ml, or 5 billion/ml is used. In one aspect, a concentration of 1 billion cells/ml is used. In yet one aspect, a concentration of cells from 75, 80, 85, 90, 95, or 100 million cells/ml is used. In further aspects, concentrations of 125 or 150 million cells/ml can be used.

Using high concentrations can result in increased cell yield, cell activation, and cell expansion. Further, use of high cell concentrations allows more efficient capture of cells that may weakly express target antigens of interest, such as CD28-negative T cells, or from samples where there are many tumor cells present (e.g., leukemic blood, tumor tissue, etc.). Such

populations of cells may have therapeutic value and would be desirable to obtain. For example, using high concentration of cells allows more efficient selection of CD8+ T cells that normally have weaker CD28 expression.

In a related aspect, it may be desirable to use lower concentrations of cells. By significantly diluting the mixture of T cells and surface (e.g., particles such as beads), interactions between the particles and cells is minimized. This selects for cells that express high amounts of desired antigens to be bound to the particles. For example, CD4+ T cells express higher levels of CD28 and are more efficiently captured than CD8+ T cells in dilute concentrations. In one aspect, the concentration of cells used is 5 x 10^6/ml. In other aspects, the concentration used can be from about 1 x 10^5/ml to 1 x 10^6/ml, and any integer value in between.

In other aspects, the cells may be incubated on a rotator for varying lengths of time at varying speeds at either 2-10°C or at room temperature.

In one embodiment, a plurality of the immune effector cells of the population do not express diaglycerol kinase (DGK), e.g., is DGK-deficient. In one embodiment, a plurality of the immune effector cells of the population do not express Ikaros, e.g., is Ikaros-deficient. In one embodiment, a plurality of the immune effector cells of the population do not express DGK and Ikaros, e.g., is both DGK and Ikaros-deficient.

T cells for stimulation can also be frozen after a washing step. Wishing not to be bound by theory, the freeze and subsequent thaw step provides a more uniform product by removing granulocytes and to some extent monocytes in the cell population. After the washing step that removes plasma and platelets, the cells may be suspended in a freezing solution. While many freezing solutions and parameters are known in the art and will be useful in this context, one method involves using PBS containing 20% DMSO and 8% human serum albumin, or culture media containing 10% Dextran 40 and 5% Dextrose, 20% Human Serum Albumin and 7.5% DMSO, or 31.25% Plasmalyte-A, 31.25% Dextrose 5%, 0.45% NaCl, 10% Dextran 40 and 5% Dextrose, 20% Human Serum Albumin, and 7.5% DMSO or other suitable cell freezing media containing for example, Hespan and PlasmaLyte A, the cells then are frozen to -80°C at a rate of 1° per minute and stored in the vapor phase of a liquid nitrogen storage tank. Other methods of controlled freezing may be used as well as uncontrolled freezing immediately at -20° C or in liquid nitrogen.

In certain aspects, cryopreserved cells are thawed and washed as described herein and allowed to rest for one hour at room temperature prior to activation using the methods of the present invention.

Also contemplated in the context of the invention is the collection of blood samples or apheresis product from a subject at a time period prior to when the expanded cells as described herein might be needed. As such, the source of the cells to be expanded can be collected at any time point necessary, and desired cells, such as T cells, isolated and frozen for later use in immune effector cell therapy for any number of diseases or conditions that would benefit from immune effector cell therapy, such as those described herein. In one aspect a blood sample or an apheresis is taken from a generally healthy subject. In certain aspects, a blood sample or an apheresis is taken from a generally healthy subject who is at risk of developing a disease, but who has not yet developed a disease, and the cells of interest are isolated and frozen for later use. In certain aspects, the T cells may be expanded, frozen, and used at a later time. In certain aspects, samples are collected from a patient shortly after diagnosis of a particular disease as described herein but prior to any treatments. In a further aspect, the cells are isolated from a blood sample or an apheresis from a subject prior to any number of relevant treatment modalities, including but not limited to treatment with agents such as natalizumab, efalizumab, antiviral agents, chemotherapy, radiation, immunosuppressive agents, such as cyclosporin, azathioprine, methotrexate, mycophenolate, and FK506, antibodies, or other immunoablative agents such as CAMPATH, anti-CD3 antibodies, cytoxan, fludarabine, cyclosporin, FK506, rapamycin, mycophenolic acid, steroids, FR901228, and irradiation.

In a further aspect of the present invention, T cells are obtained from a patient directly following treatment that leaves the subject with functional T cells. In this regard, it has been observed that following certain cancer treatments, in particular treatments with drugs that damage the immune system, shortly after treatment during the period when patients would normally be recovering from the treatment, the quality of T cells obtained may be optimal or improved for their ability to expand ex vivo. Likewise, following ex vivo manipulation using the methods described herein, these cells may be in a preferred state for enhanced engraftment and in vivo expansion. Thus, it is contemplated within the context of the present invention to collect blood cells, including T cells, dendritic cells, or other cells of the hematopoietic lineage, during this recovery phase. Further, in certain aspects, mobilization (for example, mobilization with GM-CSF) and conditioning regimens can be used to create a condition in a subject

wherein repopulation, recirculation, regeneration, and/or expansion of particular cell types is favored, especially during a defined window of time following therapy. Illustrative cell types include T cells, B cells, dendritic cells, and other cells of the immune system.

In one embodiment, the immune effector cells expressing a CAR molecule, e.g., a CAR molecule described herein, are obtained from a subject that has received a low, immune enhancing dose of an mTOR inhibitor. In an embodiment, the population of immune effector cells, e.g., T cells, to be engineered to express a CAR, are harvested after a sufficient time, or after sufficient dosing of the low, immune enhancing, dose of an mTOR inhibitor, such that the level of PD1 negative immune effector cells, e.g., T cells, or the ratio of PD1 negative immune effector cells, e.g., T cells/ PD1 positive immune effector cells, e.g., T cells, in the subject or harvested from the subject has been, at least transiently, increased.

In other embodiments, population of immune effector cells, e.g., T cells, which have, or will be engineered to express a CAR, can be treated ex vivo by contact with an amount of an mTOR inhibitor that increases the number of PD1 negative immune effector cells, e.g., T cells or increases the ratio of PD1 negative immune effector cells, e.g., T cells/ PD1 positive immune effector cells, e.g., T cells.

It is recognized that the methods of the application can utilize culture media conditions comprising 5% or less, for example 2%, human AB serum, and employ known culture media conditions and compositions, for example those described in Smith et al., "Ex vivo expansion of human T cells for adoptive immunotherapy using the novel Xeno-free CTS Immune Cell Serum Replacement" Clinical & Translational Immunology (2015) 4, e31; doi:10.1038/cti.2014.31.

In one embodiment, the methods disclosed herein can utilize culture media conditions comprising serum-free medium. In one embodiment, the serum free medium is OpTmizer CTS (LifeTech), Immunocult XF (Stemcell technologies), CellGro (CellGenix), TexMacs (Miltenyi), Stemline (Sigma), Xvivo15 (Lonza), PrimeXV (Irvine Scientific), or StemXVivo (RandD systems). The serum-free medium can be supplemented with a serum substitute such as ICSR (immune cell serum replacement) from LifeTech. The level of serum substitute (e.g., ICSR) can be, e.g., up to 5%, e.g., about 1,%, 2%, 3%, 4%, or 5%. In one embodiment, a T cell population is diaglycerol kinase (DGK)-deficient. DGK-deficient cells include cells that do not express DGK RNA or protein, or have reduced or inhibited DGK activity. DGK-deficient cells can be generated by genetic approaches, e.g., administering RNA-interfering

agents, e.g., siRNA, shRNA, miRNA, to reduce or prevent DGK expression. Alternatively, DGK-deficient cells can be generated by treatment with DGK inhibitors described herein.

In one embodiment, a T cell population is Ikaros-deficient. Ikaros-deficient cells include cells that do not express Ikaros RNA or protein, or have reduced or inhibited Ikaros activity, Ikaros-deficient cells can be generated by genetic approaches, e.g., administering RNA-interfering agents, e.g., siRNA, shRNA, miRNA, to reduce or prevent Ikaros expression. Alternatively, Ikaros-deficient cells can be generated by treatment with Ikaros inhibitors, e.g., lenalidomide.

In embodiments, a T cell population is DGK-deficient and Ikaros-deficient, e.g., does not express DGK and Ikaros, or has reduced or inhibited DGK and Ikaros activity. Such DGK and Ikaros-deficient cells can be generated by any of the methods described herein.

In an embodiment, the NK cells are obtained from the subject. In another embodiment, the NK cells are an NK cell line, e.g., NK-92 cell line (Conkwest).

In embodiments, the methods, e.g., manufacturing methods, further comprise contacting with IL-15 and/or IL-7, a cell population (e.g., a cell population in which T regulatory cells, such as CD25+ T cells, have been depleted; or a cell population that has previously contacted an anti-CD25 antibody, fragment thereof, or CD25-binding ligand). For example, the cell population (e.g., that has previously contacted an anti-CD25 antibody, fragment thereof, or CD25-binding ligand) is expanded in the presence of IL-15 and/or IL-7.

In some embodiments a CAR-expressing cell described herein is contacted with a composition comprising a interleukin-15 (IL-15) polypeptide, a interleukin-15 receptor alpha (IL-15Ra) polypeptide, or a combination of both a IL-15 polypeptide and a IL-15Ra polypeptide e.g., hetIL-15, during the manufacturing of the CAR-expressing cell, e.g., ex vivo. In embodiments, a CAR-expressing cell described herein is contacted with a composition comprising an IL-15 polypeptide during the manufacturing of the CAR-expressing cell, e.g., ex vivo. In embodiments, a CAR-expressing cell described herein is contacted with a composition comprising a combination of both a IL-15 polypeptide and a IL-15 Ra polypeptide during the manufacturing of the CAR-expressing cell, e.g., ex vivo. In embodiments, a CAR-expressing cell described herein is contacted with a composition comprising hetIL-15 during the manufacturing of the CAR-expressing cell, e.g., *ex vivo*.

In one embodiment the CAR-expressing cell described herein is contacted with a composition comprising hetIL-15 during *ex vivo* expansion. In an embodiment, the CAR-

expressing cell described herein is contacted with a composition comprising an IL-15 polypeptide during ex vivo expansion. In an embodiment, the CAR-expressing cell described herein is contacted with a composition comprising both an IL-15 polypeptide and an IL-15Ra polypeptide during ex vivo expansion. In one embodiment the contacting results in the survival and proliferation of a lymphocyte subpopulation, e.g., CD8+ T cells.

Allogeneic CAR

In embodiments described herein, the immune effector cell can be an allogeneic immune effector cell, e.g., T cell or NK cell. For example, the cell can be an allogeneic T cell, e.g., an allogeneic T cell lacking expression of a functional T cell receptor (TCR) and/or human leukocyte antigen (HLA), e.g., HLA class I and/or HLA class II.

A T cell lacking a functional TCR can be, e.g., engineered such that it does not express any functional TCR on its surface, engineered such that it does not express one or more subunits that comprise a functional TCR (e.g., engineered such that it does not express (or exhibits reduced expression) of TCR alpha, TCR beta, TCR gamma, TCR delta, TCR epsilon, and/or TCR zeta), or engineered such that it produces very little functional TCR on its surface. Alternatively, the T cell can express a substantially impaired TCR, e.g., by expression of mutated or truncated forms of one or more of the subunits of the TCR. The term "substantially impaired TCR" means that this TCR will not elicit an adverse immune reaction in a host.

A T cell described herein can be, e.g., engineered such that it does not express a functional HLA on its surface. For example, a T cell described herein, can be engineered such that cell surface expression HLA, e.g., HLA class 1 and/or HLA class II, is downregulated. In some embodiments, downregulation of HLA may be accomplished by reducing or eliminating expression of beta-2 microglobulin (B2M).In some embodiments, the T cell can lack a functional TCR and a functional HLA, e.g., HLA class I and/or HLA class II.

Modified T cells that lack expression of a functional TCR and/or HLA can be obtained by any suitable means, including a knock out or knock down of one or more subunit of TCR or HLA. For example, the T cell can include a knock down of TCR and/or HLA using siRNA, shRNA, clustered regularly interspaced short palindromic repeats (CRISPR) transcription-activator like effector nuclease (TALEN), or zinc finger endonuclease (ZFN).

In some embodiments, the allogeneic cell can be a cell which does not express or expresses at low levels an inhibitory molecule, e.g. by any method described herein. For

example, the cell can be a cell that does not express or expresses at low levels an inhibitory molecule, e.g., that can decrease the ability of a CAR-expressing cell to mount an immune effector response. Examples of inhibitory molecules include PD1, PD-L1, PD-L2, CTLA4, TIM3, CEACAM (e.g., CEACAM-1, CEACAM-3 and/or CEACAM-5), LAG3, VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4, CD80, CD86, B7-H3 (CD276), B7-H4 (VTCN1), HVEM (TNFRSF14 or CD270), KIR, A2aR, MHC class I, MHC class II, GAL9, adenosine, and TGF (e.g., TGFbeta). Inhibition of an inhibitory molecule, e.g., by inhibition at the DNA, RNA or protein level, can optimize a CAR-expressing cell performance. In embodiments, an inhibitory nucleic acid, e.g., an inhibitory nucleic acid, e.g., a dsRNA, e.g., an siRNA or shRNA, a clustered regularly interspaced short palindromic repeats (CRISPR), a transcription-activator like effector nuclease (TALEN), or a zinc finger endonuclease (ZFN), e.g., as described herein, can be used.

siRNA and shRNA to inhibit TCR or HLA

In some embodiments, TCR expression and/or HLA expression can be inhibited using siRNA or shRNA that targets a nucleic acid encoding a TCR and/or HLA, and/or an inhibitory molecule described herein (e.g., PD1, PD-L1, PD-L2, CTLA4, TIM3, CEACAM (e.g., CEACAM-1, CEACAM-3 and/or CEACAM-5), LAG3, VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4, CD80, CD86, B7-H3 (CD276), B7-H4 (VTCN1), HVEM (TNFRSF14 or CD270), KIR, A2aR, MHC class I, MHC class II, GAL9, adenosine, and TGF beta), in a cell, *e.g.*, T cell. .

Expression systems for siRNA and shRNAs, and exemplary shRNAs, are described, e.g., in paragraphs 649 and 650 of International Application WO2015/142675, filed March 13, 2015, which is incorporated by reference in its entirety.

CRISPR to inhibit TCR or HLA

"CRISPR" or "CRISPR to TCR and/or HLA" or "CRISPR to inhibit TCR and/or HLA" as used herein refers to a set of clustered regularly interspaced short palindromic repeats, or a system comprising such a set of repeats. "Cas", as used herein, refers to a CRISPR-associated protein. A "CRISPR/Cas" system refers to a system derived from CRISPR and Cas which can be used to silence or mutate a TCR and/or HLA gene, and/or an inhibitory molecule described herein (e.g., PD1, PD-L1, PD-L2, CTLA4, TIM3, CEACAM (e.g., CEACAM-1, CEACAM-3

and/or CEACAM-5), LAG3, VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4, CD80, CD86, B7-H3 (CD276), B7-H4 (VTCN1), HVEM (TNFRSF14 or CD270), KIR, A2aR, MHC class I, MHC class II, GAL9, adenosine, and TGF beta), in a cell, *e.g.*, T cell.

The CRISPR/Cas system, and uses thereof, are described, e.g., in paragraphs 651-658 of International Application WO2015/142675, filed March 13, 2015, which is incorporated by reference in its entirety.

TALEN to inhibit TCR and/or HLA

"TALEN" or "TALEN to HLA and/or TCR" or "TALEN to inhibit HLA and/or TCR" refers to a transcription activator-like effector nuclease, an artificial nuclease which can be used to edit the HLA and/or TCR gene, and/or an inhibitory molecule described herein (e.g., PD1, PD-L1, PD-L2, CTLA4, TIM3, CEACAM (e.g., CEACAM-1, CEACAM-3 and/or CEACAM-5), LAG3, VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4, CD80, CD86, B7-H3 (CD276), B7-H4 (VTCN1), HVEM (TNFRSF14 or CD270), KIR, A2aR, MHC class I, MHC class II, GAL9, adenosine, and TGF beta), in a cell, *e.g.*, T cell.

TALENs, and uses thereof, are described, e.g., in paragraphs 659-665 of International Application WO2015/142675, filed March 13, 2015, which is incorporated by reference in its entirety.

Zinc finger nuclease to inhibit HLA and/or TCR

"ZFN" or "Zinc Finger Nuclease" or "ZFN to HLA and/or TCR" or "ZFN to inhibit HLA and/or TCR" refer to a zinc finger nuclease, an artificial nuclease which can be used to edit the HLA and/or TCR gene, and/or an inhibitory molecule described herein (*e.g.*, PD1, PD-L1, PD-L2, CTLA4, TIM3, CEACAM (e.g., CEACAM-1, CEACAM-3 and/or CEACAM-5), LAG3, VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4, CD80, CD86, B7-H3 (CD276), B7-H4 (VTCN1), HVEM (TNFRSF14 or CD270), KIR, A2aR, MHC class I, MHC class II, GAL9, adenosine, and TGF beta), in a cell, *e.g.*, T cell.

ZFNs, and uses thereof, are described, e.g., in paragraphs 666-671 of International Application WO2015/142675, filed March 13, 2015, which is incorporated by reference in its entirety.

Telomerase expression

Telomeres play a crucial role in somatic cell persistence, and their length is maintained by telomerase (TERT). Telomere length in CLL cells may be very short (Roth et al., "Significantly shorter telomeres in T-cells of patients with ZAP-70+/CD38 chronic lymphocytic leukaemia" British Journal of Haematology, 143, 383-386., August 28 2008), and may be even shorter in manufactured CAR-expressing cells, e.g., CART19 cells, limiting their potential to expand after adoptive transfer to a patient. Telomerase expression can rescue CAR-expressing cells from replicative exhaustion.

While not wishing to be bound by any particular theory, in some embodiments, a therapeutic T cell has short term persistence in a patient, due to shortened telomeres in the T cell; accordingly, transfection with a telomerase gene can lengthen the telomeres of the T cell and improve persistence of the T cell in the patient. See Carl June, "Adoptive T cell therapy for cancer in the clinic", Journal of Clinical Investigation, 117:1466-1476 (2007). Thus, in an embodiment, an immune effector cell, e.g., a T cell, ectopically expresses a telomerase subunit, e.g., the catalytic subunit of telomerase, e.g., TERT, e.g., hTERT. In some aspects, this disclosure provides a method of producing a CAR-expressing cell, comprising contacting a cell with a nucleic acid encoding a telomerase subunit, e.g., the catalytic subunit of telomerase, e.g., TERT, e.g., hTERT. The cell may be contacted with the nucleic acid before, simultaneous with, or after being contacted with a construct encoding a CAR.

Telomerase expression may be stable (e.g., the nucleic acid may integrate into the cell's genome) or transient (e.g., the nucleic acid does not integrate, and expression declines after a period of time, e.g., several days). Stable expression may be accomplished by transfecting or transducing the cell with DNA encoding the telomerase subunit and a selectable marker, and selecting for stable integrants. Alternatively or in combination, stable expression may be accomplished by site-specific recombination, e.g., using the Cre/Lox or FLP/FRT system.

Transient expression may involve transfection or transduction wtih a nucleic acid, e.g., DNA or RNA such as mRNA. In some embodiments, transient mRNA transfection avoids the genetic instability sometimes associated with stable transfection with TERT. Transient expression of exogenous telomerase activity is described, e.g., in International Application WO2014/130909, which is incorporated by reference herein in its entirety. In embodiments, mRNA-based transfection of a telomerase subunit is performed according to the messenger RNA Therapeutics™ platform commercialized by Moderna Therapeutics. For instance, the

method may be a method described in US Pat. No. 8710200, 8822663, 8680069, 8754062, 8664194, or 8680069.

In an embodiment, hTERT has the amino acid sequence of GenBank Protein ID AAC51724.1 (Meyerson et al., "hEST2, the Putative Human Telomerase Catalytic Subunit Gene, Is Up-Regulated in Tumor Cells and during Immortalization" Cell Volume 90, Issue 4, 22 August 1997, Pages 785–795), provided herein as SEQ ID NO: 5.

In an embodiment, the hTERT has a sequence at least 80%, 85%, 90%, 95%, 96^, 97%, 98%, or 99% identical to the sequence of SEQ ID NO: 5. In an embodiment, the hTERT has a sequence of SEQ ID NO: 5. In an embodiment, the hTERT comprises a deletion (e.g., of no more than 5, 10, 15, 20, or 30 amino acids) at the N-terminus, the C-terminus, or both. In an embodiment, the hTERT comprises a transgenic amino acid sequence (e.g., of no more than 5, 10, 15, 20, or 30 amino acids) at the N-terminus, the C-terminus, or both.

In an embodiment, the hTERT is encoded by the nucleic acid sequence of GenBank Accession No. AF018167 (Meyerson et al., "hEST2, the Putative Human Telomerase Catalytic Subunit Gene, Is Up-Regulated in Tumor Cells and during Immortalization" Cell Volume 90, Issue 4, 22 August 1997, Pages 785–795), provided herein as SEQ ID NO: 8.

In an embodiment, the hTERT is encoded by a nucleic acid having a sequence at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to the sequence of SEQ ID NO: 8. In an embodiment, the hTERT is encoded by a nucleic acid of SEQ ID NO: 8.

RNA Transfection

Disclosed herein are methods for producing an in vitro transcribed RNA CAR. The methods described herein can include introducing a CAR encoding RNA construct that can be directly transfected into a cell. A method for generating mRNA for use in transfection can involve in vitro transcription (IVT) of a template with specially designed primers, followed by polyA addition, to produce a construct containing 3' and 5' untranslated sequence ("UTR"), a 5' cap and/or Internal Ribosome Entry Site (IRES), the nucleic acid to be expressed, and a polyA tail, typically 50-2000 bases in length (e.g., SEQ ID NO:30). RNA so produced can efficiently transfect different kinds of cells. In one aspect, the template includes sequences for the CAR. RNA CAR and methods of using the same are described, e.g., in paragraphs 553-570 of in

International Application WO2015/142675, filed March 13, 2015, which is herein incorporated by reference in its entirety.

An immune effector cell can include a CAR encoded by a messenger RNA (mRNA). In one aspect, the mRNA encoding a CAR described herein is introduced into an immune effector cell, e.g., made by a method described herein, for production of a CAR-expressing cell.

In one embodiment, the *in vitro* transcribed RNA CAR can be introduced to a cell as a form of transient transfection. The RNA is produced by *in vitro* transcription using a polymerase chain reaction (PCR)-generated template. DNA of interest from any source can be directly converted by PCR into a template for in vitro mRNA synthesis using appropriate primers and RNA polymerase. The source of the DNA can be, for example, genomic DNA, plasmid DNA, phage DNA, cDNA, synthetic DNA sequence or any other appropriate source of DNA. The desired temple for *in vitro* transcription is a CAR described herein. For example, the template for the RNA CAR comprises an extracellular region comprising a single chain variable domain of an antibody to a tumor associated antigen described herein; a hinge region (e.g., a hinge region described herein), a transmembrane domain (e.g., a transmembrane domain described herein such as a transmembrane domain of CD8a); and a cytoplasmic region that includes an intracellular signaling domain, e.g., an intracellular signaling domain described herein, e.g., comprising the signaling domain of CD3-zeta and the signaling domain of 4-1BB.

In one embodiment, the DNA to be used for PCR contains an open reading frame. The DNA can be from a naturally occurring DNA sequence from the genome of an organism. In one embodiment, the nucleic acid can include some or all of the 5' and/or 3' untranslated regions (UTRs). The nucleic acid can include exons and introns. In one embodiment, the DNA to be used for PCR is a human nucleic acid sequence. In another embodiment, the DNA to be used for PCR is a human nucleic acid sequence including the 5' and 3' UTRs. The DNA can alternatively be an artificial DNA sequence that is not normally expressed in a naturally occurring organism. An exemplary artificial DNA sequence is one that contains portions of genes that are ligated together to form an open reading frame that encodes a fusion protein. The portions of DNA that are ligated together can be from a single organism or from more than one organism.

PCR is used to generate a template for in vitro transcription of mRNA which is used for transfection. Methods for performing PCR are well known in the art. Primers for use in PCR are designed to have regions that are substantially complementary to regions of the DNA to be

used as a template for the PCR. "Substantially complementary," as used herein, refers to sequences of nucleotides where a majority or all of the bases in the primer sequence are complementary, or one or more bases are non-complementary, or mismatched. Substantially complementary sequences are able to anneal or hybridize with the intended DNA target under annealing conditions used for PCR. The primers can be designed to be substantially complementary to any portion of the DNA template. For example, the primers can be designed to amplify the portion of a nucleic acid that is normally transcribed in cells (the open reading frame), including 5' and 3' UTRs. The primers can also be designed to amplify a portion of a nucleic acid that encodes a particular domain of interest. In one embodiment, the primers are designed to amplify the coding region of a human cDNA, including all or portions of the 5' and 3' UTRs. Primers useful for PCR can be generated by synthetic methods that are well known in the art. "Forward primers" are primers that contain a region of nucleotides that are substantially complementary to nucleotides on the DNA template that are upstream of the DNA sequence that is to be amplified. "Upstream" is used herein to refer to a location 5, to the DNA sequence to be amplified relative to the coding strand. "Reverse primers" are primers that contain a region of nucleotides that are substantially complementary to a double-stranded DNA template that are downstream of the DNA sequence that is to be amplified. "Downstream" is used herein to refer to a location 3' to the DNA sequence to be amplified relative to the coding strand.

Any DNA polymerase useful for PCR can be used in the methods disclosed herein. The reagents and polymerase are commercially available from a number of sources.

Chemical structures with the ability to promote stability and/or translation efficiency may also be used. In embodiments, the RNA has 5' and 3' UTRs. In one embodiment, the 5' UTR is between one and 3000 nucleotides in length. The length of 5' and 3' UTR sequences to be added to the coding region can be altered by different methods, including, but not limited to, designing primers for PCR that anneal to different regions of the UTRs. Using this approach, one of ordinary skill in the art can modify the 5' and 3' UTR lengths required to achieve optimal translation efficiency following transfection of the transcribed RNA.

The 5' and 3' UTRs can be the naturally occurring, endogenous 5' and 3' UTRs for the nucleic acid of interest. Alternatively, UTR sequences that are not endogenous to the nucleic acid of interest can be added by incorporating the UTR sequences into the forward and reverse primers or by any other modifications of the template. The use of UTR sequences that are not endogenous to the nucleic acid of interest can be useful for modifying the stability and/or

translation efficiency of the RNA. For example, it is known that AU-rich elements in 3' UTR sequences can decrease the stability of mRNA. Therefore, 3' UTRs can be selected or designed to increase the stability of the transcribed RNA based on properties of UTRs that are well known in the art.

In one embodiment, the 5' UTR can contain the Kozak sequence of the endogenous nucleic acid. Alternatively, when a 5' UTR that is not endogenous to the nucleic acid of interest is being added by PCR as described above, a consensus Kozak sequence can be redesigned by adding the 5' UTR sequence. Kozak sequences can increase the efficiency of translation of some RNA transcripts, but does not appear to be required for all RNAs to enable efficient translation. The requirement for Kozak sequences for many mRNAs is known in the art. In other embodiments the 5' UTR can be 5'UTR of an RNA virus whose RNA genome is stable in cells. In other embodiments various nucleotide analogues can be used in the 3' or 5' UTR to impede exonuclease degradation of the mRNA.

To enable synthesis of RNA from a DNA template without the need for gene cloning, a promoter of transcription should be attached to the DNA template upstream of the sequence to be transcribed. When a sequence that functions as a promoter for an RNA polymerase is added to the 5' end of the forward primer, the RNA polymerase promoter becomes incorporated into the PCR product upstream of the open reading frame that is to be transcribed. In one embodiment, the promoter is a T7 polymerase promoter, as described elsewhere herein. Other useful promoters include, but are not limited to, T3 and SP6 RNA polymerase promoters. Consensus nucleotide sequences for T7, T3 and SP6 promoters are known in the art.

In one embodiment, the mRNA has both a cap on the 5' end and a 3' poly(A) tail which determine ribosome binding, initiation of translation and stability mRNA in the cell. On a circular DNA template, for instance, plasmid DNA, RNA polymerase produces a long concatameric product which is not suitable for expression in eukaryotic cells. The transcription of plasmid DNA linearized at the end of the 3' UTR results in normal sized mRNA which is not effective in eukaryotic transfection even if it is polyadenylated after transcription.

On a linear DNA template, phage T7 RNA polymerase can extend the 3' end of the transcript beyond the last base of the template (Schenborn and Mierendorf, Nuc Acids Res., 13:6223-36 (1985); Nacheva and Berzal-Herranz, Eur. J. Biochem., 270:1485-65 (2003).

The conventional method of integration of polyA/T stretches into a DNA template is molecular cloning. However polyA/T sequence integrated into plasmid DNA can cause plasmid

instability, which is why plasmid DNA templates obtained from bacterial cells are often highly contaminated with deletions and other aberrations. This makes cloning procedures not only laborious and time consuming but often not reliable. That is why a method which allows construction of DNA templates with polyA/T 3' stretch without cloning highly desirable.

The polyA/T segment of the transcriptional DNA template can be produced during PCR by using a reverse primer containing a polyT tail, such as 100T tail (SEQ ID NO: 31) (size can be 50-5000 T (SEQ ID NO: 32)), or after PCR by any other method, including, but not limited to, DNA ligation or in vitro recombination. Poly(A) tails also provide stability to RNAs and reduce their degradation. Generally, the length of a poly(A) tail positively correlates with the stability of the transcribed RNA. In one embodiment, the poly(A) tail is between 100 and 5000 adenosines (e.g., SEQ ID NO: 33).

Poly(A) tails of RNAs can be further extended following in vitro transcription with the use of a poly(A) polymerase, such as E. coli polyA polymerase (E-PAP). In one embodiment, increasing the length of a poly(A) tail from 100 nucleotides to between 300 and 400 nucleotides (SEQ ID NO: 34) results in about a two-fold increase in the translation efficiency of the RNA. Additionally, the attachment of different chemical groups to the 3' end can increase mRNA stability. Such attachment can contain modified/artificial nucleotides, aptamers and other compounds. For example, ATP analogs can be incorporated into the poly(A) tail using poly(A) polymerase. ATP analogs can further increase the stability of the RNA.

5' caps on also provide stability to RNA molecules. In one embodiment, RNAs produced by the methods disclosed herein include a 5' cap. The 5' cap is provided using techniques known in the art and described herein (Cougot, et al., Trends in Biochem. Sci., 29:436-444 (2001); Stepinski, et al., RNA, 7:1468-95 (2001); Elango, et al., Biochim. Biophys. Res. Commun., 330:958-966 (2005)).

The RNAs produced by the methods disclosed herein can also contain an internal ribosome entry site (IRES) sequence. The IRES sequence may be any viral, chromosomal or artificially designed sequence which initiates cap-independent ribosome binding to mRNA and facilitates the initiation of translation. Any solutes suitable for cell electroporation, which can contain factors facilitating cellular permeability and viability such as sugars, peptides, lipids, proteins, antioxidants, and surfactants can be included.

RNA can be introduced into target cells using any of a number of different methods, for instance, commercially available methods which include, but are not limited to, electroporation (Amaxa Nucleofector-II (Amaxa Biosystems, Cologne, Germany)), (ECM 830 (BTX) (Harvard Instruments, Boston, Mass.) or the Gene Pulser II (BioRad, Denver, Colo.), Multiporator (Eppendort, Hamburg Germany), cationic liposome mediated transfection using lipofection, polymer encapsulation, peptide mediated transfection, or biolistic particle delivery systems such as "gene guns" (see, for example, Nishikawa, et al. Hum Gene Ther., 12(8):861-70 (2001).

Activation and/or Expansion of Immune Effector Cells

In embodiments, the disclosure provides for methods of expanding a population of immune effector cells by contacting the population of immune effector cells with a nucleic acid encoding a CAR, under conditions suitable for expression, e.g., transient expression, of the CAR, wherein the CAR targets a cognate antigen molecule; and culturing the population of immune effector cells in the presence of a ligand, e.g., the cognate antigen molecule. In one embodiment, the nucleic acid is RNA, e.g., in vitro transcribed RNA. In another embodiment, the cognate antigen molecule is a cancer associated antigen molecule.

Methods presented herein provide for expanding a population of immune effector cells by contact with a surface having attached thereto a cognate antigen molecule that stimulates a CAR on the surface of the immune effector cells. In certain aspects, the cognate antigen molecule may be in solution or coupled to a surface. In one aspect, the cognate antigen molecule providing the stimulatory signal is bound to a cell surface. In certain aspects, the cognate antigen molecule can be in solution. In one aspect, cognate antigen molecule may be in soluble form, and then cross-linked to a surface.

In one embodiment, the cognate antigen molecule is attached to a substrate. In one embodiment, the substrate is a solid support. In one embodiment, the substrate is selected from microtiter plates (e.g., ELISA plates); membranes (e.g., nitrocellulose membranes, PVDF membranes, nylon membranes, acetate derivatives, and combinations thereof); fiber matrix, Sepharose matrix, sugar matrix; plastic chips; glass chips; or any type of bead (e.g., Luminex beads, Dynabeads, magnetic beads, flow-cytometry beads, and combinations thereof). In one embodiment, the substrate is an ELISA plate. In another embodiment, the substrate is a bead, e.g., Dynabeads.

Ratios of particles to cells from 1:500 to 500:1 and any integer values in between may be used to stimulate immune effector cells, e.g., T cells or other target cells. As those of ordinary skill in the art can readily appreciate, the ratio of particles to cells may depend on particle size relative to the target cell. For example, small sized beads could only bind a few cells, while larger beads could bind many. In certain aspects the ratio of cells to particles ranges from 1:100 to 100:1 and any integer values in-between and in further aspects the ratio comprises 1:9 to 9:1 and any integer values in between, can also be used to stimulate T cells. The ratio of cognate antigen molecule -coupled particles to immune effector cells, e.g., T cells, that result in T cell stimulation can vary as noted above, however certain preferred values include 1:100, 1:50, 1:40, 1:30, 1:20, 1:10, 1:9, 1:8, 1:7, 1:6, 1:5, 1:4, 1:3, 1:2, 1:1, 2:1, 3:1, 4:1, 5:1, 6:1, 7:1, 8:1, 9:1, 10:1, and 15:1 with one suitable ratio being at least 1:1 particles per T cell. In one aspect, a ratio of particles to cells of 1:1 or less is used. In further aspects, the ratio of particles to cells can be varied depending on the day of stimulation. For example, in one aspect, the ratio of particles to cells is from 1:1 to 10:1 on the first day and additional particles are added to the cells every day or every other day thereafter for up to 10 days, at final ratios of from 1:1 to 1:10 (based on cell counts on the day of addition). In one particular aspect, the ratio of particles to cells is 1:1 on the first day of stimulation and adjusted to 1:5 on the third and fifth days of stimulation. In one aspect, particles are added on a daily or every other day basis to a final ratio of 1:1 on the first day, and 1:5 on the third and fifth days of stimulation. In one aspect, the ratio of particles to cells is 2:1 on the first day of stimulation and adjusted to 1:10 on the third and fifth days of stimulation. In one aspect, particles are added on a daily or every other day basis to a final ratio of 1:1 on the first day, and 1:10 on the third and fifth days of stimulation. In one particular aspect, a suitable particle: cell ratio is 1:3.

In further aspects, the cells, such as T cells, are combined with cognate antigen molecule -coated beads, the beads and the cells are subsequently separated, and then the cells are cultured. In an alternative aspect, prior to culture, the cognate antigen molecule -coated beads and cells are not separated but are cultured together. In a further aspect, the beads and cells are first concentrated by application of a force, such as a magnetic force, resulting in increased ligation of cell surface markers, thereby inducing cell stimulation.

By way of example, cell surface proteins may be ligated by allowing paramagnetic beads to which cognate antigen molecules are attached (3x28 beads) to contact the T cells. In one aspect the cells (for example, 10^4 to 10^9 T cells) and beads (for example, DYNABEADS®

M-450 Tosylactivated paramagnetic beads at a ratio of 1:3) are combined in a buffer, for example PBS (without divalent cations such as, calcium and magnesium). Other cell concentrations are contemplated. For example, the target cell may be very rare in the sample and comprise only 0.01% of the sample or the entire sample (i.e., 100%) may comprise the target cell of interest. Accordingly, any cell number is within the context of the present invention. In certain aspects, it may be desirable to significantly decrease the volume in which particles and cells are mixed together (i.e., increase the concentration of cells), to ensure maximum contact of cells and particles. For example, in one aspect, a concentration of about 10 billion cells/ml, 9 billion/ml, 8 billion/ml, 7 billion/ml, 6 billion/ml, 5 billion/ml, or 2 billion cells/ml is used. In one aspect, greater than 100 million cells/ml is used. In a further aspect, a concentration of cells of 10, 15, 20, 25, 30, 35, 40, 45, or 50 million cells/ml is used. In yet one aspect, a concentration of cells from 75, 80, 85, 90, 95, or 100 million cells/ml is used. In further aspects, concentrations of 125 or 150 million cells/ml can be used. Using high concentrations can result in increased cell yield, cell activation, and cell expansion. Further, use of high cell concentrations allows more efficient capture of cells that may weakly express the expressed, e.g., transiently expressed, CAR.

In one embodiment, cells transduced with a nucleic acid encoding a CAR, e.g., a CAR described herein, e.g., a CD19 CAR described herein, are expanded, e.g., by a method described herein. In one embodiment, the cells are expanded in culture for a period of several hours (e.g., about 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 18, 21 hours) to about 40 days (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39 or 40 days). In one embodiment, the cells are expanded for a period of 4 to 9 days. In one embodiment, the cells are expanded for a period of 8 days or less, e.g., 7, 6 or 5 days. In one embodiment, the cells are expanded in culture for 5 days, and the resulting cells are more potent than the same cells expanded in culture for 9 days under the same culture conditions. Potency can be defined, e.g., by various T cell functions, e.g. proliferation, target cell killing, cytokine production, activation, migration, or combinations thereof. In one embodiment, the cells, e.g., a CD19 CAR cell described herein, expanded for 5 days show at least a one, two, three or four fold increase in cells doublings upon antigen stimulation as compared to the same cells expanded in culture for 9 days under the same culture conditions. In one embodiment, the cells, e.g., the cells expressing a CD19 CAR described herein, are expanded in culture for 5 days, and the resulting cells exhibit higher proinflammatory cytokine

production, e.g., IFN-γ and/or GM-CSF levels, as compared to the same cells expanded in culture for 9 days under the same culture conditions. In one embodiment, the cells, e.g., a CD19 CAR cell described herein, expanded for 5 days show at least a one, two, three, four, five, ten fold or more increase in pg/ml of proinflammatory cytokine production, e.g., IFN-γ and/or GM-CSF levels, as compared to the same cells expanded in culture for 9 days under the same culture conditions.

Several cycles of stimulation may also be desired such that culture time of immune effector cells, e.g., T cells, can be 60 days or more. Conditions appropriate for T cell culture include an appropriate media (e.g., Minimal Essential Media or RPMI Media 1640 or, X-vivo 15, (Lonza)) that may contain factors necessary for proliferation and viability, including serum (e.g., fetal bovine or human serum), interleukin-2 (IL-2), insulin, IFN-γ, IL-4, IL-7, GM-CSF, IL-10, IL-12, IL-15, TGFβ, and TNF-α or any other additives for the growth of cells known to the skilled artisan. Other additives for the growth of cells include, but are not limited to, surfactant, plasmanate, and reducing agents such as N-acetyl-cysteine and 2-mercaptoethanol. Media can include RPMI 1640, AIM-V, DMEM, MEM, α-MEM, F-12, X-Vivo 15, and X-Vivo 20, Optimizer, with added amino acids, sodium pyruvate, and vitamins, either serum-free or supplemented with an appropriate amount of serum (or plasma) or a defined set of hormones, and/or an amount of cytokine(s) sufficient for the growth and expansion of T cells. Antibiotics, e.g., penicillin and streptomycin, are included only in experimental cultures, not in cultures of cells that are to be infused into a subject. The target cells are maintained under conditions necessary to support growth, for example, an appropriate temperature (e.g., 37° C) and atmosphere (e.g., air plus 5% CO_2).

In one embodiment, the cells are expanded in an appropriate media (e.g., media described herein) that includes one or more interleukin that result in at least a 200-fold (e.g., 200-fold, 250-fold, 300-fold, 350-fold) increase in cells over a 14 day expansion period, e.g., as measured by a method described herein such as flow cytometry. In one embodiment, the cells are expanded in the presence IL-15 and/or IL-7 (e.g., IL-15 and IL-7). In one embodiment, the cells are expanded in the presence of IL-2.

T cells that have been exposed to varied stimulation times may exhibit different characteristics. For example, typical blood or apheresed peripheral blood mononuclear cell products have a helper T cell population (TH, CD4+) that is greater than the cytotoxic or suppressor T cell population (TC, CD8+). Ex vivo expansion of T cells by stimulating CD3 and

CD28 receptors produces a population of T cells that prior to about days 8-9 consists predominately of TH cells, while after about days 8-9, the population of T cells comprises an increasingly greater population of TC cells. Accordingly, depending on the purpose of treatment, infusing a subject with a T cell population comprising predominately of TH cells may be advantageous. Similarly, if an antigen-specific subset of TC cells has been isolated it may be beneficial to expand this subset to a greater degree.

Further, in addition to CD4 and CD8 markers, other phenotypic markers vary significantly, but in large part, reproducibly during the course of the cell expansion process. Thus, such reproducibility enables the ability to tailor an activated T cell product for specific purposes.

Various assays can be used to evaluate the efficacy of the methods described herein, such as but not limited to, transduction efficiency, the ability to express the CAR, the ability to expand immune effector cells following antigen stimulation, and to sustain immune effector cell expansion. Assays to evaluate the methods of the present invention are described in further detail below.

Transduction efficiency can be measured by flow cytometry. For example, as described herein, surface expression of CAR on immune effector cells expressing a CAR (e.g., a CD19 CAR) can be measured. Surface expression of CAR is examined by incubating cells with biotin-labeled polyclonal goat anti-mouse F(ab)2 antibodies (Jackson Immunoresearch, West Grove, PA) at 4°C for 30minutes, followed by two washes with FACs buffer (PBS plus 3% BSA) and coupling with phycoerythrin-labeled streptavidin (BD Pharmingen, San Diego, CA). Sample data can be collected on the LSRII Fortessa (BD Biosciences) and analyzed with FlowJo software (Treestar). Transduction efficiency can also be measured by any other art know method for measuring RNA levels (e.g., northern analysis, quantitative real time PCR) or protein levels (e.g., western analysis).

Expansion of immune effector cells following antigen stimulation can also be measured by flow cytometry. For example, expansion of immune effector cells expressing a CAR (e.g., a CD19 CAR) stimulated with a cognate antigen molecule (e.g., anti-idiotype CD19) can be measured as described herein. Live cells were gated on Live/Dead Aqua-negative and then gated for CD4 (or CD8)-positive. Absolute T cell counts can be determined by using CountBright Absolute Counting Beads (Life Technologies) using the formula: (Number of T cells events/number of bead events) X number of beads used.

Sustained CAR$^+$ T cell expansion in the absence of re-stimulation can also be measured. See, *e.g.*, Milone *et al.*, Molecular Therapy 17(8): 1453-1464 (2009). Briefly, mean T cell volume (fl) is measured on day 8 of culture using a Coulter Multisizer III particle counter following stimulation with αCD3/αCD28 coated magnetic beads on day 0, and transduction with the indicated CAR on day 1.

Other assays, including those described in the Example section herein, as well as those that are known in the art can also be used to evaluate the CARs described herein.

Chimeric Antigen Receptor (CAR)

The present invention provides immune effector cells that are engineered to contain one or more CARs that direct the immune effector cells to cancer. This is achieved through an antigen binding domain on the CAR that is specific for a cancer associated antigen. There are two classes of cancer associated antigens (tumor antigens) that can be targeted by the CARs described herein: (1) cancer associated antigens that are expressed on the surface of cancer cells; and (2) cancer associated antigens that itself is intracellar, however, a fragment of such antigen (peptide) is presented on the surface of the cancer cells by MHC (major histocompatibility complex).

Accordingly, an immune effector cell, e.g., obtained by a method described herein, can be engineered to contain a CAR that target one of the following cancer associated antigens (tumor antigens): CD19; CD123; CD22; CD30; CD171; CS-1 (also referred to as CD2 subset 1, CRACC, SLAMF7, CD319, and 19A24); C-type lectin-like molecule-1 (CLL-1 or CLECL1); CD33; epidermal growth factor receptor variant III (EGFRvIII); ganglioside G2 (GD2); ganglioside GD3 (aNeu5Ac(2-8)aNeu5Ac(2-3)bDGalp(1-4)bDGlcp(1-1)Cer); TNF receptor family member B cell maturation (BCMA); Tn antigen ((Tn Ag) or (GalNAcα-Ser/Thr)); prostate-specific membrane antigen (PSMA); Receptor tyrosine kinase-like orphan receptor 1 (ROR1); Fms-Like Tyrosine Kinase 3 (FLT3); Tumor-associated glycoprotein 72 (TAG72); CD38; CD44v6; Carcinoembryonic antigen (CEA); Epithelial cell adhesion molecule (EPCAM); B7H3 (CD276); KIT (CD117); Interleukin-13 receptor subunit alpha-2 (IL-13Ra2 or CD213A2); Mesothelin; Interleukin 11 receptor alpha (IL-11Ra); prostate stem cell antigen (PSCA); Protease Serine 21 (Testisin or PRSS21); vascular endothelial growth factor receptor 2 (VEGFR2); Lewis(Y) antigen; CD24; Platelet-derived growth factor receptor beta (PDGFR-beta); Stage-specific embryonic antigen-4 (SSEA-4); CD20; Folate receptor

alpha; Receptor tyrosine-protein kinase ERBB2 (Her2/neu); Mucin 1, cell surface associated (MUC1); epidermal growth factor receptor (EGFR); neural cell adhesion molecule (NCAM); Prostase; prostatic acid phosphatase (PAP); elongation factor 2 mutated (ELF2M); Ephrin B2; fibroblast activation protein alpha (FAP); insulin-like growth factor 1 receptor (IGF-I receptor), carbonic anhydrase IX (CAIX); Proteasome (Prosome, Macropain) Subunit, Beta Type, 9 (LMP2); glycoprotein 100 (gp100); oncogene fusion protein consisting of breakpoint cluster region (BCR) and Abelson murine leukemia viral oncogene homolog 1 (Abl) (bcr-abl); tyrosinase; ephrin type-A receptor 2 (EphA2); Fucosyl GM1; sialyl Lewis adhesion molecule (sLe); ganglioside GM3 (aNeu5Ac(2-3)bDGalp(1-4)bDGlcp(1-1)Cer); transglutaminase 5 (TGS5); high molecular weight-melanoma-associated antigen (HMWMAA); o-acetyl-GD2 ganglioside (OAcGD2); Folate receptor beta; tumor endothelial marker 1 (TEM1/CD248); tumor endothelial marker 7-related (TEM7R); claudin 6 (CLDN6); thyroid stimulating hormone receptor (TSHR); G protein-coupled receptor class C group 5, member D (GPRC5D); chromosome X open reading frame 61 (CXORF61); CD97; CD179a; anaplastic lymphoma kinase (ALK); Polysialic acid; placenta-specific 1 (PLAC1); hexasaccharide portion of globoH glycoceramide (GloboH); mammary gland differentiation antigen (NY-BR-1); uroplakin 2 (UPK2); Hepatitis A virus cellular receptor 1 (HAVCR1); adrenoceptor beta 3 (ADRB3); pannexin 3 (PANX3); G protein-coupled receptor 20 (GPR20); lymphocyte antigen 6 complex, locus K 9 (LY6K); Olfactory receptor 51E2 (OR51E2); TCR Gamma Alternate Reading Frame Protein (TARP); Wilms tumor protein (WT1); Cancer/testis antigen 1 (NY-ESO-1); Cancer/testis antigen 2 (LAGE-1a); Melanoma-associated antigen 1 (MAGE-A1); ETS translocation-variant gene 6, located on chromosome 12p (ETV6-AML); sperm protein 17 (SPA17); X Antigen Family, Member 1A (XAGE1); angiopoietin-binding cell surface receptor 2 (Tie 2); melanoma cancer testis antigen-1 (MAD-CT-1); melanoma cancer testis antigen-2 (MAD-CT-2); Fos-related antigen 1; tumor protein p53 (p53); p53 mutant; prostein; surviving; telomerase; prostate carcinoma tumor antigen-1 (PCTA-1 or Galectin 8), melanoma antigen recognized by T cells 1 (MelanA or MART1); Rat sarcoma (Ras) mutant; human Telomerase reverse transcriptase (hTERT); sarcoma translocation breakpoints; melanoma inhibitor of apoptosis (ML-IAP); ERG (transmembrane protease, serine 2 (TMPRSS2) ETS fusion gene); N-Acetyl glucosaminyl-transferase V (NA17); paired box protein Pax-3 (PAX3); Androgen receptor; Cyclin B1; v-myc avian myelocytomatosis viral oncogene neuroblastoma derived homolog (MYCN); Ras Homolog Family Member C (RhoC); Tyrosinase-related protein 2

(TRP-2); Cytochrome P450 1B1 (CYP1B1); CCCTC-Binding Factor (Zinc Finger Protein)-Like (BORIS or Brother of the Regulator of Imprinted Sites), Squamous Cell Carcinoma Antigen Recognized By T Cells 3 (SART3); Paired box protein Pax-5 (PAX5); proacrosin binding protein sp32 (OY-TES1); lymphocyte-specific protein tyrosine kinase (LCK); A kinase anchor protein 4 (AKAP-4); synovial sarcoma, X breakpoint 2 (SSX2); Receptor for Advanced Glycation Endproducts (RAGE-1); renal ubiquitous 1 (RU1); renal ubiquitous 2 (RU2); legumain; human papilloma virus E6 (HPV E6); human papilloma virus E7 (HPV E7); intestinal carboxyl esterase; heat shock protein 70-2 mutated (mut hsp70-2); CD79a; CD79b; CD72; Leukocyte-associated immunoglobulin-like receptor 1 (LAIR1); Fc fragment of IgA receptor (FCAR or CD89); Leukocyte immunoglobulin-like receptor subfamily A member 2 (LILRA2); CD300 molecule-like family member f (CD300LF); C-type lectin domain family 12 member A (CLEC12A); bone marrow stromal cell antigen 2 (BST2); EGF-like module-containing mucin-like hormone receptor-like 2 (EMR2); lymphocyte antigen 75 (LY75); Glypican-3 (GPC3); Fc receptor-like 5 (FCRL5); and immunoglobulin lambda-like polypeptide 1 (IGLL1).

Bispecific CARs

In an embodiment, a multispecific antibody molecule is a bispecific antibody molecule. A bispecific antibody has specificity for no more than two antigens. A bispecific antibody molecule is characterized by a first immunoglobulin variable domain sequence which has binding specificity for a first epitope and a second immunoglobulin variable domain sequence that has binding specificity for a second epitope. In an embodiment the first and second epitopes are on the same antigen, e.g., the same protein (or subunit of a multimeric protein). In an embodiment the first and second epitopes overlap. In an embodiment the first and second epitopes do not overlap. In an embodiment the first and second epitopes are on different antigens, e.g., different proteins (or different subunits of a multimeric protein). In an embodiment a bispecific antibody molecule comprises a heavy chain variable domain sequence and a light chain variable domain sequence which have binding specificity for a first epitope and a heavy chain variable domain sequence and a light chain variable domain sequence which have binding specificity for a second epitope. In an embodiment a bispecific antibody molecule comprises a half antibody having binding specificity for a first epitope and a half antibody having binding specificity for a second epitope. In an embodiment a bispecific

antibody molecule comprises a half antibody, or fragment thereof, having binding specificity for a first epitope and a half antibody, or fragment thereof, having binding specificity for a second epitope. In an embodiment a bispecific antibody molecule comprises a scFv, or fragment thereof, have binding specificity for a first epitope and a scFv, or fragment thereof, have binding specificity for a second epitope.

In certain embodiments, the antibody molecule is a multi-specific (e.g., a bispecific or a trispecific) antibody molecule. Protocols for generating bispecific or heterodimeric antibody molecules, and various configurations for bispecific antibody molecules, are described in, e.g., paragraphs 455-458 of WO2015/142675, filed March 13, 2015, which is incorporated by reference in its entirety.

In one aspect, the bispecific antibody molecule is characterized by a first immunoglobulin variable domain sequence, e.g., a scFv, which has binding specificity for CD19, e.g., comprises a scFv as described herein, or comprises the light chain CDRs and/or heavy chain CDRs from a scFv described herein, and a second immunoglobulin variable domain sequence that has binding specificity for a second epitope on a different antigen.

Chimeric TCR

In one aspect, the antibodies and antibody fragments of the present invention (e.g., CD19 antibodies and fragments) can be grafted to one or more constant domain of a T cell receptor ("TCR") chain, for example, a TCR alpha or TCR beta chain, to create a chimeric TCR. Without being bound by theory, it is believed that chimeric TCRs will signal through the TCR complex upon antigen binding. For example, an scFv as disclosed herein, can be grafted to the constant domain, e.g., at least a portion of the extracellular constant domain, the transmembrane domain and the cytoplasmic domain, of a TCR chain, for example, the TCR alpha chain and/or the TCR beta chain. As another example, an antibody fragment, for example a VL domain as described herein, can be grafted to the constant domain of a TCR alpha chain, and an antibody fragment, for example a VH domain as described herein, can be grafted to the constant domain of a TCR beta chain (or alternatively, a VL domain may be grafted to the constant domain of the TCR beta chain and a VH domain may be grafted to a TCR alpha chain). As another example, the CDRs of an antibody or antibody fragment may be grafted into a TCR alpha and/or beta chain to create a chimeric TCR. For example, the LCDRs

disclosed herein may be grafted into the variable domain of a TCR alpha chain and the HCDRs disclosed herein may be grafted to the variable domain of a TCR beta chain, or vice versa. Such chimeric TCRs may be produced, e.g., by methods known in the art (For example, Willemsen RA et al, Gene Therapy 2000; 7: 1369–1377; Zhang T et al, Cancer Gene Ther 2004; 11: 487–496; Aggen et al, Gene Ther. 2012 Apr;19(4):365-74).

Non-Antibody Scaffolds

In embodiments, the antigen binding domain comprises a non-antibody scaffold, e.g., a fibronectin, ankyrin, domain antibody, lipocalin, small modular immuno-pharmaceutical, maxybody, Protein A, or affilin. The non-antibody scaffold has the ability to bind to target antigen on a cell. In embodiments, the antigen binding domain is a polypeptide or fragment thereof of a naturally occurring protein expressed on a cell. In some embodiments, the antigen binding domain comprises a non-antibody scaffold. A wide variety of non-antibody scaffolds can be employed so long as the resulting polypeptide includes at least one binding region which specifically binds to the target antigen on a target cell.

Non-antibody scaffolds include: fibronectin (Novartis, MA), ankyrin (Molecular Partners AG, Zurich, Switzerland), domain antibodies (Domantis, Ltd., Cambridge, MA, and Ablynx nv, Zwijnaarde, Belgium), lipocalin (Pieris Proteolab AG, Freising, Germany), small modular immuno-pharmaceuticals (Trubion Pharmaceuticals Inc., Seattle, WA), maxybodies (Avidia, Inc., Mountain View, CA), Protein A (Affibody AG, Sweden), and affilin (gamma-crystallin or ubiquitin) (Scil Proteins GmbH, Halle, Germany).

In an embodiment the antigen binding domain comprises the extracellular domain, or a counter-ligand binding fragment thereof, of molecule that binds a counterligand on the surface of a target cell.The immune effector cells can comprise a recombinant DNA construct comprising sequences encoding a CAR, wherein the CAR comprises an antigen binding domain (e.g., antibody or antibody fragment, TCR or TCR fragment) that binds specifically to a tumor antigen, e.g., an tumor antigen described herein, and an intracellular signaling domain. The intracellular signaling domain can comprise a costimulatory signaling domain and/or a primary signaling domain, e.g., a zeta chain. As described elsewhere, the methods described herein can include transducing a cell, e.g., from the population of T regulatory-depleted cells, with a nucleic acid encoding a CAR, e.g., a CAR described herein.

In specific aspects, a CAR comprises a scFv domain, wherein the scFv may be preceded by an optional leader sequence such as provided in SEQ ID NO: 1, and followed by an optional hinge sequence such as provided in SEQ ID NO:2 or SEQ ID NO:36 or SEQ ID NO:23, a transmembrane region such as provided in SEQ ID NO:6, an intracellular signalling domain that includes SEQ ID NO:7 or SEQ ID NO:16 and a CD3 zeta sequence that includes SEQ ID NO:9 or SEQ ID NO:10, e.g., wherein the domains are contiguous with and in the same reading frame to form a single fusion protein.

In one aspect, an exemplary CAR constructs comprise an optional leader sequence (e.g., a leader sequence described herein), an extracellular antigen binding domain (e.g., an antigen binding domain described herein), a hinge (e.g., a hinge region described herein), a transmembrane domain (e.g., a transmembrane domain described herein), and an intracellular stimulatory domain (e.g., an intracellular stimulatory domain described herein). In one aspect, an exemplary CAR construct comprises an optional leader sequence (e.g., a leader sequence described herein), an extracellular antigen binding domain (e.g., an antigen binding domain described herein), a hinge (e.g., a hinge region described herein), a transmembrane domain (e.g., a transmembrane domain described herein), an intracellular costimulatory signaling domain (e.g., a costimulatory signaling domain described herein) and/or an intracellular primary signaling domain (e.g., a primary signaling domain described herein).

An exemplary leader sequence is provided as SEQ ID NO: 1. An exemplary hinge/spacer sequence is provided as SEQ ID NO: 2 or SEQ ID NO:36 or SEQ ID NO:23. An exemplary transmembrane domain sequence is provided as SEQ ID NO:6. An exemplary sequence of the intracellular signaling domain of the 4-1BB protein is provided as SEQ ID NO: 7. An exemplary sequence of the intracellular signaling domain of CD27 is provided as SEQ ID NO:16. An exemplary CD3zeta domain sequence is provided as SEQ ID NO: 9 or SEQ ID NO:10.

In one aspect, the immune effector cell comprises a recombinant nucleic acid construct comprising a nucleic acid molecule encoding a CAR, wherein the nucleic acid molecule comprises a nucleic acid sequence encoding an antigen binding domain, wherein the sequence is contiguous with and in the same reading frame as the nucleic acid sequence encoding an intracellular signaling domain. An exemplary intracellular signaling domain that can be used in the CAR includes, but is not limited to, one or more intracellular signaling domains of, e.g.,

CD3-zeta, CD28, CD27, 4-1BB, and the like. In some instances, the CAR can comprise any combination of CD3-zeta, CD28, 4-1BB, and the like.

The nucleic acid sequences coding for the desired molecules can be obtained using recombinant methods known in the art, such as, for example by screening libraries from cells expressing the nucleic acid molecule, by deriving the nucleic acid molecule from a vector known to include the same, or by isolating directly from cells and tissues containing the same, using standard techniques. Alternatively, the nucleic acid of interest can be produced synthetically, rather than cloned.

Nucleic acids encoding a CAR can be introduced into the immune effector cells using, e.g., a retroviral or lentiviral vector construct.

Nucleic acids encoding a CAR can also be introduced into the immune effector cell using, e.g., an RNA construct that can be directly transfected into a cell. A method for generating mRNA for use in transfection involves *in vitro* transcription (IVT) of a template with specially designed primers, followed by polyA addition, to produce a construct containing 3' and 5' untranslated sequence ("UTR") (e.g., a 3' and/or 5' UTR described herein), a 5' cap (e.g., a 5' cap described herein) and/or Internal Ribosome Entry Site (IRES) (e.g., an IRES described herein), the nucleic acid to be expressed, and a polyA tail, typically 50-2000 bases in length (e.g., described herein, e.g., SEQ ID NO:35). RNA so produced can efficiently transfect different kinds of cells. In one embodiment, the template includes sequences for the CAR. In an embodiment, an RNA CAR vector is transduced into a cell, e.g., a T cell by electroporation.

Antigen binding domain

In one aspect, a plurality of the immune effector cells, e.g., the population of T regulatory-depleted cells, include a nucleic acid encoding a CAR that comprises a target-specific binding element otherwise referred to as an antigen binding domain. The choice of binding element depends upon the type and number of ligands that define the surface of a target cell. For example, the antigen binding domain may be chosen to recognize a ligand that acts as a cell surface marker on target cells associated with a particular disease state. Thus, examples of cell surface markers that may act as ligands for the antigen binding domain in a CAR

described herein include those associated with viral, bacterial and parasitic infections, autoimmune disease and cancer cells.

In one aspect, the portion of the CAR comprising the antigen binding domain comprises an antigen binding domain that targets a tumor antigen, e.g., a tumor antigen described herein.

The antigen binding domain can be any domain that binds to the antigen including but not limited to a monoclonal antibody, a polyclonal antibody, a recombinant antibody, a human antibody, a humanized antibody, and a functional fragment thereof, including but not limited to a single-domain antibody such as a heavy chain variable domain (VH), a light chain variable domain (VL) and a variable domain (VHH) of camelid derived nanobody, and to an alternative scaffold known in the art to function as antigen binding domain, such as a recombinant fibronectin domain, a T cell receptor (TCR), or a fragment there of, e.g., single chain TCR, and the like. In some instances, it is beneficial for the antigen binding domain to be derived from the same species in which the CAR will ultimately be used in. For example, for use in humans, it may be beneficial for the antigen binding domain of the CAR to comprise human or humanized residues for the antigen binding domain of an antibody or antibody fragment.

In an embodiment, the antigen binding domain comprises an anti-CD19 antibody, or fragment thereof, e.g., an scFv. For example, the antigen binding domain comprises a variable heavy chain and a variable light chain listed in **Table 1**. The linker sequence joining the variable heavy and variable light chains can be, e.g., any of the linker sequences described herein, or alternatively, can be GSTSGSGKPGSGEGSTKG (SEQ ID NO:104).

Table 1: Anti-CD19 antibody binding domains

			SEQ ID NO:
CD19	huscFv1	EIVMTQSPATLSLSPGERATLSCRASQDISKYLNWYQQKPGQA PRLLIYHTSRLHSGIPARFSGSGSGTDYTLTISSLQPEDFAVY FCQQGNTLPYTFGQGTKLEIKGGGGSGGGGSGGGGSQVQLQES GPGLVKPSETLSLTCTVSGVSLPDYGVSWIRQPPGKGLEWIGV IWGSETTYYSSSLKSRVTISKDNSKNQVSLKLSSVTAADTAVY YCAKHYYYGGSYAMDYWGQGTLVTVSS	107
CD19	huscFv2	Eivmtqspatlslspgeratlscrasqdiskylnwyqqkpgqaprll iyhtsrlhsgiparfsgsgsgtdytltisslqpedfavyfcqqgntl pytfgqgtkleikggggsggggsggggsqvqlqesgpglvkpsetls ltctvsgvslpdygvswirqppgkglewigviwgsettyyqsslksr vtiskdnsknqvslklssvtaadtavyycakhyyyggsyamdywgqg tlvtvss	108
CD19	huscFv3	Qvqlqesgpglvkpsetlsltctvsgvslpdygvswirqppgkglew igviwgsettyyssslksrvtiskdnsknqvslklssvtaadtavyy	109

		cakhyyyggsyamdywgqgtlvtvssggggsggggsggggseivmtq spatlslspgeratlscrasqdiskylnwyqqkpgqaprlliyhtsr lhsgiparfsgsgsgtdytltisslqpedfavyfcqqgntlpytfgq gtkleik	
CD19	huscFv4	Qvqlqesgpglvkpsetlsltctvsgvslpdygvswirqppgkglew igviwgsettyyqsslksrvtiskdnsknqvslklssvtaadtavyy cakhyyyggsyamdywgqgtlvtvssggggsggggsggggseivmtq spatlslspgeratlscrasqdiskylnwyqqkpgqaprlliyhtsr lhsgiparfsgsgsgtdytltisslqpedfavyfcqqgntlpytfgq gtkleik	110
CD19	huscFv5	Eivmtqspatlslspgeratlscrasqdiskylnwyqqkpgqaprll iyhtsrlhsgiparfsgsgsgtdytltisslqpedfavyfcqqgntl pytfgqgtkleikggggsggggsggggsggggsqvqlqesgpglvkp setlsltctvsgvslpdygvswirqppgkglewigviwgsettyyss slksrvtiskdnsknqvslklssvtaadtavyycakhyyyggsyamd ywgqgtlvtvss	111
CD19	huscFv6	Eivmtqspatlslspgeratlscrasqdiskylnwyqqkpgqaprll iyhtsrlhsgiparfsgsgsgtdytltisslqpedfavyfcqqgntl pytfgqgtkleikggggsggggsggggsggggsqvqlqesgpglvkp setlsltctvsgvslpdygvswirqppgkglewigviwgsettyyqs slksrvtiskdnsknqvslklssvtaadtavyycakhyyyggsyamd ywgqgtlvtvss	112
CD19	huscFv7	Qvqlqesgpglvkpsetlsltctvsgvslpdygvswirqppgkglew igviwgsettyyssslksrvtiskdnsknqvslklssvtaadtavyy cakhyyyggsyamdywgqgtlvtvssggggsggggsggggsggggse ivmtqspatlslspgeratlscrasqdiskylnwyqqkpgqaprlli yhtsrlhsgiparfsgsgsgtdytltisslqpedfavyfcqqgntlp ytfgqgtkleik	113
CD19	huscFv8	Qvqlqesgpglvkpsetlsltctvsgvslpdygvswirqppgkglew igviwgsettyyqsslksrvtiskdnsknqvslklssvtaadtavyy cakhyyyggsyamdywgqgtlvtvssggggsggggsggggsggggse ivmtqspatlslspgeratlscrasqdiskylnwyqqkpgqaprlli yhtsrlhsgiparfsgsgsgtdytltisslqpedfavyfcqqgntlp ytfgqgtkleik	114
CD19	huscFv9	Eivmtqspatlslspgeratlscrasqdiskylnwyqqkpgqaprll iyhtsrlhsgiparfsgsgsgtdytltisslqpedfavyfcqqgntl pytfgqgtkleikggggsggggsggggsggggsqvqlqesgpglvkp setlsltctvsgvslpdygvswirqppgkglewigviwgsettyyns slksrvtiskdnsknqvslklssvtaadtavyycakhyyyggsyamd ywgqgtlvtvss	115
CD19	Hu scFv10	Qvqlqesgpglvkpsetlsltctvsgvslpdygvswirqppgkglew igviwgsettyynsslksrvtiskdnsknqvslklssvtaadtavyy cakhyyyggsyamdywgqgtlvtvssggggsggggsggggsggggse ivmtqspatlslspgeratlscrasqdiskylnwyqqkpgqaprlli yhtsrlhsgiparfsgsgsgtdytltisslqpedfavyfcqqgntlp ytfgqgtkleik	116
CD19	Hu scFv11	Eivmtqspatlslspgeratlscrasqdiskylnwyqqkpgqaprll iyhtsrlhsgiparfsgsgsgtdytltisslqpedfavyfcqqgntl pytfgqgtkleikggggsggggsggggsqvqlqesgpglvkpsetls ltctvsgvslpdygvswirqppgkglewigviwgsettyynsslksr vtiskdnsknqvslklssvtaadtavyycakhyyyggsyamdywgqg tlvtvss	117
CD19	Hu scFv12	Qvqlqesgpglvkpsetlsltctvsgvslpdygvswirqppgkglew igviwgsettyynsslksrvtiskdnsknqvslklssvtaadtavyy cakhyyyggsyamdywgqgtlvtvssggggsggggsggggseivmtq spatlslspgeratlscrasqdiskylnwyqqkpgqaprlliyhtsr lhsgiparfsgsgsgtdytltisslqpedfavyfcqqgntlpytfgq	118

		gtkleik	
CD19	muCTL 019 scFv	Diqmtqttsslsaslgdrvtiscrasqdiskylnwyqqkpdgtvkll iyhtsrlhsgvpsrfsgsgsgtdysltisnleqediatyfcqqgntl pytfgggtkleitggggsggggsggggsevklqesgpglvapsqsls vtctvsgvslpdygvswirqpprkglewlgviwgsettyynsalksr ltiikdnsksqvflkmnslqtddtaiyycakhyyyggsyamdywgqg tsvtvss	119

Antibody	VH Sequence	VL Sequence
SSJ25-C1	QVQLLESGAELVRPGSSVKISCKASGYAFSS YWMNWVKQRPGQGLEWIGQIYPGDGDTNYNG KFKGQATLTADKSSSTAYMQLSGLTSEDSAV YSCARKTISSVVDFYFDYWGQGTTVT	ELVLTQSPKFMSTSVGDRVSVTCKASQNVGT NVAWYQQKPGQSPKPLIYSATYRNSGVPDRF TGSGSGTDFTLTITNVQSKDLADYFYFCQYN RYPYTSGGGTKLEIKRRS
SEQ ID NO:	120	121

CD19 CAR constructs containing humanized anti-CD19 scFv domains are described in PCT publication WO 2014/153270, incorporated herein by reference.

The sequences of murine and humanized CDR sequences of the anti-CD19 scFv domains are shown in **Table 2** for the heavy chain variable domains and in **Table 3** for the light chain variable domains. "ID" stands for the respective SEQ ID NO for each CDR.

Table 2. Heavy Chain Variable Domain CDRs (Kabat) of CD19 Antibodies

Candidate	FW	HCDR1	ID	HCDR2	ID	HCDR3	ID
murine_CART19		DYGVS	122	VIWGSETTYYNSALKS	123	HYYYGGSYAMDY	127
humanized_CART19 a	VH4	DYGVS	122	VIWGSETTYY*S*S*S*LKS	124	HYYYGGSYAMDY	127
humanized_CART19 b	VH4	DYGVS	122	VIWGSETTYY*Q*S*S*LKS	125	HYYYGGSYAMDY	127
humanized_CART19 c	VH4	DYGVS	122	VIWGSETTYYNS*S*LKS	126	HYYYGGSYAMDY	127

Table 3 Light Chain Variable Domain CDRs (Kabat) of CD19 Antibodies

Candidate	FW	LCDR1	ID	LCDR2	ID	LCDR3	ID
murine_CART19		RASQDISKYLN	128	HTSRLHS	129	QQGNTLPYT	130
humanized_CART19 a	VK3	RASQDISKYLN	128	HTSRLHS	129	QQGNTLPYT	130
humanized_CART19 b	VK3	RASQDISKYLN	128	HTSRLHS	129	QQGNTLPYT	130
humanized_CART19 c	VK3	RASQDISKYLN	128	HTSRLHS	129	QQGNTLPYT	130

Any known CD19 CAR, e.g., the CD19 antigen binding domain of any known CD19 CAR, in the art can be used in accordance with the present disclosure. For example, LG-740; CD19 CAR described in the US Pat. No. 8,399,645; US Pat. No. 7,446,190; Xu et al., Leuk Lymphoma. 2013 54(2):255-260(2012); Cruz et al., Blood 122(17):2965-2973 (2013); Brentjens et al., Blood, 118(18):4817-4828 (2011); Kochenderfer et al., Blood 116(20):4099-102 (2010); Kochenderfer et al., Blood 122 (25):4129-39(2013); and 16th Annu Meet Am Soc Gen Cell Ther (ASGCT) (May 15-18, Salt Lake City) 2013, Abst 10.

Exemplary target antigens that can be targeted using the CAR-expressing cells, include, but are not limited to, CD19, CD123, EGFRvIII, CD33, mesothelin, BCMA, and GFR ALPHA-4, among others, as described in, for example, WO2014/153270, WO 2014/130635, WO2016/028896, WO 2014/130657, WO2016/014576, WO 2015/090230, WO2016/014565, WO2016/014535, and WO2016/025880, each of which is herein incorporated by reference in its entirety.

In one embodiment, the CAR T cell that specifically binds to CD19 has the USAN designation TISAGENLECLEUCEL-T. CTL019 is made by a gene modification of T cells is mediated by stable insertion via transduction with a self-inactivating, replication deficient Lentiviral (LV) vector containing the CTL019 transgene under the control of the EF-1 alpha promoter. CTL019 can be a mixture of transgene positive and negative T cells that are delivered to the subject on the basis of percent transgene positive T cells.

In other embodiments, the CAR-expressing cells can specifically bind to humanized CD19, *e.g.,* can include a CAR molecule, or an antigen binding domain (*e.g.*, a humanized antigen binding domain) according to Table 3 of WO2014/153270, incorporated herein by reference. The amino acid and nucleotide sequences encoding the CD19 CAR molecules and antigen binding domains (*e.g.*, including one, two, three VH CDRs; and one, two, three VL CDRs according to Kabat or Chothia), as specified in WO2014/153270, are provided in Table 1 and in the Sequence Listing submitted herewith. Amino and nucleotide sequences identical and substantially identical to the aforesaid sequences provided in the Sequence Listing are specifically incorporated into the instant specification.

In other embodiments, the CAR-expressing cells can specifically bind to CD123, *e.g.,* can include a CAR molecule (*e.g.,* any of the CAR1 to CAR8), or an antigen binding domain according to Tables 1-2 of WO 2014/130635, incorporated herein by reference. The amino

acid and nucleotide sequences encoding the CD123 CAR molecules and antigen binding domains (*e.g.*, including one, two, three VH CDRs; and one, two, three VL CDRs according to Kabat or Chothia), as specified in WO 2014/130635, are provided in the Sequence Listing submitted herewith. Amino and nucleotide sequences identical and substantially identical to the aforesaid sequences provided in the Sequence Listing are specifically incorporated into the instant specification.

In certain embodiments, the CAR molecule or antigen binding domain comprises an amino acid sequence, or is encoded by a nucleotide sequence, according to any of SEQ ID NOs: 142-193, or a sequence substantially identical thereto.

In some embodiments, the CAR molecule or antigen binding domain comprises one or more (*e.g.*, 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 147 (*e.g.*, amino acid residues 45-59, 75-81, 114-122, 183-187, 202-218, and/or 251-259 of SEQ ID NO: 147). In some embodiments, the CAR molecule or antigen binding domain comprises one or more (*e.g.*, 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 153 (*e.g.*, amino acid residues 45-59, 75-81, 114-122, 183-187, 202-218, and/or 251-259 of SEQ ID NO: 153). In some embodiments, the CAR molecule or antigen binding domain comprises one or more (*e.g.*, 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 159 (*e.g.*, amino acid residues 45-59, 75-81, 114-122, 183-187, 202-218, and/or 251-259 of SEQ ID NO: 159). In some embodiments, the CAR molecule or antigen binding domain comprises one or more (*e.g.*, 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 165 (*e.g.*, amino acid residues 45-59, 75-81, 114-122, 183-187, 202-218, and/or 251-259 of SEQ ID NO: 165). In some embodiments, the CAR molecule or antigen binding domain comprises one or more (*e.g.*, 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 171 (*e.g.*, amino acid residues 52-56, 71-87, 120-128, 183-197, 213-219, and/or 252-260 of SEQ ID NO: 171). In some embodiments, the CAR molecule or antigen binding domain comprises one or more (*e.g.*, 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 177 (*e.g.*, amino acid residues 52-56, 71-87, 120-128, 183-197, 213-219, and/or 252-260 of SEQ ID NO: 177). In some embodiments, the CAR molecule or antigen binding domain comprises one or more (*e.g.*, 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 183 (*e.g.*, amino acid residues 52-56, 71-87, 120-128, 183-197, 213-219, and/or 252-260 of SEQ ID NO: 183). In some embodiments, the CAR molecule or antigen binding domain comprises one or more (*e.g.*, 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 189 (*e.g.*,

amino acid residues 52-56, 71-87, 120-128, 183-197, 213-219, and/or 252-260 of SEQ ID NO: 189). In some embodiments, the CAR molecule or antigen binding domain comprises one or more (*e.g.,* 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 191 (*e.g.,* amino acid residues 47-61, 77-83, 116-124, 180-184, 199-215, and/or 248-256 of SEQ ID NO: 191). In some embodiments, the CAR molecule or antigen binding domain comprises one or more (*e.g.,* 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 193 (*e.g.,* amino acid residues 54-58, 73-89, 122-127, 177-187, 203-209, and/or 242-250 of SEQ ID NO: 193).

In other embodiments, the CAR-expressing cells can specifically bind to CD123, *e.g.,* can include a CAR molecule (*e.g.,* any of the CAR123-1 ro CAR123-4 and hzCAR123-1 to hzCAR123-32), or an antigen binding domain according to Tables 2, 6, and 9 of WO2016/028896, incorporated herein by reference. The amino acid and nucleotide sequences encoding the CD123 CAR molecules and antigen binding domains (*e.g.*, including one, two, three VH CDRs; and one, two, three VL CDRs according to Kabat or Chothia), as specified in WO2016/028896, are provided in the Sequence Listing submitted herewith. Amino and nucleotide sequences identical and substantially identical to the aforesaid sequences provided in the Sequence Listing are specifically incorporated into the instant specification.

In certain embodiments, the CAR molecule or antigen binding domain comprises an amino acid sequence, or is encoded by a nucleotide sequence, according to any of SEQ ID NOs: 194-413, or a sequence substantially identical thereto.

In other embodiments, the CAR-expressing cells can specifically bind to EGFRvIII, *e.g.,* can include a CAR molecule, or an antigen binding domain according to Table 2 or SEQ ID NO:11 of WO 2014/130657, incorporated herein by reference. The amino acid and nucleotide sequences encoding the EGFRvIII CAR molecules and antigen binding domains (*e.g.*, including one, two, three VH CDRs; and one, two, three VL CDRs according to Kabat or Chothia), as specified in WO 2014/130657, are provided in the Sequence Listing submitted herewith. Amino and nucleotide sequences identical and substantially identical to the aforesaid sequences provided in the Sequence Listing are specifically incorporated into the instant specification.

In certain embodiments, the CAR molecule or antigen binding domain comprises an amino acid sequence, or is encoded by a nucleotide sequence, according to any of SEQ ID NOs: 414-474, or a sequence substantially identical thereto.

In certain embodiments, the CAR molecule or antigen binding domain comprises a leader sequence, *e.g.,* amino acid residues 1-21 of SEQ ID NOs: 418, 424, 430, 436, 442, 448, 454, 460, 466, or 472. In other embodiments, the CAR molecule or antigen binding domain comprises a polyhistidine tag sequence, *e.g.,* amino acid residues 268-277 of SEQ ID NOs: 418, 424, 430, 436, 442, 448, 454, or 460, amino acid residues 265-274 of SEQ ID NO: 466, or amino acid residues 262-269 of SEQ ID NO: 472.

In some embodiments, the CAR molecule or antigen binding domain comprises one or more (*e.g.,* 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 420 (*e.g.,* amino acid residues 52-56, 71-87, 120-123, 179-194, 210-216, and/or 249-257 of SEQ ID NO: 420). In some embodiments, the CAR molecule or antigen binding domain comprises one or more (*e.g.,* 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 426 (*e.g.,* amino acid residues 45-60, 76-82, 115-123, 184-188, 203-219, and/or 251-256 of SEQ ID NO: 426). In some embodiments, the CAR molecule or antigen binding domain comprises one or more (*e.g.,* 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 432 (*e.g.,* amino acid residues 52-56, 71-87, 120-124, 179-194, 210-216, and/or 249-257 of SEQ ID NO: 432). In some embodiments, the CAR molecule or antigen binding domain comprises one or more (*e.g.,* 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 438 (*e.g.,* amino acid residues 45-60, 76-82, 115-123, 184-188, 203-219, and/or 252-256 of SEQ ID NO: 438). In some embodiments, the CAR molecule or antigen binding domain comprises one or more (*e.g.,* 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 444 (*e.g.,* amino acid residues 52-56, 71-87, 120-124, 179-194, 210-216, and/or 249-257 of SEQ ID NO: 444). In some embodiments, the CAR molecule or antigen binding domain comprises one or more (*e.g.,* 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 450 (*e.g.,* amino acid residues 52-56, 71-87, 120-124, 179-194, 210-216, and/or 249-257 of SEQ ID NO: 450). In some embodiments, the CAR molecule or antigen binding domain comprises one or more (*e.g.,* 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 456 (*e.g.,* amino acid residues 45-60, 76-82, 115-123, 184-188, 203-219, and/or 252-256 of SEQ ID NO: 456). In some embodiments, the CAR molecule or antigen binding domain comprises one or more (*e.g.,* 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 462 (*e.g.,* amino acid residues 45-60, 76-82, 115-123, 184-188, 203-219, and/or 252-256 of SEQ ID NO: 462). In some embodiments, the CAR molecule or antigen binding domain comprises one or more (*e.g.,* 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 468 (*e.g.,*

amino acid residues 52-56, 71-87, 119-124, 176-191, 207-213, and/or 246-254 of SEQ ID NO: 468).

In other embodiments, the CAR-expressing cells can specifically bind to CD33, *e.g.*, can include a CAR molecule (e.g., any of CAR33-1 to CAR-33-9), or an antigen binding domain according to Table 2 or 9 of WO2016/014576, incorporated herein by reference. The amino acid and nucleotide sequences encoding the CD33 CAR molecules and antigen binding domains (*e.g.*, including one, two, three VH CDRs; and one, two, three VL CDRs according to Kabat or Chothia), as specified in WO2016/014576, are provided in the Sequence Listing submitted herewith. Amino and nucleotide sequences identical and substantially identical to the aforesaid sequences provided in the Sequence Listing are specifically incorporated into the instant specification.

In certain embodiments, the CAR molecule or antigen binding domain comprises an amino acid sequence, or is encoded by a nucleotide sequence, according to any of SEQ ID NOs: 475-533, or a sequence substantially identical thereto. In other embodiments, the CAR-expressing cells can specifically bind to mesothelin, *e.g.*, can include a CAR molecule, or an antigen binding domain according to Tables 2-3 of WO 2015/090230, incorporated herein by reference. The amino acid and nucleotide sequences encoding the mesothelin CAR molecules and antigen binding domains (*e.g.*, including one, two, three VH CDRs; and one, two, three VL CDRs according to Kabat or Chothia), as specified in WO 2015/090230, are provided in the Sequence Listing submitted herewith. Amino and nucleotide sequences identical and substantially identical to the aforesaid sequences provided in the Sequence Listing are specifically incorporated into the instant specification.

In certain embodiments, the CAR molecule or antigen binding domain comprises an amino acid sequence, or is encoded by a nucleotide sequence, according to any of SEQ ID NOs: 534-625, or a sequence substantially identical thereto.

In some embodiments, the CAR molecule or antigen binding domain comprises one or more (*e.g.*, 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 534 (*e.g.*, amino acid residues 26-35, 50-66, 99-106, 161-171, 187-193, and/or 226-234 of SEQ ID NO: 534). In some embodiments, the CAR molecule or antigen binding domain comprises one or more (*e.g.*, 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 535 (*e.g.*, amino acid residues 47-56, 71-87, 120-127, 182-192, 208-214, and/or 247-255 of SEQ ID NO: 535). In some embodiments, the CAR molecule or antigen binding domain comprises one or

more (*e.g.*, 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 536 (*e.g.*, amino acid residues 26-35, 50-66, 99-115, 170-180, 196-202, and/or 235-243 of SEQ ID NO: 536). In some embodiments, the CAR molecule or antigen binding domain comprises one or more (*e.g.*, 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 537 (*e.g.*, amino acid residues 47-56, 71-87, 120-136, 191-201, 217-223, and/or 256-264 of SEQ ID NO: 537). In some embodiments, the CAR molecule or antigen binding domain comprises one or more (*e.g.*, 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 538 (*e.g.*, amino acid residues 26-35, 50-66, 99-109, 164-174, 190-196, and/or 229-236 of SEQ ID NO: 538). In some embodiments, the CAR molecule or antigen binding domain comprises one or more (*e.g.*, 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 539 (*e.g.*, amino acid residues 47-56, 71-87, 120-130, 185-195, 211-217, and/or 250-257 of SEQ ID NO: 539). In some embodiments, the CAR molecule or antigen binding domain comprises one or more (*e.g.*, 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 540 (*e.g.*, amino acid residues 26-35, 50-66, 99-103, 158-168, 184-189, and/or 223-232 of SEQ ID NO: 540). In some embodiments, the CAR molecule or antigen binding domain comprises one or more (*e.g.*, 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 541 (*e.g.*, amino acid residues 47-56, 71-87, 120-124, 179-189, 205-210, and/or 244-253 of SEQ ID NO: 541). In some embodiments, the CAR molecule or antigen binding domain comprises one or more (*e.g.*, 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 542 (*e.g.*, amino acid residues 26-35, 50-65, 99-104, 159-169, 185-191, and/or 224-231 of SEQ ID NO: 542). In some embodiments, the CAR molecule or antigen binding domain comprises one or more (*e.g.*, 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 543 (*e.g.*, amino acid residues 47-56, 71-86, 120-125, 180-190, 206-212, and/or 245-252 of SEQ ID NO: 543). In some embodiments, the CAR molecule or antigen binding domain comprises one or more (*e.g.*, 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 544 (*e.g.*, amino acid residues 26-35, 50-66, 99-115, 170-180, 196-202, and/or 235-243 of SEQ ID NO: 544). In some embodiments, the CAR molecule or antigen binding domain comprises one or more (*e.g.*, 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 545 (*e.g.*, amino acid residues 47-56, 71-87, 120-136, 191-201, 217-223, and/or 256-264 of SEQ ID NO: 545). In some embodiments, the CAR molecule or antigen binding domain comprises one or more (*e.g.*, 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 546 (*e.g.*, amino acid residues 26-35, 50-66, 98-110, 165-176, 192-198, and/or 231-240 of SEQ ID NO:

546). In some embodiments, the CAR molecule or antigen binding domain comprises one or more (*e.g.*, 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 547 (*e.g.*, amino acid residues 47-56, 71-87, 120-131, 186-197, 213-219, and/or 252-261 of SEQ ID NO: 547). In some embodiments, the CAR molecule or antigen binding domain comprises one or more (*e.g.*, 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 548 (*e.g.*, amino acid residues 26-35, 50-66, 99-108, 163-173, 189-195, and/or 228-236 of SEQ ID NO: 548). In some embodiments, the CAR molecule or antigen binding domain comprises one or more (*e.g.*, 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 549 (*e.g.*, amino acid residues 47-56, 71-87, 120-129, 184-194, 210-216, and/or 249-257 of SEQ ID NO: 549). In some embodiments, the CAR molecule or antigen binding domain comprises one or more (*e.g.*, 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 550 (*e.g.*, amino acid residues 26-35, 50-66, 99-110, 165-175, 191-197, and/or 230-238 of SEQ ID NO: 550). In some embodiments, the CAR molecule or antigen binding domain comprises one or more (*e.g.*, 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 551 (*e.g.*, amino acid residues 47-56, 71-87, 120-131, 186-196, 212-218, and/or 251-259 of SEQ ID NO: 551). In some embodiments, the CAR molecule or antigen binding domain comprises one or more (*e.g.*, 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 552 (*e.g.*, amino acid residues 26-35, 50-65, 99-111, 166-182, 198-204, and/or 237-245 of SEQ ID NO: 552). In some embodiments, the CAR molecule or antigen binding domain comprises one or more (*e.g.*, 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 553 (*e.g.*, amino acid residues 47-56, 71-86, 120-132, 187-203, 219-225, and/or 258-266 of SEQ ID NO: 553). In some embodiments, the CAR molecule or antigen binding domain comprises one or more (*e.g.*, 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 554 (*e.g.*, amino acid residues 26-35, 50-66, 99-104, 159-169, 185-191, and/or 224-231 of SEQ ID NO: 554). In some embodiments, the CAR molecule or antigen binding domain comprises one or more (*e.g.*, 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 555 (*e.g.*, amino acid residues 47-56, 71-87, 120-125, 180-190, 206-212, and/or 245-252 of SEQ ID NO: 555). In some embodiments, the CAR molecule or antigen binding domain comprises one or more (*e.g.*, 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 556 (*e.g.*, amino acid residues 26-35, 50-66, 99-107, 162-172, 188-194, and/or 227-236 of SEQ ID NO: 556). In some embodiments, the CAR molecule or antigen binding domain comprises one or more (*e.g.*, 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 557 (*e.g.*,

amino acid residues 47-56, 71-87, 120-128, 183-193, 209-215, and/or 248-257 of SEQ ID NO: 557). In some embodiments, the CAR molecule or antigen binding domain comprises one or more (*e.g.*, 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 558 (*e.g.*, amino acid residues 26-35, 50-66, 99-110, 165-176, 192-198, and/or 231-239 of SEQ ID NO: 558). In some embodiments, the CAR molecule or antigen binding domain comprises one or more (*e.g.*, 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 559 (*e.g.*, amino acid residues 47-56, 71-87, 120-131, 186-197, 213-219, and/or 252-260 of SEQ ID NO: 559). In some embodiments, the CAR molecule or antigen binding domain comprises one or more (*e.g.*, 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 560 (*e.g.*, amino acid residues 26-35, 50-66, 99-111, 166-176, 192-198, and/or 231-239 of SEQ ID NO: 560). In some embodiments, the CAR molecule or antigen binding domain comprises one or more (*e.g.*, 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 561 (*e.g.*, amino acid residues 47-56, 71-87, 120-132, 187-197, 213-219, and/or 252-260 of SEQ ID NO: 561). In some embodiments, the CAR molecule or antigen binding domain comprises one or more (*e.g.*, 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 562 (*e.g.*, amino acid residues 26-35, 50-65, 99-111, 160-169, 186-192, and/or 225-244 of SEQ ID NO: 562). In some embodiments, the CAR molecule or antigen binding domain comprises one or more (*e.g.*, 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 563 (*e.g.*, amino acid residues 47-56, 71-86, 120-132, 181-191, 207-213, and/or 246-255 of SEQ ID NO: 563). In some embodiments, the CAR molecule or antigen binding domain comprises one or more (*e.g.*, 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 564 (*e.g.*, amino acid residues 26-35, 50-66, 99-112, 161-171, 187-193, and/or 226-236 of SEQ ID NO: 564). In some embodiments, the CAR molecule or antigen binding domain comprises one or more (*e.g.*, 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 565 (*e.g.*, amino acid residues 47-56, 71-87, 120-133, 182-192, 208-214, and/or 247-257 of SEQ ID NO: 565). In some embodiments, the CAR molecule or antigen binding domain comprises one or more (*e.g.*, 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 566 (*e.g.*, amino acid residues 26-35, 50-66, 99-112, 161-171, 187-193, and/or 226-236 of SEQ ID NO: 566). In some embodiments, the CAR molecule or antigen binding domain comprises one or more (*e.g.*, 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 567 (*e.g.*, amino acid residues 47-56, 71-87, 120-133, 182-192, 208-214, and/or 247-257 of SEQ ID NO: 567). In some embodiments, the CAR molecule or antigen binding domain comprises one or

more (*e.g.*, 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 568 (*e.g.*, amino acid residues 26-35, 50-66, 99-111, 166-177, 193-199, and/or 232-241 of SEQ ID NO: 568). In some embodiments, the CAR molecule or antigen binding domain comprises one or more (*e.g.*, 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 569 (*e.g.*, amino acid residues 47-56, 71-87, 120-132, 187-198, 214-220, and/or 253-262 of SEQ ID NO: 569). In some embodiments, the CAR molecule or antigen binding domain comprises one or more (*e.g.*, 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 570 (*e.g.*, amino acid residues 26-35, 50-66, 99-110, 165-176, 192-198, and/or 231-240 of SEQ ID NO: 570). In some embodiments, the CAR molecule or antigen binding domain comprises one or more (*e.g.*, 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 571 (*e.g.*, amino acid residues 47-56, 71-87, 120-131, 186-197, 213-219, and/or 252-261 of SEQ ID NO: 571). In some embodiments, the CAR molecule or antigen binding domain comprises one or more (*e.g.*, 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 572 (*e.g.*, amino acid residues 26-35, 50-66, 99-111, 166-176, 192-198, and/or 231-239 of SEQ ID NO: 572). In some embodiments, the CAR molecule or antigen binding domain comprises one or more (*e.g.*, 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 573 (*e.g.*, amino acid residues 47-56, 71-87, 120-132, 187-197, 213-219, and/or 252-260 of SEQ ID NO: 573). In some embodiments, the CAR molecule or antigen binding domain comprises one or more (*e.g.*, 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 574 (*e.g.*, amino acid residues 26-35, 50-66, 99-108, 158-167, 183-190, and/or 222-230 of SEQ ID NO: 574). In some embodiments, the CAR molecule or antigen binding domain comprises one or more (*e.g.*, 2, 3, 4, 5, or all) of the heavy and/or light CDR sequences in SEQ ID NO: 575 (*e.g.*, amino acid residues 47-56, 71-86, 120-129, 179-188, 204-210, and/or 243-251 of SEQ ID NO: 575).

In some embodiments, the CAR molecule or antigen binding domain comprises a linker sequence (*e.g.*, amino acid residues 118-137 of SEQ ID NO: 534, amino acid residues 139-158 of SEQ ID NO: 535, amino acid residues 127-146 of SEQ ID NO: 536, amino acid residues 148-167 of SEQ ID NO: 537, amino acid residues 121-140 of SEQ ID NO: 538, amino acid residues 142-161 of SEQ ID NO: 539, amino acid residues 115-134 of SEQ ID NO: 540, amino acid residues 136-155 of SEQ ID NO: 541, amino acid residues 116-135 of SEQ ID NO: 542, amino acid residues 137-156 of SEQ ID NO: 543, amino acid residues 127-146 of SEQ ID NO: 544, amino acid residues 148-167 of SEQ ID NO: 545, amino acid residues 122-141 of SEQ ID

NO: 546, amino acid residues 143-162 of SEQ ID NO: 547, amino acid residues 120-139 of SEQ ID NO: 548, amino acid residues 141-160 of SEQ ID NO: 549, amino acid residues 122-141 of SEQ ID NO: 550, amino acid residues 143-162 of SEQ ID NO: 551, amino acid residues 123-142 of SEQ ID NO: 552, amino acid residues 144-163 of SEQ ID NO: 553, amino acid residues 116-135 of SEQ ID NO: 554, amino acid residues 137-156 of SEQ ID NO: 555, amino acid residues 119-138 of SEQ ID NO: 556, amino acid residues 140-159 of SEQ ID NO: 557, amino acid residues 132-141 of SEQ ID NO: 558, amino acid residues 143-162 of SEQ ID NO: 559, amino acid residues 123-142 of SEQ ID NO: 560, amino acid residues 144-163 of SEQ ID NO: 561, amino acid residues 123-137 of SEQ ID NO: 562, amino acid residues 144-158 of SEQ ID NO: 563, amino acid residues 124-138 of SEQ ID NO: 564, amino acid residues 145-159 of SEQ ID NO: 565, amino acid residues 124-138 of SEQ ID NO: 566, amino acid residues 145-159 of SEQ ID NO: 567, amino acid residues 123-142 of SEQ ID NO: 568, amino acid residues 144-163 of SEQ ID NO: 569, amino acid residues 122-141 of SEQ ID NO; 570, amino acid residues 143-162 of SEQ ID NO: 571, amino acid residues 123-142 of SEQ ID NO: 572, amino acid residues 144-163 of SEQ ID NO: 573, or amino acid residues 141-155 of SEQ ID NO: 575).

In some embodiments, the CAR molecule or antigen binding domain comprises a leader sequence (*e.g.,* amino acid residues 1-21 of SEQ ID NOs: 535, 537, 539, 541, 543, 545, 547, 549, 551, 553, 555, 557, 559, 561, 563, 565, 567, 569, 571, 573, or 575, or encoded by nucleotide residues 1-63 of SEQ ID NOs: 577, 579, 581, 583, 585, 587, 589, 591, 593, 595, 597, 599, 601. 603, 605, 607, 609, 611, 613, 615, 617, 619, 621, 623, or 625).

In other embodiments, the CAR-expressing cells can specifically bind to BCMA, *e.g.*, can include a CAR molecule, or an antigen binding domain according to Table 1 or 16, SEQ ID NO: 271 or SEQ ID NO: 273 of WO2016/014565, incorporated herein by reference. The amino acid and nucleotide sequences encoding the BCMA CAR molecules and antigen binding domains (*e.g.*, including one, two, three VH CDRs; and one, two, three VL CDRs according to Kabat or Chothia), as specified in WO2016/014565, are provided in the Sequence Listing submitted herewith. Amino and nucleotide sequences identical and substantially identical to the aforesaid sequences provided in the Sequence Listing are specifically incorporated into the instant specification.

In certain embodiments, the CAR molecule or antigen binding domain comprises an amino acid sequence, or is encoded by a nucleotide sequence, according to any of SEQ ID NOs: 626-859, or a sequence substantially identical thereto.

In other embodiments, the CAR-expressing cells can specifically bind to CLL-1, *e.g.*, can include a CAR molecule, or an antigen binding domain according to Table 2 of WO2016/014535, incorporated herein by reference. The amino acid and nucleotide sequences encoding the CLL-1 CAR molecules and antigen binding domains (*e.g.*, including one, two, three VH CDRs; and one, two, three VL CDRs according to Kabat or Chothia), as specified in WO2016/014535, are provided in the Sequence Listing submitted herewith. Amino and nucleotide sequences identical and substantially identical to the aforesaid sequences provided in the Sequence Listing are specifically incorporated into the instant specification.

In certain embodiments, the CAR molecule or antigen binding domain comprises an amino acid sequence, or is encoded by a nucleotide sequence, according to any of SEQ ID NOs: 860-941, or a sequence substantially identical thereto.

In other embodiments, the CAR-expressing cells can specifically bind to GFR ALPHA-4, *e.g.*, can include a CAR molecule, or an antigen binding domain according to Table 2 of WO2016/025880, incorporated herein by reference. The amino acid and nucleotide sequences encoding the GFR ALPHA-4 CAR molecules and antigen binding domains (*e.g.*, including one, two, three VH CDRs; and one, two, three VL CDRs according to Kabat or Chothia), as specified in WO2016/025880, are provided in the Sequence Listing submitted herewith. Amino and nucleotide sequences identical and substantially identical to the aforesaid sequences provided in the Sequence Listing are specifically incorporated into the instant specification.

In certain embodiments, the CAR molecule or antigen binding domain comprises an amino acid sequence, or is encoded by a nucleotide sequence, according to any of SEQ ID NOs: 942-981, or a sequence substantially identical thereto.

In one embodiment, the antigen binding domain of any of the CAR molecules described herein (*e.g.*, any of CD19, CD123, EGFRvIII, CD33, mesothelin, BCMA, and GFR ALPHA-4) comprises one, two three (e.g., all three) heavy chain CDRs, HC CDR1, HC CDR2 and HC CDR3, from an antibody listed above, and/or one, two, three (e.g., all three) light chain CDRs, LC CDR1, LC CDR2 and LC CDR3, from an antigen binding domain listed above. In one embodiment, the antigen binding domain comprises a heavy chain variable region and/or a variable light chain region of an antibody listed or described above.

In one aspect, the anti-tumor antigen binding domain is a fragment, e.g., a single chain variable fragment (scFv). In one aspect, the anti-a cancer associate antigen as described herein binding domain is a Fv, a Fab, a (Fab')2, or a bi-functional (e.g. bi-specific) hybrid antibody (e.g., Lanzavecchia et al., Eur. J. Immunol. 17, 105 (1987)). In one aspect, the antibodies and fragments thereof of the invention binds a cancer associate antigen as described herein protein with wild-type or enhanced affinity.

In some instances, scFvs can be prepared according to method known in the art (see, for example, Bird et al., (1988) Science 242:423-426 and Huston et al., (1988) Proc. Natl. Acad. Sci. USA 85:5879-5883). ScFv molecules can be produced by linking VH and VL regions together using flexible polypeptide linkers. The scFv molecules comprise a linker (e.g., a Ser-Gly linker) with an optimized length and/or amino acid composition. The linker length can greatly affect how the variable regions of a scFv fold and interact. In fact, if a short polypeptide linker is employed (e.g., between 5-10 amino acids) intrachain folding is prevented. Interchain folding is also required to bring the two variable regions together to form a functional epitope binding site. For examples of linker orientation and size see, e.g., Hollinger et al. 1993 Proc Natl Acad. Sci. U.S.A. 90:6444-6448, U.S. Patent Application Publication Nos. 2005/0100543, 2005/0175606, 2007/0014794, and PCT publication Nos. WO2006/020258 and WO2007/024715, is incorporated herein by reference.

An scFv can comprise a linker of at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 25, 30, 35, 40, 45, 50, or more amino acid residues between its VL and VH regions. The linker sequence may comprise any naturally occurring amino acid. In some embodiments, the linker sequence comprises amino acids glycine and serine. In another embodiment, the linker sequence comprises sets of glycine and serine repeats such as $(Gly_4Ser)n$, where n is a positive integer equal to or greater than 1 (SEQ ID NO:26). In one embodiment, the linker can be $(Gly_4Ser)_4$ (SEQ ID NO:27) or $(Gly_4Ser)_3$(SEQ ID NO:25). Variation in the linker length may retain or enhance activity, giving rise to superior efficacy in activity studies.

In another aspect, the antigen binding domain is a T cell receptor ("TCR"), or a fragment thereof, for example, a single chain TCR (scTCR). Methods to make such TCRs are known in the art. See, e.g., Willemsen RA et al, Gene Therapy 7: 1369–1377 (2000); Zhang T et al, Cancer Gene Ther 11: 487–496 (2004); Aggen et al, Gene Ther. 19(4):365-74 (2012) (references are incorporated herein by its entirety). For example, scTCR can be engineered that

contains the Vα and Vβ genes from a T cell clone linked by a linker (e.g., a flexible peptide). This approach is very useful to cancer associated target that itself is intracellar, however, a fragment of such antigen (peptide) is presented on the surface of the cancer cells by MHC.

Transmembrane domain

With respect to the transmembrane domain, in various embodiments, a CAR can be designed to comprise a transmembrane domain that is attached to the extracellular domain of the CAR. A transmembrane domain can include one or more additional amino acids adjacent to the transmembrane region, e.g., one or more amino acid associated with the extracellular region of the protein from which the transmembrane was derived (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 up to 15 amino acids of the extracellular region) and/or one or more additional amino acids associated with the intracellular region of the protein from which the transmembrane protein is derived (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 up to 15 amino acids of the intracellular region). In one aspect, the transmembrane domain is one that is associated with one of the other domains of the CAR. In some instances, the transmembrane domain can be selected or modified by amino acid substitution to avoid binding of such domains to the transmembrane domains of the same or different surface membrane proteins, e.g., to minimize interactions with other members of the receptor complex. In one aspect, the transmembrane domain is capable of homodimerization with another CAR on the cell surface of a CAR-expressing cell. In a different aspect, the amino acid sequence of the transmembrane domain may be modified or substituted so as to minimize interactions with the binding domains of the native binding partner present in the same CART.

The transmembrane domain may be derived either from a natural or from a recombinant source. Where the source is natural, the domain may be derived from any membrane-bound or transmembrane protein. In one aspect the transmembrane domain is capable of signaling to the intracellular domain(s) whenever the CAR has bound to a target. A transmembrane domain of particular use in this invention may include at least the transmembrane region(s) of e.g., the alpha, beta or zeta chain of the T-cell receptor, CD28, CD27, CD3 epsilon, CD45, CD4, CD5, CD8, CD9, CD16, CD22, CD33, CD37, CD64, CD80, CD86, CD134, CD137, CD154. In some embodiments, a transmembrane domain may include at least the transmembrane region(s) of, e.g., KIR2DS2, OX40, CD2, CD27, LFA-1 (CD11a, CD18), ICOS (CD278), 4-1BB (CD137), GITR, CD40, BAFFR, HVEM (LIGHTR), SLAMF7, NKp80 (KLRF1), NKp44,

NKp30, NKp46, CD160, CD19, IL2R beta, IL2R gamma, IL7R α, ITGA1, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CD11d, ITGAE, CD103, ITGAL, CD11a, LFA-1, ITGAM, CD11b, ITGAX, CD11c, ITGB1, CD29, ITGB2, CD18, LFA-1, ITGB7, TNFR2, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRTAM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100 (SEMA4D), SLAMF6 (NTB-A, Ly108), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, PAG/Cbp, NKG2D, NKG2C.

In some instances, the transmembrane domain can be attached to the extracellular region of the CAR, e.g., the antigen binding domain of the CAR, via a hinge, e.g., a hinge from a human protein. For example, in one embodiment, the hinge can be a human Ig (immunoglobulin) hinge, e.g., an IgG4 hinge, or a CD8a hinge. In one embodiment, the hinge or spacer comprises (e.g., consists of) the amino acid sequence of SEQ ID NO:2. In one aspect, the transmembrane domain comprises (e.g., consists of) a transmembrane domain of SEQ ID NO: 6.

In one aspect, the hinge or spacer comprises an IgG4 hinge. For example, in one embodiment, the hinge or spacer comprises a hinge of the amino acid sequence ESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNW YVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEK TISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK TTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLGKM (SEQ ID NO:36). In some embodiments, the hinge or spacer comprises a hinge encoded by a nucleotide sequence of GAGAGCAAGTACGGCCCTCCCTGCCCCCCTTGCCCTGCCCCCGAGTTCCTGGGCGG ACCCAGCGTGTTCCTGTTCCCCCCCAAGCCCAAGGACACCCTGATGATCAGCCGGA CCCCCGAGGTGACCTGTGTGGTGGTGGACGTGTCCCAGGAGGACCCCGAGGTCCA GTTCAACTGGTACGTGGACGGCGTGGAGGTGCACAACGCCAAGACCAAGCCCCGG GAGGAGCAGTTCAATAGCACCTACCGGGTGGTGTCCGTGCTGACCGTGCTGCACCA GGACTGGCTGAACGGCAAGGAATACAAGTGTAAGGTGTCCAACAAGGGCCTGCCC AGCAGCATCGAGAAAACCATCAGCAAGGCCAAGGGCCAGCCTCGGGAGCCCCAGG TGTACACCCTGCCCCCTAGCCAAGAGGAGATGACCAAGAACCAGGTGTCCCTGAC CTGCCTGGTGAAGGGCTTCTACCCCAGCGACATCGCCGTGGAGTGGGAGAGCAAC GGCCAGCCCGAGAACAACTACAAGACCACCCCCCCTGTGCTGGACAGCGACGGCA

GCTTCTTCCTGTACAGCCGGCTGACCGTGGACAAGAGCCGGTGGCAGGAGGGCAA
CGTCTTTAGCTGCTCCGTGATGCACGAGGCCCTGCACAACCACTACACCCAGAAGA
GCCTGAGCCTGTCCCTGGGCAAGATG (SEQ ID NO:37).

In one aspect, the hinge or spacer comprises an IgD hinge. For example, in one embodiment, the hinge or spacer comprises a hinge of the amino acid sequence RWPESPKAQASSVPTAQPQAEGSLAKATTAPATTRNTGRGGEEKKKEKEKEEQEERET KTPECPSHTQPLGVYLLTPAVQDLWLRDKATFTCFVVGSDLKDAHLTWEVAGKVPTG GVEEGLLERHSNGSQSQHSRLTLPRSLWNAGTSVTCTLNHPSLPPQRLMALREPAAQA PVKLSLNLLASSDPPEAASWLLCEVSGFSPPNILLMWLEDQREVNTSGFAPARPPPQPG STTFWAWSVLRVPAPPSPQPATYTCVVSHEDSRTLLNASRSLEVSYVTDH (SEQ ID NO:23). In some embodiments, the hinge or spacer comprises a hinge encoded by a nucleotide sequence of AGGTGGCCCGAAAGTCCCAAGGCCCAGGCATCTAGTGTTCCTACTGCACAGCCCCA GGCAGAAGGCAGCCTAGCCAAAGCTACTACTGCACCTGCCACTACGCGCAATACT GGCCGTGGCGGGGAGGAGAAGAAAAAGGAGAAAGAGAAAGAAGAACAGGAAGA GAGGGAGACCAAGACCCCTGAATGTCCATCCCATACCCAGCCGCTGGGCGTCTATC TCTTGACTCCCGCAGTACAGGACTTGTGGCTTAGAGATAAGGCCACCTTTACATGT TTCGTCGTGGGCTCTGACCTGAAGGATGCCCATTTGACTTGGGAGGTTGCCGGAAA GGTACCCACAGGGGGGGTTGAGGAAGGGTTGCTGGAGCGCCATTCCAATGGCTCT CAGAGCCAGCACTCAAGACTCACCCTTCCGAGATCCCTGTGGAACGCCGGGACCTC TGTCACATGTACTCTAAATCATCCTAGCCTGCCCCCACAGCGTCTGATGGCCCTTAG AGAGCCAGCCGCCCAGGCACCAGTTAAGCTTAGCCTGAATCTGCTCGCCAGTAGTG ATCCCCCAGAGGCCGCCAGCTGGCTCTTATGCGAAGTGTCCGGCTTTAGCCCGCCC AACATCTTGCTCATGTGGCTGGAGGACCAGCGAGAAGTGAACACCAGCGGCTTCG CTCCAGCCCGGCCCCCACCCCAGCCGGGTTCTACCACATTCTGGGCCTGGAGTGTC TTAAGGGTCCCAGCACCACCTAGCCCCCAGCCAGCCACATACACCTGTGTTGTGTC CCATGAAGATAGCAGGACCCTGCTAAATGCTTCTAGGAGTCTGGAGGTTTCCTACG TGACTGACCATT (SEQ ID NO:24).

In one aspect, the transmembrane domain may be recombinant, in which case it will comprise predominantly hydrophobic residues such as leucine and valine. In one aspect a triplet of phenylalanine, tryptophan and valine can be found at each end of a recombinant transmembrane domain.

Optionally, a short oligo- or polypeptide linker, between 2 and 10 amino acids in length may form the linkage between the transmembrane domain and the cytoplasmic region of the CAR. A glycine-serine doublet provides a particularly suitable linker. For example, in one aspect, the linker comprises the amino acid sequence of GGGGSGGGGS (SEQ ID NO: 14). In some embodiments, the linker is encoded by a nucleotide sequence of GGTGGCGGAGGTTCTGGAGGTGGAGGTTCC (SEQ ID NO: 19).

In one aspect, the hinge or spacer comprises a KIR2DS2 hinge.

Cytoplasmic domain

The cytoplasmic domain or region of the CAR includes an intracellular signaling domain. An intracellular signaling domain is generally responsible for activation of at least one of the normal effector functions of the immune cell in which the CAR has been introduced.

Examples of intracellular signaling domains for use in a CAR described herein include the cytoplasmic sequences of the T cell receptor (TCR) and co-receptors that act in concert to initiate signal transduction following antigen receptor engagement, as well as any derivative or variant of these sequences and any recombinant sequence that has the same functional capability.

It is known that signals generated through the TCR alone are insufficient for full activation of the T cell and that a secondary and/or costimulatory signal is also required. Thus, T cell activation can be said to be mediated by two distinct classes of cytoplasmic signaling sequences: those that initiate antigen-dependent primary activation through the TCR (primary intracellular signaling domains) and those that act in an antigen-independent manner to provide a secondary or costimulatory signal (secondary cytoplasmic domain, e.g., a costimulatory domain).

A primary signaling domain regulates primary activation of the TCR complex either in a stimulatory way, or in an inhibitory way. Primary intracellular signaling domains that act in a stimulatory manner may contain signaling motifs which are known as immunoreceptor tyrosine-based activation motifs or ITAMs.

Examples of ITAM containing primary intracellular signaling domains that are of particular use in the invention include those of TCR zeta, FcR gamma, FcR beta, CD3 gamma, CD3 delta , CD3 epsilon, CD5, CD22, CD79a, CD79b, CD278 (also known as “ICOS”), FcεRI, DAP10, DAP12, and CD66d. In one embodiment, a CAR of the invention comprises an

intracellular signaling domain, e.g., a primary signaling domain of CD3-zeta, e.g., a CD3-zeta sequence described herein.

In one embodiment, a primary signaling domain comprises a modified ITAM domain, e.g., a mutated ITAM domain which has altered (e.g., increased or decreased) activity as compared to the native ITAM domain. In one embodiment, a primary signaling domain comprises a modified ITAM-containing primary intracellular signaling domain, e.g., an optimized and/or truncated ITAM-containing primary intracellular signaling domain. In an embodiment, a primary signaling domain comprises one, two, three, four or more ITAM motifs.

Costimulatory Signaling Domain

The intracellular signalling domain of the CAR can comprise the CD3-zeta signaling domain by itself or it can be combined with any other desired intracellular signaling domain(s) useful in the context of a CAR of the invention. For example, the intracellular signaling domain of the CAR can comprise a CD3 zeta chain portion and a costimulatory signaling domain. The costimulatory signaling domain refers to a portion of the CAR comprising the intracellular domain of a costimulatory molecule. In one embodiment, the intracellular domain is designed to comprise the signaling domain of CD3-zeta and the signaling domain of CD28. In one aspect, the intracellular domain is designed to comprise the signaling domain of CD3-zeta and the signaling domain of ICOS.

A costimulatory molecule can be a cell surface molecule other than an antigen receptor or its ligands that is required for an efficient response of lymphocytes to an antigen. Examples of such molecules include CD27, CD28, 4-1BB (CD137), OX40, CD30, CD40, PD-1, ICOS, lymphocyte function-associated antigen-1 (LFA-1), CD2, CD7, LIGHT, NKG2C, B7-H3, and a ligand that specifically binds with CD83, and the like. For example, CD27 costimulation has been demonstrated to enhance expansion, effector function, and survival of human CART cells in vitro and augments human T cell persistence and antitumor activity in vivo (Song et al. Blood. 2012; 119(3):696-706). Further examples of such costimulatory molecules include CDS, ICAM-1, GITR, BAFFR, HVEM (LIGHTR), SLAMF7, NKp80 (KLRF1), NKp30, NKp44, NKp46, CD160, CD19, CD4, CD8alpha, CD8beta, IL2R beta, IL2R gamma, IL7R alpha, ITGA4, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CD11d, ITGAE, CD103, ITGAL, CD11a, LFA-1, ITGAM, CD11b, ITGAX, CD11c, ITGB1, CD29,

ITGB2, CD18, LFA-1, ITGB7, TNFR2, TRANCE/RANKL, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRTAM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100 (SEMA4D), CD69, SLAMF6 (NTB-A, Ly108), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, LAT, GADS, SLP-76, NKG2D, NKG2C and PAG/Cbp.

The intracellular signaling sequences within the cytoplasmic portion of the CAR may be linked to each other in a random or specified order. Optionally, a short oligo- or polypeptide linker, for example, between 2 and 10 amino acids (e.g., 2, 3, 4, 5, 6, 7, 8, 9, or 10 amino acids) in length may form the linkage between intracellular signaling sequence. In one embodiment, a glycine-serine doublet can be used as a suitable linker. In one embodiment, a single amino acid, e.g., an alanine, a glycine, can be used as a suitable linker.

In one aspect, the intracellular signaling domain is designed to comprise two or more, e.g., 2, 3, 4, 5, or more, costimulatory signaling domains. In an embodiment, the two or more, e.g., 2, 3, 4, 5, or more, costimulatory signaling domains, are separated by a linker molecule, e.g., a linker molecule described herein. In one embodiment, the intracellular signaling domain comprises two costimulatory signaling domains. In some embodiments, the linker molecule is a glycine residue. In some embodiments, the linker is an alanine residue.

In one aspect, the intracellular signaling domain is designed to comprise the signaling domain of CD3-zeta and the signaling domain of CD28. In one aspect, the intracellular signaling domain is designed to comprise the signaling domain of CD3-zeta and the signaling domain of 4-1BB. In one aspect, the signaling domain of 4-1BB is a signaling domain of SEQ ID NO: 7. In one aspect, the signaling domain of CD3-zeta is a signaling domain of SEQ ID NO: 9.

In one aspect, the intracellular signaling domain is designed to comprise the signaling domain of CD3-zeta and the signaling domain of CD27. In one aspect, the signaling domain of CD27 comprises an amino acid sequence of QRRKYRSNKGESPVEPAEPCRYSCPREEEGSTIPIQEDYRKPEPACSP (SEQ ID NO:16). In one aspect, the signalling domain of CD27 is encoded by a nucleic acid sequence of AGGAGTAAGAGGAGCAGGCTCCTGCACAGTGACTACATGAACATGACTCCCCGCC GCCCCGGGCCCACCCGCAAGCATTACCAGCCCTATGCCCCACCACGCGACTTCGCA GCCTATCGCTCC (SEQ ID NO:15).

In one aspect, the CAR-expressing cell described herein can further comprise a second CAR, e.g., a second CAR that includes a different antigen binding domain, e.g., to the same target or a different target (e.g., a target other than a cancer associated antigen described herein or a different cancer associated antigen described herein, *e.g.*, CD19, CD33, CLL-1, CD34, FLT3, or folate receptor beta). In one embodiment, the second CAR includes an antigen binding domain to a target expressed the same cancer cell type as the cancer associated antigen. In one embodiment, the CAR-expressing cell comprises a first CAR that targets a first antigen and includes an intracellular signaling domain having a costimulatory signaling domain but not a primary signaling domain, and a second CAR that targets a second, different, antigen and includes an intracellular signaling domain having a primary signaling domain but not a costimulatory signaling domain. While not wishing to be bound by theory, placement of a costimulatory signaling domain, *e.g.*, 4-1BB, CD28, ICOS, CD27 or OX-40, onto the first CAR, and the primary signaling domain, *e.g.*, CD3 zeta, on the second CAR can limit the CAR activity to cells where both targets are expressed. In one embodiment, the CAR expressing cell comprises a first cancer associated antigen CAR that includes an antigen binding domain that binds a target antigen described herein, a transmembrane domain and a costimulatory domain and a second CAR that targets a different target antigen (e.g., an antigen expressed on that same cancer cell type as the first target antigen) and includes an antigen binding domain, a transmembrane domain and a primary signaling domain. In another embodiment, the CAR expressing cell comprises a first CAR that includes an antigen binding domain that binds a target antigen described herein, a transmembrane domain and a primary signaling domain and a second CAR that targets an antigen other than the first target antigen (e.g., an antigen expressed on the same cancer cell type as the first target antigen) and includes an antigen binding domain to the antigen, a transmembrane domain and a costimulatory signaling domain.

In another aspect, the disclosure features a population of CAR-expressing cells, e.g., CART cells. In some embodiments, the population of CAR-expressing cells comprises a mixture of cells expressing different CARs. For example, in one embodiment, the population of CART cells can include a first cell expressing a CAR having an antigen binding domain to a cancer associated antigen described herein, and a second cell expressing a CAR having a different antigen binding domain, e.g., an antigen binding domain to a different a cancer associated antigen described herein, e.g., an antigen binding domain to a cancer associated

antigen described herein that differs from the cancer associate antigen bound by the antigen binding domain of the CAR expressed by the first cell. As another example, the population of CAR-expressing cells can include a first cell expressing a CAR that includes an antigen binding domain to a cancer associated antigen described herein, and a second cell expressing a CAR that includes an antigen binding domain to a target other than a cancer associate antigen as described herein. In one embodiment, the population of CAR-expressing cells includes, e.g., a first cell expressing a CAR that includes a primary intracellular signaling domain, and a second cell expressing a CAR that includes a secondary signaling domain.

In another aspect, the disclosure features a population of cells wherein at least one cell in the population expresses a CAR having an antigen binding domain to a cancer associated antigen described herein, and a second cell expressing another agent, e.g., an agent which enhances the activity of a CAR-expressing cell. For example, in one embodiment, the agent can be an agent which inhibits an inhibitory molecule. Inhibitory molecules, e.g., PD-1, can, in some embodiments, decrease the ability of a CAR-expressing cell to mount an immune effector response. Examples of inhibitory molecules include PD-1, PD-L1, CTLA4, TIM3, CEACAM (CEACAM-1, CEACAM-3, and/or CEACAM-5), LAG3, VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4, CD80, CD86, B7-H3 (CD276), B7-H4 (VTCN1), HVEM (TNFRSF14 or CD270), KIR, A2aR, MHC class I, MHC class II, GAL9, adenosine, and TGF (e.g., TGFbeta). In one embodiment, the agent which inhibits an inhibitory molecule comprises a first polypeptide, e.g., an inhibitory molecule, associated with a second polypeptide that provides a positive signal to the cell, e.g., an intracellular signaling domain described herein. In one embodiment, the agent comprises a first polypeptide, e.g., of an inhibitory molecule such as PD-1, PD-L1, CTLA4, TIM3, CEACAM (CEACAM-1, CEACAM-3, and/or CEACAM-5), LAG3, VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4 and TGF beta, or a fragment of any of these, and a second polypeptide which is an intracellular signaling domain described herein (e.g., comprising a costimulatory domain (e.g., 41BB, CD27, OX40 or CD28, e.g., as described herein) and/or a primary signaling domain (e.g., a CD3 zeta signaling domain described herein). In one embodiment, the agent comprises a first polypeptide of PD-1 or a fragment thereof, and a second polypeptide of an intracellular signaling domain described herein (e.g., a CD28 signaling domain described herein and/or a CD3 zeta signaling domain described herein).

Exemplary CAR Molecules

The sequences of anti-CD19 binding domains are provided above in **Table 1**. Full CAR constructs can be generated using any of the antigen binding domains described in Table 1 with one or more additional CAR component provided below.

- leader (amino acid sequence) (SEQ ID NO: 1)

MALPVTALLLPLALLLHAARP

- **leader (nucleic acid sequence) (SEQ ID NO: 12)**

ATGGCCCTGCCTGTGACAGCCCTGCTGCTGCCTCTGGCTCTGCTGCTGCATGCCGCT AGACCC

- CD8 hinge (amino acid sequence) (SEQ ID NO: 2)

TTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACD

- **CD8 hinge (nucleic acid sequence) (SEQ ID NO: 13)**

ACCACGACGCCAGCGCCGCGACCACCAACACCGGCGCCCACCATCGCGTCGCAGC CCCTGTCCCTGCGCCCAGAGGCGTGCCGGCCAGCGGCGGGGGGCGCAGTGCACAC GAGGGGGCTGGACTTCGCCTGTGAT

- CD8 transmembrane (amino acid sequence) (SEQ ID NO: 6)

IYIWAPLAGTCGVLLLSLVITLYC

- **transmembrane (nucleic acid sequence) (SEQ ID NO: 17)**

ATCTACATCTGGGCGCCCTTGGCCGGGACTTGTGGGGTCCTTCTCCTGTCACTGGTT ATCACCCTTTACTGC

- 4-1BB Intracellular domain (amino acid sequence) (SEQ ID NO: 7)

KRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCEL

- **4-1BB Intracellular domain (nucleic acid sequence) (SEQ ID NO: 18)**

AAACGGGGCAGAAAGAAACTCCTGTATATATTCAAACAACCATTTATGAGACCAG TACAAACTACTCAAGAGGAAGATGGCTGTAGCTGCCGATTTCCAGAAGAAGAAGA AGGAGGATGTGAACTG

- CD3 zeta domain (amino acid sequence) (SEQ ID NO: 9)

RVKFSRSADAPAYKQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQE
GLYNELQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR

- **CD3 zeta (nucleic acid sequence) (SEQ ID NO: 20)**

AGAGTGAAGTTCAGCAGGAGCGCAGACGCCCCCGCGTACAAGCAGGGCCAGAACC
AGCTCTATAACGAGCTCAATCTAGGACGAAGAGAGGAGTACGATGTTTTGGACAA
GAGACGTGGCCGGGACCCTGAGATGGGGGGAAAGCCGAGAAGGAAGAACCCTCA
GGAAGGCCTGTACAATGAACTGCAGAAAGATAAGATGGCGGAGGCCTACAGTGAG
ATTGGGATGAAAGGCGAGCGCCGGAGGGGCAAGGGGCACGATGGCCTTTACCAGG
GTCTCAGTACAGCCACCAAGGACACCTACGACGCCCTTCACATGCAGGCCCTGCCC
CCTCGC

- **CD3 zeta domain (amino acid sequence; NCBI Reference Sequence NM_000734.3) (SEQ ID NO:10)**

RVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQE
GLYNELQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR

- **CD3 zeta (nucleic acid sequence; NCBI Reference Sequence NM_000734.3); (SEQ ID NO:21)**

AGAGTGAAGTTCAGCAGGAGCGCAGACGCCCCCGCGTACCAGCAGGGCCAG
AACCAGCTCTATAACGAGCTCAATCTAGGACGAAGAGAGGAGTACGATGTTT
TGGACAAGAGACGTGGCCGGGACCCTGAGATGGGGGGAAAGCCGAGAAGGA
AGAACCCTCAGGAAGGCCTGTACAATGAACTGCAGAAAGATAAGATGGCGG
AGGCCTACAGTGAGATTGGGATGAAAGGCGAGCGCCGGAGGGGCAAGGGGC
ACGATGGCCTTTACCAGGGTCTCAGTACAGCCACCAAGGACACCTACGACGC
CCTTCACATGCAGGCCCTGCCCCCTCGC

IgG4 Hinge (amino acid sequence) (SEQ ID NO:36)

ESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNW
YVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEK
TISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLGKM

IgG4 Hinge (nucleotide sequence) (SEQ ID NO:37)

GAGAGCAAGTACGGCCCTCCCTGCCCCCCTTGCCCTGCCCCCGAGTTCCTGGGCGG
ACCCAGCGTGTTCCTGTTCCCCCCCAAGCCCAAGGACACCCTGATGATCAGCCGGA
CCCCCGAGGTGACCTGTGTGGTGGTGGACGTGTCCCAGGAGGACCCCGAGGTCCA
GTTCAACTGGTACGTGGACGGCGTGGAGGTGCACAACGCCAAGACCAAGCCCCGG
GAGGAGCAGTTCAATAGCACCTACCGGGTGGTGTCCGTGCTGACCGTGCTGCACCA
GGACTGGCTGAACGGCAAGGAATACAAGTGTAAGGTGTCCAACAAGGGCCTGCCC
AGCAGCATCGAGAAAACCATCAGCAAGGCCAAGGGCCAGCCTCGGGAGCCCCAGG
TGTACACCCTGCCCCCTAGCCAAGAGGAGATGACCAAGAACCAGGTGTCCCTGAC
CTGCCTGGTGAAGGGCTTCTACCCCAGCGACATCGCCGTGGAGTGGGAGAGCAAC
GGCCAGCCCGAGAACAACTACAAGACCACCCCCCCTGTGCTGGACAGCGACGGCA
GCTTCTTCCTGTACAGCCGGCTGACCGTGGACAAGAGCCGGTGGCAGGAGGGCAA
CGTCTTTAGCTGCTCCGTGATGCACGAGGCCCTGCACAACCACTACACCCAGAAGA
GCCTGAGCCTGTCCCTGGGCAAGATG

EF1 alpha promoter

CGTGAGGCTCCGGTGCCCGTCAGTGGGCAGAGCGCACATCGCCCACAGTCCCCGA
GAAGTTGGGGGGAGGGGTCGGCAATTGAACCGGTGCCTAGAGAAGGTGGCGCGGG
GTAAACTGGGAAAGTGATGTCGTGTACTGGCTCCGCCTTTTTCCCGAGGGTGGGGG
AGAACCGTATATAAGTGCAGTAGTCGCCGTGAACGTTCTTTTTCGCAACGGGTTTG
CCGCCAGAACACAGGTAAGTGCCGTGTGTGGTTCCCGCGGGCCTGGCCTCTTTACG
GGTTATGGCCCTTGCGTGCCTTGAATTACTTCCACCTGGCTGCAGTACGTGATTCTT
GATCCCGAGCTTCGGGTTGGAAGTGGGTGGGAGAGTTCGAGGCCTTGCGCTTAAG
GAGCCCCTTCGCCTCGTGCTTGAGTTGAGGCCTGGCCTGGGCGCTGGGGCCGCCGC
GTGCGAATCTGGTGGCACCTTCGCGCCTGTCTCGCTGCTTTCGATAAGTCTCTAGCC
ATTTAAAATTTTTGATGACCTGCTGCGACGCTTTTTTTCTGGCAAGATAGTCTTGTA
AATGCGGGCCAAGATCTGCACACTGGTATTTCGGTTTTTGGGGCCGCGGGCGGCGA
CGGGGCCCGTGCGTCCCAGCGCACATGTTCGGCGAGGCGGGGCCTGCGAGCGCGG
CCACCGAGAATCGGACGGGGGTAGTCTCAAGCTGGCCGGCCTGCTCTGGTGCCTGG
CCTCGCGCCGCCGTGTATCGCCCCGCCCTGGGCGGCAAGGCTGGCCCGGTCGGCAC
CAGTTGCGTGAGCGGAAAGATGGCCGCTTCCCGGCCCTGCTGCAGGGAGCTCAAA
ATGGAGGACGCGGCGCTCGGGAGAGCGGGCGGGTGAGTCACCCACACAAAGGAA
AAGGGCCTTTCCGTCCTCAGCCGTCGCTTCATGTGACTCCACGGAGTACCGGGCGC
CGTCCAGGCACCTCGATTAGTTCTCGAGCTTTTGGAGTACGTCGTCTTTAGGTTGGG
GGGAGGGGTTTTATGCGATGGAGTTTCCCCACACTGAGTGGGTGGAGACTGAAGTT
AGGCCAGCTTGGCACTTGATGTAATTCTCCTTGGAATTTGCCCTTTTTGAGTTTGGA
TCTTGGTTCATTCTCAAGCCTCAGACAGTGGTTCAAAGTTTTTTTCTTCCATTTCAG
GTGTCGTGA (SEQ ID NO: 11).

Gly/Ser (SEQ ID NO:25)

GGGGS

Gly/Ser (SEQ ID NO:26): This sequence may encompass 1-6 "Gly Gly Gly Gly Ser" repeating units

GGGGSGGGGS GGGGSGGGGS GGGGSGGGGS

Gly/Ser (SEQ ID NO:27)

GGGGSGGGGS GGGGSGGGGS

Gly/Ser (SEQ ID NO:28)

GGGGSGGGGS GGGGS

Gly/Ser (SEQ ID NO:29)

GGGS

PolyA (SEQ ID NO:30), polyA 1-5000

PolyA (SEQ ID NO:31), poly T 1-100

PolyA (SEQ ID NO:32), poly T 1-5000

PolyA (SEQ ID NO:33), Poly A 1-5000

PolyA (SEQ ID NO:34), Poly A 1-400

PolyA (SEQ ID NO:35), Poly A 1-2000

Gly/Ser (SEQ ID NO:38): This sequence may encompass 1-10 "Gly Gly Gly Ser" repeating units

GGGSGGGSGG GSGGGSGGGS GGGSGGGSGG GSGGGSGGGS

Exemplary CD19 CAR constructs that can be used in the methods described herein are shown in **Table 4**:

Table 4: CD19 CAR Constructs

Name	SEQ ID	Sequence
CAR 1		
CAR1 scFv domain	39	EIVMTQSPATLSLSPGERATLSCRASQDISKYLNWYQQKPGQAPRLLIYHT SRLHSGIPARFSGSGSGTDYTLTISSLQPEDFAVYFCQQGNTLPYTFGQGT KLEIKGGGGSGGGGSGGGGSQVQLQESGPGLVKPSETLSLTCTVSGVSLPD YGVSWIRQPPGKGLEWIGVIWGSETTYYSSSLKSRVTISKDNSKNQVSLKL SSVTAADTAVYYCAKHYYYGGSYAMDYWGQGTLVTVSS
103101 CAR1 Soluble scFv - nt	52	Atggccctccctgtcaccgccctgctgcttccgctggctcttctgctccacgccgc tcggcccgaaattgtgatgacccagtcacccgccactcttagcctttcacccggtg agcgcgcaaccctgtcttgcagagcctcccaagacatctcaaaataccttaattgg tatcaacagaagcccggacaggctcctcgccttctgatctaccacaccagccggct ccattctggaatccctgccaggttcagcggtagcggatctgggaccgactacaccc tcactatcagctcactgcagccagaggacttcgctgtctatttctgtcagcaaggg aacaccctgccctacacctttggacagggcaccaagctcgagattaaaggtggagg tggcagcggaggaggtgggtccggcggtggaggaagccaggtccaactccaagaaa gcggaccgggtcttgtgaagccatcagaaactctttcactgacttgtactgtgagc ggagtgtctctccccgattacggggtgtcttggatcagacagccaccggggaaggg tctggaatggattggagtgatttggggctctgagactacttactactcttcatccc tcaagtcacgcgtcaccatctcaaaggacaactctaagaatcaggtgtcactgaaa ctgtcatctgtgaccgcagccgacaccgccgtgtactattgcgctaagcattacta ttatggcgggagctacgcaatggattactggggacagggtactctggtcaccgtgt ccagccaccaccatcatcaccatcaccat
103101 CAR1 Soluble scFv - aa	64	**MALPVTALLLPLALLLHAARP**eivmtqspatlslspgeratlscrasqdiskylnw yqqkpgqaprlliyhtsrlhsgiparfsgsgsgtdytltisslqpedfavyfcqqg ntlpytfgqgtkleikggggsggggsggggsqvqlqesgpglvkpsetlsltctvs gvslpdygvswirqppgkglewigviwgsettyyssslksrvtiskdnsknqvslk lssvtaadtavyycakhyyyggsyamdywgqgtlvtvss**hhhhhhhh**
104875 CAR 1 – Full - nt	90	atggccctccctgtcaccgccctgctgcttccgctggctcttctgctccacgccgc tcggcccgaaattgtgatgacccagtcacccgccactcttagcctttcacccggtg agcgcgcaaccctgtcttgcagagcctcccaagacatctcaaaataccttaattgg tatcaacagaagcccggacaggctcctcgccttctgatctaccacaccagccggct ccattctggaatccctgccaggttcagcggtagcggatctgggaccgactacaccc tcactatcagctcactgcagccagaggacttcgctgtctatttctgtcagcaaggg aacaccctgccctacacctttggacagggcaccaagctcgagattaaaggtggagg tggcagcggaggaggtgggtccggcggtggaggaagccaggtccaactccaagaaa gcggaccgggtcttgtgaagccatcagaaactctttcactgacttgtactgtgagc

		ggagtgtctctccccgattacggggtgtcttggatcagacagccaccggggaaggg tctggaatggattggagtgatttggggctctgagactacttactactcttcatccc tcaagtcacgcgtcaccatctcaaaggacaactctaagaatcaggtgtcactgaaa ctgtcatctgtgaccgcagccgacaccgccgtgtactattgcgctaagcattacta ttatggcgggagctacgcaatggattactggggacagggtactctggtcaccgtgt ccagcaccactaccccagcaccgaggccacccaccccggctcctaccatcgcctcc cagcctctgtccctgcgtccggaggcatgtagacccgcagctggtggggccgtgca tacccggggtcttgacttcgcctgcgatatctacatttgggcccctctggctggta cttgcggggtcctgctgctttcactcgtgatcactctttactgtaagcgcggtcgg aagaagctgctgtacatctttaagcaacccttcatgaggcctgtgcagactactca agaggaggacggctgttcatgccggttcccagaggaggaggaaggcggctgcgaac tgcgcgtgaaattcagccgcagcgcagatgctccagcctacaagcaggggcagaac cagctctacaacgaactcaatcttggtcggagagaggagtacgacgtgctggacaa gcggagaggacgggacccagaaatgggcgggaagccgcgcagaaagaatccccaag agggcctgtacaacgagctccaaaaggataagatggcagaagcctatagcgagatt ggtatgaaaggggaacgcagaagaggcaaaggccacgacggactgtaccagggact cagcaccgccaccaaggacacctatgacgctcttcacatgcaggccctgccgcctc gg
104875 CAR 1 – Full - aa	77	MALPVTALLLPLALLLHAARPeivmtqspatlslspgeratlsc**rasqdiskyln**w yqqkpgqaprlliy**htsrlhs**giparfsgsgsgtdytltisslqpedfavyfc**qqg** **ntlpyt**fgqgtkleikggggsggggsggggsqvqlqesgpglvkpsetlsltctvs gvslp**dygvs**wirqppgkglewig**viwgsettyyssslks**rvtiskdnsknqvslk lssvtaadtavyycak**hyyyggsyamdy**wgqgtlvtvsstttpaprpptpaptias qplslrpeacrpaaggavhtrgldfacdiyiwaplagtcgvlllslvitlyckrgr kkllyifkqpfmrpvqttqeedgcscrfpeeeeggcelrvkfsrsadapaykqgqn qlynelnlgrreeydvldkrrgrdpemggkprrknpqeglynelqkdkmaeaysei gmkgerrrgkghdglyqglstatkdtydalhmqalppr
CAR 2		
CAR2 scFv domain	40	Eivmtqspatlslspgeratlscrasqdiskylnwyqqkpgqaprlliyhtsrlhs giparfsgsgsgtdytltisslqpedfavyfcqqgntlpytfgqgtkleikggggs ggggsggggsqvqlqesgpglvkpsetlsltctvsgvslpdygvswirqppgkgle wigviwgsettyyqsslksrvtiskdnsknqvslklssvtaadtavyycakhyyyg gsyamdywgqgtlvtvss
103102 CAR2 - Soluble scFv - nt	53	Atggccctccctgtcaccgccctgctgcttccgctggctcttctgctccacgccgc tcggcccgaaattgtgatgacccagtcacccgccactcttagcctttcacccggtg agcgcgcaaccctgtcttgcagagcctcccaagacatctcaaaataccttaattgg tatcaacagaagcccggacaggctcctcgccttctgatctaccacaccagccggct ccattctggaatccctgccaggttcagcggtagcggatctgggaccgactacaccc

		tcactatcagctcactgcagccagaggacttcgctgtctatttctgtcagcaaggg aacaccctgccctacacctttggacagggcaccaagctcgagattaaaggtggagg tggcagcggaggaggtgggtccggcggtggaggaagccaggtccaactccaagaaa gcggaccgggtcttgtgaagccatcagaaactctttcactgacttgtactgtgagc ggagtgtctctccccgattacggggtgtcttggatcagacagccaccggggaaggg tctggaatggattggagtgatttggggctctgagactacttactaccaatcatccc tcaagtcacgcgtcaccatctcaaaggacaactctaagaatcaggtgtcactgaaa ctgtcatctgtgaccgcagccgacaccgccgtgtactattgcgctaagcattacta ttatggcgggagctacgcaatggattactggggacagggtactctggtcaccgtgt ccagccaccaccatcatcaccatcaccat
103102 CAR2 - Soluble scFv - aa	65	**MALPVTALLLPLALLLHAARP**eivmtqspatlslspgeratlscrasqdiskylnw yqqkpgqaprlliyhtsrlhsgiparfsgsgsgtdytltisslqpedfavyfcqqg ntlpytfgqgtkleikggggsggggsggggsqvqlqesgpglvkpsetlsltctvs gvslpdygvswirqppgkglewigviwgsettyyqsslksrvtiskdnsknqvslk lssvtaadtavyycakhyyyggsyamdywgqgtlvtvss**hhhhhhhh**
104876 CAR 2 - Full - nt	91	atggccctccctgtcaccgccctgctgcttccgctggctcttctgctccacgccgc tcggcccgaaattgtgatgacccagtcacccgccactcttagcctttcacccggtg agcgcgcaaccctgtcttgcagagcctcccaagacatctcaaaataccttaattgg tatcaacagaagcccggacaggctcctcgccttctgatctaccacaccagccggct ccattctggaatccctgccaggttcagcggtagcggatctgggaccgactacaccc tcactatcagctcactgcagccagaggacttcgctgtctatttctgtcagcaaggg aacaccctgccctacacctttggacagggcaccaagctcgagattaaaggtggagg tggcagcggaggaggtgggtccggcggtggaggaagccaggtccaactccaagaaa gcggaccgggtcttgtgaagccatcagaaactctttcactgacttgtactgtgagc ggagtgtctctccccgattacggggtgtcttggatcagacagccaccggggaaggg tctggaatggattggagtgatttggggctctgagactacttactaccaatcatccc tcaagtcacgcgtcaccatctcaaaggacaactctaagaatcaggtgtcactgaaa ctgtcatctgtgaccgcagccgacaccgccgtgtactattgcgctaagcattacta ttatggcgggagctacgcaatggattactggggacagggtactctggtcaccgtgt ccagcaccactaccccagcaccgaggccacccaccccggctcctaccatcgcctcc cagcctctgtccctgcgtccggaggcatgtagacccgcagctggtggggccgtgca tacccggggtcttgacttcgcctgcgatatctacatttgggcccctctggctggta cttgcggggtcctgctgctttcactcgtgatcactctttactgtaagcgcggtcgg aagaagctgctgtacatctttaagcaacccttcatgaggcctgtgcagactactca agaggaggacggctgttcatgccggttcccagaggaggaggaaggcggctgcgaac tgcgcgtgaaattcagccgcagcgcagatgctccagcctacaagcaggggcagaac cagctctacaacgaactcaatcttggtcggagagaggagtacgacgtgctggacaa gcggagaggacgggacccagaaatgggcgggaagccgcgcagaaagaatccccaag

		agggcctgtacaacgagctccaaaaggataagatggcagaagcctatagcgagatt ggtatgaaaggggaacgcagaagaggcaaaggccacgacggactgtaccagggact cagcaccgccaccaaggacacctatgacgctcttcacatgcaggccctgccgcctc gg
104876 CAR 2 - Full - aa	78	MALPVTALLLPLALLLHAARPeivmtqspatlslspgeratlsc**rasqdiskyln**w yqqkpgqaprlliy**htsrlhs**giparfsgsgsgtdytltisslqpedfavyfc**qqg ntlpyt**fgqgtkleikggggsggggsggggsqvqlqesgpglvkpsetlsltctvs gvslp**dygvs**wirqppgkglewig**viwgsettyyqsslks**rvtiskdnsknqvslk lssvtaadtavyycak**hyyyggsyamdy**wgqgtlvtvsstttpaprpptpaptias qplslrpeacrpaaggavhtrgldfacdiyiwaplagtcgvlllslvitlyckrgr kkllyifkqpfmrpvqttqeedgcscrfpeeeeggcelrvkfsrsadapaykqgqn qlynelnlgrreeydvldkrrgrdpemggkprrknpqeglynelqkdkmaeaysei gmkgerrrgkghdglyqglstatkdtydalhmqalppr
CAR 3		
CAR3 scFv domain	41	Qvqlqesgpglvkpsetlsltctvsgvslpdygvswirqppgkglewigviwgset tyyssslksrvtiskdnsknqvslklssvtaadtavyycakhyyyggsyamdywgq gtlvtvssggggsggggsggggseivmtqspatlslspgeratlscrasqdiskyl nwyqqkpgqaprlliyhtsrlhsgiparfsgsgsgtdytltisslqpedfavyfcq qgntlpytfgqgtkleik
103104 CAR 3 - Soluble scFv - nt	54	Atggctctgcccgtgaccgcactcctcctgccactggctctgctgcttcacgccgc tcgcccacaagtccagcttcaagaatcagggcctggtctggtgaagccatctgaga ctctgtccctcacttgcaccgtgagcggagtgtccctcccagactacggagtgagc tggattagacagcctcccggaaagggactggagtggatcggagtgatttggggtag cgaaaccacttactattcatcttccctgaagtcacgggtcaccatttcaaaggata actcaaagaatcaagtgagcctcaagctctcatcagtcaccgccgctgacaccgcc gtgtattactgtgccaagcattactactatggagggtcctacgccatggactactg gggccagggaactctggtcactgtgtcatctggtggaggaggtagcggaggaggcg ggagcggtggaggtggctccgaaatcgtgatgacccagagccctgcaaccctgtcc ctttctcccggggaacgggctacccttttcttgtcgggcatcacaagatatctcaaa atacctcaattggtatcaacagaagccgggacaggcccctaggcttcttatctacc acacctctcgcctgcatagcgggattcccgcacgctttagcgggtctggaagcggg accgactacactctgaccatctcatctctccagcccgaggacttcgccgtctactt ctgccagcagggtaacaccctgccgtacaccttcggccagggcaccaagcttgaga tcaaacatcaccaccatcatcaccatcac
103104 CAR 3 - Soluble scFv - aa	66	**MALPVTALLLPLALLLHAARP**qvqlqesgpglvkpsetlsltctvsgvslpdygvs wirqppgkglewigviwgsettyyssslksrvtiskdnsknqvslklssvtaadta vyycakhyyyggsyamdywgqgtlvtvssggggsggggsggggseivmtqspatls lspgeratlscrasqdiskylnwyqqkpgqaprlliyhtsrlhsgiparfsgsgsg

		tdytltisslqpedfavyfcqqgntlpytfgqgtkleik**hhhhhhhh**
104877 CAR 3 – Full - nt	92	atggctctgcccgtgaccgcactcctcctgccactggctctgctgcttcacgccgc tcgcccacaagtccagcttcaagaatcagggcctggtctggtgaagccatctgaga ctctgtccctcacttgcaccgtgagcggagtgtccctcccagactacggagtgagc tggattagacagcctcccggaaagggactggagtggatcggagtgatttggggtag cgaaaccacttactattcatcttccctgaagtcacgggtcaccatttcaaaggata actcaaagaatcaagtgagcctcaagctctcatcagtcaccgccgctgacaccgcc gtgtattactgtgccaagcattactactatggagggtcctacgccatggactactg gggccagggaactctggtcactgtgtcatctggtggaggaggtagcggaggaggcg ggagcggtggaggtggctccgaaatcgtgatgacccagagccctgcaaccctgtcc ctttctcccggggaacgggctacccttttcttgtcgggcatcacaagatatctcaaa atacctcaattggtatcaacagaagccgggacaggcccctaggcttcttatctacc acacctctcgcctgcatagcgggattcccgcacgctttagcgggtctggaagcggg accgactacactctgaccatctcatctctccagcccgaggacttcgccgtctactt ctgccagcagggtaacaccctgccgtacaccttcggccagggcaccaagcttgaga tcaaaaccactactcccgctccaaggccacccacccctgccccgaccatcgcctct cagccgctttccctgcgtccggaggcatgtagacccgcagctggtggggccgtgca tacccggggtcttgacttcgcctgcgatatctacatttgggcccctctggctggta cttgcggggtcctgctgctttcactcgtgatcactctttactgtaagcgcggtcgg aagaagctgctgtacatctttaagcaacccttcatgaggcctgtgcagactactca agaggaggacggctgttcatgccggttcccagaggaggaggaaggcggctgcgaac tgcgcgtgaaattcagccgcagcgcagatgctccagcctacaagcaggggcagaac cagctctacaacgaactcaatcttggtcggagagaggagtacgacgtgctggacaa gcggagaggacgggacccagaaatgggcgggaagccgcgcagaaagaatccccaag agggcctgtacaacgagctccaaaaggataagatggcagaagcctatagcgagatt ggtatgaaaggggaacgcagaagaggcaaaggccacgacggactgtaccagggact cagcaccgccaccaaggacacctatgacgctcttcacatgcaggccctgccgcctc gg
104877 CAR 3 – Full - aa	79	MALPVTALLLPLALLLHAARPqvqlqesgpglvkpsetlsltctvsgvslp**dygvs** wirqppgkglewig**viwgsettyyssslks**rvtiskdnsknqvslklssvtaadta vyycak**hyyyggsyamdy**wgqgtlvtvssggggsggggsggggseivmtqspatls lspgeratlsc**rasqdiskyln**wyqqkpgqaprlliy**htsrlhs**giparfsgsgsg tdytltisslqpedfavyfc**qqgntlpyt**fgqgtkleikttt paprpptpaptias qplslrpeacrpaaggavhtrgldfacdiyiwaplagtcgvlllslvitlyckrgr kkllyifkqpfmrpvqttqeedgcscrfpeeeeggcelrvkfsrsadapaykqgqn qlynelnlgrreeydvldkrrgrdpemggkprrknpqeglynelqkdkmaeaysei gmkgerrrgkghdglyqglstatkdtydalhmqalppr
CAR 4		

CAR4 scFv domain	42	Qvqlqesgpglvkpsetlsltctvsgvslpdygvswirqppgkglewigviwgset tyyqsslksrvtiskdnsknqvslklssvtaadtavyycakhyyyggsyamdywgq gtlvtvssggggsggggsggggseivmtqspatlslspgeratlscrasqdiskyl nwyqqkpgqaprlliyhtsrlhsgiparfsgsgsgtdytltisslqpedfavyfcq qgntlpytfgqgtkleik
103106 CAR4 – Soluble scFv - nt	55	Atggctctgcccgtgaccgcactcctcctgccactggctctgctgcttcacgccgc tcgcccacaagtccagcttcaagaatcagggcctggtctggtgaagccatctgaga ctctgtccctcacttgcaccgtgagcggagtgtccctcccagactacggagtgagc tggattagacagcctcccggaaagggactggagtggatcggagtgatttggggtag cgaaaccacttactatcaatcttccctgaagtcacgggtcaccatttcaaaggata actcaaagaatcaagtgagcctcaagctctcatcagtcaccgccgctgacaccgcc gtgtattactgtgccaagcattactactatggagggtcctacgccatggactactg gggccagggaactctggtcactgtgtcatctggtggaggaggtagcggaggaggcg ggagcggtggaggtggctccgaaatcgtgatgacccagagccctgcaaccctgtcc ctttctcccggggaacgggctacccttttcttgtcgggcatcacaagatatctcaaa atacctcaattggtatcaacagaagccgggacaggcccctaggcttcttatctacc acacctctcgcctgcatagcgggattcccgcacgctttagcgggtctggaagcggg accgactacactctgaccatctcatctctccagcccgaggacttcgccgtctactt ctgccagcagggtaacaccctgccgtacaccttcggccagggcaccaagcttgaga tcaaacatcaccaccatcatcaccatcac
103106 CAR4 – Soluble scFv -aa	67	**MALPVTALLLPLALLLHAARP**qvqlqesgpglvkpsetlsltctvsgvslpdygvs wirqppgkglewigviwgsettyyqsslksrvtiskdnsknqvslklssvtaadta vyycakhyyyggsyamdywgqgtlvtvssggggsggggsggggseivmtqspatls lspgeratlscrasqdiskylnwyqqkpgqaprlliyhtsrlhsgiparfsgsgsg tdytltisslqpedfavyfcqqgntlpytfgqgtkleik**hhhhhhhh**
104878 CAR 4 – Full - nt	93	atggctctgcccgtgaccgcactcctcctgccactggctctgctgcttcacgccgc tcgcccacaagtccagcttcaagaatcagggcctggtctggtgaagccatctgaga ctctgtccctcacttgcaccgtgagcggagtgtccctcccagactacggagtgagc tggattagacagcctcccggaaagggactggagtggatcggagtgatttggggtag cgaaaccacttactatcaatcttccctgaagtcacgggtcaccatttcaaaggata actcaaagaatcaagtgagcctcaagctctcatcagtcaccgccgctgacaccgcc gtgtattactgtgccaagcattactactatggagggtcctacgccatggactactg gggccagggaactctggtcactgtgtcatctggtggaggaggtagcggaggaggcg ggagcggtggaggtggctccgaaatcgtgatgacccagagccctgcaaccctgtcc ctttctcccggggaacgggctacccttttcttgtcgggcatcacaagatatctcaaa atacctcaattggtatcaacagaagccgggacaggcccctaggcttcttatctacc acacctctcgcctgcatagcgggattcccgcacgctttagcgggtctggaagcggg accgactacactctgaccatctcatctctccagcccgaggacttcgccgtctactt

		ctgccagcagggtaacaccctgccgtacaccttcggccagggcaccaagcttgaga tcaaaaccactactcccgctccaaggccacccacccctgccccgaccatcgcctct cagccgctttccctgcgtccggaggcatgtagacccgcagctggtggggccgtgca tacccggggtcttgacttcgcctgcgatatctacatttgggcccctctggctggta cttgcggggtcctgctgctttcactcgtgatcactctttactgtaagcgcggtcgg aagaagctgctgtacatctttaagcaacccttcatgaggcctgtgcagactactca agaggaggacggctgttcatgccggttcccagaggaggaggaaggcggctgcgaac tgcgcgtgaaattcagccgcagcgcagatgctccagcctacaagcaggggcagaac cagctctacaacgaactcaatcttggtcggagagaggagtacgacgtgctggacaa gcggagaggacgggacccagaaatgggcgggaagccgcgcagaaagaatccccaag agggcctgtacaacgagctccaaaaggataagatggcagaagcctatagcgagatt ggtatgaaaggggaacgcagaagaggcaaaggccacgacggactgtaccagggact cagcaccgccaccaaggacacctatgacgctcttcacatgcaggccctgccgcctc gg
104878 CAR 4 – Full - aa	80	MALPVTALLLPLALLLHAARPqvqlqesgpglvkpsetlsltctvsgvslp**dygvs** wirqppgkglewig**viwgsettyyqsslks**rvtiskdnsknqvslklssvtaadta vyycak**hyyyggsyamdy**wgqgtlvtvssggggsggggsggggseivmtqspatls lspgeratlsc**rasqdiskyln**wyqqkpgqaprlliy**htsrlhs**giparfsgsgsg tdytltisslqpedfavyfc**qqgntlpyt**fgqgtkleikttpaprpptpaptias qplslrpeacrpaaggavhtrgldfacdiyiwaplagtcgvlllslvitlyckrgr kkllyifkqpfmrpvqttqeedgcscrfpeeeeggcelrvkfsrsadapaykqgqn qlynelnlgrreeydvldkrrgrdpemggkprrknpqeglynelqkdkmaeaysei gmkgerrrgkghdglyqglstatkdtydalhmqalppr
CAR 5		
CAR5 scFv domain	43	Eivmtqspatlslspgeratlscrasqdiskylnwyqqkpgqaprlliyhtsrlhs giparfsgsgsgtdytltisslqpedfavyfcqqgntlpytfgqgtkleikggggs ggggsggggsggggsqvqlqesgpglvkpsetlsltctvsgvslpdygvswirqpp gkglewigviwgsettyyssslksrvtiskdnsknqvslklssvtaadtavyycak hyyyggsyamdywgqgtlvtvss
99789 CAR5 - Soluble scFv - nt	56	atggccctcccagtgaccgctctgctgctgcctctcgcacttcttctccatgccgc tcggcctgagatcgtcatgacccaaagccccgctaccctgtccctgtcacccggcg agagggcaacccctttcatgcagggccagccaggacatttctaagtacctcaactgg tatcagcagaagccagggcaggctcctcgcctgctgatctaccacaccagccgcct ccacagcggtatccccgccagattttccgggagcgggtctggaaccgactacaccc tcaccatctcttctctgcagcccgaggatttcgccgtctatttctgccagcagggg aatactctgccgtacaccttcggtcaaggtaccaagctggaaatcaagggaggcgg aggatcaggcggtggcggaagcggaggaggtggctccggaggaggaggttcccaag tgcagcttcaagaatcaggacccggacttgtgaagccatcagaaaccctctccctg

		acttgtaccgtgtccggtgtgagcctccccgactacggagtctcttggattcgcca gcctccggggaagggtcttgaatggattggggtgatttggggatcagagactactt actactcttcatcacttaagtcacgggtcaccatcagcaaagataatagcaagaac caagtgtcacttaagctgtcatctgtgaccgccgctgacaccgccgtgtactattg tgccaaacattactattacggagggtcttatgctatggactactggggacagggga ccctggtgactgtctctagccatcaccatcaccaccatcatcac
99789 CAR5 - Soluble scFv -aa	68	**MALPVTALLLPLALLLHAARP**eivmtqspatlslspgeratlscrasqdiskylnw yqqkpgqaprlliyhtsrlhsgiparfsgsgsgtdytltisslqpedfavyfcqqg ntlpytfgqgtkleikggggsggggsggggsggggsqvqlqesgpglvkpsetlsl tctvsgvslpdygvswirqppgkglewigviwgsettyyssslksrvtiskdnskn qvslklssvtaadtavyycakhyyyggsyamdywgqgtlvtvss**hhhhhhhh**
104879 CAR 5 – Full - nt	94	atggccctccctgtcaccgccctgctgcttccgctggctcttctgctccacgccgc tcggcccgaaattgtgatgacccagtcacccgccactcttagcctttcacccggtg agcgcgcaaccctgtcttgcagagcctcccaagacatctcaaaataccttaattgg tatcaacagaagcccggacaggctcctcgccttctgatctaccacaccagccggct ccattctggaatccctgccaggttcagcggtagcggatctgggaccgactacaccc tcactatcagctcactgcagccagaggacttcgctgtctatttctgtcagcaaggg aacaccctgccctacacctttggacagggcaccaagctcgagattaaaggtggagg tggcagcggaggaggtgggtccggcggtggaggaagcggcggaggcgggagccagg tccaactccaagaaagcggaccgggtcttgtgaagccatcagaaactctttcactg acttgtactgtgagcggagtgtctctccccgattacggggtgtcttggatcagaca gccaccggggaagggtctggaatggattggagtgatttggggctctgagactactt actactcttcatccctcaagtcacgcgtcaccatctcaaaggacaactctaagaat caggtgtcactgaaactgtcatctgtgaccgcagccgacaccgccgtgtactattg cgctaagcattactattatggcgggagctacgcaatggattactggggacagggta ctctggtcaccgtgtccagcaccactaccccagcaccgaggccacccaccccggct cctaccatcgcctcccagcctctgtccctgcgtccggaggcatgtagacccgcagc tggtggggccgtgcatacccggggtcttgacttcgcctgcgatatctacatttggg cccctctggctggtacttgcggggtcctgctgctttcactcgtgatcactctttac tgtaagcgcggtcggaagaagctgctgtacatctttaagcaacccttcatgaggcc tgtgcagactactcaagaggaggacggctgttcatgccggttcccagaggaggagg aaggcggctgcgaactgcgcgtgaaattcagccgcagcgcagatgctccagcctac aagcaggggcagaaccagctctacaacgaactcaatcttggtcggagagaggagta cgacgtgctggacaagcggagaggacgggacccagaaatgggcgggaagccgcgca gaaagaatccccaagagggcctgtacaacgagctccaaaaggataagatggcagaa gcctatagcgagattggtatgaaaggggaacgcagaagaggcaaaggccacgacgg actgtaccagggactcagcaccgccaccaaggacacctatgacgctcttcacatgc aggccctgccgcctcgg

104879 CAR 5 – Full - aa	81	MALPVTALLLPLALLLHAARPeivmtqspatlslspgeratlsc**rasqdiskyln**w yqqkpgqaprlliy**htsrlhs**giparfsgsgsgtdytltisslqpedfavyfc**qqg ntlpyt**fgqgtkleikggggsggggsggggsggggsqvqlqesgpglvkpsetlsl tctvsgvslp**dygvs**wirqppgkglewig**viwgsettyyssslks**rvtiskdnskn qvslklssvtaadtavyycak**hyyyggsyamdy**wgqgtlvtvsstttpaprpptpa ptiasqplslrpeacrpaaggavhtrgldfacdiyiwaplagtcgvlllslvitly ckrgrkkllyifkqpfmrpvqttqeedgcscrfpeeeeggcelrvkfsrsadapay kqgqnqlynelnlgrreeydvldkrrgrdpemggkprrknpqeglynelqkdkmae ayseigmkgerrrgkghdglyqglstatkdtydalhmqalppr
CAR 6		
CAR6 scFv domain	44	Eivmtqspatlslspgeratlscrasqdiskylnwyqqkpgqaprlliyhtsrlhs giparfsgsgsgtdytltisslqpedfavyfcqqgntlpytfgqgtkleikggggs ggggsggggsggggsqvqlqesgpglvkpsetlsltctvsgvslpdygvswirqpp gkglewigviwgsettyyqsslksrvtiskdnsknqvslklssvtaadtavyycak hyyyggsyamdywgqgtlvtvss
99790 CAR6 - Soluble scFv - nt	57	atggccctcccagtgaccgctctgctgctgcctctcgcacttcttctccatgccgc tcggcctgagatcgtcatgacccaaagccccgctaccctgtccctgtcacccggcg agagggcaaccctttcatgcagggccagccaggacatttctaagtacctcaactgg tatcagcagaagccagggcaggctcctcgcctgctgatctaccacaccagccgcct ccacagcggtatccccgccagattttccgggagcgggtctggaaccgactacaccc tcaccatctcttctctgcagcccgaggatttcgccgtctatttctgccagcagggg aatactctgccgtacaccttcggtcaaggtaccaagctggaaatcaagggaggcgg aggatcaggcggtggcggaagcggaggaggtggctccggaggaggaggttcccaag tgcagcttcaagaatcaggacccggacttgtgaagccatcagaaaccctctccctg acttgtaccgtgtccggtgtgagcctccccgactacggagtctcttggattcgcca gcctccggggaagggtcttgaatggattggggtgatttggggatcagagactactt actaccagtcatcacttaagtcacgggtcaccatcagcaaagataatagcaagaac caagtgtcacttaagctgtcatctgtgaccgccgctgacaccgccgtgtactattg tgccaaacattactattacggagggtcttatgctatggactactggggacagggga ccctggtgactgtctctagccatcaccatcaccaccatcatcac
99790 CAR6 - Soluble scFv - aa	69	**MALPVTALLLPLALLLHAARP**eivmtqspatlslspgeratlscrasqdiskylnw yqqkpgqaprlliyhtsrlhsgiparfsgsgsgtdytltisslqpedfavyfcqqg ntlpytfgqgtkleikggggsggggsggggsggggsqvqlqesgpglvkpsetlsl tctvsgvslpdygvswirqppgkglewigviwgsettyyqsslksrvtiskdnskn qvslklssvtaadtavyycakhyyyggsyamdywgqgtlvtvss**hhhhhhhh**
104880 CAR6 – Full - nt	95	atggccctccctgtcaccgccctgctgcttccgctggctcttctgctccacgccgc tcggcccgaaattgtgatgacccagtcacccgccactcttagcctttcacccggtg agcgcgcaaccctgtcttgcagagcctcccaagacatctcaaaataccttaattgg

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104880 CAR6 – Full – aa	82	MALPVTALLLPLALLLHAARPeivmtqspatlslspgeratlsc**rasqdiskyln**w yqqkpgqaprlliy**htsrlhs**giparfsgsgsgtdytltisslqpedfavyfc**qqg** **ntlpyt**fgqgtkleikggggsggggsggggsggggsqvqlqesgpglvkpsetlsl tctvsgvslp**dygvs**wirqppgkglewig**viwgsettyyqsslks**rvtiskdnskn qvslklssvtaadtavyycak**hyyyggsyamdy**wgqgtlvtvsstttpaprpptpa ptiasqplslrpeacrpaaggavhtrgldfacdiyiwaplagtcgvlllslvitly ckrgrkkllyifkqpfmrpvqttqeedgcscrfpeeeeggcelrvkfsrsadapay kqgqnqlynelnlgrreeydvldkrrgrdpemggkprrknpqeglynelqkdkmae ayseigmkgerrrgkghdglyqglstatkdtydalhmqalppr
CAR 7		
CAR7 scFv domain	45	Qvqlqesgpglvkpsetlsltctvsgvslpdygvswirqppgkglewigviwgset tyyssslksrvtiskdnsknqvslklssvtaadtavyycakhyyyggsyamdywgq gtlvtvssggggsggggsggggsggggseivmtqspatlslspgeratlscrasqd iskylnwyqqkpgqaprlliyhtsrlhsgiparfsgsgsgtdytltisslqpedfa

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100796 CAR7 - Soluble scFv - nt	58	atggcactgcctgtcactgccctcctgctgcctctggccctccttctgcatgccgc caggccccaagtccagctgcaagagtcaggacccggactggtgaagccgtctgaga ctctctcactgacttgtaccgtcagcggcgtgtccctccccgactacggagtgtca tggatccgccaacctcccgggaaagggcttgaatggattggtgtcatctggggttc tgaaaccacctactactcatcttccctgaagtccagggtgaccatcagcaaggata attccaagaaccaggtcagccttaagctgtcatctgtgaccgctgctgacaccgcc gtgtattactgcgccaagcactactattacggaggaagctacgctatggactattg gggacagggcactctcgtgactgtgagcagcggcggtggagggtctggaggtggag gatccggtggtggtgggtcaggcggaggagggagcgagattgtgatgactcagtca ccagccacccttttctctttcacccggcgagagagcaaccctgagctgtagagccag ccaggacatttctaagtacctcaactggtatcagcaaaaaccggggcaggcccctc gcctcctgatctaccatacctcacgccttcactctggtatccccgctcggtttagc ggatcaggatctggtaccgactacactctgaccatttccagcctgcagccagaaga tttcgcagtgtatttctgccagcagggcaataccttccttacaccttcggtcagg gaaccaagctcgaaatcaagcaccatcaccatcatcaccaccat
100796 CAR7 - Soluble scFv - aa	70	**MALPVTALLLPLALLLHAARP**qvqlqesgpglvkpsetlsltctvsgvslpdygvs wirqppgkglewigviwgsettyyssslksrvtiskdnsknqvslklssvtaadta vyycakhyyyggsyamdywgqgtlvtvssggggsggggsggggsggggseivmtqs patlslspgeratlscrasqdiskylnwyqqkpgqaprlliyhtsrlhsgiparfs gsgsgtdytltisslqpedfavyfcqqgntlpytfgqgtkleik**hhhhhhhh**
104881 CAR 7 Full - nt	96	atggctctgcccgtgaccgcactcctcctgccactggctctgctgcttcacgccgc tcgcccacaagtccagcttcaagaatcagggcctggtctggtgaagccatctgaga ctctgtccctcacttgcaccgtgagcggagtgtccctcccagactacggagtgagc tggattagacagcctcccggaaagggactggagtggatcggagtgatttggggtag cgaaaccacttactattcatcttccctgaagtcacgggtcaccatttcaaaggata actcaaagaatcaagtgagcctcaagctctcatcagtcaccgccgctgacaccgcc gtgtattactgtgccaagcattactactatggagggtcctacgccatggactactg gggccagggaactctggtcactgtgtcatctggtggaggaggtagcggaggaggcg ggagcggtggaggtggctccggaggtggcggaagcgaaatcgtgatgacccagagc cctgcaaccctgtccctttctcccggggaacgggctacccttttcttgtcgggcatc acaagatatctcaaaatacctcaattggtatcaacagaagccgggacaggccccta ggcttcttatctaccacacctctcgcctgcatagcgggattcccgcacgctttagc gggtctggaagcgggaccgactacactctgaccatctcatctctccagcccgagga cttcgccgtctacttctgccagcagggtaacaccctgccgtacaccttcggccagg gcaccaagcttgagatcaaaaccactactcccgctccaaggccacccaccctgcc ccgaccatcgcctctcagccgctttccctgcgtccggaggcatgtagacccgcagc tggtggggccgtgcatacccggggtcttgacttcgcctgcgatatctacatttggg

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104881 CAR 7 Full - aa	83	MALPVTALLLPLALLLHAARPqvqlqesgpglvkpsetlsltctvsgvslp**dygvs** wirqppgkglewig**viwgsettyyssslks**rvtiskdnsknqvslklssvtaadta vyycak**hyyyggsyamdy**wgqgtlvtvssggggsggggsggggsggggseivmtqs patlslspgeratlsc**rasqdiskyln**wyqqkpgqaprlliy**htsrlhs**giparfs gsgsgtdytltisslqpedfavyfc**qqgntlpyt**fgqgtkleikttpaprpptpa ptiasqplslrpeacrpaaggavhtrgldfacdiyiwaplagtcgvlllslvitly ckrgrkkllyifkqpfmrpvqttqeedgcscrfpeeeeggcelrvkfsrsadapay kqgqnqlynelnlgrreeydvldkrrgrdpemggkprrknpqeglynelqkdkmae ayseigmkgerrrgkghdglyqglstatkdtydalhmqalppr
CAR 8		
CAR8 scFv domain	46	Qvqlqesgpglvkpsetlsltctvsgvslpdygvswirqppgkglewigviwgset tyyqsslksrvtiskdnsknqvslklssvtaadtavyycakhyyyggsyamdywgq gtlvtvssggggsggggsggggsggggseivmtqspatlslspgeratlscrasqd iskylnwyqqkpgqaprlliyhtsrlhsgiparfsgsgsgtdytltisslqpedfa vyfcqqgntlpytfgqgtkleik
100798 CAR8 - Soluble scFv - nt	59	atggcactgcctgtcactgccctcctgctgcctctggccctccttctgcatgccgc caggccccaagtccagctgcaagagtcaggacccggactggtgaagccgtctgaga ctctctcactgacttgtaccgtcagcggcgtgtccctccccgactacggagtgtca tggatccgccaacctcccgggaaagggcttgaatggattggtgtcatctggggttc tgaaaccacctactaccagtcttccctgaagtccagggtgaccatcagcaaggata attccaagaaccaggtcagccttaagctgtcatctgtgaccgctgctgacaccgcc gtgtattactgcgccaagcactactattacggaggaagctacgctatggactattg gggacagggcactctcgtgactgtgagcagcggcggtggagggtctggaggtggag gatccggtggtggtgggtcaggcggaggagggagcgagattgtgatgactcagtca ccagccacccttctctttcacccggcgagagagcaaccctgagctgtagagccag ccaggacatttctaagtacctcaactggtatcagcaaaaaccggggcaggccctc gcctcctgatctaccatacctcacgccttcactctggtatccccgctcggtttagc ggatcaggatctggtaccgactacactctgaccatttccagcctgcagccagaaga

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100798 CAR8 - Soluble scFv - aa	71	**MALPVTALLLPLALLLHAARP**qvqlqesgpglvkpsetlsltctvsgvslpdygvs wirqppgkglewigviwgsettyyqsslksrvtiskdnsknqvslklssvtaadta vyycakhyyyggsyamdywgqgtlvtvssggggsggggsggggsggggseivmtqs patlslspgeratlscrasqdiskylnwyqqkpgqaprlliyhtsrlhsgiparfs gsgsgtdytltisslqpedfavyfcqqgntlpytfgqgtkleik**hhhhhhhh**
104882 CAR 8 – Full - nt	97	atggctctgcccgtgaccgcactcctcctgccactggctctgctgcttcacgccgc tcgcccacaagtccagcttcaagaatcagggcctggtctggtgaagccatctgaga ctctgtccctcacttgcaccgtgagcggagtgtccctcccagactacggagtgagc tggattagacagcctcccggaaagggactggagtggatcggagtgatttggggtag cgaaaccacttactatcaatcttccctgaagtcacgggtcaccatttcaaaggata actcaaagaatcaagtgagcctcaagctctcatcagtcaccgccgctgacaccgcc gtgtattactgtgccaagcattactactatggagggtcctacgccatggactactg gggccagggaactctggtcactgtgtcatctggtggaggaggtagcggaggaggcg ggagcggtggaggtggctccggaggcggtgggtcagaaatcgtgatgacccagagc cctgcaaccctgtccctttctcccggggaacgggctacccttttcttgtcgggcatc acaagatatctcaaaatacctcaattggtatcaacagaagccgggacaggccccta ggcttcttatctaccacacctctcgcctgcatagcgggattcccgcacgctttagc gggtctggaagcgggaccgactacactctgaccatctcatctctccagcccgagga cttcgccgtctacttctgccagcagggtaacaccctgccgtacaccttcggccagg gcaccaagcttgagatcaaaaccactactcccgctccaaggccacccacccctgcc ccgaccatcgcctctcagccgctttccctgcgtccggaggcatgtagacccgcagc tggtggggccgtgcatacccggggtcttgacttcgcctgcgatatctacatttggg cccctctggctggtacttgcggggtcctgctgctttcactcgtgatcactctttac tgtaagcgcggtcggaagaagctgctgtacatctttaagcaacccttcatgaggcc tgtgcagactactcaagaggaggacggctgttcatgccggttcccagaggaggagg aaggcggctgcgaactgcgcgtgaaattcagccgcagcgcagatgctccagcctac aagcaggggcagaaccagctctacaacgaactcaatcttggtcggagagaggagta cgacgtgctggacaagcggagaggacgggacccagaaatgggcgggaagccgcgca gaaagaatccccaagagggcctgtacaacgagctccaaaaggataagatggcagaa gcctatagcgagattggtatgaaaggggaacgcagaagaggcaaaggccacgacgg actgtaccagggactcagcaccgccaccaaggacacctatgacgctcttcacatgc aggccctgccgcctcgg
104882 CAR 8 – Full - aa	84	MALPVTALLLPLALLLHAARPqvqlqesgpglvkpsetlsltctvsgvslp**dygvs** wirqppgkglewig**viwgsettyyqsslks**rvtiskdnsknqvslklssvtaadta vyycak**hyyyggsyamdy**wgqgtlvtvssggggsggggsggggsggggseivmtqs patlslspgeratlsc**rasqdiskyln**wyqqkpgqaprlliy**htsrlhs**giparfs

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CAR 9		
CAR9 scFv domain	47	Eivmtqspatlslspgeratlscrasqdiskylnwyqqkpgqaprlliyhtsrlhs giparfsgsgsgtdytltisslqpedfavyfcqqgntlpytfgqgtkleikggggs ggggsggggsggggsqvqlqesgpglvkpsetlsltctvsgvslpdygvswirqpp gkglewigviwgsettyynsslksrvtiskdnsknqvslklssvtaadtavyycak hyyyggsyamdywgqgtlvtvss
99789 CAR9 - Soluble scFv - nt	60	atggccctcccagtgaccgctctgctgctgcctctcgcacttcttctccatgccgc tcggcctgagatcgtcatgacccaaagccccgctaccctgtccctgtcacccggcg agagggcaacccctttcatgcagggccagccaggacatttctaagtacctcaactgg tatcagcagaagccagggcaggctcctcgcctgctgatctaccacaccagccgcct ccacagcggtatccccgccagattttccgggagcgggtctggaaccgactacaccc tcaccatctcttctctgcagcccgaggatttcgccgtctatttctgccagcagggg aatactctgccgtacaccttcggtcaaggtaccaagctggaaatcaagggaggcgg aggatcaggcggtggcggaagcggaggaggtggctccggaggaggaggttcccaag tgcagcttcaagaatcaggacccggacttgtgaagccatcagaaaccctctccctg acttgtaccgtgtccggtgtgagcctccccgactacggagtctcttggattcgcca gcctccggggaagggtcttgaatggattggggtgatttggggatcagagactactt actacaattcatcacttaagtcacgggtcaccatcagcaaagataatagcaagaac caagtgtcacttaagctgtcatctgtgaccgccgctgacaccgccgtgtactattg tgccaaacattactattacggagggtcttatgctatggactactggggacagggga ccctggtgactgtctctagccatcaccatcaccaccatcatcac
99789 CAR9 - Soluble scFv - aa	72	**MALPVTALLLPLALLLHAARP**eivmtqspatlslspgeratlscrasqdiskylnw yqqkpgqaprlliyhtsrlhsgiparfsgsgsgtdytltisslqpedfavyfcqqg ntlpytfgqgtkleikggggsggggsggggsggggsqvqlqesgpglvkpsetlsl tctvsgvslpdygvswirqppgkglewigviwgsettyynsslksrvtiskdnskn qvslklssvtaadtavyycakhyyyggsyamdywgqgtlvtvss**hhhhhhhh**
105974 CAR 9 – Full - nt	98	atggccctccctgtcaccgccctgctgcttccgctggctcttctgctccacgccgc tcggcccgaaattgtgatgacccagtcacccgccactcttagcctttcacccggtg agcgcgcaaccctgtcttgcagagcctcccaagacatctcaaaataccttaattgg tatcaacagaagcccggacaggctcctcgccttctgatctaccacaccagccggct ccattctggaatccctgccaggttcagcggtagcggatctgggaccgactacaccc tcactatcagctcactgcagccagaggacttcgctgtctatttctgtcagcaaggg aacaccctgccctacacctttggacagggcaccaagctcgagattaaaggtggagg

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105974 CAR 9 – Full - aa	85	MALPVTALLLPLALLLHAARPeivmtqspatlslspgeratlsc**rasqdiskyln**w yqqkpgqaprlliy**htsrlhs**giparfsgsgsgtdytltisslqpedfavyfc**qqg** **ntlpyt**fgqgtkleikggggsggggsggggsggggsqvqlqesgpglvkpsetlsl tctvsgvslp**dygvs**wirqppgkglewig**viwgsettyynsslks**rvtiskdnskn qvslklssvtaadtavyycak**hyyyggsyamdy**wgqgtlvtvsstttpaprpptpa ptiasqplslrpeacrpaaggavhtrgldfacdiyiwaplagtcgvlllslvitly ckrgrkkllyifkqpfmrpvqttqeedgcscrfpeeeeggcelrvkfsrsadapay kqgqnqlynelnlgrreeydvldkrrgrdpemggkprrknpqeglynelqkdkmae ayseigmkgerrrgkghdglyqglstatkdtydalhmqalppr
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100796 CAR10 - Soluble	61	atggcactgcctgtcactgccctcctgctgcctctggccctccttctgcatgccgc caggccccaagtccagctgcaagagtcaggacccggactggtgaagccgtctgaga ctctctcactgacttgtaccgtcagcggcgtgtccctccccgactacggagtgtca

scFv - nt		tggatccgccaacctcccgggaaagggcttgaatggattggtgtcatctggggttc tgaaaccacctactacaactcttccctgaagtccagggtgaccatcagcaaggata attccaagaaccaggtcagccttaagctgtcatctgtgaccgctgctgacaccgcc gtgtattactgcgccaagcactactattacggaggaagctacgctatggactattg gggacagggcactctcgtgactgtgagcagcggcggtggagggtctggaggtggag gatccggtggtggtgggtcaggcggaggagggagcgagattgtgatgactcagtca ccagccacccttttctctttcacccggcgagagagcaaccctgagctgtagagccag ccaggacatttctaagtacctcaactggtatcagcaaaaaccggggcaggccctc gcctcctgatctaccatacctcacgccttcactctggtatccccgctcggtttagc ggatcaggatctggtaccgactacactctgaccatttccagcctgcagccagaaga tttcgcagtgtatttctgccagcagggcaataccttccttacaccttcggtcagg gaaccaagctcgaaatcaagcaccatcaccatcatcaccaccat
100796 CAR10 - Soluble scFv - aa	73	**MALPVTALLLPLALLLHAARP**qvqlqesgpglvkpsetlsltctvsgvslpdygvs wirqppgkglewigviwgsettyynsslksrvtiskdnsknqvslklssvtaadta vyycakhyyyggsyamdywgqgtlvtvssggggsggggsggggsggggseivmtqs patlslspgeratlscrasqdiskylnwyqqkpgqaprlliyhtsrlhsgiparfs gsgsgtdytltisslqpedfavyfcqqgntlpytfgqgtkleik**hhhhhhhh**
105975 CAR 10 Full - nt	99	atggccctccctgtcaccgccctgctgcttccgctggctcttctgctccacgccgc tcggcccgaaattgtgatgacccagtcacccgccactcttagcctttcacccggtg agcgcgcaaccctgtcttgcagagcctcccaagacatctcaaaataccttaattgg tatcaacagaagcccggacaggctcctcgccttctgatctaccacaccagccggct ccattctggaatccctgccaggttcagcggtagcggatctgggaccgactacaccc tcactatcagctcactgcagccagaggacttcgctgtctatttctgtcagcaaggg aacaccctgccctacacctttggacagggcaccaagctcgagattaaaggtggagg tggcagcggaggaggtgggtccggcggtggaggaagcggaggcggtgggagccagg tccaactccaagaaagcggaccgggtcttgtgaagccatcagaaactctttcactg acttgtactgtgagcggagtgtctctccccgattacggggtgtcttggatcagaca gccaccggggaagggtctggaatggattggagtgatttggggctctgagactactt actacaactcatccctcaagtcacgcgtcaccatctcaaaggacaactctaagaat caggtgtcactgaaactgtcatctgtgaccgcagccgacaccgccgtgtactattg cgctaagcattactattatggcgggagctacgcaatggattactggggacagggta ctctggtcaccgtgtccagcaccactaccccagcaccgaggccacccaccccggct cctaccatcgcctcccagcctctgtccctgcgtccggaggcatgtagacccgcagc tggtggggccgtgcatacccggggtcttgacttcgcctgcgatatctacatttggg cccctctggctggtacttgcggggtcctgctgctttcactcgtgatcactctttac tgtaagcgcggtcggaagaagctgctgtacatctttaagcaacccttcatgaggcc tgtgcagactactcaagaggaggacggctgttcatgccggttcccagaggaggagg aaggcggctgcgaactgcgcgtgaaattcagccgcagcgcagatgctccagcctac

		aagcaggggcagaaccagctctacaacgaactcaatcttggtcggagagaggagta cgacgtgctggacaagcggagaggacgggacccagaaatgggcgggaagccgcgca gaaagaatccccaagagggcctgtacaacgagctccaaaaggataagatggcagaa gcctatagcgagattggtatgaaaggggaacgcagaagaggcaaaggccacgacgg actgtaccagggactcagcaccgccaccaaggacacctatgacgctcttcacatgc aggccctgccgcctcgg
105975 CAR 10 Full - aa	86	MALPVTALLLPLALLLHAARPEIVMTQSPATLSLSPGERATLSC**RASQDISKYLN**W YQQKPGQAPRLLIY**HTSRLHS**GIPARFSGSGSGTDYTLTISSLQPEDFAVYFC**QQG** **NTLPYT**FGQGTKLEIKGGGGSGGGGSGGGGSGGGGSQVQLQESGPGLVKPSETLSL TCTVSGVSLP**DYGVS**WIRQPPGKGLEWIG**VIWGSETTYYNSSLKS**RVTISKDNSKN QVSLKLSSVTAADTAVYYCAK**HYYYGGSYAMDY**WGQGTLVTVSSTTTPAPRPPTPA PTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLY CKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAY KQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAE AYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
CAR11		
CAR11 scFv domain	49	Eivmtqspatlslspgeratlscrasqdiskylnwyqqkpgqaprlliyhtsrlhs giparfsgsgsgtdytltisslqpedfavyfcqqgntlpytfgqgtkleikggggs ggggsggggsqvqlqesgpglvkpsetlsltctvsgvslpdygvswirqppgkgle wigviwgsettyynsslksrvtiskdnsknqvslklssvtaadtavyycakhyyyg gsyamdywgqgtlvtvss
103101 CAR11 - Soluble scFv - nt	62	Atggccctccctgtcaccgccctgctgcttccgctggctcttctgctccacgccgc tcggcccgaaattgtgatgacccagtcacccgccactcttagcctttcacccggtg agcgcgcaaccctgtcttgcagagcctcccaagacatctcaaaataccttaattgg tatcaacagaagcccggacaggctcctcgccttctgatctaccacaccagccggct ccattctggaatccctgccaggttcagcggtagcggatctgggaccgactacaccc tcactatcagctcactgcagccagaggacttcgctgtctatttctgtcagcaaggg aacaccctgccctacacctttggacagggcaccaagctcgagattaaaggtggagg tggcagcggaggaggtgggtccggcggtggaggaagccaggtccaactccaagaaa gcggaccgggtcttgtgaagccatcagaaactctttcactgacttgtactgtgagc ggagtgtctctccccgattacggggtgtcttggatcagacagccaccggggaaggg tctggaatggattggagtgatttggggctctgagactacttactacaattcatccc tcaagtcacgcgtcaccatctcaaaggacaactctaagaatcaggtgtcactgaaa ctgtcatctgtgaccgcagccgacaccgccgtgtactattgcgctaagcattacta ttatggcgggagctacgcaatggattactggggacagggtactctggtcaccgtgt ccagccaccaccatcatcaccatcaccat

103101 CAR11 - Soluble scFv - aa	74	**MALPVTALLLPLALLLHAARP**eivmtqspatlslspgeratlscrasqdiskylnw yqqkpgqaprlliyhtsrlhsgiparfsgsgsgtdytltisslqpedfavyfcqqg ntlpytfgqgtkleikggggsggggsggggsqvqlqesgpglvkpsetlsltctvs gvslpdygvswirqppgkglewigviwgsettyynsslksrvtiskdnsknqvslk lssvtaadtavyycakhyyyggsyamdywgqgtlvtvss**hhhhhhhh**
105976 CAR 11 Full - nt	100	atggctctgcccgtgaccgcactcctcctgccactggctctgctgcttcacgccgc tcgcccacaagtccagcttcaagaatcagggcctggtctggtgaagccatctgaga ctctgtccctcacttgcaccgtgagcggagtgtccctcccagactacggagtgagc tggattagacagcctcccggaaagggactggagtggatcggagtgatttggggtag cgaaaccacttactataactcttccctgaagtcacgggtcaccatttcaaaggata actcaaagaatcaagtgagcctcaagctctcatcagtcaccgccgctgacaccgcc gtgtattactgtgccaagcattactactatggagggtcctacgccatggactactg gggccagggaactctggtcactgtgtcatctggtggaggaggtagcggaggaggcg ggagcggtggaggtggctccggaggtggcggaagcgaaatcgtgatgacccagagc cctgcaaccctgtccctttctcccggggaacgggctacccttttcttgtcgggcatc acaagatatctcaaaatacctcaattggtatcaacagaagccgggacaggccccta ggcttcttatctaccacacctctcgcctgcatagcgggattcccgcacgctttagc gggtctggaagcgggaccgactacactctgaccatctcatctctccagcccgagga cttcgccgtctacttctgccagcagggtaacaccctgccgtacaccttcggccagg gcaccaagcttgagatcaaaaccactactcccgctccaaggccacccacccctgcc ccgaccatcgcctctcagccgctttccctgcgtccggaggcatgtagacccgcagc tggtggggccgtgcatacccggggtcttgacttcgcctgcgatatctacatttggg cccctctggctggtacttgcggggtcctgctgctttcactcgtgatcactctttac tgtaagcgcggtcggaagaagctgctgtacatctttaagcaacccttcatgaggcc tgtgcagactactcaagaggaggacggctgttcatgccggttcccagaggaggagg aaggcggctgcgaactgcgcgtgaaattcagccgcagcgcagatgctccagcctac aagcaggggcagaaccagctctacaacgaactcaatcttggtcggagagaggagta cgacgtgctggacaagcggagaggacgggacccagaaatgggcgggaagccgcgca gaaagaatccccaagagggcctgtacaacgagctccaaaaggataagatggcagaa gcctatagcgagattggtatgaaaggggaacgcagaagaggcaaaggccacgacgg actgtaccagggactcagcaccgccaccaaggacacctatgacgctcttcacatgc aggccctgccgcctcgg
105976 CAR 11 Full - aa	87	MALPVTALLLPLALLLHAARPQVQLQESGPGLVKPSETLSLTCTVSGVSLP**DYGVS** WIRQPPGKGLEWIG**VIWGSETTYYNSSLKS**RVTISKDNSKNQVSLKLSSVTAADTA VYYCAK**HYYYGGSYAMDY**WGQGTLVTVSSGGGGSGGGGSGGGGSGGGGSEIVMTQS PATLSLSPGERATLSC**RASQDISKYLN**WYQQKPGQAPRLLIY**HTSRLHS**GIPARFS GSGSGTDYTLTISSLQPEDFAVYFC**QQGNTLPYT**FGQGTKLEIKTTTPAPRPPTPA

		PTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLY CKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAY KQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAE AYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
CAR12		
CAR12 scFv domain	50	Qvqlqesgpglvkpsetlsltctvsgvslpdygvswirqppgkglewigviwgset tyynsslksrvtiskdnsknqvslklssvtaadtavyycakhyyyggsyamdywgq gtlvtvssggggsggggsggggseivmtqspatlslspgeratlscrasqdiskyl nwyqqkpgqaprlliyhtsrlhsgiparfsgsgsgtdytltisslqpedfavyfcq qgntlpytfgqgtkleik
103104 CAR12 - Soluble scFv - nt	63	Atggctctgcccgtgaccgcactcctcctgccactggctctgctgcttcacgccgc tcgcccacaagtccagcttcaagaatcagggcctggtctggtgaagccatctgaga ctctgtccctcacttgcaccgtgagcggagtgtccctcccagactacggagtgagc tggattagacagcctcccggaaagggactggagtggatcggagtgatttggggtag cgaaaccacttactataactcttccctgaagtcacgggtcaccatttcaaaggata actcaaagaatcaagtgagcctcaagctctcatcagtcaccgccgctgacaccgcc gtgtattactgtgccaagcattactactatggagggtcctacgccatggactactg gggccagggaactctggtcactgtgtcatctggtggaggaggtagcggaggaggcg ggagcggtggaggtggctccgaaatcgtgatgacccagagccctgcaaccctgtcc ctttctcccggggaacgggctacccttttcttgtcgggcatcacaagatatctcaaa atacctcaattggtatcaacagaagccgggacaggcccctaggcttcttatctacc acacctctcgcctgcatagcgggattcccgcacgctttagcgggtctggaagcggg accgactacactctgaccatctcatctctccagcccgaggacttcgccgtctactt ctgccagcagggtaacaccctgccgtacaccttcggccagggcaccaagcttgaga tcaaacatcaccaccatcatcaccatcac
103104 CAR12 - Soluble scFv -aa	75	**MALPVTALLLPLALLLHAARP**qvqlqesgpglvkpsetlsltctvsgvslpdygvs wirqppgkglewigviwgsettyynsslksrvtiskdnsknqvslklssvtaadta vyycakhyyyggsyamdywgqgtlvtvssggggsggggsggggseivmtqspatls lspgeratlscrasqdiskylnwyqqkpgqaprlliyhtsrlhsgiparfsgsgsg tdytltisslqpedfavyfcqqgntlpytfgqgtkleik**hhhhhhhh**
105977 CAR 12 – Full - nt	101	atggccctccctgtcaccgccctgctgcttccgctggctcttctgctccacgccgc tcggcccgaaattgtgatgacccagtcacccgccactcttagcctttcacccggtg agcgcgcaaccctgtcttgcagagcctcccaagacatctcaaaataccttaattgg tatcaacagaagcccggacaggctcctcgccttctgatctaccacaccagccggct ccattctggaatccctgccaggttcagcggtagcggatctgggaccgactacaccc tcactatcagctcactgcagccagaggacttcgctgtctatttctgtcagcaaggg aacaccctgccctacacctttggacagggcaccaagctcgagattaaaggtggagg

		tggcagcggaggaggtgggtccggcggtggaggaagccaggtccaactccaagaaa gcggaccgggtcttgtgaagccatcagaaactctttcactgacttgtactgtgagc ggagtgtctctccccgattacggggtgtcttggatcagacagccaccggggaaggg tctggaatggattggagtgatttggggctctgagactacttactacaactcatccc tcaagtcacgcgtcaccatctcaaaggacaactctaagaatcaggtgtcactgaaa ctgtcatctgtgaccgcagccgacaccgccgtgtactattgcgctaagcattacta ttatggcgggagctacgcaatggattactggggacagggtactctggtcaccgtgt ccagcaccactaccccagcaccgaggccacccaccccggctcctaccatcgcctcc cagcctctgtccctgcgtccggaggcatgtagacccgcagctggtggggccgtgca tacccggggtcttgacttcgcctgcgatatctacatttgggcccctctggctggta cttgcggggtcctgctgctttcactcgtgatcactctttactgtaagcgcggtcgg aagaagctgctgtacatctttaagcaacccttcatgaggcctgtgcagactactca agaggaggacggctgttcatgccggttcccagaggaggaggaaggcggctgcgaac tgcgcgtgaaattcagccgcagcgcagatgctccagcctacaagcaggggcagaac cagctctacaacgaactcaatcttggtcggagagaggagtacgacgtgctggacaa gcggagaggacgggacccagaaatgggcgggaagccgcgcagaaagaatccccaag agggcctgtacaacgagctccaaaaggataagatggcagaagcctatagcgagatt ggtatgaaaggggaacgcagaagaggcaaaggccacgacggactgtaccagggact cagcaccgccaccaaggacacctatgacgctcttcacatgcaggccctgccgcctc gg
105977 CAR 12 – Full - aa	88	MALPVTALLLPLALLLHAARPEIVMTQSPATLSLSPGERATLSC**RASQDISKYLN**W YQQKPGQAPRLLIY**HTSRLHS**GIPARFSGSGSGTDYTLTISSLQPEDFAVYFC**QQG** **NTLPYT**FGQGTKLEIKGGGGSGGGGSGGGGSQVQLQESGPGLVKPSETLSLTCTVS GVSLP**DYGVS**WIRQPPGKGLEWIG**VIWGSETTYYNSSLKS**RVTISKDNSKNQVSLK LSSVTAADTAVYYCAK**HYYYGGSYAMDY**WGQGTLVTVSSTTTPAPRPPTPAPTIAS QPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGR KKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQN QLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEI GMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
CTL019		
CTL019 – Soluble scFv-Histag - nt	141	Atggccctgcccgtcaccgctctgctgctgcccttgctctgcttcttcatgcagc aaggccggacatccagatgacccaaaccacctcatccctctctgcctctcttggag acagggtgaccatttcttgtcgcgccagccaggacatcagcaagtatctgaactgg tatcagcagaagccggacggaaccgtgaagctcctgatctaccatacctctcgcct gcatagcggcgtgccctcacgcttctctggaagcggatcaggaaccgattattctc tcactatttcaaatcttgagcaggaagatattgccacctatttctgccagcagggt

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CTL019 – Soluble scFv-Histag - aa	76	**MALPVTALLLPLALLLHAARP**diqmtqttsslsaslgdrvtiscrasqdiskylnw yqqkpdgtvklliyhtsrlhsgvpsrfsgsgsgtdysltisnleqediatyfcqqg ntlpytfgggtkleitggggsggggsggggsevklqesgpglvapsqslsvtctvs gvslpdygvswirqpprkglewlgviwgsettyynsalksrltiikdnsksqvflk mnslqtddtaiyycakhyyyggsyamdywgqgtsvtvss**hhhhhhhh**
CTL019 Full - nt	102	atggccttaccagtgaccgccttgctcctgccgctggccttgctgctccacgccgc caggccggacatccagatgacacagactacatcctccctgtctgcctctctgggag acagagtcaccatcagttgcagggcaagtcaggacattagtaaatatttaaattgg tatcagcagaaaccagatggaactgttaaactcctgatctaccatacatcaagatt acactcaggagtcccatcaaggttcagtggcagtgggtctggaacagattattctc tcaccattagcaacctggagcaagaagatattgccacttacttttgccaacagggt aatacgcttccgtacacgttcggaggggggaccaagctggagatcacaggtggcgg tggctcgggcggtggtgggtcgggtggcggcggatctgaggtgaaactgcaggagt caggacctggcctggtggcgccctcacagagcctgtccgtcacatgcactgtctca ggggtctcattacccgactatggtgtaagctggattcgccagcctccacgaaaggg tctggagtggctgggagtaatatggggtagtgaaaccacatactataattcagctc tcaaatccagactgaccatcatcaaggacaactccaagagccaagttttcttaaaa atgaacagtctgcaaactgatgacacagccatttactactgtgccaaacattatta ctacggtggtagctatgctatggactactggggccaaggaacctcagtcaccgtct cctcaaccacgacgccagcgccgcgaccaccaacaccggcgcccaccatcgcgtcg cagcccctgtccctgcgcccagaggcgtgccggccagcggcgggggggcgcagtgca cacgaggggggctggacttcgcctgtgatatctacatctgggcgcccttggccggga cttgtggggtccttctcctgtcactggttatcacccctttactgcaaacggggcaga aagaaactcctgtatatattcaaacaaccatttatgagaccagtacaaactactca agaggaagatggctgtagctgccgatttccagaagaagaagaaggaggatgtgaac tgagagtgaagttcagcaggagcgcagacgcccccgcgtacaagcagggccagaac cagctctataacgagctcaatctaggacgaagagaggagtacgatgttttggacaa gagacgtggccgggaccctgagatgggggggaaagccgagaaggaagaaccctcagg aaggcctgtacaatgaactgcagaaagataagatggcggaggcctacagtgagatt

		gggatgaaaggcgagcgccggaggggcaaggggcacgatggcctttaccagggtct cagtacagccaccaaggacacctacgacgcccttcacatgcaggccctgcccctc gc
CTL019 Full – aa (including signal sequence shown in bold)	89	**MALPVTALLLPLALLLHAARP**diqmtqttsslsaslgdrvtiscrasqdiskylnw yqqkpdgtvklliyhtsrlhsgvpsrfsgsgsgtdysltisnleqediatyfcqqg ntlpytfgggtkleitggggsggggsggggsevklqesgpglvapsqslsvtctvs gvslpdygvswirqpprkglewlgviwgsettyynsalksrltiikdnsksqvflk mnslqtddtaiyycakhyyyggsyamdywgqgtsvtvsstttpaprpptpaptias qplslrpeacrpaaggavhtrgldfacdiyiwaplagtcgvlllslvitlyckrgr kkllyifkqpfmrpvqttqeedgcscrfpeeeeggcelrvkfsrsadapaykqgqn qlynelnlgrreeydvldkrrgrdpemggkprrknpqeglynelqkdkmaeaysei gmkgerrrgkghdglyqglstatkdtydalhmqalppr
CTL019 scFv domain	51	Diqmtqttsslsaslgdrvtiscrasqdiskylnwyqqkpdgtvklliyhtsrlhs gvpsrfsgsgsgtdysltisnleqediatyfcqqgntlpytfgggtkleitggggs ggggsggggsevklqesgpglvapsqslsvtctvsgvslpdygvswirqpprkgle wlgviwgsettyynsalksrltiikdnsksqvflkmnslqtddtaiyycakhyyyg gsyamdywgqgtsvtvss

Co-expression of CAR with Other Molecules or Agents

Co-expression of a Second CAR

In one aspect, the CAR-expressing cell described herein can further comprise a second CAR, e.g., a second CAR that includes a different antigen binding domain, e.g., to the same target (e.g., CD19) or a different target (e.g., a target other than CD19, e.g., a target described herein). In one embodiment, the CAR-expressing cell comprises a first CAR that targets a first antigen and includes an intracellular signaling domain having a costimulatory signaling domain but not a primary signaling domain, and a second CAR that targets a second, different, antigen and includes an intracellular signaling domain having a primary signaling domain but not a costimulatory signaling domain. Placement of a costimulatory signaling domain, e.g., 4-1BB, CD28, CD27, OX-40 or ICOS, onto the first CAR, and the primary signaling domain, e.g., CD3 zeta, on the second CAR can limit the CAR activity to cells where both targets are expressed. In one embodiment, the CAR expressing cell comprises a first CAR that includes an antigen binding domain, a transmembrane domain and a costimulatory domain and a second CAR that targets another antigen and includes an antigen binding domain, a transmembrane domain and a primary signaling domain. In another embodiment, the CAR expressing cell comprises a first CAR that includes an antigen binding domain, a transmembrane domain and a

primary signaling domain and a second CAR that targets another antigen and includes an antigen binding domain to the antigen, a transmembrane domain and a costimulatory signaling domain.

In one embodiment, the CAR-expressing cell comprises an XCAR described herein and an inhibitory CAR. In one embodiment, the inhibitory CAR comprises an antigen binding domain that binds an antigen found on normal cells but not cancer cells, e.g., normal cells that also express X. In one embodiment, the inhibitory CAR comprises the antigen binding domain, a transmembrane domain and an intracellular domain of an inhibitory molecule. For example, the intracellular domain of the inhibitory CAR can be an intracellular domain of PD1, PD-L1, PD-L2, CTLA4, TIM3, CEACAM (CEACAM-1, CEACAM-3, and/or CEACAM-5), LAG3, VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4, CD80, CD86, B7-H3 (CD276), B7-H4 (VTCN1), HVEM (TNFRSF14 or CD270), KIR, A2aR, MHC class I, MHC class II, GAL9, adenosine, and TGF (e.g., TGFbeta).

In one embodiment, when the CAR-expressing cell comprises two or more different CARs, the antigen binding domains of the different CARs can be such that the antigen binding domains do not interact with one another. For example, a cell expressing a first and second CAR can have an antigen binding domain of the first CAR, e.g., as a fragment, e.g., an scFv, that does not form an association with the antigen binding domain of the second CAR, e.g., the antigen binding domain of the second CAR is a VHH.

In some embodiments, the antigen binding domain comprises a single domain antigen binding (SDAB) molecules include molecules whose complementary determining regions are part of a single domain polypeptide. Examples include, but are not limited to, heavy chain variable domains, binding molecules naturally devoid of light chains, single domains derived from conventional 4-chain antibodies, engineered domains and single domain scaffolds other than those derived from antibodies. SDAB molecules may be any of the art, or any future single domain molecules. SDAB molecules may be derived from any species including, but not limited to mouse, human, camel, llama, lamprey, fish, shark, goat, rabbit, and bovine. This term also includes naturally occurring single domain antibody molecules from species other than Camelidae and sharks.

In one aspect, an SDAB molecule can be derived from a variable region of the immunoglobulin found in fish, such as, for example, that which is derived from the immunoglobulin isotype known as Novel Antigen Receptor (NAR) found in the serum of

shark. Methods of producing single domain molecules derived from a variable region of NAR ("IgNARs") are described in WO 03/014161 and Streltsov (2005) Protein Sci. 14:2901-2909.

According to another aspect, an SDAB molecule is a naturally occurring single domain antigen binding molecule known as heavy chain devoid of light chains. Such single domain molecules are disclosed in WO 9404678 and Hamers-Casterman, C. et al. (1993) Nature 363:446-448, for example. For clarity reasons, this variable domain derived from a heavy chain molecule naturally devoid of light chain is known herein as a VHH or nanobody to distinguish it from the conventional VH of four chain immunoglobulins. Such a VHH molecule can be derived from Camelidae species, for example in camel, llama, dromedary, alpaca and guanaco. Other species besides Camelidae may produce heavy chain molecules naturally devoid of light chain; such VHHs are within the scope of the invention.

The SDAB molecules can be recombinant, CDR-grafted, humanized, camelized, de-immunized and/or in vitro generated (e.g., selected by phage display).

It has also been discovered, that cells having a plurality of chimeric membrane embedded receptors comprising an antigen binding domain that interactions between the antigen binding domain of the receptors can be undesirable, e.g., because it inhibits the ability of one or more of the antigen binding domains to bind its cognate antigen. Accordingly, disclosed herein are cells having a first and a second non-naturally occurring chimeric membrane embedded receptor comprising antigen binding domains that minimize such interactions. Also disclosed herein are nucleic acids encoding a first and a second non-naturally occurring chimeric membrane embedded receptor comprising an antigen binding domains that minimize such interactions, as well as methods of making and using such cells and nucleic acids. In an embodiment the antigen binding domain of one of the first and the second non-naturally occurring chimeric membrane embedded receptor, comprises an scFv, and the other comprises a single VH domain, e.g., a camelid, shark, or lamprey single VH domain, or a single VH domain derived from a human or mouse sequence.

In some embodiments, a composition herein comprises a first and second CAR, wherein the antigen binding domain of one of the first and the second CAR does not comprise a variable light domain and a variable heavy domain. In some embodiments, the antigen binding domain of one of the first and the second CAR is an scFv, and the other is not an scFv. In some embodiments, the antigen binding domain of one of the first and the second CAR comprises a single VH domain, e.g., a camelid, shark, or lamprey single VH domain, or a single VH domain

derived from a human or mouse sequence. In some embodiments, the antigen binding domain of one of the first and the second CAR comprises a nanobody. In some embodiments, the antigen binding domain of one of the first and the second CAR comprises a camelid VHH domain.

In some embodiments, the antigen binding domain of one of the first and the second CAR comprises an scFv, and the other comprises a single VH domain, e.g., a camelid, shark, or lamprey single VH domain, or a single VH domain derived from a human or mouse sequence. In some embodiments, the antigen binding domain of one of the first and the second CAR comprises an scFv, and the other comprises a nanobody. In some embodiments, the antigen binding domain of one of the first and the second CAR comprises an scFv, and the other comprises a camelid VHH domain.

In some embodiments, when present on the surface of a cell, binding of the antigen binding domain of the first CAR to its cognate antigen is not substantially reduced by the presence of the second CAR. In some embodiments, binding of the antigen binding domain of the first CAR to its cognate antigen in the presence of the second CAR is 85%, 90%, 95%, 96%, 97%, 98% or 99% of binding of the antigen binding domain of the first CAR to its cognate antigen in the absence of the second CAR.

In some embodiments, when present on the surface of a cell, the antigen binding domains of the first and the second CAR, associate with one another less than if both were scFv antigen binding domains. In some embodiments, the antigen binding domains of the first and the second CAR, associate with one another 85%, 90%, 95%, 96%, 97%, 98% or 99% less than if both were scFv antigen binding domains.

Co-expression of an Agent that Enhances CAR Activity

In another aspect, the CAR-expressing cell described herein can further express another agent, e.g., an agent that enhances the activity or fitness of a CAR-expressing cell.

For example, in one embodiment, the agent can be an agent which inhibits a molecule that modulates or regulates, e.g., inhibits, T cell function. In some embodiments, the molecule that modulates or regulates T cell function is an inhibitory molecule. Inhibitory molecules, e.g., PD1, can, in some embodiments, decrease the ability of a CAR-expressing cell to mount an immune effector response. Examples of inhibitory molecules include PD1, PD-L1, CTLA4, TIM3, LAG3, VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4, CD80, CD86, B7-H3 (CD276),

B7-H4 (VTCN1), HVEM (TNFRSF14 or CD270), KIR, A2aR, MHC class I, MHC class II, GAL9, adenosine, or TGF beta.

In embodiments, an agent, e.g., an inhibitory nucleic acid, e.g., a dsRNA, e.g., an siRNA or shRNA; or e.g., an inhibitory protein or system, e.g., a clustered regularly interspaced short palindromic repeats (CRISPR), a transcription-activator like effector nuclease (TALEN), or a zinc finger endonuclease (ZFN), e.g., as described herein, can be used to inhibit expression of a molecule that modulates or regulates, e.g., inhibits, T-cell function in the CAR-expressing cell. In an embodiment the agent is an shRNA, e.g., an shRNA described herein. In an embodiment, the agent that modulates or regulates, e.g., inhibits, T-cell function is inhibited within a CAR-expressing cell. For example, a dsRNA molecule that inhibits expression of a molecule that modulates or regulates, e.g., inhibits, T-cell function is linked to the nucleic acid that encodes a component, e.g., all of the components, of the CAR.

In one embodiment, the agent that inhibits an inhibitory molecule comprises a first polypeptide, e.g., an inhibitory molecule, associated with a second polypeptide that provides a positive signal to the cell, e.g., an intracellular signaling domain described herein. In one embodiment, the agent comprises a first polypeptide, e.g., of an inhibitory molecule such as PD1, PD-L1, CTLA4, TIM3, LAG3, VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4, CD80, CD86, B7-H3 (CD276), B7-H4 (VTCN1), HVEM (TNFRSF14 or CD270), KIR, A2aR, MHC class I, MHC class II, GAL9, adenosine, or TGF beta, or a fragment of any of these (e.g., at least a portion of an extracellular domain of any of these), and a second polypeptide which is an intracellular signaling domain described herein (e.g., comprising a costimulatory domain (e.g., 41BB, CD27 or CD28, e.g., as described herein) and/or a primary signaling domain (e.g., a CD3 zeta signaling domain described herein). In one embodiment, the agent comprises a first polypeptide of PD1 or a fragment thereof (e.g., at least a portion of an extracellular domain of PD1), and a second polypeptide of an intracellular signaling domain described herein (e.g., a CD28 signaling domain described herein and/or a CD3 zeta signaling domain described herein). PD1 is an inhibitory member of the CD28 family of receptors that also includes CD28, CTLA-4, ICOS, and BTLA. PD-1 is expressed on activated B cells, T cells and myeloid cells (Agata et al. 1996 Int. Immunol 8:765-75). Two ligands for PD1, PD-L1 and PD-L2 have been shown to downregulate T cell activation upon binding to PD1 (Freeman et a. 2000 J Exp Med 192:1027-34; Latchman et al. 2001 Nat Immunol 2:261-8; Carter et al. 2002 Eur J Immunol 32:634-43). PD-L1 is abundant in human cancers (Dong et al. 2003 J Mol Med 81:281-7;

Blank et al. 2005 Cancer Immunol. Immunother 54:307-314; Konishi et al. 2004 Clin Cancer Res 10:5094). Immune suppression can be reversed by inhibiting the local interaction of PD1 with PD-L1.

In one embodiment, the agent comprises the extracellular domain (ECD) of an inhibitory molecule, e.g., Programmed Death 1 (PD1), can be fused to a transmembrane domain and intracellular signaling domains such as 41BB and CD3 zeta (also referred to herein as a PD1 CAR). In one embodiment, the PD1 CAR, when used in combinations with an XCAR described herein, improves the persistence of the T cell. In one embodiment, the CAR is a PD1 CAR comprising the extracellular domain of PD1 indicated as underlined in SEQ ID NO: 105. In one embodiment, the PD1 CAR comprises the amino acid sequence of SEQ ID NO: 105.

Malpvtalllplalllhaarppgwfldspdrpwnpptfspallvvtegdnatftcsfsntsesfvlnwyrmspsnqtdklaafpedrsqpgqdcrfrvtqlpngrdfhmsvvrarrndsgtylcgaislapkaqikeslraelrvterraevptahpspsprpagqfqtlvtttpaprpptpaptiasqplslrpeacrpaaggavhtrgldfacdiyiwaplagtcgvlllslvitlyckrgrkkllyifkqpfmrpvqttqeedgcscrfpeeeeggcelrvkfsrsadapaykqgqnqlynelnlgrreeydvldkrrgrdpemggkprrknpqeglynelqkdkmaeayseigmkgerrrgkghdglyqglstatkdtydalhmqalppr (SEQ ID NO:105).

In one embodiment, the PD1 CAR comprises the amino acid sequence provided below (SEQ ID NO:106).

pgwfldspdrpwnpptfspallvvtegdnatftcsfsntsesfvlnwyrmspsnqtdklaafpedrsqpgqdcrfrvtqlpngrdfhmsvvrarrndsgtylcgaislapkaqikeslraelrvterraevptahpspsprpagqfqtlvtttpaprpptpaptiasqplslrpeacrpaaggavhtrgldfacdiyiwaplagtcgvlllslvitlyckrgrkkllyifkqpfmrpvqttqeedgcscrfpeeeeggcelrvkfsrsadapaykqgqnqlynelnlgrreeydvldkrrgrdpemggkprrknpqeglynelqkdkmaeayseigmkgerrrgkghdglyqglstatkdtydalhmqalppr (SEQ ID NO:106).

In one embodiment, the agent comprises a nucleic acid sequence encoding the PD1 CAR, e.g., the PD1 CAR described herein. In one embodiment, the nucleic acid sequence for the PD1 CAR is shown below, with the PD1 ECD underlined below in SEQ ID NO: 103:

atggccctccctgtcactgccctgcttctccccctcgcactcctgctccacgccgctagaccacccggatggtttctggactctccggatcgcccgtggaatcccccaaccttctcaccggcactcttggttgtgactgagggcgataatgcgaccttcacgtgctcgttctccaacacctccgaatcattcgtgctgaactggtaccgcatgagcccgtcaaaccagaccgacaagctcgccgcgtttccggaagatcggtcgcaaccgggacaggattgtcggttccgcgtgactcaactgccgaatggcagagacttccacatgagcgtggtccgcgctaggcgaaacgactccgggacctacctgtgcggagccatctcgctggcgcctaaggcccaaatcaaagagagcttgagggccgaactgagagtgaccgagcgcagag

ctgaggtgccaactgcacatccatccccatcgcctcggcctgcggggcagtttcagaccctggtcacgaccactccggcgccgcgccc
accgactccggccccaactatcgcgagccagcccctgtcgctgaggccggaagcatgccgccctgccgccggaggtgctgtgcatac
ccggggattggacttcgcatgcgacatctacatttgggctcctctcgccggaacttgtggcgtgctccttctgtccctggtcatcaccctgta
ctgcaagcggggtcggaaaaagcttctgtacattttcaagcagcccttcatgaggcccgtgcaaaccacccaggaggaggacggttgct
cctgccggttccccgaagaggaagaaggaggttgcgagctgcgcgtgaagttctcccggagcgccgacgcccccgcctataagcagg
gccagaaccagctgtacaacgaactgaacctgggacggcgggaagagtacgatgtgctggacaagcggcgcggccgggaccccga
aatgggcgggaagcctagaagaaagaaccctcaggaaggcctgtataacgagctgcagaaggacaagatggccgaggcctactccg
aaattgggatgaagggagagcggcggaggggaaaggggcacgacggcctgtaccaaggactgtccaccgccaccaaggacacata
cgatgccctgcacatgcaggcccttcccccctcgc (SEQ ID NO: 103).

In another example, in one embodiment, the agent that enhances the activity of a CAR-expressing cell can be a costimulatory molecule or costimulatory molecule ligand. Examples of costimulatory molecules include MHC class I molecule, BTLA and a Toll ligand receptor, as well as OX40, CD27, CD28, CDS, ICAM-1, LFA-1 (CD11a/CD18), ICOS (CD278), and 4-1BB (CD137). Further examples of such costimulatory molecules include CDS, ICAM-1, GITR, BAFFR, HVEM (LIGHTR), SLAMF7, NKp80 (KLRF1), NKp44, NKp30, NKp46, CD160, CD19, CD4, CD8alpha, CD8beta, IL2R beta, IL2R gamma, IL7R alpha, ITGA4, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CD11d, ITGAE, CD103, ITGAL, CD11a, LFA-1, ITGAM, CD11b, ITGAX, CD11c, ITGB1, CD29, ITGB2, CD18, LFA-1, ITGB7, NKG2D, NKG2C, TNFR2, TRANCE/RANKL, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRTAM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100 (SEMA4D), CD69, SLAMF6 (NTB-A, Ly108), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, LAT, GADS, SLP-76, PAG/Cbp, CD19a, and a ligand that specifically binds with CD83., e.g., as described herein. Examples of costimulatory molecule ligands include CD80, CD86, CD40L, ICOSL, CD70, OX40L, 4-1BBL, GITRL, and LIGHT. In embodiments, the costimulatory molecule ligand is a ligand for a costimulatory molecule different from the costimulatory molecule domain of the CAR. In embodiments, the costimulatory molecule ligand is a ligand for a costimulatory molecule that is the same as the costimulatory molecule domain of the CAR. In an embodiment, the costimulatory molecule ligand is 4-1BBL. In an embodiment, the costimulatory ligand is CD80 or CD86. In an embodiment, the costimulatory molecule ligand is CD70. In embodiments, a CAR-expressing immune effector cell described herein can be

further engineered to express one or more additional costimulatory molecules or costimulatory molecule ligands.

Co-expression of CAR with a Chemokine Receptor

In embodiments, the CAR-expressing cell described herein, e.g., CD19 CAR-expressing cell, further comprises a chemokine receptor molecule. Transgenic expression of chemokine receptors CCR2b or CXCR2 in T cells enhances trafficking to CCL2- or CXCL1-secreting solid tumors including melanoma and neuroblastoma (Craddock et al., *J Immunother.* 2010 Oct; 33(8):780-8 and Kershaw et al., *Hum Gene Ther.* 2002 Nov 1; 13(16):1971-80). Thus, without wishing to be bound by theory, it is believed that chemokine receptors expressed in CAR-expressing cells that recognize chemokines secreted by tumors, e.g., solid tumors, can improve homing of the CAR-expressing cell to the tumor, facilitate the infiltration of the CAR-expressing cell to the tumor, and enhances antitumor efficacy of the CAR-expressing cell. The chemokine receptor molecule can comprise a naturally occurring or recombinant chemokine receptor or a chemokine-binding fragment thereof. A chemokine receptor molecule suitable for expression in a CAR-expressing cell (e.g., CAR-Tx) described herein include a CXC chemokine receptor (e.g., CXCR1, CXCR2, CXCR3, CXCR4, CXCR5, CXCR6, or CXCR7), a CC chemokine receptor (e.g., CCR1, CCR2, CCR3, CCR4, CCR5, CCR6, CCR7, CCR8, CCR9, CCR10, or CCR11), a CX3C chemokine receptor (e.g., CX3CR1), a XC chemokine receptor (e.g., XCR1), or a chemokine-binding fragment thereof. In one embodiment, the chemokine receptor molecule to be expressed with a CAR described herein is selected based on the chemokine(s) secreted by the tumor. In one embodiment, the CAR-expressing cell described herein further comprises, e.g., expresses, a CCR2b receptor or a CXCR2 receptor. In an embodiment, the CAR described herein and the chemokine receptor molecule are on the same vector or are on two different vectors. In embodiments where the CAR described herein and the chemokine receptor molecule are on the same vector, the CAR and the chemokine receptor molecule are each under control of two different promoters or are under the control of the same promoter.

Nucleic Acid Constructs Encoding a CAR

The present invention also provides an immune effector cell, e.g., made by a method described herein, that includes a nucleic acid molecules encoding one or more CAR constructs

described herein. In one aspect, the nucleic acid molecule is provided as a messenger RNA transcript. In one aspect, the nucleic acid molecule is provided as a DNA construct.

The nucleic acid molecules described herein can be a DNA molecule, an RNA molecule, or a combination thereof. In one embodiment, the nucleic acid molecule is an mRNA encoding a CAR polypeptide as described herein. In other embodiments, the nucleic acid molecule is a vector that includes any of the aforesaid nucleic acid molecules.

In one aspect, the antigen binding domain of a CAR of the invention (e.g., a scFv) is encoded by a nucleic acid molecule whose sequence has been codon optimized for expression in a mammalian cell. In one aspect, entire CAR construct of the invention is encoded by a nucleic acid molecule whose entire sequence has been codon optimized for expression in a mammalian cell. Codon optimization refers to the discovery that the frequency of occurrence of synonymous codons (i.e., codons that code for the same amino acid) in coding DNA is biased in different species. Such codon degeneracy allows an identical polypeptide to be encoded by a variety of nucleotide sequences. A variety of codon optimization methods is known in the art, and include, e.g., methods disclosed in at least US Patent Numbers 5,786,464 and 6,114,148.

Accordingly, in one aspect, an immune effector cell, e.g., made by a method described herein, includes a nucleic acid molecule encoding a chimeric antigen receptor (CAR), wherein the CAR comprises an antigen binding domain that binds to a tumor antigen described herein, a transmembrane domain (e.g., a transmembrane domain described herein), and an intracellular signaling domain (e.g., an intracellular signaling domain described herein) comprising a stimulatory domain, e.g., a costimulatory signaling domain (e.g., a costimulatory signaling domain described herein) and/or a primary signaling domain (e.g., a primary signaling domain described herein, e.g., a zeta chain described herein).

The present invention also provides vectors in which a nucleic acid molecule encoding a CAR, e.g., a nucleic acid molecule described herein, is inserted. Vectors derived from retroviruses such as the lentivirus are suitable tools to achieve long-term gene transfer since they allow long-term, stable integration of a transgene and its propagation in daughter cells. Lentiviral vectors have the added advantage over vectors derived from onco-retroviruses such as murine leukemia viruses in that they can transduce non-proliferating cells, such as hepatocytes. They also have the added advantage of low immunogenicity. A retroviral vector may also be, e.g., a gammaretroviral vector. A gammaretroviral vector may include, e.g., a

promoter, a packaging signal (ψ), a primer binding site (PBS), one or more (e.g., two) long terminal repeats (LTR), and a transgene of interest, e.g., a gene encoding a CAR. A gammaretroviral vector may lack viral structural gens such as gag, pol, and env. Exemplary gammaretroviral vectors include Murine Leukemia Virus (MLV), Spleen-Focus Forming Virus (SFFV), and Myeloproliferative Sarcoma Virus (MPSV), and vectors derived therefrom. Other gammaretroviral vectors are described, e.g., in Tobias Maetzig et al., "Gammaretroviral Vectors: Biology, Technology and Application" Viruses. 2011 Jun; 3(6): 677–713.

In another embodiment, the vector comprising the nucleic acid encoding the desired CAR is an adenoviral vector (A5/35). In another embodiment, the expression of nucleic acids encoding CARs can be accomplished using of transposons such as sleeping beauty, crisper, CAS9, and zinc finger nucleases. See below June et al. 2009*Nature Reviews Immunology* 9.10: 704-716, is incorporated herein by reference.

In brief summary, the expression of natural or synthetic nucleic acids encoding CARs is typically achieved by operably linking a nucleic acid encoding the CAR polypeptide or portions thereof to a promoter, and incorporating the construct into an expression vector. The vectors can be suitable for replication and integration eukaryotes. Typical cloning vectors contain transcription and translation terminators, initiation sequences, and promoters useful for regulation of the expression of the desired nucleic acid sequence.

The nucleic acid can be cloned into a number of types of vectors. For example, the nucleic acid can be cloned into a vector including, but not limited to a plasmid, a phagemid, a phage derivative, an animal virus, and a cosmid. Vectors of particular interest include expression vectors, replication vectors, probe generation vectors, and sequencing vectors.

Further, the expression vector may be provided to a cell in the form of a viral vector. Viral vector technology is well known in the art and is described, for example, in Sambrook et al., 2012, MOLECULAR CLONING: A LABORATORY MANUAL, volumes 1 -4, Cold Spring Harbor Press, NY), and in other virology and molecular biology manuals. Viruses, which are useful as vectors include, but are not limited to, retroviruses, adenoviruses, adeno-associated viruses, herpes viruses, and lentiviruses. In general, a suitable vector contains an origin of replication functional in at least one organism, a promoter sequence, convenient restriction endonuclease sites, and one or more selectable markers, (e.g., WO 01/96584; WO 01/29058; and U.S. Pat. No. 6,326,193).

A number of viral based systems have been developed for gene transfer into mammalian cells. For example, retroviruses provide a convenient platform for gene delivery systems. A selected gene can be inserted into a vector and packaged in retroviral particles using techniques known in the art. The recombinant virus can then be isolated and delivered to cells of the subject either in vivo or ex vivo. A number of retroviral systems are known in the art. In some embodiments, adenovirus vectors are used. A number of adenovirus vectors are known in the art. In one embodiment, lentivirus vectors are used.

Additional promoter elements, e.g., enhancers, regulate the frequency of transcriptional initiation. Typically, these are located in the region 30-110 bp upstream of the start site, although a number of promoters have been shown to contain functional elements downstream of the start site as well. The spacing between promoter elements frequently is flexible, so that promoter function is preserved when elements are inverted or moved relative to one another. In the thymidine kinase (tk) promoter, the spacing between promoter elements can be increased to 50 bp apart before activity begins to decline. Depending on the promoter, it appears that individual elements can function either cooperatively or independently to activate transcription. Exemplary promoters include the CMV IE gene, EF-1α, ubiquitin C, or phosphoglycerokinase (PGK) promoters.

An example of a promoter that is capable of expressing a CAR encoding nucleic acid molecule in a mammalian T cell is the EF1a promoter. The native EF1a promoter drives expression of the alpha subunit of the elongation factor-1 complex, which is responsible for the enzymatic delivery of aminoacyl tRNAs to the ribosome. The EF1a promoter has been extensively used in mammalian expression plasmids and has been shown to be effective in driving CAR expression from nucleic acid molecules cloned into a lentiviral vector. See, e.g., Milone et al., Mol. Ther. 17(8): 1453–1464 (2009). In one aspect, the EF1a promoter comprises the sequence provided in the Examples.

Another example of a promoter is the immediate early cytomegalovirus (CMV) promoter sequence. This promoter sequence is a strong constitutive promoter sequence capable of driving high levels of expression of any polynucleotide sequence operatively linked thereto. However, other constitutive promoter sequences may also be used, including, but not limited to the simian virus 40 (SV40) early promoter, mouse mammary tumor virus (MMTV), human immunodeficiency virus (HIV) long terminal repeat (LTR) promoter, MoMuLV promoter, an avian leukemia virus promoter, an Epstein-Barr virus immediate early promoter, a Rous

sarcoma virus promoter, as well as human gene promoters such as, but not limited to, the actin promoter, the myosin promoter, the elongation factor-1α promoter, the hemoglobin promoter, and the creatine kinase promoter. Further, the invention should not be limited to the use of constitutive promoters. Inducible promoters are also contemplated as part of the invention. The use of an inducible promoter provides a molecular switch capable of turning on expression of the polynucleotide sequence which it is operatively linked when such expression is desired, or turning off the expression when expression is not desired. Examples of inducible promoters include, but are not limited to a metallothionine promoter, a glucocorticoid promoter, a progesterone promoter, and a tetracycline promoter.

Another example of a promoter is the phosphoglycerate kinase (PGK) promoter. In embodiments, a truncated PGK promoter (e.g., a PGK promoter with one or more, e.g., 1, 2, 5, 10, 100, 200, 300, or 400, nucleotide deletions when compared to the wild-type PGK promoter sequence) may be desired. The nucleotide sequences of exemplary PGK promoters are provided below.

WT PGK Promoter:

ACCCCTCTCTCCAGCCACTAAGCCAGTTGCTCCCTCGGCTGACGGCTGCACG CGAGGCCTCCGAACGTCTTACGCCTTGTGGCGCGCCCGTCCTTGTCCCGGGTGTGA TGGCGGGGTGTGGGGCGGAGGGCGTGGCGGGGAAGGGCCGGCGACGAGAGCCGC GCGGGACGACTCGTCGGCGATAACCGGTGTCGGGTAGCGCCAGCCGCGCGACGGT AACGAGGGACCGCGACAGGCAGACGCTCCCATGATCACTCTGCACGCCGAAGGCA AATAGTGCAGGCCGTGCGGCGCTTGGCGTTCCTTGGAAGGGCTGAATCCCCGCCTC GTCCTTCGCAGCGGCCCCCCGGGTGTTCCCATCGCCGCTTCTAGGCCCACTGCGAC GCTTGCCTGCACTTCTTACACGCTCTGGGTCCCAGCCGCGGCGACGCAAAGGGCCT TGGTGCGGGTCTCGTCGGCGCAGGGACGCGTTTGGGTCCCGACGGAACCTTTTCCG CGTTGGGGTTGGGGCACCATAAGCT (SEQ ID NO: 982).

Exemplary truncated PGK Promoters:

PGK100:

ACCCCTCTCTCCAGCCACTAAGCCAGTTGCTCCCTCGGCTGACGGCTGCACG CGAGGCCTCCGAACGTCTTACGCCTTGTGGCGCGCCCGTCCTTGTCCCGGGTGTGA TGGCGGGGTG (SEQ ID NO: 983).

PGK200:

ACCCCTCTCTCCAGCCACTAAGCCAGTTGCTCCCTCGGCTGACGGCTGCACG CGAGGCCTCCGAACGTCTTACGCCTTGTGGCGCGCCCGTCCTTGTCCCGGGTGTGA TGGCGGGGTGTGGGGCGGAGGGCGTGGCGGGGAAGGGCCGGCGACGAGAGCCGC GCGGGACGACTCGTCGGCGATAACCGGTGTCGGGTAGCGCCAGCCGCGCGACGGT AACG (SEQ ID NO: 984).

PGK300:

ACCCCTCTCTCCAGCCACTAAGCCAGTTGCTCCCTCGGCTGACGGCTGCACG CGAGGCCTCCGAACGTCTTACGCCTTGTGGCGCGCCCGTCCTTGTCCCGGGTGTGA TGGCGGGGTGTGGGGCGGAGGGCGTGGCGGGGAAGGGCCGGCGACGAGAGCCGC GCGGGACGACTCGTCGGCGATAACCGGTGTCGGGTAGCGCCAGCCGCGCGACGGT AACGAGGGACCGCGACAGGCAGACGCTCCCATGATCACTCTGCACGCCGAAGGCA AATAGTGCAGGCCGTGCGGCGCTTGGCGTTCCTTGGAAGGGCTGAATCCCCG (SEQ ID NO:985).

PGK400:

ACCCCTCTCTCCAGCCACTAAGCCAGTTGCTCCCTCGGCTGACGGCTGCACG CGAGGCCTCCGAACGTCTTACGCCTTGTGGCGCGCCCGTCCTTGTCCCGGGTGTGA TGGCGGGGTGTGGGGCGGAGGGCGTGGCGGGGAAGGGCCGGCGACGAGAGCCGC GCGGGACGACTCGTCGGCGATAACCGGTGTCGGGTAGCGCCAGCCGCGCGACGGT AACGAGGGACCGCGACAGGCAGACGCTCCCATGATCACTCTGCACGCCGAAGGCA AATAGTGCAGGCCGTGCGGCGCTTGGCGTTCCTTGGAAGGGCTGAATCCCCGCCTC GTCCTTCGCAGCGGCCCCCCGGGTGTTCCCATCGCCGCTTCTAGGCCCACTGCGAC GCTTGCCTGCACTTCTTACACGCTCTGGGTCCCAGCCG (SEQ ID NO: 986).

A vector may also include, e.g., a signal sequence to facilitate secretion, a polyadenylation signal and transcription terminator (e.g., from Bovine Growth Hormone (BGH) gene), an element allowing episomal replication and replication in prokaryotes (e.g. SV40 origin and ColE1 or others known in the art) and/or elements to allow selection (e.g., ampicillin resistance gene and/or zeocin marker).

In order to assess the expression of a CAR polypeptide or portions thereof, the expression vector to be introduced into a cell can also contain either a selectable marker gene or a reporter gene or both to facilitate identification and selection of expressing cells from the population of cells sought to be transfected or infected through viral vectors. In other aspects, the selectable marker may be carried on a separate piece of DNA and used in a co- transfection

procedure. Both selectable markers and reporter genes may be flanked with appropriate regulatory sequences to enable expression in the host cells. Useful selectable markers include, for example, antibiotic-resistance genes, such as neo and the like.

Reporter genes are used for identifying potentially transfected cells and for evaluating the functionality of regulatory sequences. In general, a reporter gene is a gene that is not present in or expressed by the recipient organism or tissue and that encodes a polypeptide whose expression is manifested by some easily detectable property, e.g., enzymatic activity. Expression of the reporter gene is assayed at a suitable time after the DNA has been introduced into the recipient cells. Suitable reporter genes may include genes encoding luciferase, beta-galactosidase, chloramphenicol acetyl transferase, secreted alkaline phosphatase, or the green fluorescent protein gene (e.g., Ui-Tei et al., 2000 FEBS Letters 479: 79-82). Suitable expression systems are well known and may be prepared using known techniques or obtained commercially. In general, the construct with the minimal 5' flanking region showing the highest level of expression of reporter gene is identified as the promoter. Such promoter regions may be linked to a reporter gene and used to evaluate agents for the ability to modulate promoter-driven transcription.

In embodiments, the vector may comprise two or more nucleic acid sequences encoding a CAR, e.g., a CAR described herein, e.g., a CD19 CAR, and a second CAR, e.g., an inhibitory CAR or a CAR that specifically binds to an antigen other than CD19. In such embodiments, the two or more nucleic acid sequences encoding the CAR are encoded by a single nucleic molecule in the same frame and as a single polypeptide chain. In this aspect, the two or more CARs, can, e.g., be separated by one or more peptide cleavage sites. (e.g., an auto-cleavage site or a substrate for an intracellular protease). Examples of peptide cleavage sites include T2A, P2A, E2A, or F2A sites.Methods of introducing and expressing genes into a cell are known in the art. In the context of an expression vector, the vector can be readily introduced into a host cell, e.g., mammalian, bacterial, yeast, or insect cell by any method in the art. For example, the expression vector can be transferred into a host cell by physical, chemical, or biological means.

Physical methods for introducing a polynucleotide into a host cell include calcium phosphate precipitation, lipofection, particle bombardment, microinjection, electroporation, and the like. Methods for producing cells comprising vectors and/or exogenous nucleic acids are well-known in the art. See, for example, Sambrook et al., 2012, MOLECULAR CLONING: A

LABORATORY MANUAL, volumes 1 -4, Cold Spring Harbor Press, NY). A suitable method for the introduction of a polynucleotide into a host cell is calcium phosphate transfection

Biological methods for introducing a polynucleotide of interest into a host cell include the use of DNA and RNA vectors. Viral vectors, and especially retroviral vectors, have become the most widely used method for inserting genes into mammalian, e.g., human cells. Other viral vectors can be derived from lentivirus, poxviruses, herpes simplex virus I, adenoviruses and adeno-associated viruses, and the like. See, for example, U.S. Pat. Nos. 5,350,674 and 5,585,362.

Chemical means for introducing a polynucleotide into a host cell include colloidal dispersion systems, such as macromolecule complexes, nanocapsules, microspheres, beads, and lipid-based systems including oil-in-water emulsions, micelles, mixed micelles, and liposomes. An exemplary colloidal system for use as a delivery vehicle in vitro and in vivo is a liposome (e.g., an artificial membrane vesicle). Other methods of state-of-the-art targeted delivery of nucleic acids are available, such as delivery of polynucleotides with targeted nanoparticles or other suitable sub-micron sized delivery system.

In the case where a non-viral delivery system is utilized, an exemplary delivery vehicle is a liposome. The use of lipid formulations is contemplated for the introduction of the nucleic acids into a host cell (in vitro, ex vivo or in vivo). In another aspect, the nucleic acid may be associated with a lipid. The nucleic acid associated with a lipid may be encapsulated in the aqueous interior of a liposome, interspersed within the lipid bilayer of a liposome, attached to a liposome via a linking molecule that is associated with both the liposome and the oligonucleotide, entrapped in a liposome, complexed with a liposome, dispersed in a solution containing a lipid, mixed with a lipid, combined with a lipid, contained as a suspension in a lipid, contained or complexed with a micelle, or otherwise associated with a lipid. Lipid, lipid/DNA or lipid/expression vector associated compositions are not limited to any particular structure in solution. For example, they may be present in a bilayer structure, as micelles, or with a "collapsed" structure. They may also simply be interspersed in a solution, possibly forming aggregates that are not uniform in size or shape. Lipids are fatty substances which may be naturally occurring or synthetic lipids. For example, lipids include the fatty droplets that naturally occur in the cytoplasm as well as the class of compounds which contain long-chain aliphatic hydrocarbons and their derivatives, such as fatty acids, alcohols, amines, amino alcohols, and aldehydes.

Lipids suitable for use can be obtained from commercial sources. For example, dimyristyl phosphatidylcholine ("DMPC") can be obtained from Sigma, St. Louis, MO; dicetyl phosphate ("DCP") can be obtained from K & K Laboratories (Plainview, NY); cholesterol ("Choi") can be obtained from Calbiochem-Behring; dimyristyl phosphatidylglycerol ("DMPG") and other lipids may be obtained from Avanti Polar Lipids, Inc. (Birmingham, AL.). Stock solutions of lipids in chloroform or chloroform/methanol can be stored at about -20ºC. Chloroform is used as the only solvent since it is more readily evaporated than methanol. "Liposome" is a generic term encompassing a variety of single and multilamellar lipid vehicles formed by the generation of enclosed lipid bilayers or aggregates. Liposomes can be characterized as having vesicular structures with a phospholipid bilayer membrane and an inner aqueous medium. Multilamellar liposomes have multiple lipid layers separated by aqueous medium. They form spontaneously when phospholipids are suspended in an excess of aqueous solution. The lipid components undergo self-rearrangement before the formation of closed structures and entrap water and dissolved solutes between the lipid bilayers (Ghosh et al., 1991 Glycobiology 5: 505-10). However, compositions that have different structures in solution than the normal vesicular structure are also encompassed. For example, the lipids may assume a micellar structure or merely exist as nonuniform aggregates of lipid molecules. Also contemplated are lipofectamine-nucleic acid complexes.

Regardless of the method used to introduce exogenous nucleic acids into a host cell or otherwise expose a cell to the inhibitor of the present invention, in order to confirm the presence of the recombinant nucleic acid sequence in the host cell, a variety of assays may be performed. Such assays include, for example, "molecular biological" assays well known to those of skill in the art, such as Southern and Northern blotting, RT-PCR and PCR; "biochemical" assays, such as detecting the presence or absence of a particular peptide, e.g., by immunological means (ELISAs and Western blots) or by assays described herein to identify agents falling within the scope of the invention.

Once a CAR described herein is made, various assays can be used to evaluate the activity of the molecule, such as but not limited to, the ability to expand T cells following antigen stimulation, sustain T cell expansion in the absence of re-stimulation, and anti-cancer activities in appropriate in vitro and animal models. Assays to evaluate the effects of a CAR of the present invention are described in further detail below

Western blot analysis of CAR expression in primary T cells can be used to detect the presence of monomers and dimers, *e.g.*, as described in paragraph 695 of International Application WO2015/142675, filed March 13, 2015, which is herein incorporated by reference in its entirety.

In vitro expansion of CAR^+ T cells following antigen stimulation can be measured by flow cytometry. For example, a mixture of $CD4^+$ and $CD8^+$ T cells are stimulated with αCD3/αCD28 aAPCs followed by transduction with lentiviral vectors expressing GFP under the control of the promoters to be analyzed. Exemplary promoters include the CMV IE gene, EF-1α, ubiquitin C, or phosphoglycerokinase (PGK) promoters. GFP fluorescence is evaluated on day 6 of culture in the $CD4^+$ and/or $CD8^+$ T cell subsets by flow cytometry. See, *e.g.*, Milone *et al.*, Molecular Therapy 17(8): 1453-1464 (2009). Alternatively, a mixture of $CD4^+$ and $CD8^+$ T cells are stimulated with αCD3/αCD28 coated magnetic beads on day 0, and transduced with CAR on day 1 using a bicistronic lentiviral vector expressing CAR along with eGFP using a 2A ribosomal skipping sequence. Cultures are re-stimulated with either a cancer associated antigen as described herein$^+$ K562 cells (K562-expressing a cancer associated antigen as described herein), wild-type K562 cells (K562 wild type) or K562 cells expressing hCD32 and 4-1BBL in the presence of antiCD3 and anti-CD28 antibody (K562-BBL-3/28) following washing. Exogenous IL-2 is added to the cultures every other day at 100 IU/ml. GFP^+ T cells are enumerated by flow cytometry using bead-based counting. See, *e.g.*, Milone *et al.*, Molecular Therapy 17(8): 1453-1464 (2009).

Sustained CAR^+ T cell expansion in the absence of re-stimulation can also be measured. See, *e.g.*, Milone *et al.*, Molecular Therapy 17(8): 1453-1464 (2009). Briefly, mean T cell volume (fl) is measured on day 8 of culture using a Coulter Multisizer III particle counter, a Nexcelom Cellometer Vision or Millipore Scepter, following stimulation with αCD3/αCD28 coated magnetic beads on day 0, and transduction with the indicated CAR on day 1.

Animal models can also be used to measure a CAR-expressing cell activity, *e.g.*, as described in paragraph 698 of International Application WO2015/142675, filed March 13, 2015, which is herein incorporated by reference in its entirety.

Dose dependent CAR treatment response can be evaluated, *e.g.*, as described in paragraph 699 of International Application WO2015/142675, filed March 13, 2015, which is herein incorporated by reference in its entirety. Assessment of cell proliferation and cytokine production has been previously described, *e.g.*, at Milone *et al.*, Molecular Therapy 17(8):

1453-1464 (2009), *e.g.*, as described in paragraph 700 of International Application WO2015/142675, filed March 13, 2015, which is herein incorporated by reference in its entirety. Cytotoxicity can be assessed by a standard 51Cr-release assay, *e.g.*, as described in paragraph 701 of International Application WO2015/142675, filed March 13, 2015, which is herein incorporated by reference in its entirety. Cytotoxicity can also be assessed by measuring changes in adherent cell's electrical impedance, e.g., using an xCELLigence real time cell analyzer (RTCA). In some embodiments, cytotoxicity is measured at multiple time points.

Imaging technologies can be used to evaluate specific trafficking and proliferation of CARs in tumor-bearing animal models, *e.g.*, as described in paragraph 702 of International Application WO2015/142675, filed March 13, 2015, which is herein incorporated by reference in its entirety. Other assays, including those described in the Example section herein as well as those that are known in the art can also be used to evaluate the CARs described herein.

Strategies for Regulating Chimeric Antigen Receptors

There are many ways CAR activities can be regulated. For example, inducible apoptosis using, e.g., a caspase fused to a dimerization domain (see, e.g., Di Stasa et al., N Egnl. J. Med. 2011 Nov. 3; 365(18):1673-1683), can be used as a safety switch in the CAR therapy of the instant invention. In one embodiment, the cells (e.g., T cells or NK cells) expressing a CAR of the present invention further comprise an inducible apoptosis switch, wherein a human caspase (e.g., caspase 9) or a modified version is fused to a modification of the human FKB protein that allows conditional dimerization. In the presence of a small molecule, such as a rapalog (e.g., AP 1903, AP20187), the inducible caspase (e.g., caspase 9) is activated and leads to the rapid apoptosis and death of the cells (e.g., T cells or NK cells) expressing a CAR of the present invention. Examples of a caspase-based inducible apoptosis switch (or one or more aspects of such a switch) have been described in, e.g., US2004040047; US20110286980; US20140255360; WO1997031899; WO2014151960; WO2014164348; WO2014197638; WO2014197638; all of which are incorporated by reference herein.

In another example, CAR-expressing cells can also express an inducible Caspase-9 (iCaspase-9) molecule that, upon administration of a dimerizer drug (e.g., rimiducid (also called AP1903 (Bellicum Pharmaceuticals) or AP20187 (Ariad)) leads to activation of the Caspase-9 and apoptosis of the cells. The iCaspase-9 molecule contains a chemical inducer of dimerization (CID) binding domain that mediates dimerization in the presence of a CID. This

results in inducible and selective depletion of CAR-expressing cells. In some cases, the iCaspase-9 molecule is encoded by a nucleic acid molecule separate from the CAR-encoding vector(s). In some cases, the iCaspase-9 molecule is encoded by the same nucleic acid molecule as the CAR-encoding vector. The iCaspase-9 can provide a safety switch to avoid any toxicity of CAR-expressing cells. See, e.g., Song et al. *Cancer Gene Ther.* 2008; 15(10):667-75; Clinical Trial Id. No. NCT02107963; and Di Stasi et al. *N. Engl. J. Med.* 2011; 365:1673-83.

Alternative strategies for regulating the CAR therapy of the instant invention include utilizing small molecules or antibodies that deactivate or turn off CAR activity, e.g., by depleting CAR-expressing cells, e.g., by inducing antibody dependent cell-mediated cytotoxicity (ADCC).

In one embodiment, the CAR therapy includes administration of a T cell depleting agent. In one embodiment, the T cell depleting agent is an agent that depletes CAR-expressing cells, e.g., by inducing antibody dependent cell-mediated cytotoxicity (ADCC) and/or complement-induced cell death. For example, CAR-expressing cells described herein may also express an antigen (e.g., a target antigen) that is recognized by molecules capable of inducing cell death, e.g., ADCC or complement-induced cell death. For example, CAR expressing cells described herein may also express a target protein (e.g., a receptor) capable of being targeted by an antibody or antibody fragment. Examples of such target proteins include, but are not limited to, EpCAM, VEGFR, integrins (e.g., integrins αvβ3, α4, αI3/4β3, α4β7, α5β1, αvβ3, αv), members of the TNF receptor superfamily (e.g., TRAIL-R1 , TRAIL-R2), PDGF Receptor, interferon receptor, folate receptor, GPNMB, ICAM-1, HLA-DR, CEA, CA-125, MUC1, TAG-72, IL-6 receptor, 5T4, GD2, GD3, CD2, CD3, CD4, CD5, CD11 , CD11a/LFA-1, CD15, CD18/ITGB2, CD19, CD20, CD22, CD23/lgE Receptor, CD25, CD28, CD30, CD33, CD38, CD40, CD41 , CD44, CD51 , CD52, CD62L, CD74, CD80, CD125, CD147/basigin, CD152/CTLA-4, CD154/CD40L, CD195/CCR5, CD319/SLAMF7, and EGFR, and truncated versions thereof (e.g., versions preserving one or more extracellular epitopes but lacking one or more regions within the cytoplasmic domain).

In other embodiments, a CAR-expressing cell described herein may also express a truncated epidermal growth factor receptor (EGFR) which lacks signaling capacity but retains the epitope that is recognized by molecules capable of inducing ADCC, e.g., cetuximab (ERBITUX®), such that administration of cetuximab induces ADCC and subsequent depletion

of the CAR-expressing cells (see, e.g., WO2011/056894, and Jonnalagadda et al., Gene Ther. 2013; 20(8)853-860). Another strategy includes expressing a highly compact marker/suicide gene that combines target epitopes from both CD32 and CD20 antigens in the CAR-expressing cells described herein, which binds rituximab, resulting in selective depletion of the CAR-expressing cells, e.g., by ADCC (see, e.g., Philip et al., Blood. 2014; 124(8)1277-1287). Other methods for depleting CAR-expressing cells described herein include administration of CAMPATH, a monoclonal anti-CD52 antibody that selectively binds and targets mature lymphocytes, e.g., CAR-expressing cells, for destruction, e.g., by inducing ADCC. In other embodiments, the CAR-expressing cell can be selectively targeted using a CAR ligand, e.g., an anti-idiotypic antibody. In some embodiments, the anti-idiotypic antibody can cause effector cell activity, e.g., ADCC or ADC activities, thereby reducing the number of CAR-expressing cells. In other embodiments, the CAR ligand, e.g., the anti-idiotypic antibody, can be coupled to an agent that induces cell killing, e.g., a toxin, thereby reducing the number of CAR-expressing cells. Alternatively, the CAR molecules themselves can be configured such that the activity can be regulated, e.g., turned on and off, as described below.

In other embodiments, a CAR-expressing cell described herein may also express a target protein recognized by the T cell depleting agent. In one embodiment, the target protein is CD20 and the T cell depleting agent is an anti-CD20 antibody, e.g., rituximab. In such embodiment, the T cell depleting agent is administered once it is desirable to reduce or eliminate the CAR-expressing cell, e.g., to mitigate the CAR induced toxicity. In other embodiments, the T cell depleting agent is an anti-CD52 antibody, e.g., alemtuzumab, as described in the Examples herein.

In some embodiments, the methods disclosed herein further include administering a T cell depleting agent after treatment with the cell (e.g., an immune effector cell as described herein), thereby reducing (e.g., depleting) the CAR-expressing cells (e.g., the CD19CAR-expressing cells). Such T cell depleting agents can be used to effectively deplete CAR-expressing cells (e.g., CD19CAR-expressing cells) to mitigate toxicity. In some embodiments, the CAR-expressing cells were manufactured according to a method herein, e.g., assayed (e.g., before or after transfection or transduction) according to a method herein.

In some embodiments, the T cell depleting agent is administered one, two, three, four, or five weeks after administration of the cell, e.g., the population of immune effector cells, described herein.

In some embodiments, the CAR expressing cell co-expresses the CAR and the target protein, e.g., naturally expresses the target protein or is engineered to express the target protein. For example, the cell, e.g., the population of immune effector cells, can include a nucleic acid (e.g., vector) comprising the CAR nucleic acid (e.g., a CAR nucleic acid as described herein) and a nucleic acid encoding the target protein.

In one embodiment, the T cell depleting agent is a CD52 inhibitor, e.g., an anti-CD52 antibody molecule, e.g., alemtuzumab.

In other embodiments, the cell, e.g., the population of immune effector cells, expresses a CAR molecule as described herein (e.g., CD19CAR) and the target protein recognized by the T cell depleting agent. In one embodiment, the target protein is CD20. In embodiments where the target protein is CD20, the T cell depleting agent is an anti-CD20 antibody, e.g., rituximab.

In further embodiments of any of the aforesaid methods, the methods further include transplanting a cell, e.g., a hematopoietic stem cell, or a bone marrow, into the subject.

In another aspect, the invention features a method of conditioning a subject prior to cell transplantation. The method includes administering to the subject an effective amount of the cell comprising a CAR nucleic acid or polypeptide, e.g., a CD19 CAR nucleic acid or polypeptide. In some embodiments, the cell transplantation is a stem cell transplantation, e.g., a hematopoietic stem cell transplantation, or a bone marrow transplantation. In other embodiments, conditioning a subject prior to cell transplantation includes reducing the number of target-expressing cells in a subject, e.g., CD19-expressing normal cells or CD19-expressing cancer cells.

RCARs

In other embodiments, a regulatable CAR (RCAR) where the CAR activity can be controlled is desirable to optimize the safety and efficacy of a CAR therapy. An RCAR can comprise a set of polypeptides, typically two in the simplest embodiments, in which the components of a standard CAR described herein, e.g., an antigen binding domain and an intracellular signaling domain, are partitioned on separate polypeptides or members. In some embodiments, the set of polypeptides include a dimerization switch that, upon the presence of a dimerization molecule, can couple the polypeptides to one another, e.g., can couple an antigen binding domain to an intracellular signaling domain. In one embodiment, a CAR of the present

invention utilizes a dimerization switch as those described in, e.g., WO2014127261, which is incorporated by reference herein.

Additional description and exemplary configurations of such regulatable CARs are provided herein and in, e.g., paragraphs 527-551 of International Publication No. WO 2015/090229 filed March 13, 2015, which is incorporated by reference in its entirety. In some embodiments, an RCAR involves a switch domain, e.g., a FKBP switch domain, as set out SEQ ID NO: 131, or comprise a fragment of FKBP having the ability to bind with FRB, e.g., as set out in SEQ ID NO: 132. In some embodiments, the RCAR involves a switch domain comprising a FRB sequence, e.g., as set out in SEQ ID NO: 116, or a mutant FRB sequence, e.g., as set out in any of SEQ ID Nos. 134-139.

In an aspect, an RCAR comprises two polypeptides or members: 1) an intracellular signaling member comprising an intracellular signaling domain, e.g., a primary intracellular signaling domain described herein, and a first switch domain; 2) an antigen binding member comprising an antigen binding domain, e.g., that targets CD19, as described herein and a second switch domain. Optionally, the RCAR comprises a transmembrane domain described herein. In an embodiment, a transmembrane domain can be disposed on the intracellular signaling member, on the antigen binding member, or on both. (Unless otherwise indicated, when members or elements of an RCAR are described herein, the order can be as provided, but other orders are included as well. In other words, in an embodiment, the order is as set out in the text, but in other embodiments, the order can be different. E.g., the order of elements on one side of a transmembrane region can be different from the example, e.g., the placement of a switch domain relative to a intracellular signaling domain can be different, e.g., reversed).

In an embodiment, the first and second switch domains can form an intracellular or an extracellular dimerization switch. In an embodiment, the dimerization switch can be a homodimerization switch, e.g., where the first and second switch domain are the same, or a heterodimerization switch, e.g., where the first and second switch domain are different from one another.

In embodiments, an RCAR can comprise a "multi switch." A multi switch can comprise heterodimerization switch domains or homodimerization switch domains. A multi switch comprises a plurality of, e.g., 2, 3, 4, 5, 6, 7, 8, 9, or 10, switch domains, independently, on a first member, e.g., an antigen binding member, and a second member, e.g., an intracellular signaling member. In an embodiment, the first member can comprise a plurality of first switch

domains, e.g., FKBP-based switch domains, and the second member can comprise a plurality of second switch domains, e.g., FRB-based switch domains. In an embodiment, the first member can comprise a first and a second switch domain, e.g., a FKBP-based switch domain and a FRB-based switch domain, and the second member can comprise a first and a second switch domain, e.g., a FKBP-based switch domain and a FRB-based switch domain.

In an embodiment, the intracellular signaling member comprises one or more intracellular signaling domains, e.g., a primary intracellular signaling domain and one or more costimulatory signaling domains.

In an embodiment, the antigen binding member may comprise one or more intracellular signaling domains, e.g., one or more costimulatory signaling domains. In an embodiment, the antigen binding member comprises a plurality, e.g., 2 or 3 costimulatory signaling domains described herein, e.g., selected from 41BB, CD28, CD27, ICOS, and OX40, and in embodiments, no primary intracellular signaling domain. In an embodiment, the antigen binding member comprises the following costimulatory signaling domains, from the extracellular to intracellular direction: 41BB-CD27; 41BB-CD27; CD27-41BB; 41BB-CD28; CD28-41BB; OX40-CD28; CD28-OX40; CD28-41BB; or 41BB-CD28. In such embodiments, the intracellular binding member comprises a CD3zeta domain. In one such embodiment the RCAR comprises (1) an antigen binding member comprising, an antigen binding domain, a transmembrane domain, and two costimulatory domains and a first switch domain; and (2) an intracellular signaling domain comprising a transmembrane domain or membrane tethering domain and at least one primary intracellular signaling domain, and a second switch domain.

An embodiment provides RCARs wherein the antigen binding member is not tethered to the surface of the CAR cell. This allows a cell having an intracellular signaling member to be conveniently paired with one or more antigen binding domains, without transforming the cell with a sequence that encodes the antigen binding member. In such embodiments, the RCAR comprises: 1) an intracellular signaling member comprising: a first switch domain, a transmembrane domain, an intracellular signaling domain, e.g., a primary intracellular signaling domain, and a first switch domain; and 2) an antigen binding member comprising: an antigen binding domain, and a second switch domain, wherein the antigen binding member does not comprise a transmembrane domain or membrane tethering domain, and, optionally, does not comprise an intracellular signaling domain. In some embodiments, the RCAR may further comprise 3) a second antigen binding member comprising: a second antigen binding

domain, e.g., a second antigen binding domain that binds a different antigen than is bound by the antigen binding domain; and a second switch domain.

Also provided herein are RCARs wherein the antigen binding member comprises bispecific activation and targeting capacity. In this embodiment, the antigen binding member can comprise a plurality, e.g., 2, 3, 4, or 5 antigen binding domains, e.g., scFvs, wherein each antigen binding domain binds to a target antigen, e.g. different antigens or the same antigen, e.g., the same or different epitopes on the same antigen. In an embodiment, the plurality of antigen binding domains are in tandem, and optionally, a linker or hinge region is disposed between each of the antigen binding domains. Suitable linkers and hinge regions are described herein.

An embodiment provides RCARs having a configuration that allows switching of proliferation. In this embodiment, the RCAR comprises: 1) an intracellular signaling member comprising: optionally, a transmembrane domain or membrane tethering domain; one or more co-stimulatory signaling domain, e.g., selected from 41BB, CD28, CD27, ICOS, and OX40, and a switch domain; and 2) an antigen binding member comprising: an antigen binding domain, a transmembrane domain, and a primary intracellular signaling domain, e.g., a CD3zeta domain, wherein the antigen binding member does not comprise a switch domain, or does not comprise a switch domain that dimerizes with a switch domain on the intracellular signaling member. In an embodiment, the antigen binding member does not comprise a co-stimulatory signaling domain. In an embodiment, the intracellular signaling member comprises a switch domain from a homodimerization switch. In an embodiment, the intracellular signaling member comprises a first switch domain of a heterodimerization switch and the RCAR comprises a second intracellular signaling member which comprises a second switch domain of the heterodimerization switch. In such embodiments, the second intracellular signaling member comprises the same intracellular signaling domains as the intracellular signaling member. In an embodiment, the dimerization switch is intracellular. In an embodiment, the dimerization switch is extracellular.

In any of the RCAR configurations described here, the first and second switch domains comprise a FKBP-FRB based switch as described herein.

Also provided herein are cells comprising an RCAR described herein. Any cell that is engineered to express a RCAR can be used as a RCARX cell. In an embodiment the RCARX

cell is a T cell, and is referred to as a RCART cell. In an embodiment the RCARX cell is an NK cell, and is referred to as a RCARN cell.

Also provided herein are nucleic acids and vectors comprising RCAR encoding sequences. Sequence encoding various elements of an RCAR can be disposed on the same nucleic acid molecule, e.g., the same plasmid or vector, e.g., viral vector, e.g., lentiviral vector. In an embodiment, (i) sequence encoding an antigen binding member and (ii) sequence encoding an intracellular signaling member, can be present on the same nucleic acid, e.g., vector. Production of the corresponding proteins can be achieved, e.g., by the use of separate promoters, or by the use of a bicistronic transcription product (which can result in the production of two proteins by cleavage of a single translation product or by the translation of two separate protein products). In an embodiment, a sequence encoding a cleavable peptide, e.g., a P2A or F2A sequence, is disposed between (i) and (ii). In an embodiment, a sequence encoding an IRES, e.g., an EMCV or EV71 IRES, is disposed between (i) and (ii). In these embodiments, (i) and (ii) are transcribed as a single RNA. In an embodiment, a first promoter is operably linked to (i) and a second promoter is operably linked to (ii), such that (i) and (ii) are transcribed as separate mRNAs.

Alternatively, the sequence encoding various elements of an RCAR can be disposed on the different nucleic acid molecules, e.g., different plasmids or vectors, e.g., viral vector, e.g., lentiviral vector. E.g., the (i) sequence encoding an antigen binding member can be present on a first nucleic acid, e.g., a first vector, and the (ii) sequence encoding an intracellular signaling member can be present on the second nucleic acid, e.g., the second vector.

Dimerization switches

Dimerization switches can be non-covalent or covalent. In a non-covalent dimerization switch, the dimerization molecule promotes a non-covalent interaction between the switch domains. In a covalent dimerization switch, the dimerization molecule promotes a covalent interaction between the switch domains.

In an embodiment, the RCAR comprises a FKBP/FRAP, or FKBP/FRB,-based dimerization switch. FKBP12 (FKBP, or FK506 binding protein) is an abundant cytoplasmic protein that serves as the initial intracellular target for the natural product immunosuppressive drug, rapamycin. Rapamycin binds to FKBP and to the large PI3K homolog FRAP (RAFT, mTOR). FRB is a 93 amino acid portion of FRAP, that is sufficient for binding the FKBP-

rapamycin complex (Chen, J., Zheng, X. F., Brown, E. J. & Schreiber, S. L. (1995) Proc Natl Acad Sci U S A 92: 4947-51.)

In embodiments, an FKBP/FRAP, e.g., an FKBP/FRB, based switch can use a dimerization molecule, e.g., rapamycin or a rapamycin analog.

The amino acid sequence of FKBP is as follows:

D V P D Y A S L G G P S S P K K K R K V S R G V Q V E T I S P G D G R T F P K R G Q T C V V H Y T G M L E D G K K F D S S R D R N K P F K F M L G K Q E V I R G W E E G V A Q M S V G Q R A K L T I S P D Y A Y G A T G H P G I I P P H A T L V F D V E L L K L E T S Y (SEQ ID NO: 131)

In embodiments, an FKBP switch domain can comprise a fragment of FKBP having the ability to bind with FRB, or a fragment or analog thereof, in the presence of rapamycin or a rapalog, e.g., the underlined portion of SEQ ID NO: 131, which is:

V Q V E T I S P G D G R T F P K R G Q T C V V H Y T G M L E D G K K F D S S R D R N K P F K F M L G K Q E V I R G W E E G V A Q M S V G Q R A K L T I S P D Y A Y G A T G H P G I I P P H A T L V F D V E L L K L E T S (SEQ ID NO: 132)

The amino acid sequence of FRB is as follows:

ILWHEMWHEG LEEASRLYFG ERNVKGMFEV LEPLHAMMER GPQTLKETSF NQAYGRDLME AQEWCRKYMK SGNVKDLTQA WDLYYHVFRR ISK (SEQ ID NO: 133)

"FKBP/FRAP, e.g., an FKBP/FRB, based switch" as that term is used herein, refers to a dimerization switch comprising: a first switch domain, which comprises an FKBP fragment or analog thereof having the ability to bind with FRB, or a fragment or analog thereof, in the presence of rapamycin or a rapalog, e.g., RAD001, and has at least 70, 75, 80, 85, 90, 95, 96, 97, 98, or 99% identity with, or differs by no more than 30, 25, 20, 15, 10, 5, 4, 3, 2, or 1 amino acid residues from, the FKBP sequence of SEQ ID NO: 131 or 132; and a second switch domain, which comprises an FRB fragment or analog thereof having the ability to bind with FRB, or a fragment or analog thereof, in the presence of rapamycin or a rapalog, and has at least 70, 75, 80, 85, 90, 95, 96, 97, 98, or 99% identity with, or differs by no more than 30, 25, 20, 15, 10, 5, 4, 3, 2, or 1 amino acid residues from, the FRB sequence of SEQ ID NO: 133. In an embodiment, a RCAR described herein comprises one switch domain comprises amino acid residues disclosed in SEQ ID NO: 131 (or SEQ ID NO: 132), and one switch domain comprises amino acid residues disclosed in SEQ ID NO: 133.

In embodiments, the FKBP/FRB dimerization switch comprises a modified FRB switch domain that exhibits altered, e.g., enhanced, complex formation between an FRB-based switch domain, e.g., the modified FRB switch domain, a FKBP-based switch domain, and the dimerization molecule, e.g., rapamycin or a rapalogue, e.g., RAD001. In an embodiment, the modified FRB switch domain comprises one or more mutations, e.g., 2, 3, 4, 5, 6, 7, 8, 9, 10 or more, selected from mutations at amino acid position(s) L2031, E2032, S2035, R2036, F2039, G2040, T2098, W2101, D2102, Y2105, and F2108, where the wild-type amino acid is mutated to any other naturally-occurring amino acid. In an embodiment, a mutant FRB comprises a mutation at E2032, where E2032 is mutated to phenylalanine (E2032F), methionine (E2032M), arginine (E2032R), valine (E2032V), tyrosine (E2032Y), isoleucine (E2032I), e.g., SEQ ID NO: 134, or leucine (E2032L), e.g., SEQ ID NO: 135. In an embodiment, a mutant FRB comprises a mutation at T2098, where T2098 is mutated to phenylalanine (T2098F) or leucine (T2098L), e.g., SEQ ID NO: 136. In an embodiment, a mutant FRB comprises a mutation at E2032 and at T2098, where E2032 is mutated to any amino acid, and where T2098 is mutated to any amino acid, e.g., SEQ ID NO: 137. In an embodiment, a mutant FRB comprises an E2032I and a T2098L mutation, e.g., SEQ ID NO: 138. In an embodiment, a mutant FRB comprises an E2032L and a T2098L mutation, e.g., SEQ ID NO: 139.

Table 10. Exemplary mutant FRB having increased affinity for a dimerization molecule.

FRB mutant	Amino Acid Sequence	SEQ ID NO:
E2032I mutant	ILWHEMWHEGLIEASRLYFGERNVKGMFEVLEPLHAMMERGPQTLKETSFNQ AYGRDLMEAQEWCRKYMKSGNVKDLTQAWDLYYHVFRRISKTS	134
E2032L mutant	ILWHEMWHEGLLEASRLYFGERNVKGMFEVLEPLHAMMERGPQTLKETSFNQ AYGRDLMEAQEWCRKYMKSGNVKDLTQAWDLYYHVFRRISKTS	135
T2098L mutant	ILWHEMWHEGLEEASRLYFGERNVKGMFEVLEPLHAMMERGPQTLKETSFNQ AYGRDLMEAQEWCRKYMKSGNVKDLLQAWDLYYHVFRRISKTS	136
E2032, T2098 mutant	ILWHEMWHEGL**X**EASRLYFGERNVKGMFEVLEPLHAMMERGPQTLKETSFNQ AYGRDLMEAQEWCRKYMKSGNVKDL**X**QAWDLYYHVFRRISKTS	137
E2032I, T2098L mutant	ILWHEMWHEGLIEASRLYFGERNVKGMFEVLEPLHAMMERGPQTLKETSFNQ AYGRDLMEAQEWCRKYMKSGNVKDLLQAWDLYYHVFRRISKTS	138
E2032L, T2098L mutant	ILWHEMWHEGLLEASRLYFGERNVKGMFEVLEPLHAMMERGPQTLKETSFNQ AYGRDLMEAQEWCRKYMKSGNVKDLLQAWDLYYHVFRRISKTS	139

Other suitable dimerization switches include a GyrB-GyrB based dimerization switch, a Gibberellin-based dimerization switch, a tag/binder dimerization switch, and a halo-tag/snap-tag dimerization switch. Following the guidance provided herein, such switches and relevant dimerization molecules will be apparent to one of ordinary skill.

Dimerization molecule

Association between the switch domains is promoted by the dimerization molecule. In the presence of dimerization molecule interaction or association between switch domains allows for signal transduction between a polypeptide associated with, e.g., fused to, a first switch domain, and a polypeptide associated with, e.g., fused to, a second switch domain. In the presence of non-limiting levels of dimerization molecule signal transduction is increased by 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2, 5, 10, 50, 100 fold, e.g., as measured in a system described herein.

Rapamycin and rapamycin analogs (sometimes referred to as rapalogues), e.g., RAD001, can be used as dimerization molecules in a FKBP/FRB-based dimerization switch described herein. In an embodiment the dimerization molecule can be selected from rapamycin (sirolimus), RAD001 (everolimus), zotarolimus, temsirolimus, AP-23573 (ridaforolimus), biolimus and AP21967. Additional rapamycin analogs suitable for use with FKBP/FRB-based dimerization switches are further described in the section entitled "Combination Therapies", or in the subsection entitled "Exemplary mTOR inhibitors".

Natural Killer Cell Receptor (NKR) CARs

In an embodiment, the CAR molecule described herein comprises one or more components of a natural killer cell receptor (NKR), thereby forming an NKR-CAR. The NKR component can be a transmembrane domain, a hinge domain, or a cytoplasmic domain from any of the following natural killer cell receptors: killer cell immunoglobulin-like receptor (KIR), e.g., KIR2DL1, KIR2DL2/L3, KIR2DL4, KIR2DL5A, KIR2DL5B, KIR2DS1, KIR2DS2, KIR2DS3, KIR2DS4, DIR2DS5, KIR3DL1/S1, KIR3DL2, KIR3DL3, KIR2DP1, and KIR3DP1; natural cytotoxicity receptor (NCR), e.g., NKp30, NKp44, NKp46; signaling lymphocyte activation molecule (SLAM) family of immune cell receptors, e.g., CD48, CD229, 2B4, CD84, NTB-A, CRACC, BLAME, and CD2F-10; Fc receptor (FcR), e.g., CD16, and CD64; and Ly49 receptors, e.g., LY49A, LY49C. The NKR-CAR molecules described herein may interact with an adaptor molecule or intracellular signaling domain, e.g., DAP12. Exemplary configurations and sequences of CAR molecules comprising NKR components are described in International Publication No. WO2014/145252, the contents of which are hereby incorporated by reference.

Split CAR

In some embodiments, the CAR-expressing cell comprises a split CAR. The split CAR approach is described in more detail in publications WO2014/055442 and WO2014/055657. Briefly, a split CAR system comprises a cell expressing a first CAR having a first antigen binding domain and a costimulatory domain (e.g., 41BB), and the cell also expresses a second CAR having a second antigen binding domain and an intracellular signaling domain (e.g., CD3 zeta). When the cell encounters the first antigen, the costimulatory domain is activated, and the cell proliferates. When the cell encounters the second antigen, the intracellular signaling domain is activated and cell-killing activity begins. Thus, the CAR-expressing cell is only fully activated in the presence of both antigens.

CAR ligands and uses thereof

Alternatively, or in combination to the methods disclosed herein, methods and compositions for one or more of: detection and/or quantification of CAR-expressing cells (*e.g.*, *in vitro* or *in vivo* (e.g., clinical monitoring)); immune cell expansion and/or activation; and/or CAR-specific selection, that involve the use of a CAR ligand, are disclosed. In one exemplary embodiment, the CAR ligand is an antibody that binds to the CAR molecule, e.g., binds to the extracellular antigen binding domain of CAR (e.g., an antibody that binds to the antigen binding domain, e.g., an anti-idiotypic antibody; or an antibody that binds to a constant region of the extracellular binding domain). In other embodiments, the CAR ligand is a CAR antigen molecule (e.g., a CAR antigen molecule as described herein).

In one aspect, a method for detecting and/or quantifying CAR-expressing cells is disclosed. For example, the CAR ligand can be used to detect and/or quantify CAR-expressing cells *in vitro* or *in vivo* (e.g., clinical monitoring of CAR-expressing cells in a patient, or dosing a patient). The method includes:

providing the CAR ligand (optionally, a labelled CAR ligand, e.g., a CAR ligand that includes a tag, a bead, a radioactive or fluorescent label);

acquiring the CAR-expressing cell (e.g., acquiring a sample containing CAR-expressing cells, such as a manufacturing sample or a clinical sample);

contacting the CAR-expressing cell with the CAR ligand under conditions where binding occurs, thereby detecting the level (e.g., amount) of the CAR-expressing cells present.

Binding of the CAR-expressing cell with the CAR ligand can be detected using standard techniques such as FACS, ELISA and the like.

In another aspect, a method of expanding and/or activating cells (e.g., immune effector cells) is disclosed. The method includes:

providing a CAR-expressing cell (e.g., a first CAR-expressing cell or a transiently expressing CAR cell);

contacting said CAR-expressing cell with a CAR ligand, e.g., a CAR ligand as described herein), under conditions where immune cell expansion and/or proliferation occurs, thereby producing the activated and/or expanded cell population.

In certain embodiments, the CAR ligand is present on (e.g., is immobilized or attached to a substrate, e.g., a non-naturally occurring substrate). In some embodiments, the substrate is a non-cellular substrate. The non-cellular substrate can be a solid support chosen from, e.g., a plate (e.g., a microtiter plate), a membrane (e.g., a nitrocellulose membrane), a matrix, a chip or a bead. In embodiments, the CAR ligand is present in the substrate (e.g., on the substrate surface). The CAR ligand can be immobilized, attached, or associated covalently or non-covalently (e.g., cross-linked) to the substrate. In one embodiment, the CAR ligand is attached (e.g., covalently attached) to a bead. In the aforesaid embodiments, the immune cell population can be expanded *in vitro* or *ex vivo*. The method can further include culturing the population of immune cells in the presence of the ligand of the CAR molecule, e.g., using any of the methods described herein.

In other embodiments, the method of expanding and/or activating the cells further comprises addition of a second stimulatory molecule, e.g., CD28. For example, the CAR ligand and the second stimulatory molecule can be immobilized to a substrate, e.g., one or more beads, thereby providing increased cell expansion and/or activation.

In yet another aspect, a method for selecting or enriching for a CAR expressing cell is provided. The method includes contacting the CAR expressing cell with a CAR ligand as described herein; and selecting the cell on the basis of binding of the CAR ligand.

In yet other embodiments, a method for depleting, reducing and/or killing a CAR expressing cell is provided. The method includes contacting the CAR expressing cell with a CAR ligand as described herein; and targeting the cell on the basis of binding of the CAR ligand, thereby reducing the number, and/or killing, the CAR-expressing cell. In one

embodiment, the CAR ligand is coupled to a toxic agent (e.g., a toxin or a cell ablative drug). In another embodiment, the anti-idiotypic antibody can cause effector cell activity, e.g., ADCC or ADC activities.

Exemplary anti-CAR antibodies that can be used in the methods disclosed herein are described, e.g., in WO 2014/190273 and by Jena et al., "Chimeric Antigen Receptor (CAR)-Specific Monoclonal Antibody to Detect CD19-Specific T cells in Clinical Trials", PLOS March 2013 8:3 e57838, the contents of which are incorporated by reference. In one embodiment, the anti-idiotypic antibody molecule recognizes an anti-CD19 antibody molecule, e.g., an anti-CD19 scFv. For instance, the anti-idiotypic antibody molecule can compete for binding with the CD19-specific CAR mAb clone no. 136.20.1 described in Jena et al., PLOS March 2013 8:3 e57838; may have the same CDRs (e.g., one or more of, e.g., all of, VH CDR1, VH CDR2, CH CDR3, VL CDR1, VL CDR2, and VL CDR3, using the Kabat definition, the Chothia definition, or a combination of tthe Kabat and Chothia definitions) as the CD19-specific CAR mAb clone no. 136.20.1; may have one or more (e.g., 2) variable regions as the CD19-specific CAR mAb clone no. 136.20.1, or may comprise the CD19-specific CAR mAb clone no. 136.20.1. In some embodiments, the anti-idiotypic antibody was made according to a method described in Jena et al. In another embodiment, the anti-idiotypic antibody molecule is an anti-idiotypic antibody molecule described in WO 2014/190273. In some embodiments, the anti-idiotypic antibody molecule has the same CDRs (e.g., one or more of, e.g., all of, VH CDR1, VH CDR2, CH CDR3, VL CDR1, VL CDR2, and VL CDR3) as an antibody molecule of WO 2014/190273 such as 136.20.1; may have one or more (e.g., 2) variable regions of an antibody molecule of WO 2014/190273, or may comprise an antibody molecule of WO 2014/190273 such as 136.20.1. In other embodiments, the anti-CAR antibody binds to a constant region of the extracellular binding domain of the CAR molecule, e.g., as described in WO 2014/190273. In some embodiments, the anti-CAR antibody binds to a constant region of the extracellular binding domain of the CAR molecule, e.g., a heavy chain constant region (e.g., a CH2-CH3 hinge region) or light chain constant region. For instance, in some embodiments the anti-CAR antibody competes for binding with the 2D3 monoclonal antibody described in WO 2014/190273, has the same CDRs (e.g., one or more of, e.g., all of, VH CDR1, VH CDR2, CH CDR3, VL CDR1, VL CDR2, and VL CDR3) as 2D3, or has one or more (e.g., 2) variable regions of 2D3, or comprises 2D3 as described in WO 2014/190273.

In some aspects and embodiments, the compositions and methods herein are optimized for a specific subset of T cells, e.g., as described in US Serial No. PCT/US2015/043219 filed July 31, 2015, the contents of which are incorporated herein by reference in their entirety. In some embodiments, the optimized subsets of T cells display an enhanced persistence compared to a control T cell, e.g., a T cell of a different type (e.g., CD8+ or CD4+) expressing the same construct.

In some embodiments, a CD4+ T cell comprises a CAR described herein, which CAR comprises an intracellular signaling domain suitable for (e.g., optimized for, e.g., leading to enhanced persistence in) a CD4+ T cell, e.g., an ICOS domain. In some embodiments, a CD8+ T cell comprises a CAR described herein, which CAR comprises an intracellular signaling domain suitable for (e.g., optimized for, e.g., leading to enhanced persistence of) a CD8+ T cell, e.g., a 4-1BB domain, a CD28 domain, or another costimulatory domain other than an ICOS domain. In some embodiments, the CAR described herein comprises an antigen binding domain described herein, e.g., a CAR comprising an antigen binding domain.

In an aspect, described herein is a method of treating a subject, e.g., a subject having cancer. The method includes administering to said subject, an effective amount of:

1) a CD4+ T cell comprising a CAR (the CARCD4+) comprising:

an antigen binding domain, e.g., an antigen binding domain described herein;

a transmembrane domain; and

an intracellular signaling domain, e.g., a first costimulatory domain, e.g., an ICOS domain; and

2) a CD8+ T cell comprising a CAR (the CARCD8+) comprising:

an antigen binding domain, e.g., an antigen binding domain described herein;

a transmembrane domain; and

an intracellular signaling domain, e.g., a second costimulatory domain, e.g., a 4-1BB domain, a CD28 domain, or another costimulatory domain other than an ICOS domain;

wherein the CARCD4+ and the CARCD8+ differ from one another.

Optionally, the method further includes administering:

3) a second CD8+ T cell comprising a CAR (the second CARCD8+) comprising:

an antigen binding domain, e.g., an antigen binding domain described herein;

a transmembrane domain; and

an intracellular signaling domain, wherein the second CARCD8+ comprises an intracellular signaling domain, e.g., a costimulatory signaling domain, not present on the CARCD8+, and, optionally, does not comprise an ICOS signaling domain.

Non-viral delivery methods

In some aspects, non-viral methods can be used to deliver a nucleic acid encoding a CAR described herein into a cell or tissue or a subject.

In some embodiments, the non-viral method includes the use of a transposon (also called a transposable element). In some embodiments, a transposon is a piece of DNA that can insert itself at a location in a genome, for example, a piece of DNA that is capable of self-replicating and inserting its copy into a genome, or a piece of DNA that can be spliced out of a longer nucleic acid and inserted into another place in a genome. For example, a transposon comprises a DNA sequence made up of inverted repeats flanking genes for transposition.

Exemplary methods of nucleic acid delivery using a transposon include a Sleeping Beauty transposon system (SBTS) and a piggyBac (PB) transposon system. See, e.g., Aronovich et al. Hum. Mol. Genet. 20.R1(2011):R14-20; Singh et al. Cancer Res. 15(2008):2961–2971; Huang et al. Mol. Ther. 16(2008):580–589; Grabundzija et al. Mol. Ther. 18(2010):1200–1209; Kebriaei et al. Blood. 122.21(2013):166; Williams. Molecular Therapy 16.9(2008):1515–16; Bell et al. Nat. Protoc. 2.12(2007):3153-65; and Ding et al. Cell. 122.3(2005):473-83, all of which are incorporated herein by reference.

The SBTS includes two components: 1) a transposon containing a transgene and 2) a source of transposase enzyme. The transposase can transpose the transposon from a carrier plasmid (or other donor DNA) to a target DNA, such as a host cell chromosome/genome. For example, the transposase binds to the carrier plasmid/donor DNA, cuts the transposon (including transgene(s)) out of the plasmid, and inserts it into the genome of the host cell. See, e.g., Aronovich et al. *supra.*

Exemplary transposons include a pT2-based transposon. See, e.g., Grabundzija et al. Nucleic Acids Res. 41.3(2013):1829-47; and Singh et al. Cancer Res. 68.8(2008): 2961–2971, all of which are incorporated herein by reference. Exemplary transposases include a Tc1/mariner-type transposase, e.g., the SB10 transposase or the SB11 transposase (a hyperactive transposase which can be expressed, e.g., from a cytomegalovirus promoter). See, e.g., Aronovich et al.; Kebriaei et al.; and Grabundzija et al., all of which are incorporated

herein by reference.

Use of the SBTS permits efficient integration and expression of a transgene, e.g., a nucleic acid encoding a CAR described herein. Provided herein are methods of generating a cell, e.g., T cell or NK cell, that stably expresses a CAR described herein, e.g., using a transposon system such as SBTS.

In accordance with methods described herein, in some embodiments, one or more nucleic acids, e.g., plasmids, containing the SBTS components are delivered to a cell (e.g., T or NK cell). For example, the nucleic acid(s) are delivered by standard methods of nucleic acid (e.g., plasmid DNA) delivery, e.g., methods described herein, e.g., electroporation, transfection, or lipofection. In some embodiments, the nucleic acid contains a transposon comprising a transgene, e.g., a nucleic acid encoding a CAR described herein. In some embodiments, the nucleic acid contains a transposon comprising a transgene (e.g., a nucleic acid encoding a CAR described herein) as well as a nucleic acid sequence encoding a transposase enzyme. In other embodiments, a system with two nucleic acids is provided, e.g., a dual-plasmid system, e.g., where a first plasmid contains a transposon comprising a transgene, and a second plasmid contains a nucleic acid sequence encoding a transposase enzyme. For example, the first and the second nucleic acids are co-delivered into a host cell.

In some embodiments, cells, e.g., T or NK cells, are generated that express a CAR described herein by using a combination of gene insertion using the SBTS and genetic editing using a nuclease (e.g., Zinc finger nucleases (ZFNs), Transcription Activator-Like Effector Nucleases (TALENs), the CRISPR/Cas system, or engineered meganuclease re-engineered homing endonucleases).

In some embodiments, use of a non-viral method of delivery permits reprogramming of cells, e.g., T or NK cells, and direct infusion of the cells into a subject. Advantages of non-viral vectors include but are not limited to the ease and relatively low cost of producing sufficient amounts required to meet a patient population, stability during storage, and lack of immunogenicity.

Biopolymer delivery methods

In some embodiments, one or more CAR-expressing cells as disclosed herein can be administered or delivered to the subject via a biopolymer scaffold, e.g., a biopolymer implant. Biopolymer scaffolds can support or enhance the delivery, expansion, and/or dispersion of the

CAR-expressing cells described herein. A biopolymer scaffold comprises a biocompatible (e.g., does not substantially induce an inflammatory or immune response) and/or a biodegradable polymer that can be naturally occurring or synthetic. Exemplary biopolymers are described, e.g., in paragraphs 1004-1006 of International Application WO2015/142675, filed March 13, 2015, which is herein incorporated by reference in its entirety.

Pharmaceutical compositions and treatments

In some aspects, the disclosure provides a method of treating a patient, comprising administering CAR-expressing cells manufactured as described herein, optionally in combination with one or more other therapies. In some aspects, the disclosure provides a method of treating a patient, comprising administering a reaction mixture comprising CAR-expressing cells as described herein, optionally in combination with one or more other therapies. In some aspects, the disclosure provides a method of shipping or receiving a reaction mixture comprising CAR-expressing cells as described herein. In some aspects, the disclosure provides a method of treating a patient, comprising receiving a CAR-expressing cell that was manufactured as described herein, and further comprising administering the CAR-expressing cell to the patient, optionally in combination with one or more other therapies. In some aspects, the disclosure provides a method of treating a patient, comprising manufacturing a CAR-expressing cell as described herein, and further comprising administering the CAR-expressing cell to the patient, optionally in combination with one or more other therapies. The other therapy may be, e.g., a cancer therapy such as chemotherapy.

The methods described herein can further include formulating a CAR-expressing cell in a pharmaceutical composition. Pharmaceutical compositions may comprise a CAR-expressing cell, e.g., a plurality of CAR-expressing cells, as described herein, in combination with one or more pharmaceutically or physiologically acceptable carriers, diluents or excipients. Such compositions may comprise buffers such as neutral buffered saline, phosphate buffered saline and the like; carbohydrates such as glucose, mannose, sucrose or dextrans, mannitol; proteins; polypeptides or amino acids such as glycine; antioxidants; chelating agents such as EDTA or glutathione; adjuvants (e.g., aluminum hydroxide); and preservatives. Compositions can be formulated, e.g., for intravenous administration.

In one embodiment, the pharmaceutical composition is substantially free of, e.g., there are no detectable levels of a contaminant, e.g., selected from the group consisting of endotoxin,

mycoplasma, replication competent lentivirus (RCL), p24, VSV-G nucleic acid, HIV gag, residual anti-CD3/anti-CD28 coated beads, mouse antibodies, pooled human serum, bovine serum albumin, bovine serum, culture media components, vector packaging cell or plasmid components, a bacterium and a fungus. In one embodiment, the bacterium is at least one selected from the group consisting of Alcaligenes faecalis, Candida albicans, Escherichia coli, Haemophilus influenza, Neisseria meningitides, Pseudomonas aeruginosa, Staphylococcus aureus, Streptococcus pneumonia, and Streptococcus pyogenes group A.

When "an immunologically effective amount," "an anti-cancer effective amount," "a cancer-inhibiting effective amount," or "therapeutic amount" is indicated, the precise amount of the compositions to be administered can be determined by a physician with consideration of individual differences in age, weight, tumor size, extent of infection or metastasis, and condition of the patient (subject). It can generally be stated that a pharmaceutical composition comprising the immune effector cells (e.g., T cells, NK cells) described herein may be administered at a dosage of 10^4 to 10^9 cells/kg body weight, in some instances 10^5 to 10^6 cells/kg body weight, including all integer values within those ranges. T cell compositions may also be administered multiple times at these dosages. The cells can be administered by using infusion techniques that are commonly known in immunotherapy (see, e.g., Rosenberg et al., New Eng. J. of Med. 319:1676, 1988).

In some embodiments, a dose of CAR cells (e.g., CD19 CAR cells) comprises about 1 x 10^6, 1.1 x 10^6, 2 x 10^6, 3.6 x 10^6, 5 x 10^6, 1 x 10^7, 1.8 x 10^7, 2 x 10^7, 5 x 10^7, 1 x 10^8, 2 x 10^8, or 5 x 10^8 cells/kg. In some embodiments, a dose of CAR cells (e.g., CD19 CAR cells) comprises at least about 1 x 10^6, 1.1 x 10^6, 2 x 10^6, 3.6 x 10^6, 5 x 10^6, 1 x 10^7, 1.8 x 10^7, 2 x 10^7, 5 x 10^7, 1 x 10^8, 2 x 10^8, or 5 x 10^8 cells/kg. In some embodiments, a dose of CAR cells (e.g., CD19 CAR cells) comprises up to about 1 x 10^6, 1.1 x 10^6, 2 x 10^6, 3.6 x 10^6, 5 x 10^6, 1 x 10^7, 1.8 x 10^7, 2 x 10^7, 5 x 10^7, 1 x 10^8, 2 x 10^8, or 5 x 10^8 cells/kg. In some embodiments, a dose of CAR cells (e.g., CD19 CAR cells) comprises about 1.1 x 10^6 – 1.8 x 10^7 cells/kg. In some embodiments, a dose of CAR cells (e.g., CD19 CAR cells) comprises about 1 x 10^7, 2 x 10^7, 5 x 10^7, 1 x 10^8, 2 x 10^8, 5 x 10^8, 1 x 10^9, 2 x 10^9, or 5 x 10^9 cells. In some embodiments, a dose of CAR cells (e.g., CD19 CAR cells) comprises at least about 1 x 10^7, 2 x 10^7, 5 x 10^7, 1 x 10^8, 2 x 10^8, 5 x 10^8, 1 x 10^9, 2 x 10^9, or 5 x 10^9 cells. In some embodiments, a dose of CAR cells (e.g., CD19 CAR cells) comprises up to about 1 x 10^7, 2 x 10^7, 5 x 10^7, 1 x 10^8, 2 x 10^8, 5 x 10^8, 1 x 10^9, 2 x 10^9, or 5 x 10^9 cells. In certain aspects, it may be desired to administer

activated immune effector cells (e.g., T cells, NK cells) to a subject and then subsequently redraw blood (or have an apheresis performed), activate immune effector cells (e.g., T cells, NK cells) therefrom, and reinfuse the patient with these activated and expanded immune effector cells (e.g., T cells, NK cells). This process can be carried out multiple times every few weeks. In certain aspects, immune effector cells (e.g., T cells, NK cells) can be activated from blood draws of from 10cc to 400cc. In certain aspects, immune effector cells (e.g., T cells, NK cells) are activated from blood draws of 20cc, 30cc, 40cc, 50cc, 60cc, 70cc, 80cc, 90cc, or 100cc.

In embodiments, the CAR-expressing cells (e.g., the CD19 CAR-expressing cells) are administered in a plurality of doses, e.g., a first dose, a second dose, and optionally a third dose. In embodiments, the method comprises treating a subject (e.g., an adult subject) having a cancer (e.g., acute lymphoid leukemia (ALL)), comprising administering to the subject a first dose, a second dose, and optionally one or more additional doses, each dose comprising immune effector cells expressing a CAR molecule, e.g., a CD19 CAR molecule, e.g., a CAR molecule according to SEQ ID NO: 89.

In embodiments, the method comprises administering a dose of 2-5x10^6 viable CAR-expressing cells/kg, wherein the subject has a body mass of less than 50 kg; or

administering a dose of 1.0 -2.5 x10^8 viable CAR-expressing cells, wherein the subject has a body mass of at least 50 kg.

In embodiments, a single dose is administered to the subject, e.g., pediatric subject.

In embodiments, the doses are administered on sequential days, e.g., the first dose is administered on day 1, the second dose is administered on day 2, and the optional third dose (if administered) is administered on day 3.

In embodiments, a fourth, fifth, or sixth dose, or more doses, are administered.

In embodiments, the first dose comprises about 10% of the total dose, the second dose comprises about 30% of the total dose, and the third dose comprises about 60% of the total dose, wherein the aforementioned percentages have a sum of 100%. In embodiments, the first dose comprises about 9-11%, 8-12%, 7-13%, or 5-15% of the total dose. In embodiments, the second dose comprises about 29-31%, 28-32%, 27-33%, 26-34%, 25-35%, 24-36%, 23-37%, 22-38%, 21-39%, or 20-40% of the total dose. In embodiments, the third dose comprises about 55-65%, 50-70%, 45-75%, or 40-80% of the total dose. In embodiments, the total dose refers to the total number of viable CAR-expressing cells administered over the course of 1 week, 2

weeks, 3 weeks, or 4 weeks. In some embodiments wherein two doses are administered, the total dose refers to the sum of the number of viable CAR-expressing cells administered to the subject in the first and second doses. In some embodiments wherein three doses are administered, the total dose refers to the sum of the number of viable CAR-expressing cells administered to the subject in the first, second, and third doses.

In embodiments, the dose is measured according to the number of viable CAR-expressing cells therein. CAR expression can be measured, e.g., by flow cytometry using an antibody molecule that binds the CAR molecule and a detectable label. Viability can be measured, e.g., by Cellometer.

In embodiments, the viable CAR-expressing cells are administered in ascending doses. In embodiments, the second dose is larger than the first dose, e.g., larger by 10%, 20%, 30%, or 50%. In embodiments, the second dose is twice, three times, four times, or five times the size of the first dose. In embodiments, the third dose is larger than the second dose, e.g., larger by 10%, 20%, 30%, or 50%. In embodiments, the third dose is twice, three times, four times, or five times the size of the second dose.

In certain embodiments, the method includes one, two, three, four, five, six, seven or all of a)-h) of the following:

a) the number of CAR-expressing, viable cells administered in the first dose is no more than 1/3, of the number of CAR-expressing, viable cells administered in the second dose;

b) the number of CAR-expressing, viable cells administered in the first dose is no more than 1/X, wherein X is 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 30, 40 or 50, of the total number of CAR-expressing, viable cells administered;

c) the number of CAR-expressing, viable cells administered in the first dose is no more than 1×10^7, 2×10^7, 3×10^7, 4×10^7, 5×10^7, 6×10^7, 7×10^7, 8×10^7, 9×10^7, 1×10^8, 2×10^8, 3×10^8, 4×10^8, or 5×10^8 CAR-expressing, viable cells, and the second dose is greater than the first dose;

d) the number of CAR-expressing, viable cells administered in the second dose is no more than 1/2, of the number of CAR-expressing, viable cells administered in the third dose;

e) the number of CAR-expressing, viable cells administered in the second dose is no more than 1/Y, wherein Y is 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 30, 40 or 50, of the total number of CAR-expressing, viable cells administered;

f) the number of CAR-expressing, viable cells administered in the second dose is no more than 1 x 10^7, 2 x 10^7, 3 x 10^7, 4 x 10^7, 5 x 10^7, 6 x 10^7, 7 x 10^7, 8 x 10^7, 9 x 10^7, 1 x 10^8, 2 x 10^8, 3 x 10^8, 4 x 10^8, or 5 x 10^8 CAR-expressing, viable cells, and the third dose is greater than the second dose;

h) the dosages and time periods of administration of the first, second, and optionally third doses are selected such that the subject experiences CRS at a level no greater than 4, 3, 2, or 1.

In embodiments, the total dose is about 5 x 10^8 CAR-expressing, viable cells. In embodiments, the total dose is about 5 x 10^7 - 5 x 10^8 CAR-expressing, viable cells. In embodiments, the first dose is about 5 x 10^7 (e.g., ± 10%, 20%, or 30%) CAR-expressing, viable cells, the second dose is about 1.5 x 10^8 (e.g., ± 10%, 20%, or 30%) CAR-expressing, viable cells, and the third dose is about 3 x 10^8 (e.g., ± 10%, 20%, or 30%) CAR-expressing, viable cells.

In embodiments, the subject is evaluated for CRS after receiving a dose, e.g., after receiving the first dose, the second dose, and/or the third dose.

In embodiments, the subject receives a CRS treatment, e.g., tocilizumab, a corticosteroid, etanercept, or siltuximab. In embodiments, the CRS treatment is administered before or after the first dose of cells comprising the CAR molecule. In embodiments, the CRS treatment is administered before or after the second dose of cells comprising the CAR molecule. In embodiments, the CRS treatment is administered before or after the third dose of cells comprising the CAR molecule. In embodiments, the CRS treatment is administered between the first and second doses of cells comprising the CAR molecule, and/or between the second and third doses of cells comprising the CAR molecule.

The administration of the subject compositions may be carried out in any convenient manner. The compositions described herein may be administered to a patient trans arterially, subcutaneously, intradermally, intratumorally, intranodally, intramedullary, intramuscularly, by intravenous (i.v.) injection, or intraperitoneally, e.g., by intradermal or subcutaneous injection. The compositions of immune effector cells (e.g., T cells, NK cells) may be injected directly into a tumor, lymph node, or site of infection.

In an embodiment, cells expressing a CAR described herein are administered to a subject in combination with a molecule that decreases the T_{REG} cell population. Methods that decrease the number of (e.g., deplete) T_{REG} cells are known in the art and include, e.g., CD25

depletion, cyclophosphamide administration, and modulating GITR function. Without wishing to be bound by theory, it is believed that reducing the number of T_{REG} cells in a subject prior to apheresis or prior to administration of a CAR-expressing cell described herein reduces the number of unwanted immune cells (e.g., Tregs) in the tumor microenvironment and reduces the subject's risk of relapse.

In one embodiment, cells expressing a CAR described herein are administered to a subject in combination with a molecule targeting GITR and/or modulating GITR functions, such as a GITR agonist and/or a GITR antibody that depletes regulatory T cells (T_{REG}s). In embodiments, cells expressing a CAR described herein are administered to a subject in combination with cyclophosphamide. In one embodiment, the GITR binding molecules and/or molecules modulating GITR functions (e.g., GITR agonist and/or Treg depleting GITR antibodies) are administered prior to administration of the CAR-expressing cell. For example, in one embodiment, the GITR agonist can be administered prior to apheresis of the cells. In embodiments, cyclophosphamide is administered to the subject prior to administration (e.g., infusion or re-infusion) of the CAR-expressing cell or prior to aphersis of the cells. In embodiments, cyclophosphamide and an anti-GITR antibody are administered to the subject prior to administration (e.g., infusion or re-infusion) of the CAR-expressing cell or prior to apheresis of the cells. In one embodiment, the subject has cancer (e.g., a solid cancer or a hematological cancer such as ALL or CLL). In an embodiment, the subject has CLL. In embodiments, the subject has ALL. In embodiments, the subject has a solid cancer, e.g., a solid cancer described herein. Exemplary GITR agonists include, e.g., GITR fusion proteins and anti-GITR antibodies (e.g., bivalent anti-GITR antibodies) such as, e.g., a GITR fusion protein described in U.S. Patent No.: 6,111,090, European Patent No.: 090505B1, U.S Patent No.: 8,586,023, PCT Publication Nos.: WO 2010/003118 and 2011/090754, or an anti-GITR antibody described, e.g., in U.S. Patent No.: 7,025,962, European Patent No.: 1947183B1, U.S. Patent No.: 7,812,135, U.S. Patent No.: 8,388,967, U.S. Patent No.: 8,591,886, European Patent No.: EP 1866339, PCT Publication No.: WO 2011/028683, PCT Publication No.:WO 2013/039954, PCT Publication No.: WO2005/007190, PCT Publication No.: WO 2007/133822, PCT Publication No.: WO2005/055808, PCT Publication No.: WO 99/40196, PCT Publication No.: WO 2001/03720, PCT Publication No.: WO99/20758, PCT Publication No.: WO2006/083289, PCT Publication No.: WO 2005/115451, U.S. Patent No.: 7,618,632, and PCT Publication No.: WO 2011/051726.

In one embodiment, a CAR expressing cell described herein is administered to a subject in combination with a GITR agonist, e.g., a GITR agonist described herein. In one embodiment, the GITR agonist is administered prior to the CAR-expressing cell. For example, in one embodiment, the GITR agonist can be administered prior to apheresis of the cells. In one embodiment, the subject has CLL.

Therapeutic Methods

In one aspect, the disclosure provides methods for treating a disease associated with expression of a tumor antigen described herein.

In one aspect the invention features a method of treating, or providing anti-tumor immunity to, a subject having a cancer, comprising administering to the subject an effective amount of an immune effector cell population, wherein the immune effector cell population is expanded by contacting the population of immune effector cells transiently expressing a first CAR with a cognate antigen.

In another aspect, the invention features a method of treating, or providing anti-tumor immunity to, a subject having a cancer, comprising administering to the subject an effective amount of an immune effector cell population expressing a second CAR, wherein the immune effector cell population is expanded by contacting the population of immune effector cells transiently expressing a first CAR with a cognate antigen, and is further transduced with a vector comprising a nucleic acid encoding a second CAR.

In one aspect, the present disclosure provides methods of treating cancer (e.g., a hematological cancer such as ALL and CLL) by providing to the subject in need thereof immune effector cells (e.g., T cells, NK cells) that are engineered to express a CAR, e.g., a CAR described herein. In one embodiment, the cancer to be treated is a B cell malignancy. In one embodiment, the cancer to be treated is ALL (acute lymphoblastic leukemia), CLL (chronic lymphocytic leukemia), DLBCL (diffuse large B-cell lymphoma), MCL (Mantle cell lymphoma, or MM (multiple myeloma).

In one aspect, the disclosure provides methods of treating cancer (e.g., a hematological cancer such as ALL and CLL) by providing to the subject in need thereof immune effector cells (e.g., T cells, NK cells) that are engineered to express a CAR, e.g., a CAR as described herein, e.g., CD19 CAR, wherein the cancer cells express CD19. In one embodiment, the cancer to be treated is a B cell malignancy. In one embodiment, the cancer to be treated is ALL (acute

lymphoblastic leukemia), CLL (chronic lymphocytic leukemia), DLBCL (diffuse large B-cell lymphoma), MCL (Mantle cell lymphoma), Hodgkin's lymphoma, or MM (multiple myeloma).

The disclosure includes a type of cellular therapy where immune effector cells (e.g., T cells, NK cells) are genetically modified (e.g., via transduction of a lentiviral vector) to express a CAR and the CAR-expressing cell is infused to a recipient in need thereof. The infused cell is able to kill tumor cells in the recipient. Unlike antibody therapies, CAR-modified immune effector cells (e.g., T cells, NK cells) are able to replicate in vivo resulting in long-term persistence that can lead to sustained tumor control. CAR-expressing cells (e.g., T cells or NK cells) generated using lentiviral vectors will have stable CAR expression. In various aspects, the immune effector cells (e.g., T cells, NK cells) administered to the patient, or their progeny, persist in the patient for at least four months, five months, six months, seven months, eight months, nine months, ten months, eleven months, twelve months, thirteen months, fourteen month, fifteen months, sixteen months, seventeen months, eighteen months, nineteen months, twenty months, twenty-one months, twenty-two months, twenty-three months, two years, three years, four years, or five years after administration of the T cell to the patient.

The invention also includes a type of cellular therapy where immune effector cells (e.g., T cells, NK cells) are modified, e.g., by in vitro transcribed RNA, to transiently express a CAR and the CAR-expressing cell is infused to a recipient in need thereof. CAR-expressing cells (e.g., T cells, NK cells) generated through transduction of CAR RNA (e.g., by transfection or electroporation) transiently express RNA CARs for 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 days after transduction. The infused cell is able to kill tumor cells in the recipient. Thus, in various aspects, the immune effector cells (e.g., T cells, NK cells) administered to the patient, is present for less than one month, e.g., three weeks, two weeks, one week, after administration of the T cell to the patient.

In one embodiment, the present disclosure provides methods of treating cancer (e.g., a hematological cancer such as ALL and CLL) by providing to the subject in need thereof immune effector cells (e.g., T cells, NK cells) that are engineered to express a CAR that specifically targets or binds to a tumor antigen (or cancer associated antigen) described herein. In yet another embodiment, the method of treatment includes altering the manufacturing of a CAR-expressing cell to enrich for naïve T cells, e.g., as described herein.

In one embodiment, the immune effector cells (e.g., T cells, NK cells) are engineered to express CD19 CAR, for treating a subject having cancer (e.g., a hematological cancer such as

ALL and CLL), wherein the cancer cells express CD19. In one embodiment, the cancer to be treated is ALL or CLL. The CD19 CAR molecules to be expressed in an immune effector cell can comprise any anti-CD19 antigen binding domain in the art (e.g., those provided in **Table 1 or 4**) in combination with any of the CAR domains described herein to generate a full CAR construct. For example, the full CAR construct is a CAR listed in **Table 4**. **Table 4** provides the exemplary full CD19 CAR constructs generated using the various CAR domains (e.g., transmembrane and intracellular signaling domains) described herein, and the anti-CD19 antigen binding domains listed in **Table 1 or 4**. Amino acid sequences are designated (aa) and nucleic acid sequences are designated (nt).

In one aspect, the disclosure provides methods for treating cancer, e.g., a cancer associated with CD19 expression, with a CAR-expressing cell (e.g., T cell, NK cell) therapy. Exemplary cancers include, but are not limited to e.g., one or more acute leukemias including but not limited to, e.g., B-ALL, T-ALL, ALL; one or more chronic leukemias including but not limited to, e.g., chronic myelogenous leukemia (CML), chronic lymphocytic leukemia (CLL).

Additional cancers or hematological conditions that can be treated with the methods described herein include, but are not limited to, e.g., B cell promyelocytic leukemia, blastic plasmacytoid dendritic cell neoplasm, Burkitt's lymphoma, diffuse large B cell lymphoma, follicular lymphoma, hairy cell leukemia, small cell- or a large cell-follicular lymphoma, malignant lymphoproliferative conditions, MALT lymphoma, mantle cell lymphoma (MCL), marginal zone lymphoma, multiple myeloma, myelodysplasia and myelodysplastic syndrome, non-Hodgkin's lymphoma, Hodgkin's lymphoma, plasmablastic lymphoma, plasmacytoid dendritic cell neoplasm, Waldenstrom macroglobulinemia, and "preleukemia" which are a diverse collection of hematological conditions united by ineffective production (or dysplasia) of myeloid blood cells, and the like.

The aforesaid hematological conditions can be associated with expression of CD19. Further, a disease associated with CD19 expression include, but not limited to, e.g., atypical and/or non-classical cancers, malignancies, precancerous conditions or proliferative diseases associated with expression of CD19.

In one embodiment, the disclosure provides methods for treating CLL.

In another embodiment, the disclosure provides methods for treating ALL.

In another embodiment, the disclosure provides methods for treating B-cell ALL.

In one aspect, the disclosure provides methods of treating a subject having cancer (e.g., a hematological cancer such as ALL and CLL) with a CAR-expressing cell (e.g., T cell, NK cell) (e.g., a CD19 CAR-expressing cell (e.g., T cell, NK cell) as described herein, such as, e.g., CTL019). In an embodiment, the disclosure provides methods of treating a subject with a CAR-expressing cell (e.g., T cell, NK cell) in combination with another therapeutic agent, e.g., another therapeutic agent described herein (e.g., another CAR, e.g., another CAR described herein, an inhibitory CAR, e.g., an inhibitory CAR described herein; a chemotherapy; a kinase inhibitor (e.g., a kinase inhibitor described herein, e.g., an mTOR inhibitor, a BTK inhibitor), a checkpoint inhibitor, e.g., a checkpoint inhibitor described herein, a standard of care therapy, etc.). The combination can be, e.g., with any agent described herein.

In an embodiment, stem cell transplantation comprises an autogeneic stem cell transplant. In an embodiment, stem cell transplantation comprises an allogenic stem cell transplant. In an embodiment, stem cell transplantation comprises allogeneic bone marrow transplantation. In an embodiment, stem cell transplantation comprises a hematopoietic stem cell transplantation (HSCT). In an embodiment, hematopoietic stem cells are derived from various tissues including, but not limited to bone marrow, peripheral blood, umbilical cord blood, and combinations thereof.

In one aspect, the disclosure provides methods for treating a disease associated with CD19 expression. In one aspect, the invention provides methods for treating a disease wherein part of the tumor is negative for CD19 and part of the tumor is positive for CD19. For example, provided methods are useful for treating subjects that have undergone treatment for a disease associated with elevated expression of CD19, wherein the subject that has undergone treatment for elevated levels of CD19 exhibits a disease associated with elevated levels of CD19.

In one aspect, provided methods comprise a vector comprising CD19 CAR operably linked to promoter for expression in mammalian cells (e.g., T cells or NK cells). In one aspect, provided methods comprise a recombinant cell (e.g., T cell or NK cell) expressing a CD19 CAR for use in treating CD19-expressing tumors, wherein the recombinant T cell expressing the CD19 CAR is termed a CD19 CAR-expressing cell. In one aspect, a CD19 CAR-expressing cell (e.g., T cell, NK cell) administered according to provided methods is capable of contacting a tumor cell with at least one CD19 CAR expressed on its surface such that the CAR-expressing cell targets the tumor cell and growth of the tumor is inhibited.

In one aspect, the disclosure features to a method of inhibiting growth of a CD19-expressing tumor cell, comprising contacting the tumor cell with a CD19 CAR-expressing cell (e.g., T cell, NK cell) described herein such that the CAR-expressing cell is activated in response to the antigen and targets the cancer cell, wherein the growth of the tumor is inhibited.

In one aspect, the disclosure includes a type of cellular therapy where T cells are genetically modified to express a CAR and the CAR-expressing cell (e.g., T cell, NK cell) is infused to a recipient in need thereof. The infused cell is able to kill tumor cells in the recipient. Unlike antibody therapies, CAR-modified cells (e.g., T cells or NK cells) are able to replicate in vivo resulting in long-term persistence that can lead to sustained tumor control. In various aspects, the cells administered to the patient, or their progeny, persist in the patient for at least four months, five months, six months, seven months, eight months, nine months, ten months, eleven months, twelve months, thirteen months, fourteen month, fifteen months, sixteen months, seventeen months, eighteen months, nineteen months, twenty months, twenty-one months, twenty-two months, twenty-three months, two years, three years, four years, or five years after administration of the cell to the patient.

The disclosure also includes a type of cellular therapy where cells (e.g., T cells, NK cells) are modified, e.g., by in vitro transcribed RNA, to transiently express a chimeric antigen receptor (CAR) and the CAR-expressing cell (e.g., T cell, NK cell) is infused to a recipient in need thereof. The infused cell is able to kill tumor cells in the recipient. Thus, in various aspects, the cells administered to the patient, are present for less than one month, e.g., three weeks, two weeks, one week, after administration of the cell (e.g., T cell, NK cell) to the patient.

Without wishing to be bound by any particular theory, the anti-tumor immunity response elicited by the CAR-modified cells (e.g, T cells, NK cells) may be an active or a passive immune response, or alternatively may be due to a direct vs indirect immune response. In one aspect, the CAR transduced T cells exhibit specific proinflammatory cytokine secretion and potent cytolytic activity in response to human cancer cells expressing the CD19, resist soluble CD19 inhibition, mediate bystander killing and mediate regression of an established human tumor. For example, antigen-less tumor cells within a heterogeneous field of CD19-expressing tumor may be susceptible to indirect destruction by CD19-redirected T cells that has previously reacted against adjacent antigen-positive cancer cells.

In one aspect, the fully-human CAR-modified cells (e.g., T cells, NK cells) described herein may be a type of vaccine for ex vivo immunization and/or in vivo therapy in a mammal. In one aspect, the mammal is a human.

With respect to ex vivo immunization, at least one of the following occurs in vitro prior to administering the cell into a subject: i) expansion of the cells, ii) introducing a nucleic acid encoding a CAR to the cells or iii) cryopreservation of the cells.

Ex vivo procedures are known in the art and are discussed more fully below. Briefly, cells are isolated from a subject (e.g., a human) and genetically modified (i.e., transduced or transfected in vitro) with a vector expressing a CAR disclosed herein. The CAR-modified cell can be administered to a mammalian recipient to provide a therapeutic benefit. The mammalian recipient may be a human and the CAR-modified cell can be autologous with respect to the recipient. Alternatively, the cells can be allogeneic, syngeneic or xenogeneic with respect to the recipient.

Hematological Cancers

Hematological cancer conditions are types of cancer such as leukemia and malignant lymphoproliferative conditions that affect blood, bone marrow and the lymphatic system.

Leukemia can be classified as acute leukemia and chronic leukemia. Acute leukemia can be further classified as acute myelogenous leukemia (AML) and acute lymphoid leukemia (ALL). Chronic leukemia includes chronic myelogenous leukemia (CML) and chronic lymphoid leukemia (CLL). Other related conditions include myelodysplastic syndromes (MDS, formerly known as "preleukemia") which are a diverse collection of hematological conditions united by ineffective production (or dysplasia) of myeloid blood cells and risk of transformation to AML.

The present disclosure provides for compositions and methods for treating cancer. In one aspect, the cancer is a hematologic cancer including but is not limited to a leukemia or a lymphoma. In one aspect, the CAR-expressing cells (e.g., T cells, NK cells) of the invention may be used to treat cancers and malignancies such as, but not limited to, e.g., acute leukemias including but not limited to, e.g., B-ALL, T-ALL, ALL; one or more chronic leukemias including but not limited to, e.g., CML, CLL; additional hematologic cancers or hematologic conditions including, but not limited to, e.g., B cell promyelocytic leukemia, blastic plasmacytoid dendritic cell neoplasm, Burkitt's lymphoma, diffuse large B cell lymphoma, follicular lymphoma, hairy cell leukemia, small cell- or a large cell-follicular lymphoma,

malignant lymphoproliferative conditions, MALT lymphoma, mantle cell lymphoma (MCL), marginal zone lymphoma, multiple myeloma, myelodysplasia and myelodysplastic syndrome, non-Hodgkin's lymphoma, Hodgkin's lymphoma , plasmablastic lymphoma, plasmacytoid dendritic cell neoplasm, Waldenstrom macroglobulinemia, and "preleukemia" which are a diverse collection of hematological conditions united by ineffective production (or dysplasia) of myeloid blood cells, and the like.

The present disclosure also provides methods for inhibiting the proliferation or reducing a CD19-expressing cell population, the methods comprising contacting a population of cells comprising a CD19-expressing cell with a CD19 CAR-expressing cell (e.g., T cell, NK cell) described herein that binds to the CD19-expressing cell. In a specific aspect, the disclosure provides methods for inhibiting the proliferation or reducing the population of cancer cells expressing CD19, the methods comprising contacting the CD19-expressing cancer cell population with a CD19 CAR-expressing cell (e.g., T cell, NK cell) described herein that binds to the CD19-expressing cell. In one aspect, the present disclosure provides methods for inhibiting the proliferation or reducing the population of cancer cells expressing CD19, the methods comprising contacting the CD19-expressing cancer cell population with a CD19 CAR-expressing cell (e.g., T cell, NK cell) described herein that binds to the CD19-expressing cell. In certain aspects, the anti-CD19 CAR-expressing cell (e.g., T cell, NK cell) reduces the quantity, number, amount or percentage of cells and/or cancer cells by at least 25%, at least 30%, at least 40%, at least 50%, at least 65%, at least 75%, at least 85%, at least 95%, or at least 99% in a subject with or animal model for myeloid leukemia or another cancer associated with CD19-expressing cells relative to a negative control. In one aspect, the subject is a human.

The present disclosure also provides methods for preventing, treating and/or managing a disease associated with CD19-expressing cells (e.g., a hematologic cancer or atypical cancer expressing CD19), the methods comprising administering to a subject in need a CAR-expressing cell (e.g., T cell, NK cell) described herein that binds to the CD19-expressing cell. In one aspect, the subject is a human. Non-limiting examples of disorders associated with CD19-expressing cells include autoimmune disorders (such as lupus), inflammatory disorders (such as allergies and asthma) and cancers (such as hematological cancers or atypical cancers expressing CD19).

The present disclosure also provides methods for preventing, treating and/or managing a disease associated with CD19-expressing cells, the methods comprising administering to a subject in need a CD19 CAR-expressing cell (e.g., T cell, NK cell) described herein that binds to the CD19-expressing cell. In one aspect, the subject is a human.

The present disclosure provides methods for preventing relapse of cancer associated with CD19-expressing cells (e.g., a hematological cancer such as ALL and CLL), the methods comprising administering to a subject in need thereof a CD19 CAR-expressing cell (e.g., T cell, NK cell) described herein that binds to the CD19-expressing cell. In one aspect, the methods comprise administering to the subject in need thereof an effective amount of a CD19 CAR-expressing cell (e.g., T cell, NK cell) described herein that binds to the CD19-expressing cell in combination with an effective amount of another therapy.

Combination Therapy

It will be appreciated that any cancer therapy as described above and herein can be administered in combination with one or more additional therapies to treat and/or reduce the symptoms of cancer described herein. The pharmaceutical compositions can be administered concurrently with, prior to, or subsequent to, one or more other additional therapies or therapeutic agents. In an embodiment, a CAR-expressing cell described herein may be used in combination with other known agents and therapies. Administered "in combination", as used herein, means that two (or more) different treatments are delivered to the subject during the course of the subject's affliction with the disorder, e.g., the two or more treatments are delivered after the subject has been diagnosed with the disorder and before the disorder has been cured or eliminated or treatment has ceased for other reasons. In some embodiments, the delivery of one treatment is still occurring when the delivery of the second begins, so that there is overlap in terms of administration. This is sometimes referred to herein as "simultaneous" or "concurrent delivery". In other embodiments, the delivery of one treatment ends before the delivery of the other treatment begins. In some embodiments of either case, the treatment is more effective because of combined administration. For example, the second treatment is more effective, e.g., an equivalent effect is seen with less of the second treatment, or the second treatment reduces symptoms to a greater extent, than would be seen if the second treatment were administered in the absence of the first treatment or the analogous situation is seen with the first treatment. In some embodiments, delivery is such that the reduction in a symptom, or

other parameter related to the disorder is greater than what would be observed with one treatment delivered in the absence of the other. The effect of the two treatments can be partially additive, wholly additive, or greater than additive. The delivery can be such that an effect of the first treatment delivered is still detectable when the second is delivered.

A CAR-expressing cell described herein and the at least one additional therapeutic agent can be administered simultaneously, in the same or in separate compositions, or sequentially. For sequential administration, the CAR-expressing cell described herein can be administered first, and the additional agent can be administered second, or the order of administration can be reversed.

In further aspects, a CAR-expressing cell described herein may be used in a treatment regimen in combination with surgery, chemotherapy, radiation, immunosuppressive agents, such as cyclosporin, azathioprine, methotrexate, mycophenolate, and FK506, antibodies, or other immunoablative agents such as CAMPATH, anti-CD3 antibodies or other antibody therapies, cytoxin, fludarabine, cyclosporin, FK506, rapamycin, mycophenolic acid, steroids, FR901228, cytokines, and irradiation peptide vaccine, such as that described in Izumoto et al. 2008 J NEUROSURG 108:963-971.

In one embodiment, a CAR-expressing cell described herein can be used in combination with a chemotherapeutic agent. Exemplary chemotherapeutic agents include an anthracycline (e.g., doxorubicin (e.g., liposomal doxorubicin)), a vinca alkaloid (e.g., vinblastine, vincristine, vindesine, vinorelbine), an alkylating agent (e.g., bendamustine, cyclophosphamide, decarbazine, melphalan, ifosfamide, temozolomide), an immune cell antibody (e.g., alemtuzamab, gemtuzumab, rituximab, tositumomab), an antimetabolite (including, e.g., folic acid antagonists, pyrimidine analogs, purine analogs and adenosine deaminase inhibitors (e.g., fludarabine)), an mTOR inhibitor, a TNFR glucocorticoid induced TNFR related protein (GITR) agonist, a proteasome inhibitor (e.g., aclacinomycin A, gliotoxin or bortezomib), an immunomodulator such as thalidomide or a thalidomide derivative (e.g., lenalidomide), and combinations thereof.

Exemplary mTOR inhibitors include, without limitation, RAD001, temsirolimus; ridaforolimus (formally known as deferolimus, (1*R*,2*R*,4*S*)-4-[(2*R*)-2 [(1*R*,9*S*,12*S*,15*R*,16*E*,18*R*,19*R*,21*R*, 23*S*,24*E*,26*E*,28*Z*,30*S*,32*S*,35*R*)-1,18-dihydroxy-19,30-dimethoxy-15,17,21,23, 29,35-hexamethyl-2,3,10,14,20-pentaoxo-11,36-dioxa-4-azatricyclo[30.3.1.$0^{4,9}$] hexatriaconta-16,24,26,28-tetraen-12-yl]propyl]-2-methoxycyclohexyl

dimethylphosphinate, also known as AP23573 and MK8669, and described in PCT Publication No. WO 03/064383); everolimus (Afinitor® or RAD001); rapamycin (AY22989, Sirolimus®); simapimod (CAS 164301-51-3); emsirolimus, (5-{2,4-Bis[(3*S*)-3-methylmorpholin-4-yl]pyrido[2,3-*d*]pyrimidin-7-yl}-2-methoxyphenyl)methanol (AZD8055); 2-Amino-8-[*trans*-4-(2-hydroxyethoxy)cyclohexyl]-6-(6-methoxy-3-pyridinyl)-4-methyl-pyrido[2,3-*d*]pyrimidin-7(8*H*)-one (PF04691502, CAS 1013101-36-4); and N^2-[1,4-dioxo-4-[[4-(4-oxo-8-phenyl-4*H*-1-benzopyran-2-yl)morpholinium-4-yl]methoxy]butyl]-L-arginylglycyl-L-α-aspartylL-serine-, inner salt (SF1126, CAS 936487-67-1) (SEQ ID NO: 140), XL765 and combinations thereof.

Exemplary immunomodulators include, without limitation, afutuzumab (available from Roche®); pegfilgrastim (Neulasta®); lenalidomide (CC-5013, Revlimid®); thalidomide (Thalomid®), actimid (CC4047); IRX-2 (mixture of human cytokines including interleukin 1, interleukin 2, and interferon γ, CAS 951209-71-5, available from IRX Therapeutics) and combinations thereof.

Exemplary anthracyclines include, without limitation, doxorubicin (Adriamycin® and Rubex®); bleomycin (lenoxane®); daunorubicin (dauorubicin hydrochloride, daunomycin, and rubidomycin hydrochloride, Cerubidine®); daunorubicin liposomal (daunorubicin citrate liposome, DaunoXome®); mitoxantrone (DHAD, Novantrone®); epirubicin (Ellence™); idarubicin (Idamycin®, Idamycin PFS®); mitomycin C (Mutamycin®); geldanamycin; herbimycin; ravidomycin; desacetylravidomycin and combinations thereof.

Exemplary vinca alkaloids include, without limitation, vinorelbine tartrate (Navelbine®), Vincristine (Oncovin®), Vindesine (Eldisine®)); vinblastine (also known as vinblastine sulfate, vincaleukoblastine and VLB, Alkaban-AQ® and Velban®); vinorelbine (Navelbine®) and combinations thereof.

Exemplary proteosome inhibitors include, without limitation, bortezomib (Velcade®); carfilzomib (PX-171-007, (*S*)-4-Methyl-*N*-((*S*)-1-(((*S*)-4-methyl-1-((*R*)-2-methyloxiran-2-yl)-1-oxopentan-2-yl)amino)-1-oxo-3-phenylpropan-2-yl)-2-((*S*)-2-(2-morpholinoacetamido)-4-phenylbutanamido)-pentanamide); marizomib (NPI-0052); ixazomib citrate (MLN-9708); delanzomib (CEP-18770); *O*-Methyl-*N*-[(2-methyl-5-thiazolyl)carbonyl]-L-seryl-*O*-methyl-*N*-[(1*S*)-2-[(2*R*)-2-methyl-2-oxiranyl]-2-oxo-1-(phenylmethyl)ethyl]- L-serinamide (ONX-0912) and combinations thereof.

Exemplary GITR agonists include, without limitation, GITR fusion proteins and anti-GITR antibodies (e.g., bivalent anti-GITR antibodies) such as, e.g., a GITR fusion protein

described in U.S. Patent No.: 6,111,090, European Patent No.: 090505B1, U.S Patent No.: 8,586,023, PCT Publication Nos.: WO 2010/003118 and 2011/090754, or an anti-GITR antibody described, e.g., in U.S. Patent No.: 7,025,962, European Patent No.: 1947183B1, U.S. Patent No.: 7,812,135, U.S. Patent No.: 8,388,967, U.S. Patent No.: 8,591,886, European Patent No.: EP 1866339, PCT Publication No.: WO 2011/028683, PCT Publication No.:WO 2013/039954, PCT Publication No.: WO2005/007190, PCT Publication No.: WO 2007/133822, PCT Publication No.: WO2005/055808, PCT Publication No.: WO 99/40196, PCT Publication No.: WO 2001/03720, PCT Publication No.: WO99/20758, PCT Publication No.: WO2006/083289, PCT Publication No.: WO 2005/115451, U.S. Patent No.: 7,618,632, and PCT Publication No.: WO 2011/051726.

In an embodiment, a CAR expressing cell described herein, such as, e.g., a CD19 CAR-expressing cell (e.g., T cell, NK cell), e.g., CTL019 is administered to a subject, e.g., a subject identified as a partial responder or non-responder, in combination with an mTOR inhibitor, e.g., an mTOR inhibitor described herein, e.g., a target of the rapamycin signaling pathway such as RAD001. In an embodiment, the mTOR inhibitor is administered prior to the CAR-expressing cell. For example, in an embodiment, the mTOR inhibitor can be administered prior to apheresis of the cells. In an embodiment, the subject has cancer (e.g., a hematological cancer such as ALL and CLL). In an embodiment, the subject has ALL. In an embodiment, the subject has CLL.

In an embodiment, a CAR expressing cell described herein, such as, e.g., a CD19 CAR-expressing cell (e.g., T cell, NK cell), e.g., CTL019, is administered to a subject, e.g., a subject identified as a partial responder or non-responder, in combination with a GITR agonist, e.g., a GITR agonist described herein. In an embodiment, the GITR agonist is administered prior to the CAR-expressing cell. For example, in an embodiment, the GITR agonist can be administered prior to apheresis of the cells. In an embodiment, the subject has cancer (e.g., a hematological cancer such as ALL and CLL). In an embodiment, the subject has ALL. In an embodiment, the subject has CLL.

In one embodiment, the subject can be administered an agent which enhances the activity of a CAR-expressing cell. For example, in one embodiment, the agent can be an agent which inhibits an inhibitory molecule. Inhibitory molecules, e.g., Programmed Death 1 (PD1), can, in some embodiments, decrease the ability of a CAR-expressing cell to mount an immune effector response. Examples of inhibitory molecules include PD1, PD-L1, CTLA-4, TIM3,

CEACAM (e.g., CEACAM-1, CEACAM-3 and/or CEACAM-5), LAG3, VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4 and TGF beta. Inhibition of an inhibitory molecule, e.g., by inhibition at the DNA, RNA or protein level, can optimize a CAR-expressing cell performance. In embodiments, an inhibitory nucleic acid, e.g., an inhibitory nucleic acid, e.g., a dsRNA, e.g., an siRNA or shRNA, or a clustered regularly interspaced short palindromic repeats (CRISPR), a transcription-activator like effector nuclease (TALEN), or a zinc finger endonuclease (ZFN), can be used to inhibit expression of an inhibitory molecule in the CAR-expressing cell. In an embodiment the inhibitor is an shRNA. In an embodiment, the inhibitory molecule is inhibited within a CAR-expressing cell. In these embodiments, a dsRNA molecule that inhibits expression of the inhibitory molecule is linked to the nucleic acid that encodes a component, e.g., all of the components, of the CAR. In one embodiment, the inhibitor of an inhibitory signal can be, e.g., an antibody or antibody fragment that binds to an inhibitory molecule. For example, the agent can be an antibody or antibody fragment that binds to PD1, PD-L1, PD-L2 or CTLA4 (e.g., ipilimumab (also referred to as MDX-010 and MDX-101, and marketed as Yervoy®; Bristol-Myers Squibb; Tremelimumab (IgG2 monoclonal antibody available from Pfizer, formerly known as ticilimumab, CP-675,206).). In an embodiment, the agent is an antibody or antibody fragment that binds to TIM3. In an embodiment, the agent is an antibody or antibody fragment that binds to LAG3. In an embodiment, the agent is an antibody or antibody fragment that binds to CEACAM (e.g., CEACAM-1, CEACAM-3 and/or CEACAM-5).

PD1 is an inhibitory member of the CD28 family of receptors that also includes CD28, CTLA-4, ICOS, and BTLA. PD1 is expressed on activated B cells, T cells and myeloid cells (Agata et al. 1996 Int. Immunol 8:765-75). Two ligands for PD1, PD-L1 and PD-L2 have been shown to downregulate T cell activation upon binding to PD1 (Freeman et a. 2000 J Exp Med 192:1027-34; Latchman et al. 2001 Nat Immunol 2:261-8; Carter et al. 2002 Eur J Immunol 32:634-43). PD-L1 is abundant in human cancers (Dong et al. 2003 J Mol Med 81:281-7; Blank et al. 2005 Cancer Immunol. Immunother 54:307-314; Konishi et al. 2004 Clin Cancer Res 10:5094). Immune suppression can be reversed by inhibiting the local interaction of PD1 with PD-L1. Antibodies, antibody fragments, and other inhibitors of PD1, PD-L1 and PD-L2 are available in the art and may be used combination with a CD19 CAR described herein.

For example, nivolumab (also referred to as BMS-936558 or MDX1106; Bristol-Myers Squibb) is a fully human IgG4 monoclonal antibody which specifically blocks PD1.

Nivolumab (clone 5C4) and other human monoclonal antibodies that specifically bind to PD1 are disclosed in US 8,008,449 and WO2006/121168. Pidilizumab (CT-011; Cure Tech) is a humanized IgG1k monoclonal antibody that binds to PD1. Pidilizumab and other humanized anti-PD1 monoclonal antibodies are disclosed in WO2009/101611. Pembrolizumab (formerly known as lambrolizumab, and also referred to as Keytruda, MK03475; Merck) is a humanized IgG4 monoclonal antibody that binds to PD1. Pembrolizumab and other humanized anti-PD1 antibodies are disclosed in US 8,354,509 and WO2009/114335. MEDI4736 (Medimmune) is a human monoclonal antibody that binds to PDL1, and inhibits interaction of the ligand with PD1. MDPL3280A (Genentech / Roche) is a human Fc optimized IgG1 monoclonal antibody that binds to PD-L1. MDPL3280A and other human monoclonal antibodies to PD-L1 are disclosed in U.S. Patent No.: 7,943,743 and U.S Publication No.: 20120039906. Other anti-PD-L1 binding agents include YW243.55.S70 (heavy and light chain variable regions are shown in SEQ ID NOs 20 and 21 in WO2010/077634) and MDX-1 105 (also referred to as BMS-936559, and, e.g., anti-PD-L1 binding agents disclosed in WO2007/005874). AMP-224 (B7-DCIg; Amplimmune; e.g., disclosed in WO2010/027827 and WO2011/066342), is a PD-L2 Fc fusion soluble receptor that blocks the interaction between PD1 and B7-H1. Other anti-PD1 antibodies include AMP 514 (Amplimmune), among others, e.g., anti-PD1 antibodies disclosed in US 8,609,089, US 2010028330, and/or US 20120114649.

In one embodiment, the anti-PD-1 antibody or fragment thereof is an anti-PD-1 antibody molecule as described in US 2015/0210769, entitled "Antibody Molecules to PD-1 and Uses Thereof," incorporated by reference in its entirety. In one embodiment, the anti-PD-1 antibody molecule includes at least one, two, three, four, five or six CDRs (or collectively all of the CDRs) from a heavy and light chain variable region from an antibody chosen from any of BAP049-hum01, BAP049-hum02, BAP049-hum03, BAP049-hum04, BAP049-hum05, BAP049-hum06, BAP049-hum07, BAP049-hum08, BAP049-hum09, BAP049-hum10, BAP049-hum11, BAP049-hum12, BAP049-hum13, BAP049-hum14, BAP049-hum15, BAP049-hum16, BAP049-Clone-A, BAP049-Clone-B, BAP049-Clone-C, BAP049-Clone-D, or BAP049-Clone-E; or as described in Table 1, or encoded by the nucleotide sequence in Table 1; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences, or closely related CDRs, *e.g.*, CDRs which are identical or which have at least one amino acid alteration, but not more than

two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions).

In yet another embodiment, the anti-PD-1 antibody molecule comprises at least one, two, three or four variable regions from an antibody described herein, *e.g.*, an antibody chosen from any of BAP049-hum01, BAP049-hum02, BAP049-hum03, BAP049-hum04, BAP049-hum05, BAP049-hum06, BAP049-hum07, BAP049-hum08, BAP049-hum09, BAP049-hum10, BAP049-hum11, BAP049-hum12, BAP049-hum13, BAP049-hum14, BAP049-hum15, BAP049-hum16, BAP049-Clone-A, BAP049-Clone-B, BAP049-Clone-C, BAP049-Clone-D, or BAP049-Clone-E; or as described in Table 1, or encoded by the nucleotide sequence in Table 1; or as described in Table 1 of US 2015/0210769; or encoded by the nucleotide sequence in Tables 1; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences.

In one embodiment, the anti-PD-1 antibody molecule includes:

(a) a heavy chain variable region (VH) comprising a VHCDR1 amino acid sequence of SEQ ID NO: 4, a VHCDR2 amino acid sequence of SEQ ID NO: 5, and a VHCDR3 amino acid sequence of SEQ ID NO: 3; and a light chain variable region (VL) comprising a VLCDR1 amino acid sequence of SEQ ID NO: 13, a VLCDR2 amino acid sequence of SEQ ID NO: 14, and a VLCDR3 amino acid sequence of SEQ ID NO: 33, each disclosed in Table 1 of US 2015/0210769;

(b) a VH comprising a VHCDR1 amino acid sequence chosen from SEQ ID NO: 1; a VHCDR2 amino acid sequence of SEQ ID NO: 2; and a VHCDR3 amino acid sequence of SEQ ID NO: 3; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 10, a VLCDR2 amino acid sequence of SEQ ID NO: 11, and a VLCDR3 amino acid sequence of SEQ ID NO: 32, each disclosed in Table 1 of US 2015/0210769;

(c) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 224, a VHCDR2 amino acid sequence of SEQ ID NO: 5, and a VHCDR3 amino acid sequence of SEQ ID NO: 3; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 13, a VLCDR2 amino acid sequence of SEQ ID NO: 14, and a VLCDR3 amino acid sequence of SEQ ID NO: 33, each disclosed in Table 1 of US 2015/0210769; or

(d) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 224; a VHCDR2 amino acid sequence of SEQ ID NO: 2; and a VHCDR3 amino acid sequence of SEQ ID NO: 3; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 10, a VLCDR2

amino acid sequence of SEQ ID NO: 11, and a VLCDR3 amino acid sequence of SEQ ID NO: 32, each disclosed in Table 1 of US 2015/0210769.

In the combinations herein below, in another embodiment, the anti-PD-1 antibody molecule comprises (i) a heavy chain variable region (VH) comprising a VHCDR1 amino acid sequence chosen from SEQ ID NO: 1, SEQ ID NO: 4, or SEQ ID NO: 224; a VHCDR2 amino acid sequence of SEQ ID NO: 2 or SEQ ID NO: 5; and a VHCDR3 amino acid sequence of SEQ ID NO: 3; and (ii) a light chain variable region (VL) comprising a VLCDR1 amino acid sequence of SEQ ID NO: 10 or SEQ ID NO: 13, a VLCDR2 amino acid sequence of SEQ ID NO: 11 or SEQ ID NO: 14, and a VLCDR3 amino acid sequence of SEQ ID NO: 32 or SEQ ID NO: 33, each disclosed in Table 1 of US 2015/0210769.

In certain embodiments, the anti-PD-1 antibody molecule is administered by injection (*e.g.*, subcutaneously or intravenously) at a dose of about 1 to 30 mg/kg, *e.g.*, about 5 to 25 mg/kg, about 10 to 20 mg/kg, about 1 to 5 mg/kg, or about 3 mg/kg. The dosing schedule can vary from *e.g.*, once a week to once every 2, 3, or 4 weeks. In one embodiment, the anti-PD-1 antibody molecule is administered at a dose from about 1 to 20 mg/kg every other week.

In some embodiments, the dose of a PD-1 inhibitor, *e.g.*, an anti-PD-1 antibody molecule, is a flat dose. In some embodiments, the anti-PD-1 antibody molecule is administered by injection (*e.g.*, subcutaneously or intravenously) at a dose (*e.g.,* a flat dose) of about 200 mg to 500 mg, *e.g.,* about 250 mg to 450 mg, about 300 mg to 400 mg, about 250 mg to 350 mg, about 350 mg to 450 mg, or about 300 mg or about 400 mg. The dosing schedule (*e.g.,* flat dosing schedule) can vary from e.g., once a week to once every 2, 3, 4, 5, or 6 weeks. In one embodiment, the anti-PD-1 antibody molecule is administered at a dose from about 300 mg to 400 mg once every three weeks or once every four weeks. In one embodiment, the anti-PD-1 antibody molecule is administered at a dose from about 300 mg once every three weeks. In one embodiment, the anti-PD-1 antibody molecule is administered at a dose from about 400 mg once every four weeks, e.g., via i.v. infusion. In one embodiment, the anti-PD-1 antibody molecule is administered at a dose from about 300 mg once every four weeks, e.g., via i.v. infusion. In one embodiment, the anti-PD-1 antibody molecule is administered at a dose from about 400 mg once every three weeks, e.g., via i.v. infusion.

In another embodiment, the anti-PD-L1 antibody molecule includes at least one, two, three, four, five or six CDRs (or collectively all of the CDRs) from a heavy and light chain variable region of any of BAP058-hum01, BAP058-hum02, BAP058-hum03, BAP058-hum04,

BAP058-hum05, BAP058-hum06, BAP058-hum07, BAP058-hum08, BAP058-hum09, BAP058-hum10, BAP058-hum11, BAP058-hum12, BAP058-hum13, BAP058-hum14, BAP058-hum15, BAP058-hum16, BAP058-hum17, BAP058-Clone-K, BAP058-Clone-L, BAP058-Clone-M, BAP058-Clone-N, or BAP058-Clone-O; or as described in Table 1, or encoded by a nucleotide sequence shown in Table 1 of US-2016/0108123. In one embodiment, one or more of the CDRs (or collectively all of the CDRs) have one, two, three, four, five, six or more changes, *e.g.*, amino acid substitutions or deletions, relative to the amino acid sequence shown in Table 1, or encoded by a nucleotide sequence shown in Table 1.

In yet another embodiment, the anti-PD-L1 antibody molecule includes at least one or two heavy chain variable domain (optionally including a constant region), at least one or two light chain variable domain (optionally including a constant region), or both, comprising the amino acid sequence of any of BAP058-hum01, BAP058-hum02, BAP058-hum03, BAP058-hum04, BAP058-hum05, BAP058-hum06, BAP058-hum07, BAP058-hum08, BAP058-hum09, BAP058-hum10, BAP058-hum11, BAP058-hum12, BAP058-hum13, BAP058-hum14, BAP058-hum15, BAP058-hum16, BAP058-hum17, BAP058-Clone-K, BAP058-Clone-L, BAP058-Clone-M, BAP058-Clone-N, or BAP058-Clone-O; or as described in Table 1 of US-2016/0108123, or encoded by the nucleotide sequence in Table 1; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences.

In one embodiment, the anti-PD-L1 antibody molecule includes:

(i) a heavy chain variable region (VH) including a VHCDR1 amino acid sequence chosen from SEQ ID NO: 1, SEQ ID NO: 4 or SEQ ID NO: 195; a VHCDR2 amino acid sequence of SEQ ID NO: 2; and a VHCDR3 amino acid sequence of SEQ ID NO: 3, each disclosed in Table 1 of USSN 14/881,888; and

(ii) a light chain variable region (VL) including a VLCDR1 amino acid sequence of SEQ ID NO: 9, a VLCDR2 amino acid sequence of SEQ ID NO: 10, and a VLCDR3 amino acid sequence of SEQ ID NO: 11, each disclosed in Table 1 of US-2016/0108123.

In another embodiment, the anti-PD-L1 antibody molecule includes:

(i) a heavy chain variable region (VH) including a VHCDR1 amino acid sequence chosen from SEQ ID NO: 1, SEQ ID NO: 4 or SEQ ID NO: 195; a VHCDR2 amino acid sequence of SEQ ID NO: 5, and a VHCDR3 amino acid sequence of SEQ ID NO: 3, each disclosed in Table 1 of US-2016/0108123; and

(ii) a light chain variable region (VL) including a VLCDR1 amino acid sequence of SEQ ID NO: 12, a VLCDR2 amino acid sequence of SEQ ID NO: 13, and a VLCDR3 amino acid sequence of SEQ ID NO: 14, each disclosed in Table 1 of US-2016/0108123.

In one embodiment, the anti-PD-L1 antibody molecule comprises the VHCDR1 amino acid sequence of SEQ ID NO: 1. In another embodiment, the anti-PD-L1 antibody molecule comprises the VHCDR1 amino acid sequence of SEQ ID NO: 4. In yet another embodiment, the anti-PD-L1 antibody molecule comprises the VHCDR1 amino acid sequence of SEQ ID NO: 195, each disclosed in Table 1 of US-2016/0108123.

TIM3 (T cell immunoglobulin-3) also negatively regulates T cell function, particularly in IFN-g-secreting CD4+ T helper 1 and CD8+ T cytotoxic 1 cells, and plays a critical role in T cell exhaustion. Inhibition of the interaction between TIM3 and its ligands, e.g., galectin-9 (Gal9), phosphotidylserine (PS), and HMGB1, can increase immune response. Antibodies, antibody fragments, and other inhibitors of TIM3 and its ligands are available in the art and may be used combination with a CAR, e.g., a CD19 CAR, described herein. For example, antibodies, antibody fragments, small molecules, or peptide inhibitors that target TIM3 binds to the IgV domain of TIM3 to inhibit interaction with its ligands. Antibodies and peptides that inhibit TIM3 are disclosed in WO2013/006490 and US20100247521. Other anti-TIM3 antibodies include humanized versions of RMT3-23 (disclosed in Ngiow et al., 2011, Cancer Res, 71:3540-3551), and clone 8B.2C12 (disclosed in Monney et al., 2002, Nature, 415:536-541). Bi-specific antibodies that inhibit TIM3 and PD-1 are disclosed in US20130156774.

In one embodiment, the anti-TIM3 antibody or fragment thereof is an anti-TIM3 antibody molecule as described in US 2015/0218274, entitled "Antibody Molecules to TIM3 and Uses Thereof," incorporated by reference in its entirety. In one embodiment, the anti-TIM3 antibody molecule includes at least one, two, three, four, five or six CDRs (or collectively all of the CDRs) from a heavy and light chain variable region from an antibody chosen from any of ABTIM3, ABTIM3-hum01, ABTIM3-hum02, ABTIM3-hum03, ABTIM3-hum04, ABTIM3-hum05, ABTIM3-hum06, ABTIM3-hum07, ABTIM3-hum08, ABTIM3-hum09, ABTIM3-hum10, ABTIM3-hum11, ABTIM3-hum12, ABTIM3-hum13, ABTIM3-hum14, ABTIM3-hum15, ABTIM3-hum16, ABTIM3-hum17, ABTIM3-hum18, ABTIM3-hum19, ABTIM3-hum20, ABTIM3-hum21, ABTIM3-hum22, ABTIM3-hum23; or as described in Tables 1-4 of US 2015/0218274; or encoded by the nucleotide sequence in Tables 1-4; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%,

99% or higher identical) to any of the aforesaid sequences, or closely related CDRs, *e.g.*, CDRs which are identical or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions).

In yet another embodiment, the anti-TIM3 antibody molecule comprises at least one, two, three or four variable regions from an antibody described herein, *e.g.*, an antibody chosen from any of ABTIM3, ABTIM3-hum01, ABTIM3-hum02, ABTIM3-hum03, ABTIM3-hum04, ABTIM3-hum05, ABTIM3-hum06, ABTIM3-hum07, ABTIM3-hum08, ABTIM3-hum09, ABTIM3-hum10, ABTIM3-hum11, ABTIM3-hum12, ABTIM3-hum13, ABTIM3-hum14, ABTIM3-hum15, ABTIM3-hum16, ABTIM3-hum17, ABTIM3-hum18, ABTIM3-hum19, ABTIM3-hum20, ABTIM3-hum21, ABTIM3-hum22, ABTIM3-hum23; or as described in Tables 1-4 of US 2015/0218274; or encoded by the nucleotide sequence in Tables 1-4; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences.In other embodiments, the agent which enhances the activity of a CAR-expressing cell is a CEACAM inhibitor (e.g., CEACAM-1, CEACAM-3, and/or CEACAM-5 inhibitor). In one embodiment, the inhibitor of CEACAM is an anti-CEACAM antibody molecule. Exemplary anti-CEACAM-1 antibodies are described in WO 2010/125571, WO 2013/082366 WO 2014/059251 and WO 2014/022332, e.g., a monoclonal antibody 34B1, 26H7, and 5F4; or a recombinant form thereof, as described in, e.g., US 2004/0047858, US 7,132,255 and WO 99/052552. In other embodiments, the anti-CEACAM antibody binds to CEACAM-5 as described in, e.g., Zheng et al. PLoS One. 2010 Sep 2;5(9). pii: e12529 (DOI:10:1371/journal.pone.0021146), or crossreacts with CEACAM-1 and CEACAM-5 as described in, e.g., WO 2013/054331 and US 2014/0271618.

Without wishing to be bound by theory, carcinoembryonic antigen cell adhesion molecules (CEACAM), such as CEACAM-1 and CEACAM-5, are believed to mediate, at least in part, inhibition of an anti-tumor immune response (see e.g., Markel et al. J Immunol. 2002 Mar 15;168(6):2803-10; Markel et al. J Immunol. 2006 Nov 1;177(9):6062-71; Markel et al. Immunology. 2009 Feb;126(2):186-200; Markel et al. Cancer Immunol Immunother. 2010 Feb;59(2):215-30; Ortenberg et al. Mol Cancer Ther. 2012 Jun;11(6):1300-10; Stern et al. J Immunol. 2005 Jun 1;174(11):6692-701; Zheng et al. PLoS One. 2010 Sep 2;5(9). pii: e12529). For example, CEACAM-1 has been described as a heterophilic ligand for TIM-3 and as playing a role in TIM-3-mediated T cell tolerance and exhaustion (see e.g., WO 2014/022332; Huang,

et al. (2014) Nature doi:10.1038/nature13848). In embodiments, co-blockade of CEACAM-1 and TIM-3 has been shown to enhance an anti-tumor immune response in xenograft colorectal cancer models (see e.g., WO 2014/022332; Huang, et al. (2014), supra). In other embodiments, co-blockade of CEACAM-1 and PD-1 reduce T cell tolerance as described, e.g., in WO 2014/059251. Thus, CEACAM inhibitors can be used with the other immunomodulators described herein (e.g., anti-PD-1 and/or anti-TIM-3 inhibitors) to enhance an immune response against a cancer, e.g., a melanoma, a lung cancer (e.g., NSCLC), a bladder cancer, a colon cancer an ovarian cancer, and other cancers as described herein.

LAG3 (lymphocyte activation gene-3 or CD223) is a cell surface molecule expressed on activated T cells and B cells that has been shown to play a role in CD8+ T cell exhaustion. Antibodies, antibody fragments, and other inhibitors of LAG3 and its ligands are available in the art and may be used combination with a CAR, e.g., a CD19 CAR, described herein. For example, BMS-986016 (Bristol-Myers Squib) is a monoclonal antibody that targets LAG3. IMP701 (Immutep) is an antagonist LAG3 antibody and IMP731 (Immutep and GlaxoSmithKline) is a depleting LAG3 antibody. Other LAG3 inhibitors include IMP321 (Immutep), which is a recombinant fusion protein of a soluble portion of LAG3 and Ig that binds to MHC class II molecules and activates antigen presenting cells (APC). Other antibodies are disclosed, e.g., in WO2010/019570.

In one embodiment, the anti-LAG3 antibody or fragment thereof is an anti-LAG3 antibody molecule as described in US 2015/0259420, entitled "Antibody Molecules to LAG3 and Uses Thereof," incorporated by reference in its entirety. In one embodiment, the anti-LAG3 antibody molecule includes at least one, two, three, four, five or six CDRs (or collectively all of the CDRs) from a heavy and light chain variable region from an antibody chosen from any of BAP050-hum01, BAP050-hum02, BAP050-hum03, BAP050-hum04, BAP050-hum05, BAP050-hum06, BAP050-hum07, BAP050-hum08, BAP050-hum09, BAP050-hum10, BAP050-hum11, BAP050-hum12, BAP050-hum13, BAP050-hum14, BAP050-hum15, BAP050-hum16, BAP050-hum17, BAP050-hum18, BAP050-hum19, BAP050-hum20, huBAP050(Ser) (*e.g.,* BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum03-Ser, BAP050-hum04-Ser, BAP050-hum05-Ser, BAP050-hum06-Ser, BAP050-hum07-Ser, BAP050-hum08-Ser, BAP050-hum09-Ser, BAP050-hum10-Ser, BAP050-hum11-Ser, BAP050-hum12-Ser, BAP050-hum13-Ser, BAP050-hum14-Ser, BAP050-hum15-Ser, BAP050-hum18-Ser, BAP050-hum19-Ser, or BAP050-hum20-Ser), BAP050-Clone-F,

BAP050-Clone-G, BAP050-Clone-H, BAP050-Clone-I, or BAP050-Clone-J; or as described in Table 1 of US 2015/0259420; or encoded by the nucleotide sequence in Table 1; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences, or closely related CDRs, *e.g.*, CDRs which are identical or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions).

In yet another embodiment, the anti-LAG3 antibody molecule comprises at least one, two, three or four variable regions from an antibody described herein, *e.g.*, an antibody chosen from any of BAP050-hum01, BAP050-hum02, BAP050-hum03, BAP050-hum04, BAP050-hum05, BAP050-hum06, BAP050-hum07, BAP050-hum08, BAP050-hum09, BAP050-hum10, BAP050-hum11, BAP050-hum12, BAP050-hum13, BAP050-hum14, BAP050-hum15, BAP050-hum16, BAP050-hum17, BAP050-hum18, BAP050-hum19, BAP050-hum20, huBAP050(Ser) (*e.g.,* BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum03-Ser, BAP050-hum04-Ser, BAP050-hum05-Ser, BAP050-hum06-Ser, BAP050-hum07-Ser, BAP050-hum08-Ser, BAP050-hum09-Ser, BAP050-hum10-Ser, BAP050-hum11-Ser, BAP050-hum12-Ser, BAP050-hum13-Ser, BAP050-hum14-Ser, BAP050-hum15-Ser, BAP050-hum18-Ser, BAP050-hum19-Ser, or BAP050-hum20-Ser), BAP050-Clone-F, BAP050-Clone-G, BAP050-Clone-H, BAP050-Clone-I, or BAP050-Clone-J; or as described in Table 1 of US 2015/0259420; or encoded by the nucleotide sequence in Tables 1; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences.In some embodiments, the agent which enhances the activity of a CAR-expressing cell can be, e.g., a fusion protein comprising a first domain and a second domain, wherein the first domain is an inhibitory molecule, or fragment thereof, and the second domain is a polypeptide that is associated with a positive signal, e.g., a polypeptide comprising an intracellular signaling domain as described herein. In some embodiments, the polypeptide that is associated with a positive signal can include a costimulatory domain of CD28, CD27, ICOS, e.g., an intracellular signaling domain of CD28, CD27 and/or ICOS, and/or a primary signaling domain, e.g., of CD3 zeta, e.g., described herein. In one embodiment, the fusion protein is expressed by the same cell that expressed the CAR. In another embodiment, the fusion protein is expressed by a cell, e.g., a T cell or NK cell that does not express a CD19 CAR.

In one embodiment, the agent which enhances activity of a CAR-expressing cell described herein is miR-17-92.

ROR1 inhibitors

Also provided herein are ROR1 inhibitors and combination therapies, e.g., combinations of a CAR-expressing cell described herein with a ROR1 inhibitor. The ROR1 inhibitor can be, e.g., a small molecule, antibody, or fragment thereof (e.g., a monospecific or bispecific antibody or fragment thereof); a recombinant protein, e.g., fusion protein, that binds to ROR1; inhibitory nucleic acid; or a cell expressing a ROR1 CAR, e.g., a ROR1 CAR-expressing T cell or NK cell. In one embodiment, the ROR1 inhibitor is an anti-ROR1 expressing cell, e.g., ROR1 CART or ROR1-expressing NK cell. Exemplary ROR1 inhibitors are described in more detail below.

In one embodiment, the present disclosure provides a population of CAR-expressing cells, e.g., CART cells or CAR-expressing NK cells, comprising a mixture of cells expressing ROR1 CARs. For example, in one embodiment, the population of CAR-expressing cells can include a first cell expressing a CD19 CAR and a second cell expressing a ROR1 CAR.

ROR1 inhibitors include but are not limited to anti-ROR1 CAR-expressing cells, e.g. CARTs, and anti-ROR antibodies (e.g., an anti-ROR1 mono- or bispecific antibody) and fragments thereof. In some embodiments, anti-ROR1 inhibitors can be used to treat a disease described herein.

An exemplary anti-ROR1 inhibitor is described in Hudecek, et al. Clin. Cancer Res. 19.12(2013):3153-64, incorporated herein by reference. For example, an anti-ROR1 inhibitor includes the anti-ROR1 CARTs described in Hudecek et al. (for example, generated as described in Hudecek et al. at page 3155, first full paragraph, incorporated herein by reference). In other examples, an anti-ROR1 inhibitor includes an antibody or fragment thereof comprising the VH and/or VL sequences of the 2A2 and R12 anti-ROR1 monoclonal antibodies described in Hudecek et al. at paragraph bridging pages 3154-55; Baskar et al. MAbs 4(2012):349–61; and Yang et al. PLoS ONE 6(2011):e21018, incorporated herein by reference.

In other embodiments, a ROR1 inhibitor includes an antibody or fragment thereof (e.g., single chain variable fragment (scFv)) that targets ROR1, including those described in US 2013/0101607, e.g., SEQ ID NOs: 1 or 2 of US 2013/0101607, incorporated herein by reference. In some embodiments, anti-ROR1 antibody fragments (e.g., scFvs) are conjugated or

fused to a biologically active molecule, e.g., to form a chimeric antigen receptor (CAR) that directs immune cells, e.g., T cells or NK cells, to respond to ROR1-expressing cells.

In some embodiments, an exemplary ROR1 inhibitor includes an anti-ROR1 monoclonal antibody called UC-961 (Cirmtuzumab). See, e.g., Clinical Trial Identifier No. NCT02222688. Cirmtuzumab can be used to treat cancers, such as chronic lymphocytic leukemia (CLL), ovarian cancer, and melanoma. See, e.g., Hojjat-Farsangi et al. PLoS One. 8(4): e61167; and NCT02222688. In some embodiments, cirmtuzumab is administered intravenously, e.g., as an intravenous infusion.

In some embodiments, the anti-ROR1 antibody is conjugated or otherwise bound to a therapeutic agent.

In some embodiments, a ROR1 inhibitor includes an anti-ROR1 CAR-expressing cell, e.g., CART, e.g., a cell expressing an anti-ROR1 CAR construct or encoded by a ROR1 binding CAR comprising a scFv, CDRs, or VH and VL chains. For example, an anti-ROR1 CAR-expressing cell, e.g., CART is a generated by engineering a ROR1-CAR (that comprises a ROR1 binding domain) into a cell (e.g., a T cell or NK cell), e.g., for administration in combination with a CAR-expressing cell described herein. Also provided herein are methods of use of the CAR-expressing cells described herein for adoptive therapy.

In another aspect, provided herein is a population of CAR-expressing cells, e.g., CART cells or CAR-expressing NK cells, comprising a mixture of cells expressing CD19 CARs and ROR1 CARs. For example, in one embodiment, the population of CAR-expressing cell can include a first cell expressing a CD19 CAR and a second cell expressing a ROR1 CAR. In one embodiment, the population of CAR-expressing cells includes, e.g., a first cell expressing a CAR (e.g., a CD19 CAR, a ROR1 CAR, a CD20 CAR, or a CD22 CAR) that includes a primary intracellular signaling domain, and a second cell expressing a CAR (e.g., a CD19 CAR, a ROR1 CAR, a CD20 CAR, or a CD22 CAR)) that includes a secondary signaling domain.

CD20 inhibitors

Provided herein are CD20 inhibitors and combination therapies, e.g., combinations of a CAR-expressing cell described herein with a CD20 inhibitor. The CD20 inhibitor can be, e.g., a small molecule, antibody, or fragment thereof (e.g., a monospecific or bispecific antibody or fragment thereof); a recombinant protein, e.g., fusion protein, that binds to CD20; inhibitory

nucleic acid; or a cell expressing a CD20 CAR, e.g., a CD20 CAR-expressing T cell or NK cell. In one embodiment, the CD20 inhibitor is an anti-CD20 CAR expressing cell, e.g., CD20 CART or CD20 CAR-expressing NK cell. Exemplary CD20 inhibitors are described in more detail below.

In an embodiment, the present disclosure provides a population of CAR-expressing cells, e.g., CART cells or CAR-expressing NK cells, comprising a mixture of cells expressing CD20 CARs. For example, in one embodiment, the population of CAR-expressing cells includes a first cell expressing a CD20 CAR and a second cell expressing a CD19 CAR.

In one embodiment, the second CD20 inhibitor is an anti-CD20 antibody or fragment thereof. In an embodiment, the antibody is a monospecific antibody, and in another embodiment, the antibody is a bispecific antibody. In an embodiment, the CD20 inhibitor is a chimeric mouse/human monoclonal antibody, e.g., rituximab. In an embodiment, the CD20 inhibitor is a human monoclonal antibody such as ofatumumab. In an embodiment, the CD20 inhibitor is a humanized antibody such as ocrelizumab, veltuzumab, obinutuzumab, ocaratuzumab, or PRO131921 (Genentech). In an embodiment, the CD20 inhibitor is a fusion protein comprising a portion of an anti-CD20 antibody, such as TRU-015 (Trubion Pharmaceuticals).

For example, the anti-CD20 antibodyis chosen from rituximab, ofatumumab, ocrelizumab, veltuzumab, obinutuzumab, TRU-015 (Trubion Pharmaceuticals), ocaratuzumab, or Pro131921 (Genentech). See, e.g., Lim et al. Haematologica. 95.1(2010):135-43.

In some embodiments, the anti-CD20 antibody comprises rituximab. Rituximab is a chimeric mouse/human monoclonal antibody IgG1 kappa that binds to CD20 and causes cytolysis of a CD20 expressing cell, e.g., as described in www.accessdata.fda.gov/drugsatfda_docs/label/2010/103705s5311lbl.pdf.

In some embodiments, the anti-CD20 antibody comprises ofatumumab. Ofatumumab is an anti-CD20 IgG1κ human monoclonal antibody with a molecular weight of approximately 149 kDa. For example, ofatumumab is generated using transgenic mouse and hybridoma technology and is expressed and purified from a recombinant murine cell line (NS0). See, e.g., www.accessdata.fda.gov/drugsatfda_docs/label/2009/125326lbl.pdf; and Clinical Trial Identifier number NCT01363128, NCT01515176, NCT01626352, and NCT01397591.

In some embodiments, the anti-CD20 antibody comprises ocrelizumab. Ocrelizumab is a humanized anti-CD20 monoclonal antibody, e.g., as described in Clinical Trials Identifier

Nos. NCT00077870, NCT01412333, NCT00779220, NCT00673920, NCT01194570, and Kappos et al. Lancet. 19.378(2011):1779-87. In some embodiments, ocrelizumab is administered as an intravenous infusion.

In some embodiments, the anti-CD20 antibody comprises veltuzumab. Veltuzumab is a humanized monoclonal antibody against CD20. See, e.g., Clinical Trial Identifier No. NCT00547066, NCT00546793, NCT01101581, and Goldenberg et al. Leuk Lymphoma. 51(5)(2010):747-55. In some embodiments, veltuzumab is administered subcutaneously or intravenously, e.g., as an intravenous infusion.

In some embodiments, the anti-CD20 antibody comprises GA101. GA101 (also called obinutuzumab or RO5072759) is a humanized and glyco-engineered anti-CD20 monoclonal antibody. See, e.g., Robak. Curr. Opin. Investig. Drugs. 10.6(2009):588-96; Clinical Trial Identifier Numbers: NCT01995669, NCT01889797, NCT02229422, and NCT01414205; and www.accessdata.fda.gov/drugsatfda_docs/label/2013/125486s000lbl.pdf. In some embodiments, GA101 is administered intravenously, e.g., as an intravenous infusion.

In some embodiments, the anti-CD20 antibody comprises AME-133v. AME-133v (also called LY2469298 or ocaratuzumab) is a humanized IgG1 monoclonal antibody against CD20 with increased affinity for the FcγRIIIa receptor and an enhanced antibody dependent cellular cytotoxicity (ADCC) activity compared with rituximab. See, e.g., Robak et al. BioDrugs 25.1(2011):13-25; and Forero-Torres et al. Clin Cancer Res. 18.5(2012):1395-403.

In some embodiments, the anti-CD20 antibody comprises PRO131921. PRO131921 is a humanized anti-CD20 monoclonal antibody engineered to have better binding to FcγRIIIa and enhanced ADCC compared with rituximab. See, e.g., Robak et al. BioDrugs 25.1(2011):13-25; and Casulo et al. Clin Immunol. 154.1(2014):37-46; Clinical Trial Identifier No. NCT00452127. In some embodiments, PRO131921 is administered intravenously, e.g., as an intravenous infusion.

In some embodiments, the anti-CD20 antibody comprises TRU-015. TRU-015 is an anti-CD20 fusion protein derived from domains of an antibody against CD20. TRU-015 is smaller than monoclonal antibodies, but retains Fc-mediated effector functions. See, e.g., Robak et al. BioDrugs 25.1(2011):13-25. TRU-015 contains an anti-CD20 single-chain variable fragment (scFv) linked to human IgG1 hinge, CH2, and CH3 domains but lacks CH1 and CL domains. In some cases, TRU-015 is administered intravenously, e.g., as an intravenous infusion.

In some embodiments, an anti-CD20 antibody described herein is conjugated or otherwise bound to a therapeutic agent, e.g., a chemotherapeutic agent (e.g., a chemotherapeutic agent described herein, e.g,. cytoxan, fludarabine, histone deacetylase inhibitor, demethylating agent, peptide vaccine, anti-tumor antibiotic, tyrosine kinase inhibitor, alkylating agent, anti-microtubule or anti-mitotic agent, CD20 antibody, or CD20 antibody drug conjugate described herein), anti-allergic agent, anti-nausea agent (or anti-emetic), pain reliever, or cytoprotective agent described herein.

In one embodiment, the CD20 inhibitor includes a CD20 CAR-expressing cell, e.g., a CD20 CART, or e.g., a CD20-CAR that comprises a CD20 binding domain and is engineered into a cell (e.g., T cell or NK cell) for administration in combination with CD19 CART, and methods of their use for adoptive therapy. In some embodiments, the CD20 inhibitor includes a cell expressing a CD20 CAR construct or encoded by a CD20 CAR comprising a scFv, CDRs, or VH and VL chains. For example, a CD20 CAR-expressing cell, e.g., CART, is generated by engineering a CD20-CAR (that comprises a CD20 binding domain) into a cell (e.g., a T cell or NK cell), e.g., for administration in combination with a CAR-expressing cell described herein, e.g., a CD20 CART described herein.

In another aspect, the present invention provides a population of CAR-expressing cells, e.g., CAR-expressing cell, comprising a mixture of cells expressing CD20 CARs and CD19 CARs. For example, in one embodiment, the population of CAR-expressing cell can include a first cell expressing a CD20 CAR and a second cell expressing a CD19 CAR. In one embodiment, the population of CAR-expressing cells includes, e.g., a first cell expressing a CAR (e.g., a CD20 CAR or CD19 CAR) that includes a primary intracellular signaling domain, and a second cell expressing a CAR (e.g., a CD20 CAR or CD19 CAR) that includes a secondary signaling domain.

CD19 inhibitors

Provided herein are CD19 inhibitors and combination therapies, e.g., one or more CD19 inhibitors. In some embodiments, the methods and compositions (e.g., CD19 CAR-expressing cells) described herein further include a second CD19 inhibitor. For example, a CD19 CAR-expressing cell described herein is administered in combination with a second CD19 inhibitor. A CD19 inhibitor includes but is not limited to a CD19 CAR-expressing cell, e.g., a CD19

CART cell, a CD19 CAR-expressing NK cell, or an anti-CD19 antibody (e.g., an anti-CD19 mono- or bispecific antibody) or a fragment thereof.

Exemplary anti-CD19 antibodies or fragments or conjugates thereof include but are not limited to blinatumomab, SAR3419 (Sanofi), MEDI-551 (MedImmune LLC), Combotox, DT2219ARL (Masonic Cancer Center), MOR-208 (also called XmAb-5574; MorphoSys), XmAb-5871 (Xencor), MDX-1342 (Bristol-Myers Squibb), SGN-CD19A (Seattle Genetics), and AFM11 (Affimed Therapeutics). See, e.g., Hammer. MAbs. 4.5(2012): 571–77.

In some embodiments, the anti-CD19 antibody or fragment or conjugate thereof comprises blinatomomab. Blinatomomab is a bispecific antibody comprised of two scFvs—one that binds to CD19 and one that binds to CD3. Blinatomomab directs T cells to attack cancer cells. See, e.g., Hammer et al.; Clinical Trial Identifier No. NCT00274742 and NCT01209286. In some embodiments, blinatomomab can be used to treat NHL (e.g., DLBCL) or ALL.

In some embodiments, the anti-CD19 antibody comprises MEDI-551. MEDI-551 is a humanized anti-CD19 antibody with a Fc engineered to have enhanced antibody-dependent cell-mediated cytotoxicity (ADCC). See, e.g., Hammer et al.; and Clinical Trial Identifier No. NCT01957579. In some embodiments, MEDI-551 can be used to treat B cell malignancies (e.g., NHL, CLL, DLBCL, and multiple myeloma), multiple sclerosis, and scleroderma.

In some embodiments, the anti-CD19 antibody or fragment or conjugate thereof comprises Combotox. Combotox is a mixture of immunotoxins that bind to CD19 and CD22. The immunotoxins are made up of scFv antibody fragments fused to a deglycosylated ricin A chain. See, e.g., Hammer et al.; and Herrera et al. J. Pediatr. Hematol. Oncol. 31.12(2009):936-41; Schindler et al. Br. J. Haematol. 154.4(2011):471-6. In some embodiments, Combotox can be used to treat B cell leukemia, e.g., ALL.

In some embodiments, the anti-CD19 antibody or fragment or conjugate thereof comprises DT2219ARL. DT2219ARL is a bispecific immunotoxin targeting CD19 and CD22, comprising two scFvs and a truncated diphtheria toxin. See, e.g., Hammer et al.; and Clinical Trial Identifier No. NCT00889408. In some embodiments, DT2219ARL can be used to treat B cell malignancies, e.g., B cell leukemias and lymphomas.

In some embodiments, DT2219ARL is administered intravenously, e.g., as an intravenous infusion.

In some embodiments, the anti-CD19 antibody or fragment or conjugate thereof comprises SGN-CD19A. SGN-CD19A is an antibody-drug conjugate (ADC) comprised of an anti-CD19 humanized monoclonal antibody linked to a synthetic cytotoxic cell-killing agent, monomethyl auristatin F (MMAF). See, e.g., Hammer et al.; and Clinical Trial Identifier Nos. NCT01786096 and NCT01786135. In some embodiments, SGN-CD19A can be used to treat B-cell ALL, NHL (e.g., DLBCL, mantle cell lymphoma, or follicular lymphoma), Burkitt lymphoma or leukemia, or B-lineage lymphoblastic lymphoma (B-LBL). In some embodiments, SGN-CD19A is administered intravenously, e.g., as an intravenous infusion.

In some embodiments, the anti-CD19 antibody comprises MOR-208 (also called XmAb-5574). MOR-208 is an Fc-engineered anti-CD19 humanized monoclonal antibody with enhanced FcγRIIIA binding, which results in improved ADCC activity. See, e.g., ClinicalTrials.gov Identifier Nos. NCT01685008, NCT01685021, NCT02005289, and NCT01161511; Hammer et al.; Woyach et al. Blood 124.24(2014).

In some embodiments, MOR-208 can be used to treat NHL (e.g., FL, MCL, DLBCL), CLL, small lymphocytic lymphoma, prolymphocytic leukemia, or B-cell Acute Lymphoblastic Leukemia (B-ALL). In some embodiments, MOR-208 is administered intravenously, e.g., as an intravenous infusion.

In some aspect, the anti-CD19 antibody or fragment or conjugate thereof comprises SAR3419. SAR3419 is an anti-CD19 antibody-drug conjugate (ADC) comprising an anti-CD19 humanized monoclonal antibody conjugated to a maytansine derivative via a cleavable linker. See, e.g., Younes et al. J. Clin. Oncol. 30.2(2012): 2776-82; Hammer et al.; Clinical Trial Identifier No. NCT00549185; and Blanc et al. Clin Cancer Res. 2011;17:6448-58. In some embodiments, SAR3419 can be used to treat NHL (diffuse large B-cell lymphoma (DLBCL) and follicular small cleaved cell lymphoma) or B-cell ALL.

In some embodiments, the anti-CD19 antibody comprises XmAb-5871. XmAb-5871 is an Fc-engineered, humanized anti-CD19 antibody. In some embodiments, XmAb-5871 can be used to treat autoimmune diseases, such as lupus. See, e.g., Hammer et al.

In some embodiments, the anti-CD19 antibody comprises MDX-1342, which is a human Fc-engineered anti-CD19 antibody with enhanced ADCC. In some embodiments, MDX-1342 can be used to treat CLL and rheumatoid arthritis. See, e.g., Hammer et al.

In some embodiments, the anti-CD19 antibody comprises AFM11. AFM11 is a bispecific antibody that targets CD19 and CD3. In some embodiments, AFM11 can be used to

treat NHL (e.g., DLBCL), ALL, or CLL. See, e.g., Hammer et al.; and Clinical Trial Identifier No. NCT02106091. In some embodiments, AFM11 is administered as an intravenous infusion.

In some embodiments, an anti-CD19 antibody described herein is conjugated or otherwise bound to a therapeutic agent, e.g., a chemotherapeutic agent (e.g., a chemotherapeutic agent described herein), peptide vaccine (such as that described in Izumoto et al. 2008 J Neurosurg 108:963-971), immunosuppressive agent (e.g., an immunosuppressive agent described herein), or immunoablative agent (e.g., an immunoablative agent described herein), e.g., cyclosporin, azathioprine, methotrexate, mycophenolate, FK506, CAMPATH, anti-CD3 antibody, cytoxin, fludarabine, rapamycin, mycophenolic acid, steroid, FR901228, or cytokine.

In some embodiments, a CD19 inhibitor includes an anti-CD19 CAR-expressing cell, e.g., CART, e.g., a cell expressing an anti-CD19 CAR construct. In an embodiment, the anti-CD19 CAR construct comprises a murine scFv sequence. For example, the anti-CD19 CAR construct comprising a murine scFv sequence is the CAR19 construct provided in PCT publication WO2012/079000 and provided herein.

For example, an anti-CD19 CAR-expressing cell, e.g., CART, is a generated by engineering a CD19-CAR (that comprises a CD19 binding domain) into a cell (e.g., a T cell or NK cell), e.g., for administration in combination with a CAR-expressing cell described herein. Also provided herein are methods of use of the CAR-expressing cells described herein for adoptive therapy.

In another aspect, provided herein is a population of CAR-expressing cells, e.g., CAR-expressing cell, comprising a mixture of cells expressing CD22 CARs and CD19 CARs. For example, in one embodiment, the population of CAR-expressing cell can include a first cell expressing a CD22 CAR and a second cell expressing a CD19 CAR.

CD123 Inhibitors

Provided herein are CD123 inhibitors and combination therapies. CD123 inhibitors include but are not limited to small molecules, recombinant proteins, anti-CD123 CAR-expressing cells, e.g. CARTs, and anti-CD123 antibodies (e.g., an anti-CD123 mono- or bispecific antibody) and fragments thereof. In some embodiments, anti-CD123 inhibitors can be used to treat a B-cell malignancy described herein. In an embodiment, the CD123 inhibitor is administered in combination with a CD19 inhibitor, e.g., a CD19 CAR-expressing cell, e.g.,

a CAR-expressing cell described herein, e.g., a cell expressing a CAR comprising an antibody binding domain that is murine, human, or humanized.

In one embodiment, the CD123 inhibitor is a recombinant protein, e.g., comprising the natural ligand (or a fragment) of the CD123 receptor. For example, the recombinant protein is SL-401 (also called DT388IL3; University of Texas Southwestern Medical Center), which is a fusion protein comprising human IL-3 fused to a truncated diphtheria toxin. See, e.g., Testa et al. Biomark Res. 2014; 2: 4; and Clinical Trial Identifier No. NCT00397579.

In another embodiment, the CD123 inhibitor is an anti-CD123 antibody or fragment thereof. In one embodiment, the anti-CD123 antibody or fragment thereof comprises a monoclonal antibody, e.g., a monospecific or bispecific antibody or fragment thereof. For example, the anti-CD123 antibody or fragment thereof comprises CSL360 (CSL Limited). CSL360 is a recombinant chimeric monoclonal antibody that binds to CD123. In some embodiments, CSL360 is administered intravenously, e.g., by intravenous infusion. See, e.g., Clinical Trial Identifier No. NCT01632852; and Testa et al.

In another embodiment, the CD123 antibody or fragment thereof comprises CSL362 (CSL Limited). CSL362 is a humanized monoclonal antibody that targets the CD123 and is optimized for enhanced activation of antibody dependent cell-mediated cytotoxicity (ADCC). In some embodiments, CSL362 is administered intravenously, e.g., by intravenous infusion. See, e.g., Clinical Trial Identifier No. NCT01632852.

In one embodiment, the CD123 antibody or fragment thereof comprises a bispecific antibody, e.g., MGD006 (MacroGenics). MGD006 is a bispecific antibody that targets CD123 and CD3. See, e.g., Clinical Trial Identifier No. NCT02152956.

In some embodiments, the CD123 inhibitor is conjugated or otherwise bound to a therapeutic agent.

In some embodiments, a CD123 inhibitor includes an anti-CD123 CAR-expressing cell, e.g., CART, e.g., a cell expressing an anti-CD123 CAR construct or encoded by a CD123 binding CAR comprising a scFv, CDRs, or VH and VL chains. For example, an anti-CD123 CAR-expressing cell, e.g., CART is a generated by engineering a CD123-CAR (that comprises a CD123 binding domain) into a cell (e.g., a T cell or NK cell), e.g., for administration in combination with a CAR-expressing cell described herein. In an embodiment, the anti-CD123 CAR construct comprises a scFv sequence, e.g., a scFv sequence provided in US 2014/0322212 A1, incorporated herein by reference. In one embodiment, the anti-CD123 binding domain is a

scFv described in US 2014/0322212 A1. In an embodiment, the anti-CD123 binding domain is part of a CAR construct provided in US 2014/0322212 A1. Also provided herein are methods of use of the CAR-expressing cells described herein for adoptive therapy.

In another aspect, provided herein is a population of CAR-expressing cells, e.g., CART cells or CAR-expressing NK cells, comprising a mixture of cells expressing CD19 CARs and CD123 CARs. For example, in one embodiment, the population of CAR-expressing cellscan include a first cell expressing a CD19 CAR and a second cell expressing a CD123 CAR.

CD10 Inhibitors

Also provided herein are CD10 inhibitors and combination therapies. CD10 inhibitors include but are not limited to small molecules, recombinant proteins, anti-CD10 CAR-expressing cells, e.g. CARTs, and anti-CD10 antibodies (e.g., an anti-CD10 mono- or bispecific antibody) and fragments thereof. In some embodiments, anti-CD10 inhibitors can be used to treat a B-cell malignancy described herein. In an embodiment, the CD10 inhibitor is administered in combination with a CD19 inhibitor, e.g., a CD19 CAR-expressing cell, e.g., a CAR-expressing cell described herein, e.g., a cell expressing a CAR comprising an antibody binding domain that is murine, human, or humanized.

In an embodiment, the CD10 inhibitor comprises a small molecule, such as sacubitril (Novartis), valsartan/sacubritril (Novartis), omapatrilat (Bristol-Myers Squibb), RB-101, UK-414,495 (Pfizer), or a pharmaceutically acceptable salt or a derivative thereof.

In an embodiment, the CD10 inhibitor comprises sacubitril (AHU-377; Novartis) (4-{[(2*S*,4*R*)-1-(4-Biphenylyl)-5-ethoxy-4-methyl-5-oxo-2-pentanyl]amino}-4-oxobutanoic acid), or a pharmaceutically acceptable salt or a derivative thereof.

In another embodiment, the CD10 inhibitor comprises valsartan/sacubritril (LCZ696; Novartis) or a pharmaceutically acceptable salt or a derivative thereof. Valsartan/sacubritril is a combination drug comprising a 1:1 mixture of valsartan and sacubitril. The structure of Valsartan has the following chemical name: ((*S*)-3-methyl-2-(*N*-{[2'-(2*H*-1,2,3,4-tetrazol-5-yl)biphenyl-4-yl]methyl}pentanamido)butanoic acid).

In an embodiment, the CD10 inhibitor comprises omapatrilat (Bristol-Myers Squibb) ((4*S*,7*S*,10a*S*)-5-oxo-4-{[(2*S*)-3-phenyl-2- sulfanylpropanoyl]amino}-2,3,4,7,8,9,10,10a-octahydropyrido[6,1-*b*] [1,3]thiazepine-7-carboxylic acid), or a pharmaceutically acceptable salt or a derivative thereof.

In an embodiment, the CD10 inhibitor comprises RB-101 (benzyl *N*-(3-{[(2*S*)-2-amino-4-(methylthio)butyl]dithio}-2-benzylpropanoyl)-L-phenylalaninate), or a pharmaceutically acceptable salt or a derivative thereof.

In an embodiment, the CD10 inhibitor comprises UK-414,495 (Pfizer) ((R)-2-({1-[(5-ethyl-1,3,4-thiadiazol-2-yl)carbamoyl]cyclopentyl}methyl)valeric acid), or a pharmaceutically acceptable salt or a derivative thereof.

In some embodiments, the CD10 inhibitor is conjugated or otherwise bound to a therapeutic agent.

In some embodiments, a CD10 inhibitor includes an anti-CD10 CAR-expressing cell, e.g., CART, e.g., a cell expressing an anti-CD10 CAR construct or encoded by a CD10 binding CAR comprising a scFv, CDRs, or VH and VL chains. For example, an anti-CD10 CAR-expressing cell, e.g., CART is a generated by engineering a CD10-CAR (that comprises a CD10 binding domain) into a cell (e.g., a T cell or NK cell), e.g., for administration in combination with a CAR-expressing cell described herein. Also provided herein are methods of use of the CAR-expressing cells described herein for adoptive therapy.

In another aspect, provided herein is a population of CAR-expressing cells, e.g., CART cells or CAR-expressing NK cells, comprising a mixture of cells expressing CD19 CARs and CD10 CARs. For example, in one embodiment, the population of CAR-expressing cells can include a first cell expressing a CD19 CAR and a second cell expressing a CD10 CAR.

CD34 Inhibitors

Also provided herein are CD34 inhibitors and combination therapies. CD34 inhibitors include but are not limited to small molecules, recombinant proteins, anti-CD34 CAR-expressing cells, e.g. CARTs, and anti-CD34 antibodies (e.g., an anti-CD34 mono- or bispecific antibody) and fragments thereof. In some embodiments, anti-CD34 inhibitors can be used to treat a B-cell malignancy described herein. In an embodiment, the CD34 inhibitor is administered in combination with a CD19 inhibitor, e.g., a CD19 CAR-expressing cell, e.g., a CAR-expressing cell described herein, e.g., a cell expressing a CAR comprising an antibody binding domain that is murine, human, or humanized.

In an embodiment, the CD34 inhibitor comprises a monoclonal antibody or fragment thereof that targets CD34 or an immunoliposome comprising an anti-CD34 monoclonal antibody or fragment thereof.

In an embodiment, the CD34 inhibitor comprises an antibody or fragment thereof, e.g., the My-10 monoclonal antibody or an immunoliposome comprising the My-10 monoclonal antibody, as described in Mercadal et al. Biochim. Biophys. Acta. 1371.1(1998):17-23. In other embodiments, the CD34 inhibitor comprises an immunoliposome containing a cancer drug, e.g., doxorubicin, that is targeted to CD34-expressing cells, as described in Carrion et al. Life Sci. 75.3(2004):313-28. In an embodiment, the CD34 inhibitor comprises a monoclonal antibody against CD34 as described in Maleki et al. Hum. Antibodies. 22(2013):1-8. In another embodiment, the CD34 inhibitor comprises a monoclonal antibody that targets CD34, as described in Maleki et al. Cell J. 16.3(2014):361-66.

In some embodiments, the CD34 inhibitor is conjugated or otherwise bound to a therapeutic agent.

In some embodiments, a CD34 inhibitor includes an anti-CD34 CAR-expressing cell, e.g., CART, e.g., a cell expressing an anti-CD34 CAR construct or encoded by a CD34 binding CAR comprising a scFv, CDRs, or VH and VL chains. For example, an anti-CD34 CAR-expressing cell, e.g., CART is a generated by engineering a CD34-CAR (that comprises a CD34 binding domain) into a cell (e.g., a T cell or NK cell), e.g., for administration in combination with a CAR-expressing cell described herein. Also provided herein are methods of use of the CAR-expressing cells described herein for adoptive therapy.

In another aspect, provided herein is a population of CAR-expressing cells, e.g., CART cells or CAR-expressing NK cells, comprising a mixture of cells expressing CD19 CARs and CD34 CARs. For example, in one embodiment, the population of CAR-expressing cells can include a first cell expressing a CD19CAR and a second cell expressing a CD34 CAR.

FLT-3 Inhibitors

Fms-like tyrosine kinase 3 (FLT-3), also called Cluster of differentiation antigen 135 (CD135), receptor-type tyrosine-protein kinase FLT3, or fetal liver kinase-2 (Flk2), is a receptor tyrosine kinase. FLT-3 is a cytokine receptor for the ligand, cytokine Flt3 ligand (FLT3L). FLT-3 is expressed on the surface of many hematopoietic progenitor cells and is important for lymphocyte development. The FLT3 gene is commonly mutated in leukemia, e.g., acute myeloid leukemia (AML).

Also provided herein are FLT-3 inhibitors and combination therapies. FLT-3 inhibitors include but are not limited to small molecules, recombinant proteins, anti-FLT-3 CAR-

expressing cells, e.g. CARTs, and anti-FLT-3 antibodies (e.g., an anti-FLT-3 mono- or bispecific antibody) and fragments thereof. In some embodiments, anti-FLT-3 inhibitors can be used to treat a B-cell malignancy described herein. In an embodiment, the FLT-3 inhibitor is administered in combination with a CD19 inhibitor, e.g., a CD19 CAR-expressing cell, e.g., a CAR-expressing cell described herein, e.g., a cell expressing a CAR comprising an antibody binding domain that is murine, human, or humanized.

In some embodiments, the FLT-3 inhibitor comprises a small molecule, such as quizartinib (Ambit Biosciences), midostaurin (Technische Universitat Dresden), sorafenib (Bayer and Onyx Pharmaceuticals), sunitinib (Pfizer), lestaurtinib (Cephalon), or a pharmaceutically acceptable salt or derivative thereof.

In some embodiments, the FLT-3 inhibitor comprises quizartinib (AC220; Ambit Biosciences) or a pharmaceutically acceptable salt or a derivative thereof. Quizartinib is a small molecule receptor tyrosine kinase inhibitor. Quizartinib has the following chemical name: (1-(5-(*tert*-Butyl)isoxazol-3-yl)-3-(4-(7-(2-morpholinoethoxy)benzo[*d*]imidazo[2,1-b]thiazol-2-yl)phenyl)urea).

In some embodiments, the FLT-3 inhibitor comprises midostaurin is (PKC412; Technische Universität Dresden) or a pharmaceutically acceptable salt or a derivative thereof. Midostaurin is a protein kinase inhibitor that is a semi-synthetic derivative of staurosporine, an alkaloid from the bacterium Streptomyces staurosporeus. The chemical name of midostaurin is as follows: ((9S,10R,11R,13R)-2,3,10,11,12,13-Hexahydro-10-methoxy-9-methyl-11-(methylamino)-9,13-epoxy-1H,9H-diindolo[1,2,3-gh:3',2',1'-lm]pyrrolo[3,4-j][1,7]benzodiamzonine-1-one).

In an embodiment, the FLT-3 inhibitor comprises sorafenib (Bayer and Onyx Pharmaceuticals) or a pharmaceutically acceptable salt or a derivative thereof. See, e.g., labeling.bayerhealthcare.com/html/products/pi/Nexavar_PI.pdf. The chemical name of sorafenib is (4-[4-[[4-chloro-3-(trifluoromethyl)phenyl]carbamoylamino] phenoxy]-*N*-methyl-pyridine-2-carboxamide).

In some embodiments, the FLT-3 inhibitor comprises sunitinib (previously known as SU11248; Pfizer) or a pharmaceutically acceptable salt or derivative thereof.Sunitinib has the following chemical name: (*N*-(2-diethylaminoethyl)-5-[(*Z*)-(5-fluoro-2-oxo-1H-indol-3-ylidene)methyl]-2,4-dimethyl-1*H*-pyrrole-3-carboxamide).

In some embodiments, the FLT-3 inhibitor comprises lestaurtinib (CEP-701; Cephalon) or a pharmaceutically acceptable salt or derivative thereof. Lestaurtinib has the following chemical name: ((9*S*,10*S*,12*R*)-2,3,9,10,11,12-Hexahydro-10-hydroxy-10-(hydroxymethyl)-9-methyl-9,12-epoxy-1*H*-diindolo[1,2,3-*fg*:3',2',1'-*kl*]pyrrolo[3,4-*i*][1,6]benzodiazocin-1-one).

In some embodiments, a FLT-3 inhibitor includes an anti-FLT-3 CAR-expressing cell, e.g., CART, e.g., a cell expressing an anti-FLT-3 CAR construct or encoded by a FLT-3 binding CAR comprising a scFv, CDRs, or VH and VL chains. For example, an anti-FLT-3 CAR-expressing cell, e.g., CART is a generated by engineering a FLT-3-CAR (that comprises a FLT-3 binding domain) into a cell (e.g., a T cell or NK cell), e.g., for administration in combination with a CAR-expressing cell described herein. Also provided herein are methods of use of the CAR-expressing cells described herein for adoptive therapy.

In another aspect, provided herein is a population of CAR-expressing cells, e.g., CART cells or CAR-expressing NK cells, comprising a mixture of cells expressing CD19 CARs and FLT-3 CARs. For example, in one embodiment, the population of CAR-expressing cells can include a first cell expressing a CD19 CAR and a second cell expressing a FLT-3 CAR.

CD79b Inhibitors

Provided herein are CD79b inhibitors and combination therapies. CD79b inhibitors include but are not limited to small molecules, recombinant proteins, anti-CD79b CAR-expressing cells, e.g. CARTs, and anti-CD79b antibodies (e.g., an anti-CD79b mono- or bispecific antibody) and fragments thereof. In some embodiments, anti-CD79b inhibitors can be used to treat a B-cell malignancy described herein. In an embodiment, the CD79b inhibitor is administered in combination with a CD19 inhibitor, e.g., a CD19 CAR-expressing cell, e.g., a CAR-expressing cell described herein, e.g., a cell expressing a CAR comprising an antibody binding domain that is murine, human, or humanized.

In an embodiment, the CD79b inhibitor is an anti-CD79b antibody or fragment thereof. In one embodiment, the anti-79b antibody or fragment thereof comprises a monoclonal antibody, e.g., a monospecific or bispecific antibody or fragment thereof. For example, the anti-CD79b antibody or fragment thereof comprises polatuzumab vedotin (Roche), an anti-CD79b antibody drug conjugate. In embodiments, polatuzumab vedotin is used to treat a cancer, e.g., NHL, e.g., follicular lymphoma or DLBCL, e.g., relapsed or refractory follicular lymphoma or DLBCL. See, e.g., NCT02257567. In embodiments, the anti-CD79b antibody or

fragment thereof comprises MGD010 (MacroGenics), which is a bispecific antibody comprising components that bind to CD32B and D79B. See, e.g., NCT02376036.

In some embodiments, the CD79b inhibitor is conjugated or otherwise bound to a therapeutic agent.

In some embodiments, a CD79b inhibitor includes an anti-CD79b CAR-expressing cell, e.g., CART, e.g., a cell expressing an anti-CD79b CAR construct or encoded by a CD79b binding CAR comprising a scFv, CDRs, or VH and VL chains. For example, an anti-CD79b CAR-expressing cell, e.g., CART is a generated by engineering a CD79b-CAR (that comprises a CD79b binding domain) into a cell (e.g., a T cell or NK cell), e.g., for administration in combination with a CAR-expressing cell described herein. Also provided herein are methods of use of the CAR-expressing cells described herein for adoptive therapy.

In another aspect, provided herein is a population of CAR-expressing cells, e.g., CART cells or CAR-expressing NK cells, comprising a mixture of cells expressing CD19 CARs and CD79b CARs. For example, in one embodiment, the population of CAR-expressing cells can include a first cell expressing a CD19 CAR and a second cell expressing a CD79b CAR.

CD79a Inhibitors

Provided herein are CD79a inhibitors and combination therapies. CD79a inhibitors include but are not limited to small molecules, recombinant proteins, anti-CD79a CAR-expressing cells, e.g. CARTs, and anti-CD79a antibodies (e.g., an anti-CD79a mono- or bispecific antibody) and fragments thereof. In some embodiments, anti-CD79a inhibitors can be used to treat a B-cell malignancy described herein. In an embodiment, the CD79a inhibitor is administered in combination with a CD19 inhibitor, e.g., a CD19 CAR-expressing cell, e.g., a CAR-expressing cell described herein, e.g., a cell expressing a CAR comprising an antibody binding domain that is murine, human, or humanized.

In an embodiment, the CD79a inhibitor is an anti-CD79a antibody or fragment thereof. In one embodiment, the anti-CD79a antibody or fragment thereof comprises a monoclonal antibody, e.g., a monospecific or bispecific antibody or fragment thereof. For example, the anti-CD79a antibody or fragment thereof comprises an anti-CD79a antibody or fragment thereof described in Polson et al. Blood 110.2(2007):616-23, incorporated herein by reference. For example, the anti-CD79a antibody or fragment thereof comprises the 7H7, 15E4, or 16C11 antibody or fragment thereof described in Polson et al. See Id.

In some embodiments, the CD79a inhibitor is conjugated or otherwise bound to a therapeutic agent.

In some embodiments, a CD79a inhibitor includes an anti-CD79a CAR-expressing cell, e.g., CART, e.g., a cell expressing an anti-CD79a CAR construct or encoded by a CD79a binding CAR comprising a scFv, CDRs, or VH and VL chains. For example, an anti-CD79a CAR-expressing cell, e.g., CART is a generated by engineering a CD79a-CAR (that comprises a CD79a binding domain) into a cell (e.g., a T cell or NK cell), e.g., for administration in combination with a CAR-expressing cell described herein. Also provided herein are methods of use of the CAR-expressing cells described herein for adoptive therapy.

In another aspect, provided herein is a population of CAR-expressing cells, e.g., CART cells or CAR-expressing NK cells, comprising a mixture of cells expressing CD19 CARs and CD79a CARs. For example, in one embodiment, the population of CAR-expressing cells can include a first cell expressing a CD19 CAR and a second cell expressing a CD79a CAR.

CD179b Inhibitors

Provided herein are CD179b inhibitors and combination therapies. CD179b inhibitors include but are not limited to small molecules, recombinant proteins, anti-CD179b CAR-expressing cells, e.g. CARTs, and anti-CD179b antibodies (e.g., an anti-CD179b mono- or bispecific antibody) and fragments thereof.

In some embodiments, anti-CD179b inhibitors can be used to treat a B-cell malignancy described herein. In an embodiment, the CD179b inhibitor is administered in combination with a CD19 inhibitor, e.g., a CD19 CAR-expressing cell, e.g., a CAR-expressing cell described herein, e.g., a cell expressing a CAR comprising an antibody binding domain that is murine, human, or humanized.

In an embodiment, the CD179b inhibitor is an anti-CD179b antibody or fragment thereof. In one embodiment, the anti-179b antibody or fragment thereof comprises a monoclonal antibody, e.g., a monospecific or bispecific antibody or fragment thereof.

In some embodiments, the CD179b inhibitor is conjugated or otherwise bound to a therapeutic agent.

In some embodiments, a CD179b inhibitor includes an anti-CD179b CAR-expressing cell, e.g., CART, e.g., a cell expressing an anti-CD179b CAR construct or encoded by a CD179b binding CAR comprising a scFv, CDRs, or VH and VL chains. For example, an anti-

CD179b CAR-expressing cell, e.g., CART is a generated by engineering a CD179b-CAR (that comprises a CD179b binding domain) into a cell (e.g., a T cell or NK cell), e.g., for administration in combination with a CAR-expressing cell described herein. Also provided herein are methods of use of the CAR-expressing cells described herein for adoptive therapy.

In another aspect, provided herein is a population of CAR-expressing cells, e.g., CART cells or CAR-expressing NK cells, comprising a mixture of cells expressing CD19 CARs and CD179b CARs. For example, in one embodiment, the population of CAR-expressing cells can include a first cell expressing a CD19 CAR and a second cell expressing a CD179b CAR.

CD22 inhibitors

Provided herein are CD22 inhibitors and combination therapies. CD22 inhibitors include but are not limited to small molecules, recombinant proteins, anti-CD22 CAR-expressing cells, e.g. CARTs, and anti-CD22 antibodies (e.g., an anti-CD22 mono- or bispecific antibody) and fragments thereof. In some embodiments, anti-CD22 inhibitors can be used to treat a B-cell malignancy described herein. In an embodiment, the CD22 inhibitor is administered in combination with a CD19 inhibitor, e.g., a CD19 CAR-expressing cell, e.g., a CAR-expressing cell described herein, e.g., a cell expressing a CAR comprising an antibody binding domain that is murine, human, or humanized.

In one embodiment, the CD22 inhibitor is a CD22 inhibitor described herein. The CD22 inhibitor can be, e.g., an anti-CD22 antibody (e.g., an anti-CD22 mono- or bispecific antibody) or a CD22 CART. In some embodiments the anti-CD22 antibody is conjugated or otherwise bound to a therapeutic agent. Exemplary therapeutic agents include, e.g., microtubule disrupting agents (*e.g.,* monomethyl auristatin E) and toxins (*e.g.,* diphtheria toxin or Pseudomonas exotoxin-A, ricin).

In an embodiment, the anti-CD22 antibody is an anti-CD22 monoclonal antibody-MMAE conjugate (e.g., DCDT2980S). In an embodiment, the antibody is a scFv of an anti-CD22 antibody, e.g., a scFv of antibody RFB4. This scFv can be fused to all of or a fragment of Pseudomonas exotoxin-A (e.g., BL22). In an embodiment, the antibody is a humanized anti-CD22 monoclonal antibody (e.g., epratuzumab). In an embodiment, the antibody or fragment thereof comprises the Fv portion of an anti-CD22 antibody, which is optionally covalently fused to all or a fragment or (e.g., a 38 KDa fragment of) Pseudomonas exotoxin-A (e.g., moxetumomab pasudotox). In an embodiment, the anti-CD22 antibody is an anti-CD19/CD22

bispecific antibody, optionally conjugated to a toxin. For instance, in one embodiment, the anti-CD22 antibody comprises an anti-CD19/CD22 bispecific portion, (e.g., two scFv ligands, recognizing human CD19 and CD22) optionally linked to all of or a portion of diphtheria toxin (DT), e.g., first 389 amino acids of diphtheria toxin (DT), DT 390, e.g., a ligand-directed toxin such as DT2219ARL). In another embodiment, the bispecific portion (e.g., anti-CD19/anti-CD22) is linked to a toxin such as deglycosylated ricin A chain (e.g., Combotox).

In one embodiment, the anti-CD22 antibody is selected from an anti-CD19/CD22 bispecific ligand-directed toxin (e.g., two scFv ligands, recognizing human CD19 and CD22, linked to the first 389 amino acids of diphtheria toxin (DT), DT 390, e.g., DT2219ARL); anti-CD22 monoclonal antibody-MMAE conjugate (e.g., DCDT2980S); scFv of an anti-CD22 antibody RFB4 fused to a fragment of Pseudomonas exotoxin-A (e.g., BL22); deglycosylated ricin A chain-conjugated anti-CD19/anti-CD22 (e.g., Combotox); humanized anti-CD22 monoclonal antibody (e.g., epratuzumab); or the Fv portion of an anti-CD22 antibody covalently fused to a 38 KDa fragment of Pseudomonas exotoxin-A (e.g., moxetumomab pasudotox).

In some embodiments, the present disclosure encompasses a recombinant nucleic acid construct comprising a nucleic acid molecule encoding a CAR (e.g., a CD19 CAR, a ROR1 CAR, a CD20 CAR, a CD22 CAR, a CD123 CAR, a CD10 CAR, a CD34 CAR, or a FLT-3 CAR), wherein the nucleic acid molecule comprises the nucleic acid sequence encoding an antigen binding domain, e.g., described herein, e.g., that is contiguous with and in the same reading frame as a nucleic acid sequence encoding an intracellular signaling domain. An exemplary intracellular signaling domain that can be used in the CAR includes, but is not limited to, one or more intracellular signaling domains of, e.g., CD3-zeta, CD28, 4-1BB, and the like. In some instances, the CAR can comprise any combination of CD3-zeta, CD28, 4-1BB, and the like.

In one embodiment, the antigen binding domain (e.g., a CD19, ROR1, CD20, CD22, CD123, CD10, CD34, or FLT-3 antigen binding domain) is characterized by particular functional features or properties of an antibody or antibody fragment. For example, in one embodiment, the portion of a CAR composition of the invention that comprises an antigen binding domain specifically binds a human B-cell antigen (e.g., CD19, ROR1, CD20, CD22, CD123, CD10, CD34, or FLT-3) or a fragment thereof. In certain embodiments, the scFv is

contiguous with and in the same reading frame as a leader sequence. In one aspect the leader sequence is the polypeptide sequence provided as SEQ ID NO:1.

In one embodiment, the antigen binding domain is a fragment, e.g., a single chain variable fragment (scFv). In one embodiments, the antigen binding domain is a Fv, a Fab, a (Fab')2, or a bi-functional (e.g. bi-specific) hybrid antibody (e.g., Lanzavecchia et al., Eur. J. Immunol. 17, 105 (1987)). In one aspect, the antibodies and fragments thereof of the invention binds a B-cell protein or a fragment thereof with wild-type or enhanced affinity. In some instances, a human scFv can be derived from a display library.

In one embodiment, the antigen binding domain, e.g., scFv comprises at least one mutation such that the mutated scFv confers improved stability to the CAR construct. In another embodiment, the antigen binding domain, e.g., scFv comprises at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 mutations arising from, e.g., the humanization process such that the mutated scFv confers improved stability to the CAR construct.

In one embodiment, the population of CAR-expressing cells includes, e.g., a first cell expressing a CAR (e.g., a CD19 CAR, a ROR1 CAR, a CD20 CAR, a CD22 CAR, a CD123 CAR, a CD10 CAR, a CD34 CAR, or a FLT-3 CAR) that includes a primary intracellular signaling domain, and a second cell expressing a CAR (e.g., a CD19 CAR, a ROR1 CAR, a CD20 CAR, a CD22 CAR, a CD123 CAR, a CD10 CAR, a CD34 CAR, or a FLT-3 CAR)) that includes a secondary signaling domain.

Kinase Inhibitor

In one embodiment, a CAR-expressing cell described herein may be used in a treatment regimen in combination with a kinase inhibitor, e.g., a CDK4 inhibitor, a BTK inhibitor, an MNK inhibitor, an mTOR inhibitor, an ITK inhibitor, etc. In one embodiment, the subject is a complete responder, and the subject is administered a treatment regimen that includes administration of a CAR-expressing cell described herein in combination with a kinase inhibitor, e.g., a kinase inhibitor described herein, e.g., at a dose or dosing schedule described herein. In one embodiment, the subject is a partial responder or a non- responder, and the subject is administered a treatment regimen that includes administration of a CAR-expressing cell described herein in combination with a kinase inhibitor, e.g., a kinase inhibitor described herein, e.g., at a dose or dosing schedule described herein.

In an embodiment, the kinase inhibitor is a CDK4 inhibitor, e.g., a CDK4 inhibitor described herein, e.g., a CDK4/6 inhibitor, such as, e.g., 6-Acetyl-8-cyclopentyl-5-methyl-2-(5-piperazin-1-yl-pyridin-2-ylamino)-8*H*-pyrido[2,3-*d*]pyrimidin-7-one, hydrochloride (also referred to as palbociclib or PD0332991). In one embodiment, the kinase inhibitor is a BTK inhibitor, e.g., a BTK inhibitor described herein, such as, e.g., ibrutinib. In one embodiment, the kinase inhibitor is an mTOR inhibitor, e.g., an mTOR inhibitor described herein, such as, e.g., rapamycin, a rapamycin analog, OSI-027. The mTOR inhibitor can be, e.g., an mTORC1 inhibitor and/or an mTORC2 inhibitor, e.g., an mTORC1 inhibitor and/or mTORC2 inhibitor described herein. In one embodiment, the kinase inhibitor is a MNK inhibitor, e.g., a MNK inhibitor described herein, such as, e.g., 4-amino-5-(4-fluoroanilino)-pyrazolo [3,4-*d*] pyrimidine. The MNK inhibitor can be, e.g., a MNK1a, MNK1b, MNK2a and/or MNK2b inhibitor.

In one embodiment, the kinase inhibitor is a CDK4 inhibitor selected from aloisine A; flavopiridol or HMR-1275, 2-(2-chlorophenyl)-5,7-dihydroxy-8-[(3S,4R)-3-hydroxy-1-methyl-4-piperidinyl]-4-chromenone; crizotinib (PF-02341066; 2-(2-Chlorophenyl)-5,7-dihydroxy-8-[(2*R*,3*S*)-2-(hydroxymethyl)-1-methyl-3-pyrrolidinyl]- 4*H*-1-benzopyran-4-one, hydrochloride (P276-00); 1-methyl-5-[[2-[5-(trifluoromethyl)-1*H*-imidazol-2-yl]-4-pyridinyl]oxy]-*N*-[4-(trifluoromethyl)phenyl]-1*H*-benzimidazol-2-amine (RAF265); indisulam (E7070); roscovitine (CYC202); palbociclib (PD0332991); dinaciclib (SCH727965); N-[5-[[(5-*tert*-butyloxazol-2-yl)methyl]thio]thiazol-2-yl]piperidine-4-carboxamide (BMS 387032); 4-[[9-chloro-7-(2,6-difluorophenyl)-5*H*-pyrimido[5,4-*d*][2]benzazepin-2-yl]amino]-benzoic acid (MLN8054); 5-[3-(4,6-difluoro-1H-benzimidazol-2-yl)-1H-indazol-5-yl]-N-ethyl-4-methyl-3-pyridinemethanamine (AG-024322); 4-(2,6-dichlorobenzoylamino)-1H-pyrazole-3-carboxylic acid N-(piperidin-4-yl)amide (AT7519); 4-[2-methyl-1-(1-methylethyl)-1*H*-imidazol-5-yl]-*N*-[4-(methylsulfonyl)phenyl]- 2-pyrimidinamine (AZD5438); and XL281 (BMS908662).

In one embodiment, the kinase inhibitor is a CDK4 inhibitor, e.g., palbociclib (PD0332991), and the palbociclib is administered at a dose of about 50 mg, 60 mg, 70 mg, 75 mg, 80 mg, 90 mg, 100 mg, 105 mg, 110 mg, 115 mg, 120 mg, 125 mg, 130 mg, 135 mg (e.g., 75 mg, 100 mg or 125 mg) daily for a period of time, e.g., daily for 14-21 days of a 28 day cycle, or daily for 7-12 days of a 21 day cycle. In one embodiment, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12 or more cycles of palbociclib are administered.

In one embodiment, the kinase inhibitor is a BTK inhibitor selected from ibrutinib (PCI-32765); GDC-0834; RN-486; CGI-560; CGI-1764; HM-71224; CC-292; ONO-4059; CNX-774; and LFM-A13.

In one embodiment, the kinase inhibitor is a BTK inhibitor, e.g., ibrutinib (PCI-32765), and the ibrutinib is administered at a dose of about 250 mg, 300 mg, 350 mg, 400 mg, 420 mg, 440 mg, 460 mg, 480 mg, 500 mg, 520 mg, 540 mg, 560 mg, 580 mg, 600 mg (e.g., 250 mg, 420 mg or 560 mg) daily for a period of time, e.g., daily for 21 day cycle, or daily for 28 day cycle. In one embodiment, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12 or more cycles of ibrutinib are administered.

In one embodiment, the kinase inhibitor is an mTOR inhibitor selected from temsirolimus; ridaforolimus (1*R*,2*R*,4*S*)-4-[(2*R*)-2 [(1*R*,9*S*,12*S*,15*R*,16*E*,18*R*,19*R*,21*R*, 23*S*,24*E*,26*E*,28*Z*,30*S*,32*S*,35*R*)-1,18-dihydroxy-19,30-dimethoxy-15,17,21,23, 29,35-hexamethyl-2,3,10,14,20-pentaoxo-11,36-dioxa-4-azatricyclo[30.3.1.$0^{4,9}$] hexatriaconta-16,24,26,28-tetraen-12-yl]propyl]-2-methoxycyclohexyl dimethylphosphinate, also known as AP23573 and MK8669; everolimus (RAD001); rapamycin (AY22989); simapimod; (5-{2,4-bis[(3*S*)-3-methylmorpholin-4-yl]pyrido[2,3-*d*]pyrimidin-7-yl}-2-methoxyphenyl)methanol (AZD8055); 2-mmino-8-[*trans*-4-(2-hydroxyethoxy)cyclohexyl]-6-(6-methoxy-3-pyridinyl)-4-methyl-pyrido[2,3-*d*]pyrimidin-7(8*H*)-one (PF04691502); and N^2-[1,4-dioxo-4-[[4-(4-oxo-8-phenyl-4*H*-1-benzopyran-2-yl)morpholinium-4-yl]methoxy]butyl]-L-arginylglycyl-L-α-aspartylL-serine-, inner salt (SF1126) (SEQ ID NO: 140); and XL765.

In one embodiment, the kinase inhibitor is an MNK inhibitor selected from CGP052088; 4-amino-3-(p-fluorophenylamino)-pyrazolo [3,4-*d*] pyrimidine (CGP57380); cercosporamide; ETC-1780445-2; and 4-amino-5-(4-fluoroanilino)-pyrazolo [3,4-*d*] pyrimidine.

Combination with a low dose of an mTOR inhibitor

In one embodiment, the cells expressing a CAR molecule, e.g., a CAR molecule described herein, are administered in combination with a low, immune enhancing dose of an mTOR inhibitor.

In an embodiment, a dose of an mTOR inhibitor is associated with, or provides, mTOR inhibition of at least 5 but no more than 90%, 80%, 70%, 60%, 50%, 40%, or 30%; at least 10 but no more than 90%, 80%, 70%, 60%, 50%, 40%, or 30%; at least 15, but no more than 90%, 80%, 70%, 60%, 50%, 40%, or 30%; at least 20 but no more than 90%, 80%, 70%, 60%, 50%,

40%, or 30%; at least 30 but no more than 90%, 80%, 70%, 60%, 50%, or 40%; at least 40 but no more than 90%, 80%, 70%, 60%, 50%, 40%, or 30%; at least 50 but no more than 90%, 80%, 70%, or 60%; at least 60 but no more than 90%, 80% or 70%; or at least 70 but no more than 90% or 80%.

In an embodiment, a dose of an mTOR inhibitor is associated with, or provides, mTOR inhibition of at least 5 but no more than 30%, at least 10 but no more than 30%, at least 15, but no more than 30%, at least 20 but no more than 30%, or at least 25 but no more than 30%.

In an embodiment, a dose of an mTOR inhibitor is associated with, or provides, mTOR inhibition of at least 1, 2, 3, 4 or 5 but no more than 20%, at least 1, 2, 3, 4 or 5 but no more than 30%, at least 1, 2, 3, 4 or 5, but no more than 35, at least 1, 2, 3, 4 or 5 but no more than 40%, or at least 1, 2, 3, 4 or 5 but no more than 45%.

In an embodiment, a dose of an mTOR inhibitor is associated with, or provides, mTOR inhibition of at least 1, 2, 3, 4 or 5 but no more than 90%.

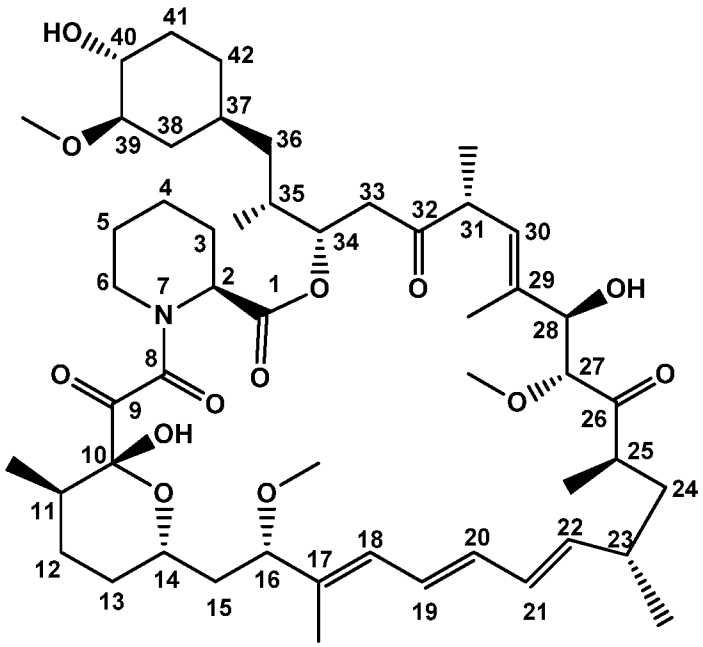
As is discussed herein, the extent of mTOR inhibition can be expressed as the extent of P70 S6 kinase inhibition, e.g., the extent of mTOR inhibition can be determined by the level of decrease in P70 S6 kinase activity, e.g., by the decrease in phosphorylation of a P70 S6 kinase substrate. The level of mTOR inhibition can be evaluated by a method described herein, e.g. by the Boulay assay, or measurement of phosphorylated S6 levels by Western blot.

EXEMPLARY MTOR INHIBITORS

As used herein, the term "mTOR inhibitor" refers to a compound or ligand, or a pharmaceutically acceptable salt thereof, which inhibits the mTOR kinase in a cell. In an embodiment an mTOR inhibitor is an allosteric inhibitor. In an embodiment an mTOR inhibitor is a catalytic inhibitor.

Allosteric mTOR inhibitors include the neutral tricyclic compound rapamycin (sirolimus), rapamycin-related compounds, that is compounds having structural and functional similarity to rapamycin including, e.g., rapamycin derivatives, rapamycin analogs (also referred to as rapalogs) and other macrolide compounds that inhibit mTOR activity.

Rapamycin is a known macrolide antibiotic produced by Streptomyces hygroscopicus having the structure shown in Formula A.



(A)

Other suitable rapamycin analogs include, but are not limited to, RAD001, otherwise known as everolimus (Afinitor®), has the chemical name (1R,9S,12S,15R,16E,18R,19R,21R,23S,24E,26E,28E,30S,32S,35R)-1,18-dihydroxy-12-{(1R)-2-[(1S,3R,4R)-4-(2-hydroxyethoxy)-3-methoxycyclohexyl]-1-methylethyl}-19,30-dimethoxy-15,17,21,23,29,35-hexamethyl-11,36-dioxa-4-aza-tricyclo[30.3.1.04,9]hexatriaconta-16,24,26,28-tetraene-2,3,10,14,20-pentaone,sirolimus (rapamycin, AY-22989), 40-[3-hydroxy-2-(hydroxymethyl)-2-methylpropanoate]-rapamycin (also called temsirolimus or CCI-779) and ridaforolimus (AP-23573/MK-8669).b Other examples of allosteric mTor inhibtors include zotarolimus (ABT578) and umirolimus as described in US2005/0101624 the contents of which are incorporated by reference. Other suitable mTOR inhibitors are described in paragraphs 946 to 964 of International Publication WO2015/142675, filed March 13, 2015, which is incorporated by reference in its entirety. Low, immune enhancing doses of an mTOR inhibitor, suitable levels of mTOR inhibition associated with low doses of an mTOR inhibitor, methods for detecting the level of mTOR inhibition, and suitable pharmaceutical compositions thereof are further described in paragraphs 936 to 945 and 965 to 1003 of International Publication WO2015/142675, filed March 13, 2015, which is incorporated by reference in its entirety.

EXAMPLES

The invention is further described in detail by reference to the following experimental examples. These examples are provided for purposes of illustration only, and are not intended to be limiting unless otherwise specified. Thus, the invention should in no way be construed as being limited to the following examples, but rather, should be construed to encompass any and all variations which become evident as a result of the teaching provided herein.

Example 1: Optimizing CART production with exogenous cytokines

Cytokines have important functions related to T cell expansion, differentiation, survival and homeostasis. One of the most important cytokine families for clinical use is the common γ-chain (γ_c) family cytokines, which includes interleukin (IL)-2, IL-4, IL-7, IL-9, IL-15 and IL-21 (Liao et al., 2013, *Immunity*, 38:13-25. IL-2 has been widely studied as an immunotherapeutic agent for cancer. The supplement of IL-2 enhanced the antitumor ability of anti-CD19 CAR-T cells in the clinical trials (Xu et al., 2013, *Lymphoma*, 54:255-60). However, the administration of IL-2 is limited by side effects and a propensity for expansion of regulatory T cells and the effect of activated induced cell death (AICD) (Malek et al., 2010, *Immunity*, 33:153-65; and Lenardo et al., 1999, *Annu Rev Immunol*, 17:221-53). IL-7, IL-15, and IL-21 each can enhance the effectiveness of adoptive immunotherapies and seems to be less toxicity compared with IL-2 (Alves et al., 2007, *Immunol Lett,* 108:113-20). Despite extensive preclinical and clinical studies on the role of the above cytokines, multi-parameter comparative studies on the roles of various exogenous γ_c cytokines on CAR-T cell adoptive therapy are lacking.

Besides γ-chain cytokines, IL-18 is another immunostimulatory cytokine regulating immune responses, which enhances the production of IFN-γ by T cells and augments the cytolytic activity of CTLs (Srivastava et al., 2010, *Curr Med Chem*, 17:3353-7). Administration of IL-18 is safe and well tolerated, even when the dose reaching as high as 1000μg/kg (Robertson et al., 2006, *Clin Cancer Res*, 12:4265-73). Therefore, IL-18 could be another candidate used to boost the antitumor of CAR-T cells.

In this example, the effect of administration of different exogenous cytokines was examined for expansion, phenotype, *in vitro* effector functions, and *in vivo* anti-tumor efficacy of T cells and folate receptor alpha (FRα) CART cells.

The following materials and methods were used in the experiments described in this example.

CAR construction and lentivirus preparation

The pELNS-C4-27z CAR vector was constructed as described previously (manuscript under review), Briefly, the pHEN2 plasmid containing the anti-FRα C4/AFRA4 scFv was used as a template for PCR amplification of C4 fragment using the primers of 5′-ataggatcccagctggtggagtctgggggaggc-3′ (SEQ ID NO: 3) and 5′-atagctagcacctaggacggtcagcttggtccc-3′ (SEQ ID NO: 4) (BamHI and NheI were underlined). The PCR product and the third generation self-inactivating lentiviral expression vectors pELNS were digested with BamHI and NheI. The digested PCR products were then inserted into the pELNS vector containing CD27-CD3z T-cell signaling domain in which transgene expression is driven by the elongation factor-1α (EF-1α) promoter.

High-titer replication-defective lentivirus was generated by transfection of human embryonic kidney cell line 293T (293T) cells with four plasmids (pVSV-G, pRSV.REV, pMDLg/p.RRE and pELNS-C4-27z CAR) by using Express In (Open Biosystems) as described previously. Supernatants were collected at 24h and 48h after transfection and concentrated by ultracentrifugation. The virus titers were determined based on the transduction efficiency of lentivirus to SupT1 cells by using limiting dilution method.

T cells and cell lines

Peripheral blood lymphocytes were obtained from healthy donors after informed consent under a protocol approved by University Institutional Review Board at the University of Pennsylvania. The primary T cells were purchased from the Human Immunology Core after purified by negative selection. T cells were cultured in complete media (RPMI 1640 supplemented with 10% FBS, 100U/mL penicillin, 100μg/mL streptomycin sulfate) and stimulated with anti-CD3 and anti-CD28 mAbs-coated beads (Invitrogen) at a ratio of 1:1 following the instruction. Twenty-four hours after activation, cells were transduced with lentivirus at MOI of 5. Indicated cytokines were added to the transduced T cells from the next day with a final concentration of 10ng/mL. The cytokines were replaced every 3 days.

The 293T cell used for lentivirus packaging and the SupT1 cell used for lentiviral titration were obtained from ATCC. The established ovarian cancer cell lines SKOV3 (FRα+) and C30 (FRα-) was used as target cell for cytokine-secreting and cytotoxicity assay. For

bioluminescence assays, SKOV3 was transduced with lentivirus to express firefly luciferase (fLuc).

Flow cytometric analysis and cell sorting

Flow cytometry was performed on a BD FACSCanto. Anti-human CD45 (HI30), CD3 (HIT3a), CD8 (HIT8a), CD45RA (HI100), CD62L (DREG-56), CCR7 (G043H7), IL-7Rα (A019D5), CD27 (M-T271), CD28 (CD28.2), CD95 (DX2), TNF-α (MAb11), IFN-γ (4S.B3), IL-2 (MQ1-17H12), perforin (B-D48), granzym-B (GB11) were obtained from Biolegend. Biotin-SP-conjugated rabbit anti-human IgG (H+L) was purchased from Jackson Immunoresearch and APC conjugated streptavidin was purchased from Biolegand. Anti-human Bcl-xl (7B2.5) was purchased from SouhernBiotech. Apoptosis kit and TruCount tubes were obtained from BD Bioscience. For peripheral blood T cell count, blood was obtained via retro-orbital bleeding and stained for the presence of human CD45, CD3, CD4 and CD8 T cells. Human CD45+-gated, CD3+, CD4+ and CD8+ subsets were quantified with the TruCount tubes following the manufacturer's instructions.

In vivo study of adoptive cell therapy

Female non-obese diabetic/severe combined immunodeficiency/γ-chain$^{-/-}$(NSG) mice 8 to 12 weeks of age were obtained from the Stem Cell and Xenograft Core of the Abramson Cancer Center, University of Pennsylvania. The mice were inoculated subcutaneously with 3×10^6 fLuc$^+$ SKOV3 cells on the flank on day 0. Four or Five mice were randomized per group before treatment. After tumors became palpable, human primary T cells were activated and transduced as described previously. T cells were expanded in the presence of IL-2 (5ng/mL) for about 2 weeks. When the tumor burden was ~250-300 mm^3, the mice were injected with 5×10^6 CAR-T cells or 100μl saline intravenously and then received daily intraperitoneal injection of 5μg of IL-2, IL-7, IL-15, IL-18, IL-21 or phosphate buffer solution (PBS) for 7 days. Tumor dimensions were measured with calipers and tumor volumes were calculated with the following formula: tumor volume = (length×width^2)/2. The number and phenotype of transferred T cells in recipient mouse blood was determined by flow cytometry after retro-orbital bleeding. The mice were euthanized when the tumor volumes were more than 2000 mm^3 and tumors were resected immediately for further analysis.

Statistical analysis

Statistical analysis was performed with Prism 5 (GraphPad software) and IBM SPSS Statistics 20.0 software. The data were shown as mean±SEM unless clarified. Paired sample t-tests or nonparametric Wilcoxon rank tests were used for comparison of two groups and repeated measures ANOVA or Friedman test were used to test statistical significance of differences among three or more groups. Findings were considered as statistically significant when P-values were less than 0.05.

RESULTS

1. Construction and expression of anti-FRα C4 CAR

The pELNS-C4-27z CAR comprised of the anti-FRα C4 scFv linked to a CD8α hinge and transmembrane region, followed by a CD3ζ signaling moiety in tandem with the CD27 intracellular signaling motif (**Figure 1A**). Primary human T cells were efficiently transduced with C4 CAR lentiviral vectors with transduction efficiencies of 43%~65% when detected at 48h after transduction. CAR expression levels were comparable between CD4+ and CD8+ T cells (52.6±10.2% vs. 49.5±17.1%, P=0.713).

2. Influence of cytokines on expansion of CAR transduced T (CAR-T) cell

The expansion and accumulation of CAR-T cells in the presence of various γc cytokines and IL-18 was investigated. Three weeks after exposure to the different cytokines in culture, CAR-T cells that had been cultured in the presence of IL2, IL-7 or IL-5 had expanded 1000-2000 fold. CAR-T cells that had been cultured in the presence of IL-18, IL-21 or NC (control, no cytokine) demonstrated a less than 200 fold expansion (**Figure 1B**).

The reasons contributing to the higher accumulation of CAR-T cells were analyzed, specifically, proliferation and apoptosis of the T cells was assessed. The proliferative response was measured by monitoring cell division of CFSE labeled T cells cultured for 7 days. As shown in **Figure 1C**, T cells cultured with IL-2 and IL-15 showed the highest proliferative ability, followed by IL-7; while IL-21 and IL-18 were less potent mitogenic stimulants. Apoptosis of the T cells cultured in the different cytokines was tested using Annexin-V staining. The results indicated that T cells cultured in IL-2, IL-7 and IL-15 underwent less apoptosis when compared with NC, IL-18 and IL-21 groups (**Figure 1D**). These results indicate that increased accumulation of T cells expanded in the presence of cytokines, e.g., IL-

2, IL-7, or IL-15, may be caused by both an increase in proliferation and a decrease in apoptosis, e.g., by activation of the Bcl-xl anti-apoptotic pathway.

3. Influence of cytokines on the phenotypes of CAR-T cells

Next, the phenotype of the CAR-T cells expanded in the presence of exogenous cytokines was examined. The fresh T cells from healthy donors were generally divided into four subsets based on CD45RA and CD62L expression: 1) naïve T cell (CD45RA+CD62L+, referred to as Tn), 2) central memory T cell (CD45RA-CD62L+, referred to as Tcm), 3) effector memory T cell (CD45RA-CD62L-, referred to as Tem) and 4) CD45RA positive effector T cell (CD45RA+CD62L-, referred to as Temra). Then the expression of CCR7, CD27, CD28, and CD95 are further evaluated for each subset. The CD95 expression was significantly upregulated upon lentiviral transduction. The latter three T cell subsets were positive for CD95 while only small part of Tn expressed CD95 (3.6±1.4% in CD4+ and 3.7±1.3% in CD8+ T cells). This small population also co-expressed CD27, CD28 and CCR7, and was considered as memory stem T cells (Tscm). However, after stimulation with anti-CD3/CD28 beads before and after lentiviral transduction with CAR, CD95 was greatly up-regulated to nearly 100% in this population (**Figure 2A**). The percentages of CD45RA+CD62L+CD95+ T cells were greatly expanded after anti-CD3/CD28 bead stimulation in both CD4+ and CD8+ T and CAR-T cells when compared with the fresh T cells (**Figures 2B** and **2C**). This population highly expressed CD27, CD28 and CCR7 simultaneously, indicating it could be defined as Tscm. Furthermore, CD8+ CAR-T cells had a higher percentage of Tscm cells, which may be related to the higher proportion of Tn in initial CD8+ T cells (**Figure 2D**).

Fourteen days after co-culture with various cytokines, the proportion of T cell subsets of CAR-T cells were investigated by measuring the expression of CD45RA, CD62L and CD95. Of the CD4+ CAR-T cells, a significantly higher percentage of Tscm cells existed in the IL-7 group compared with the IL-2 group, while the no cytokine (NC) and IL-18 groups presented lower percentages of Tscm but higher percentages of Tcm. The distribution of T cell subsets in the IL-15 group was similar with the IL-2 group, while the IL-21 group presented a higher percentage of Tcm, while percentage of Tscm was comparable with the IL-2 group. The CD8+ CAR-T cells demonstrated a similar trend as that of the CD4+ CAR-T cells on the differentiation and distribution of the four T cell subsets for each cytokine-administered group,

with higher proportions of Tscm compared with CD4+ CAR-T cells in the corresponding group of CD8+ CAR-T cells.

The abilities of various CAR-T cell subpopulations to self-renew and to differentiate into other cell types were further studied. The four subsets of CAR-T cells were sorted based on CAR, CD45RA and CD62L expression and cultured separately in medium containing IL-2 for 3 days. As shown in **Figure 2E**, the Tscm subset was able to differentiate into all the other three subsets, and Tcm and Temra subsets were able to differentiate into Tem. These results indicate that CD62L+ and CD45RA+ T cells were able to differentiate into CD62L- and CD45RA- T cells, respectively. The proliferation capacity of the four subsets was assessed by CFSE dilution and then compared. The results showed the Tscm presented stronger proliferation ability than other subsets (**Figure 2F**). Furthermore, CD45RAexpression inversely correlated with CFSE intensity while CD62L and CCR7 expression directly correlated with proliferation. In all cytokine groups, CD45RA+ T cells exhibited much lower CFSE levels than CD45RA dim and negative T cells (**Figure 3A-3B**), indicating that CD45RA+ T cells had stronger proliferation activity than CD45RA- T cells. Thus, the increased accumulation of T cells grown in the presence of IL-2, IL-7 and IL-15 may be related to the increased proportion of CD45RA+ T cells (which have increased proliferation capacity) (**Figure 4**).

With regard to the phenotype of the CAR-T cells, CAR-T cells presented lower expression of CD45RA, CD62L, CD27 and CD28, but higher expression of CCR7 on the surface of T cells. The influence of cytokines on the phenotype of CAR-T cells were further assessed based on the expression of the following surface markers: CD27, CD28, CD62L, CCR7 and IL7Rα. CAR-T cells grow in the presence of IL-18 showed quite similar expression pattern with those grown without cytokine supplement. IL-2 dramatically down-regulated the expressions of CD27, CD28 CD62L, CCR7 and ILR7α when compared with NC control. Of the other γc cytokines, compared with IL-2 exposed CAR-T cells, IL-7 exposed CAR-T cells presented higher CD62L, CD27 and CD28 expression but significantly decreased CCR7 expression; IL-15 group CAR-T cells presented higher CD27 and CD28 expression; and IL-21 exposed CAR-T cells presented higher CD62L, CCR7, CD27 and CD28 expression, indicating that IL-2 exposure induced the expansion of a subset of T cells with a much more mature T cell phenotype than all other groups (**Figure 4**).

4. Influence of cytokines on the effector function of CAR-T cells

To investigate the influence of cytokines on CAR-T cell effector function, the cytokine production capability of CAR-T cells after stimulation with FRα-expressing SKOV3 cells was assessed. Following 5 hours stimulation, TNF-α, IFN-γ and IL-2 were detectable in the cytoplasm of CAR-T cells, with 41.5-54.0% of the CAR-T cells produced TNF-α, 12.4-15.3% of the CAR-T cells produced IFNγ, and 4.3-6.5% of CAR-T cells produced and IL-2 (**Figures 5A-5C**). IL-2, IL-7 and IL-15 exposure during expansion promoted CAR-T cells to produce TNF-α, while the numbers of IFN-γ and IL-2 producing CAR-T cells were comparable among all the cytokine groups (**Figures 5A, 5B,** and **5C**). Next, the fractions of responding CAR-T cells and their polyfunctionality were compared. In comparison to exposure to IL-2 during expansion, exposure to IL-18, IL-21 or no cytokine exposure during expansion induced less cytokine-producing CAR-T cells, and less CAR-T cells possessed the ability to produce multiple cytokines when stimulated by target cells. These results are consistent with the phenotype that the CAR-T cells in IL-18, IL-21 and NC groups were less differentiated than those in the IL-2 exposed group.

Then, the effect of cytokine exposure during expansion on the expression of the cytolytic molecules perforin and granzyme-B after antigen stimulation was determined. Similar with TNF-α production, the CAR-T cells exposed to IL-2, IL-7, and IL-15 demonstrated increased perforin expression compared with CAR-T cells exposed to NC, IL-18 and IL-21. However, although CAR-T cells exposed to IL-21 produce less TNF-α and perforin, they produced the highest level of granzyme-B. The next highest levels of granzyme-B production were observed in CAR-T cells exposed to IL-2 and IL-15 during expansion. CAR-T cells in IL-18 group presented the least amount of both perforin and granzyme-B expression after antigen stimulation.

Finally, the tumor lysis activity by CAR-T cells exposed to various cytokines during exposure was quantified by luciferase assay. As shown in Figure 5D, CAR-T cells co-cultured with IL-2 and IL-15 lysed the SKOV3 more efficiently than those with NC and IL-18 (both $P<0.05$).

The association between phenotype of the CAR-T cells and their function was further confirmed. The T cells 14 days were sorted after lentiviral transduction based on CAR and CD62L expression. The CD62L+ CAR-T cells (Tscm and Tcm) exhibited less cytokine production activity and weaker cytolytic capacity when compared with CD62L- CAR-T cells

(Tem and Temra) (**Figures 6A-6C**). In this perspective, CAR-T cells exposed to IL-2 and IL-15 produced more cytokines and presented stronger tumor lysis activity, which might be partially attributed to the higher proportions of Tem and Temra in these groups.

5. Expansion and phenotype of CAR-T cells after antigen challenge

To investigate the influence of cytokines on CAR-T cell expansion under the challenge of specific antigen, the CAR-T cells exposed to IL-2 for two weeks were co-cultured with SKOV3 (FRα+) or C30 (FRα-) cells in the presence of indicated cytokines for 7 days. Similar to the antigen-free circumstance, CAR-T cells exposed to IL-2, IL-7 and IL-15 presented higher fold expansion than CAR-T cells exposed to other cytokines. The CAR-T cells exposed to IL-21 during expansion were more likely to undergo apoptosis. However, when the CAR-T cells exposed to the indicated cytokines for two weeks were co-cultured with SKOV3 or C30 cells without further cytokine supplement for 7 days, the accumulation of CAR-T cells were comparable among all groups, with those having been exposed to IL-15 and IL-18 undergoing the least amount of apoptosis (**Figure 7A**). The phenotypes of CAR-T cells were also analyzed. As to the four subsets of memory T cells, the results were different from antigen-free study: Tscm was rare and Tem accounted for more than 50% in no cytokine, IL-18 and IL-21 all groups. Cytokines had no significant impact on the composition of memory T subsets and IL-7 exposure did not favor the increase of Tscm (**Figure 7B**).

6. Anti-tumor efficacy of various cytokines in animal models

To evaluate the effects of various cytokines during ex vivo expansion of CAR-T cells on the efficacy of CAR-T cells in vivo, the persistence of CAR-T cells and outcome was investigated by using a NSG mouse xenograft model of ovarian cancer. Mice bearing subcutaneous SKOV3 tumors were intravenously injected with two doses of 5×106 C4-27z CAR-T cells which had been exposed to the indicated cytokines *ex vivo* for 2 weeks previously. All mice receiving C4-27z CAR-T cell infusion presented less tumor burden when compared with those injected with untransduced T cells and anti-CD19 CAR-T cells (**Figure 8A**). Of the various cytokine groups, mice receiving CAR-T cells with previous IL-2 exposure showed the highest tumor burden, consistent with the least amount of circulating human T cell in these mice. The tumors in NC, IL-7, IL-15, IL-18 and IL-21 groups were all significantly suppressed or even disappeared, without any statistical difference on tumor size. The persistence of

transferred T cells in the peripheral blood was determined 15 and 32 days after adoptive transfer. Mice receiving IL-7 and IL-21 treated CAR-T cells seemed to have higher amount of human T cells than other groups in the peripheral blood on day +15, while mice receiving IL-2 treated CAR-T cells had the lowest number of human T cells (**Figures 8B-8C**). As to the percentages of different CAR-T cell populations, NC, IL-15, IL-18 and IL-21 exposed groups all presented higher CD4+ CAR-T cells when compared with IL-2 group, while the percentages of CD8+ CAR-T cells were comparable among all the groups. Of the T cell phenotypes, CD62L, CD27 and CD28 were expressed only on about 5-10% of T cells and were comparable among all groups, except that CD8+ T cells in IL-21 group expressed higher CD28 than those in IL-2 and NC group (both $P<0.05$). On day +32, the circulating human T cells in all CAR-T cell groups expanded significantly except the IL-2 group, with an average T cell account of 14907/μl to 19651/μl (and only 242/μl in the IL-2 group). Two mice died although the tumors were regressed.

DISCUSSION

IL-2 is the most frequently used cytokine for generating lymphocytes for adoptive immunotherapy. It promotes T cell survival and expansion, enhances tumor-killing ability of T cells. However, the action of IL-2 is limited as it results in activation induced cell death (AICD) of T-cell and the development of regulatory T-cell (Malek et al., *Immunity*, 2010, 33:153-65; and Lenardo et al., *Annu Rev Immunol*, 1999, 17:221-53). In this example, IL-2 significantly increased the accumulation of CAR-T cells and their cytotoxicity ability, but IL-2 exposed CAR-T cells presented inferior antitumor immunity in vivo following adoptive transfer. This finding demonstrates an inverse relationship between in vitro tumor-lysis and in vivo tumor eradication. IL-2 exposed CAR-T cells displayed a relative mature phenotype with low expression of CD62L, CCR7, CD27 and CD28, which are less persistent in vivo (Yang et al., *Cancer Immunol Immunother*, 2013, 62:727-36). Recent studies have indicated that adoptive transfer of less differentiated T cells correlates with superior tumor regression, which supports the finding that IL-2 exposed CAR-T cells are less effective than other group (Gattinoni et al., *Nat Med*, 2011, 17:1290-7; and Markley et al., *Blood*, 2010, 115:3508-19).

IL-15 presented similar performance of stimulating CAR-T cell expansion and tumor-lysis function as IL-2, but induced a less differentiated phenotype (higher expression of CD27 and CD28). Therefore, IL-15 supports the persistence of CAR-T cells in vivo and shows better

antitumor immunity in animal models.

Compared with IL-2 and IL-15, IL-7 showed similar capability to promote CAR-T cell expansion, but induced higher level of CD62L expression and exhibited the highest proportion of CAR-Tscm cells in an antigen-free circumstance. Therefore, compared to CAR-T cells exposed to IL-2, ex vivo exposure of IL-7 without antigen challenge enhanced the antitumor efficacy of the CAR-T cells. IL-7 exposed CAR-T cells did not result in better in vivo antitumor efficacy than IL-2, and efficacy was inferior to IL-15 due to the less expansion of CAR-T cells under antigen challenge.

IL-21 exerted few effects on CAR-T cell accumulation as it could not enhance anti-apoptosis ability, e.g., by promoting Bcl-xL expression. However, IL-21 induced the expansion of less differentiated CAR-T cells, with a phenotype of high expression of CD62L, CCR7, CD27 and CD28, even under the circumstance of antigen challenge. Therefore, IL-21 exposed CAR-T cells showed best persistence in animal models and IL-21 injection in vivo, and also presented a better efficacy in promoting tumor eradication than other cytokine groups except IL-15. These results are consistent with previous finding that less differentiated CAR-T cells correlates with superior tumor regression.

IL-18 is proinflammatory cytokine belonging to the IL-1 family, which regulates both innate and adaptive immune responses by activating monocytes, NK cells, and T cells and production of IFN-γ as well as other cytokines in vivo (Srivastava et al., *Curr Med Chem*, 2010, 17:3353-7). The results presented herein indicates that IL-18 has little impact on CAR-T cell's expansion, phenotype and function in ex vivo experiments, as most of the results in IL-18 groups are similar and comparable with NC group. IL-18 promoted little proliferation of T cells and maintained more T cell survival under antigen challenge compared to the control (NC) group. In vivo studies show that IL-18 has no significant impact on CAR-T cell efficacy when compared with mice without cytokine supplement.

In summary, the findings of these experiments indicate that IL-2 supplement ex vivo for CAR-T cell expansion is not an optimal strategy although it is widely used. As to IL-18, IL-21 or no cytokine supplement, although they may induced relative effective CAR-T cells, they do not promote CAR-T cell expansion effectively enough, such that enough CAR-T cells could be prepared for clinical use in a limited expansion time. Therefore, IL-15 and IL-7 may be better agents for CAR-T cell expansion. Furthermore, the combination of IL-7 and IL-15 supplement instructs the generation of Tscm, which is beneficial to produce more "young" CAR-T cells. As

to in vivo cytokine injection, all γc cytokines supplement enhance antitumor efficacy, as many of them favor the expansion of CAR-T cells, with IL-15 presenting best effect. Mice receiving IL-15 exposed CAR-T cells by injection had increased efficacy, due in part to the increased expansion ability and increased persistence of the CAR-T cells during tumor treatment. Thus, the results of these experiments indicate that IL-7 and IL-15 show promise to promote CAR-T cell expansion and induce T cell phenotypes that are most efficacious for therapeutic treatment.

Example 2: Effect of CD25 depletion on cell growth and transduction efficiency

The interleukin-2 a-chain, also known as CD25, is expressed by regulatory T cells (Tregs) but has also been observed on chronic B cell leukemia (CLL) cells (in greater than 85% of CLL patients). Tregs have immune suppressing functions and can impede the efficacy of immunotherapy, e.g., by inhibiting T cell proliferation. Current isolation or enrichment of T cells from CLL patients by apheresis usually contains a significantly increased proportion of Tregs as well as CLL cells. The depletion of Tregs and CLL cells in the starting material by CD25 depletion methods may significantly improve the purity of effector T cells, and thereby increase the potency of CAR19 expressing T cells, e.g., CART19 cells.

Optimizing CD25 depletion

A validation experiment was performed to identify the optimal conditions for CD25 depletion from the aphereses from two patients using CD25 Reagent from Miltenyi in a CliniMACS System. CD25 depletion reagent was used at 100%, 70%, and 30% of the manufacturer's recommended amount to identify whether the same depletion efficiency could be obtained by using less reagent. Two different tubing sets from Miltenyi were also tested. The depletion was performed in accordance with the manufacturer's directions. The results from the experiments are shown in the table below. For control, selection using anti-CD3/CD28 immunomagnetic beads was performed.

Table 2. Experimental results from CD25 depletion.

CD25 depletion arms		100%	70%	30%
Miltenyi tubing set	161-01			
CliniMACS program	ENRICHMENT1.1			
Patient cells	UPCC04409-15			
%CD45+CD25+ cells	83.56%			
%CD45+CD3+ cells	8.66%			
%CD45+CD3+CD25- cells	5.70%			
#CD25+ cells to target		2.E+09	2.E+09	2.E+09
#apheresed cells for CD25 depletion		2.39E+09	3.41E+09	7.97.E+09
CD25 bead volume used (mL)		2.5	2.5	2.5
Cell# in CD25-depleted fraction		1.05E+09	1.86E+09	3.36E+09
Cell# in CD25-enriched fraction		2.05E+08	2.58E+08	5.19E+08
Expected CD25- T-cell yield		1.36E+08	1.95E+08	4.54E+08
%T cells in depleted fraction		6.26%	4.06%	2.50%
Observed yield CD25- T cells		6.57E+07	7.55E+07	8.40E+07
Yield of CD3+CD25- as % of expected		**48%**	**39%**	**18%**
%B cells in depleted fraction		90.50%	91.6%	95.30%
Viability CD25+ fraction		94.4%	96.2%	91.1%
Viability CD25- fraction		95.8%	95.0%	99.0%

The expected CD25- (CD25-negative) T cell yield represents the calculated CD25- T cell yield calculated by assuming 100% efficiency in the respective manipulations. The observed yield of CD25- T cells represents the number of CD25- T cells after the respective manipulations. As shown in Table 2, using less reagent than recommended by the manufacturer did not result in the same efficiency in CD25 depletion. Using different tubing resulted in an increase in T cell enrichment by one log.

Figure 9 shows representative flow cytometry analysis plots demonstrating the efficiency of CD25 depletion compared to the total cells from the apheresis, control CD3/CD28 selected cells, CD25 depleted cells, and CD25 enriched cells. The monocyte content of the cell population, as determined by CD14 expression of the CD3-CD19- subset. These results indicate efficient CD25 depletion and that CD25 depletion also resulted in significant monocyte content (61.1% CD14-expressing cells compared to less than 2% in the total cells from apheresis, control, and the CD25 enriched cells.

Effect of CD25 depletion on T cell population and proliferation

Next, the quality of the T cell product after CD25 depletion was assessed by determining the proportion of CD4+ and CD8+ T cells and proliferation capacity.

To determine the proportion of specific T cells populations, cells were analyzed by flow cytometry nine days after selection by anti-CD3/CD28 or CD25 depletion as described above. The results show that CD3/CD28-selected T cells had a greater proportion of CD4+ T cells compared to CD25 depleted cells (84.6% compared to 46.8% CD4+ T cells). Conversely, CD25 depleted cells had a greater proportion of CD8+ T cells compared to the CD3/CD28-selected cells (47.2% compared to 11.5% CD8+ T cells). Therefore, CD25 depletion results in T cells with a greater proportion of CD8+ T effector cells.

Proliferation capacity and cell viability was also assessed in control (CD3/CD28 selected cells) and CD25 depleted cells. $1.6x10^7$ cells from control and CD25 depleted cells were plated and the cell number and viability was determined over 10-13 days. Figure 10A shows the total cell number over time and Figure 10B shows the calculated population doublings (calculated from the total number of cells). The results indicate that the CD25 depleted cells demonstrated similar growth characteristics to the control cells. Figure 10C shows the percentage of viable cells, and the results show that viability was also similar between control and CD25 depleted cells.

Effect of CD25 depletion on lentiviral transduction efficiency

The effect of CD25 depletion on lentiviral transduction efficiency was assessed by determining the expression of CAR after transduction. A patient apheresis was depleted with CD25 cells as described above. The efficiency of the CD25 depletion is demonstrated in the flow cytometry analysis plots comparing the CD25-expressing population before (apheresis sample) and after CD25 depletion (CD25-depeleted fraction). After CD25 depletion, the CD25 depleted fraction contained about 59.2% of CD25 negative cells and only 10.3% CD25 positive cells.

The CD25 depleted fraction was transduced with a lentiviral construct encoding CAR19. After 11 days of culture, CAR expression was assessed by flow cytometry. Cells that were untransduced and transduced CD3 selected cells were used as controls. CAR19 expression was significantly higher in CD25 depleted cells compared to CD3 selected cells (51.4% compared to 12.8%). This result demonstrates that CD25 depleted cells have improved

lentiviral transduction efficiency, which may be important for improved therapeutic effect in CART therapy.

Example 3: Using cytokines with CD25-depleted cells

In this example, the effect of CD25 depletion with cytokine supplement during expansion in culture was examined. Peripheral blood mononuclear cells (PBMCs) were isolated from a patient and were either left unmanipulated or were depleted of CD25-expressing cells as described in Example 2. T cell enrichment was achieved by stimulation with anti-CD3 and CD28 coated beads. The T cells were immediately cultured in media supplemented with 10ng/ml IL-7, 10ng/ml IL-15, or the combination of 10ng/ml IL-7 and 10ng/ml IL-15. At day 3, medium was changed with the same cytokines added. At day 5, the medium containing 100 IU IL-2/ml was added, and the cells were grown for a total of 10 days.

Flow cytometric analysis shows the change in distribution of CD3 and CD19 cells in CD25 depleted cells compared to unmanipulated PBMC (standard CD3/CD28 selection) after culture in the presence of IL7, IL-15, or IL7 and IL15. The distribution of CD3, CD19, and CD25 expressing cells in the starting population (e.g., before CD25 depletion and before culture with cytokine supplementation) was assessed. The starting population had a high proportion of CD3-CD19+ cells (~97.2%) and a high proportion of CD25-expressing cells (~94.5% CD25+ CD3-; and ~93.8% CD25+ CD19+). After manipulation (CD25 depletion) and culture with cytokines, the distribution changed as shown in Figure 11. CD25 depleted cells overall showed greater reduction in CD19-expressing cells compared to the unmanipulated cells.

Proliferation capacity was also assessed for the same cell samples by determining the total number of cells in culture at day 10 after stimulation with anti-CD3 and anti-CD28 coated beads. The cell numbers for each cell sample are shown below.

Table 3. In vitro expansion

Cells	Cytokines added	# Cells in culture
Unmanipulated	IL-7	1.24×10^6
	IL-15	0.92×10^6
	IL-7 + IL-15	0.52×10^6
CD25-depleted	IL-7	0.93×10^6

	IL-15	1.95×10^6
	IL-7 + IL-15	3.03×10^6

These results show that supplementation of IL-15 during culture of CD25 depleted T cells resulted in increased expansion compared to unmanipulated cells. Addition of IL-7 and IL-15 in the media during culture resulted in significant increase in expansion compared to unmanipulated cells, and compared to adding the cytokines IL-7 or IL-15 independently. Thus, the combination IL-7 and IL-15 supplement resulted in T cells with the most increased proliferation capacity.

Example 4: Stimulation and expansion of mesothelin CAR T cells

CD4 or CD8 T cells are obtained from peripheral or cord blood. By means of electroporation, in vitro transcribed RNA is introduced into the cells. After an over-night incubation to allow maximum CAR surface expression, the cells are incubated with a cognate antigen immobilized on to tosylactivated magnetic beads (Invitrogen Cat 14013) in media supplemented by cytokines. The cells are allowed to expand in vitro with regular supplementation of fresh media every 48 hours (Figure 22).

Cultures were started with a 50:50 mix of CD4 and CD8 T cells. Cells were mock electroporated or electroporated with SS1-BBz RNA. After 8 hours, cells were then exposed to mesothelin conjugated beads (left in culture or for 1 day), or CD3/CD28 beads left in culture. The next day the cells were either mock transfected or transfected with lentivirus. (Figure 23) Growth rate and cell size was measured. Cells stimulated with CD3/28 beads show highest population doublings. However, transduction with lentivirus lowers population by 2 (dark red). (Figure 24A). Cells pre-electroporated with SS1-BBz RNA show no difference in population doublings and cell size whether stimulated with meso beads for 1d or more, nor with the transduction with lentivirus. (**Figures 24A** and **24B**). Cells stimulated with CD3/28 beads and SS1-BBz CART cells stimulated with mesothelin coated beads showed similar transduction efficiency. (**Figures 25A** and **25B**).

Mesothelin CARs consisting of a single-chain variable fragment (scFv) of the heavy and light chain of an antibody specific to a tumor target protein are shown in Figure 26A. Although this invention is not restricted to any individual scFv, the results demonstrated here have been obtained, in part, using a mesothelin specific scFv. These CARs have costimulatory

domains attached in tandem to the scFv via a CD8z hinge and a transmembrane domain (as shown in the schematic **Figure 26A**). Surface expression level of the mesothelin CARs on human CD4 or CD8 T cells is shown in **Figure 26B**.

Expansion of peripheral blood CD8 T cells (**Figure 27A**) CD4 T cells (**Figure 27B**) and cord blood CD8 T cells (**Figure 27C**) in culture through mesothelin CAR stimulation was studied. Mesothelin CAR expressing CD4 or CD8 T cells shown were co-cultured with mesothelin immobilized on magnetic beads in the presence of cytokines. CD4 T cells received IL2 (30units/mL). CD8 T cells were cultured in the presence of either IL2 (100units/mL) or IL7+IL15 (10ng/mL each). Cell number was counted (using Multisizer 3 Coulter counter) every 48hours, and replated at $0.75e^6$/mL with fresh media (supplemented with the corresponding cytokines). All T cells with CARs received CAR-specific stimulation and expanded in culture. Different CAR costimulatory domains had different effects on expansion of T cells in culture, the best combination being the BBz CAR construct in CD8 T cells. These numbers are comparable to the expansions seen using the CD3/28 stimulation conditions.

Example 5: Activation and expansion of T cells via transiently expressed Chimeric Antigen Receptors (CARs)

Figure 28 shows a schematic representation of a method for stimulation through a transiently expressed Chimeric Antigen Receptor (CAR) on the surface of T cells, by its cognate antigen. CD4 or CD8 T cells are obtained from peripheral or cord blood. By means of electroporation, *in vitro* transcribed RNA is introduced into the cells. After an over-night incubation to allow maximum CAR surface expression, the cells are incubated with a cognate antigen immobilized onto tosylactivated magnetic beads (Invitrogen Cat 14013) in media supplemented by cytokines. The cells are allowed to expand *in vitro* with regular supplementation of fresh media every 48 hours. (**Figure 29**)

Population doublings (**Figure 30A**) and cell size (**Figure 30B**) of mesothelin CAR expressing cells after exposure to mesothelin coated beads were measured as well as expansion of peripheral blood T cells stimulated with mesothelin CAR (**Figure 31A**), or CD19 CAR (**Figure 31B**) and cord blood CD8 T cells stimulated with mesothelin CAR (**Figure 31C**) in culture. CAR expressing T cells were co-cultured with CAR-specific antigen immobilized on magnetic beads in the presence of cytokines. CD8 T cells were cultured in the presence of IL7+IL15 (10ng/mL each). Cell number was counted (using Multisizer 3 Coulter counter)

every 48hours, and replated at $0.75e^6$/mL with fresh media (supplemented with the corresponding cytokines).

All T cells with CARs received CAR-specific stimulation and expanded in culture. Different CAR costimulatory domains had different effects on expansion of T cells in culture, the best combination being the BBz CAR construct in CD8 T cells. These numbers are comparable to (and in some cases, higher than) the expansions seen using the CD3/28 stimulation conditions.

Example 6: Reprogramming metabolic fate of T cells by distinct signaling domains in chimeric antigen receptors

Chimeric antigen receptors (CAR) redirect T cell cytotoxicity against cancer cells, providing a promising new approach to cancer immunotherapy. Despite extensive clinical use, the attributes of CAR co-stimulatory domains that impact persistence and functions (e.g., resistance to exhaustion) of CAR-T cells remain largely undefined. This example reports the influence of signaling domains of coreceptors CD28 and 4-1BB on proliferation, cell longevity, memory differentiation and metabolic characteristics of CAR-grafted human T cells. Inclusion of 4-1BB, a member of the TNF receptor family in the CAR architecture, promotes the outgrowth of CD8 central memory T cells that had significantly enhanced respiratory capacity, increased fatty acid oxidation and enhanced mitochondrial biogenesis. In contrast, CAR T cells with CD28 domains yielded effector memory cells with a genetic signature consistent with enhanced glycolysis. These results provide, at least in part, a mechanistic insight into the differential persistence of CAR-T cells expressing 4-1BB or CD28 signaling domains in clinical trials and inform the design of future CAR T cell therapies.

Adoptive immunotherapy based on the infusion of genetically redirected autologous T cells has demonstrated promise for the treatment of both hematologic malignancies and solid tumors. Accordingly, multiple gain-of-function strategies to endow T cells with desired antigen receptors, based on either T cell receptors (TCRs) or chimeric antigen receptors (CARs) have been described (June et al., Sci. Transl. Med. 7, 280ps7, 2015). Among several proposed strategies, the use of CARs has shown potent effects in augmenting immune response to cancers, particularly B cell malignancies (Brentjens et al., Sci. Transl. Med. 5, 177ra38, 2013; Grupp et al., N. Engl. J. Med. 368, 1509–1518, 2013; Kalos et al., Sci. Transl. Med. 3, 95ra73, 2011). Although CAR T cell therapy can have a significant impact on disease clearance, the

essential components of a clinically successful CAR, and how they influence therapeutic efficacy, remain largely undefined (Kalos and June, Immunity 39, 49–60, 2013).

CARs are synthetic molecules that combine the effector functions of T cells with the exquisite specificity of antibody-binding domains. In their simplest form, these receptors consist of the TCR grafted to extracellular variable regions of an antibody (Eshhar et al., Proc. Natl. Acad. Sci. USA 90, 720–724, 1993; Kuwana et al., Biochem. Biophys. Res. Commun. 149, 960–968, 1987). One advantage of antibody-based receptors is that they can recognize pre-defined tumor targets independent of antigen processing and major histocompatibility complex (MHC)-restricted presentation, rendering a single design applicable to a wide range of patients. First-generation CARs consisting of the cytoplasmic domain of the Fc receptor-gamma chain (g chain) or the CD3z signaling modules alone often become anergic and do not elicit potent T cell antitumor effects (Brocker, Blood 96, 1999–2001, 2000; Kershaw et al., Clin. Cancer Res. 12, 6106–6115, 2006; Lamers et al., J. Clin. Oncol. 24, e20–e22, 2006). This led to the development of second- and third-generation CARs that incorporate additional costimulatory cytoplasmic domains such as CD28, 4-1BB (CD137), ICOS, and OX40, either individually or in combination (Dotti et al., Immunol. Rev. 257, 107–126, 2014; Sadelain et al., Cancer Discov. 3, 388–398, 2013). This modular design successfully recapitulates many aspects of natural costimulation and enhances proliferation and function of CAR T cells (Maus et al., Cancer Immunol. Res. 1, 26–31, 2014).

The CD19-specific CAR T cells have shown encouraging clinical responses against various hematological malignancies, including chronic lymphocytic leukemia (CLL), acute lymphoblastic leukemia (ALL) and diffuse large B cell lymphoma. The success rates, however, have been difficult to compare because of several variations in study design, as well as differences in the single chain variable antibody fragment (scFv), costimulatory domains, gene-transfer protocols and interventions following CAR T cell infusion, among others. Trials conducted with CARs incorporating CD28 or 4-1BB costimulatory domains have shown similar initial response rates in patients with ALL (Brentjens et al., Sci. Transl. Med. 5, 177ra38, 2013; Lee et al., Lancet 385, 517–528, 2015; Maude et al. N. Engl. J. Med. 371, 1507–1517, 2014). However, in CLL the clinical efficacy of CAR T cells with 4-1BB costimulatory domains (Porter et al., Sci. Transl. Med. 7, 303ra139, 2015) appears superior to that of CD28 domains (Brentjens et al., Blood 118, 4817–4828, 2011Porter et al., Sci. Transl. Med. 7, 303ra139, 2015). The reported persistence of CD28 based CAR T cells in vivo is about

30 days (Brentjens et al., Sci. Transl. Med. 5, 177ra38, 2013; Lee et al., Lancet 385, 517–528, 2015), compared to the sustained expression and effector function of 4-1BB CAR T cells, which may exceed 4 years in some patients (Porter et al., Sci. Transl. Med. 7, 303ra139, 2015). In addition, the incorporation of 4-1BB signaling domains in certain CARs ameliorates exhaustion (Long et al., 2015). Another important consideration is that endogenous CD28 and members of the tumor necrosis factor receptor family (TNFR), such as 4-1BB, invoke distinct signaling cascades in T cells. CD28 leads to activation of the P13K-Akt pathway with downstream effects on glucose metabolism and increased glycolysis (Frauwirth et al., Immunity 16, 769–777, 2002). In contrast, endogenous 4-1BB signaling has been implicated in imparting long-term survival benefits to T cells (Sabbagh et al., J. Immunol. 180, 8093–8101, 2008) and signaling pathways used by 4-1BB are distinct from CD28 (Martinez-Forero et al., J. Immunol. 190, 6694–6706, 2013). Thus, a thorough understanding of the molecular signaling effects of CARs may in part explain the observed differences in clinical efficacy for CLL.

A challenge for the identification of optimal CAR designs has been the lack of a physiological in vitro model investigating the impact of CAR-based stimulation. Moreover, current gene transfer protocols with retroviruses require concomitant activation of T cells via its endogenous TCR, potentially obscuring effects due to signaling through the CAR *per se*. In this Example, an approach is described allowing for CAR expression in over 90% of the T cells without the need to activate the endogenous TCR. Stimulating the CAR T cells with cognate antigen permitted identification of distinct effects on the differentiation and metabolism of primary human T cells. It was found that CAR signaling domains can mediate metabolic reprogramming while modifying bioenergetics and mitochondrial biogenesis. It was found that 4-1BBz CAR T cells demonstrate enhanced survival associated with an increased frequency of central memory T (Tcm) cells, mitochondrial biogenesis, and greater oxidative metabolism. In contrast, antigen stimulation of CD28z CAR T cells promoted effector memory differentiation and led to enhanced aerobic glycolysis.

As described in this example, distinct signaling of coreceptors can regulate specific metabolism pathways and impact memory development in CAR T cells.

Experimental Procedures

CAR constructs and generation of CAR-encoding in vitro transcribed (IVT) RNA

For the purpose of these studies, CARs specific to the human CD19 or mesothelin antigen were used. Figure 32A shows the schematic of the CARs used in this study. All CARs contained the single-chain variable fragment (scFv) against human CD19 (clone FMC-63), or the SS1 scFv against human mesothelin protein, wherever indicated (Hassan et al., Clin. Cancer Res. 8, 3520–3526, 2002; Nicholson et al., Mol. Immunol. 34, 1157–1165, 1997). The mesothelin CAR was previously described (Carpenito et al., Proc. Natl. Acad. Sci. USA 106, 3360–3365, 2009). The CD28z CAR consisted of the scFv linked in cis to the intracellular domains of CD28 and CD3z through the CD8a hinge and a CD28-transmembrane domain, as described previously (Milone et al., Mol. Ther. 17, 1453–1464, 2009). Similarly the BBz CAR contained the scFv linked to the 4-1BB intracellular portion and the CD3z domain through a CD8a hinge and transmembrane domain (Milone et al., Mol. Ther. 17, 1453–1464, 2009). For preparation of *in-vitro*-transcribed (IVT) RNA, the CAR-encoding gene constructs were subcloned into the pGEM.64A based vector, as described previously (Zhao et al., Cancer Res. 70, 9053–9061, 2010).

CAR RNA preparation

For *in vitro* transcribed (IVT) RNA, the T7 mScript™ RNA system (Cellscript, Madison WI) was used as per the manufacturer's instructions and as described previously (Zhao et al., Cancer Res. 70, 9053–9061, 2010). The IVT products were purified with an RNeasy Mini Kit (Qiagen Inc., Valencia, CA) and the purified RNA was eluted in RNase-free water at 1μg/μL.

Isolation, electroporation and expansion of primary human T lymphocytes

Primary human T lymphocytes were obtained from anonymous healthy donors at the University of Pennsylvania Apheresis Unit. Using the BTX CM380 (Harvard Apparatus BTX) electroporation machine, the IVT RNA was introduced into the T cells at a ratio of 1ug RNA/10^6 cells. This technique was optimized to promote uniform CAR expression on the cell surface (Figure 32B). T cells were stimulated with magnetic beads coated with a recombinant anti-CD19 idiotype or mesothelin-Fc.

Preparation of stimulation beads

For *in vitro* stimulation of CAR T cells, recombinant anti-CD19 idiotype antibody or mesothelin-Fc fusion protein was coupled to Dynabeads M-450 Tosylactivated (Invitrogen, USA). For the coupling, every $4x10^8$ beads were washed once and resuspended in 1mL of sterile Borate solution (0.1M Boric acid, pH 9.5). To this, 150μg of protein in 1mL of Borate

solution was added and incubated overnight (16-24 hours) at 37°C with constant mixing. After magnet bead capture, the solution was decanted and the beads were washed three times with Bead-wash solution (3% human albumin, 0.1% sodium azide and 0.4% 0.5M EDTA in PBS) for 10 minutes each time, and then another overnight wash in fresh Bead-wash solution with continuous rocking. The coated beads were washed three times in R10 (RPMI supplemented with 10% FCS, 100-U/ml penicillin, 100μg/ml streptomycin sulfate) before use for *in vitro* stimulation. For stimulation, the CAR RNA-electroporated cells were co-cultured with beads in a bead:cells ratio of 3:1.

T cell culture

The cells were maintained in R10 at 37°C for the entire culture and fed with fresh media every 48 hours. The cells were counted using a Coulter Multisizer III particle counter. Population doubling for each time point was measured as a ratio of the total cells on the day to the last time point measured. Cumulative population doublings were plotted. The media was supplemented with cytokines as follows: for CD4+ T cells 30U/mL human IL2 (Chiron) and for CD8+ T cells 10ng/mL IL7 + 10ng/mL IL15 (R&D systems).

Surface staining for flow cytometry analysis

Cell viability was measured by staining with Live/Dead Fixable Aqua amine-reactive viability dye (Life Technologies) for 15 minutes at room temperature. The following fluorescent probe conjugated antibodies were purchased from BD Biosciences: αCD4-BV711, αCD8-APCH7, αCD45RO-PE, αCD69-PECF594, αCCR7-PE-Cy7, αCD25-PE-Cy7, αCD127-FITC and αCD215-PE. Surface staining was performed at 4°C for 30 minutes in phosphate-buffered saline (PBS) supplemented with 3% fetal bovine serum. Surface expression of CAR was examined by incubating cells with biotin-labelled polyclonal goat anti-mouse F(ab)2 antibodies (Jackson Immunoresearch, West Grove, PA) at 4°C for 30 minutes, followed by two washes with FACs buffer (PBS plus 3% BSA) and detection with phycoerythrin-labeled streptavidin (BD Pharmingen, San Diego, CA). Sample data was collected on the LSRII Fortessa (BD Biosciences) and analyzed with FlowJo software (Treestar).

Flow cytometry analysis

Live cells were gated on live/dead aqua-negative and then gated for CD3-, CD4-, and CD8-positive events. Using markers for memory, CCR7, and CD45RO, we analyzed cells in culture and sorted them for the three different memory phenotypes using the BD FACSCalibur analyzer. Absolute T cell counts were determined with the aid of CountBright Absolute

Counting Beads (Life Technologies) using the following formula: (Number of T cells events/number of bead events) x number of beads used

Analysis of metabolic parameters

Mitochondrial function was assessed with an extracellular flux analyzer (Seahorse Bioscience). Individual wells of an XF24 (Figures 34B-34C and 34F-34G) or XF96 (Figures 34H-34K) cell culture microplates were coated with CellTak in accordance with the manufacturer's instructions. The matrix was adsorbed overnight at 37°C, aspirated, air-dried, and stored at 4°C until use. Mitochondrial function was assessed on days 0, 7, and 21. To assay mitochondrial function, T cells were centrifuged at 1200 x g for 5 minutes. Cell pellets were resuspended in XF assay medium (non-buffered RPMI 1640) containing 5.5 mM glucose, 2mM L-glutamine, 1mM sodium pyruvate and seeded at 1 x 10^6 cell per well. The microplate was centrifuged at 1000 x g for 5 minutes and incubated in standard culture conditions for 60 minutes. During instrument calibration (30 minutes), the cells were switched to a CO_2-free (37°C) incubator. XF24 and XF96 assay cartridges were calibrated in accordance with the manufacturer's instructions. Cellular oxygen consumption rates (OCRs) were measured under basal conditions and following treatment with 5 mM oligomycin, 5 mM fluoro-carbonyl cyanide phenlhdrazone (FCCP), and 40nM rotenone, with 1 mM antimycin A (XF Cell Mito Stress kit, Seahorse Bioscience).

Gene expression analysis by RT-PCR

Quantitative reverse-transcription polymerase chain reaction (qRT-PCR) was used to quantify expression levels of certain candidate genes. Total RNA from cells was used as a template to synthesize cDNA with a High Capacity RNA-to-cDNA Kit (Applied Biosystems). qRT-PCR was performed in triplicates with Taqman Universal Master Mix on a ViiA 7 Real Time PCR System as per the manufacturer's instructions. mRNA levels of each candidate gene as quantified by the PCR system were normalized to a housekeeping gene, GADPH. All probes used are commercially available (Applied Biosystems).

Glucose uptake assay

Cells at day 7 after stimulation were starved in PBS at room temperature for 30 min followed by incubation at 37°C in regular RPMI culture media supplemented with 11 mM glucose, 10% FCS, 100 U/ml penicillin, 100 mg/ml streptomycin sulfate, and 2 mM glutamax. 500 uL aliquots of cell culture was collected at indicated time points and spun down, and the

supernatants were analyzed for glucose and lactate concentrations with the Nova BioProfile Analyzer (Nova Biomedical).

Palmitic acid uptake assay

[$^{13}C_{16}$] palmitic acid was purchased from Sigma-Aldrich. All solvents for liquid chromatography mass spectrometry were Optima grade and purchased from Fisher Scientific. For palmitic acid-labeled isotope experiments, cells were cultured overnight in RPMI 1,640 without D-glucose or L-glutamine (Biological Industries) and supplemented with 10% charcoal-stripped FBS (GIBCO), 2 mM L glutamine (Life Technologies), 5.0 mM glucose, and 100 mM [$^{13}C_{16}$] palmitic acid.

Short-chain acyl-CoA extraction

Extractions were performed as described previously (Basu and Blair, Nat. Protoc. 7, 1–12, 2012; Worth et al., J. Biol. Chem. 289, 26895–26903, 2014). In brief, lymphocytes were centrifuged at 1,200 rcf for 5 min. Cell pellets were resuspended in 750 ml of ice-cold 10% trichloroacetic acid and pulse-sonicated with a sonic dismembrator (Fisher Scientific). The samples were centrifuged at 15,000 rcf for 15 min, and the supernatants were purified by solid-phase extraction. In brief, Oasis HLB 1 ml (30 mg) solid-phase extraction columns were conditioned with 1 ml methanol followed by 1 ml of H_2O. The supernatants were applied to the column and washed with 1 ml of H_2O. The analytes were eluted in methanol containing 25 mM ammonium acetate, dried overnight in N_2 gas, and resuspended in 50 ml of 5% 5-sulfosalicylic acid. 10 ml injections were applied in LC/ESI/MS/MS analysis.

LC/MS analysis of acyl-CoA thioesters

Acyl-CoAs were separated with a Phenomenex Luna C18 reverse-phase highperformance liquid chromatography column (2.0 3 150 mm, 5 mm pore size) with 5mMammonium acetate in water as solvent A, 5mMammonium acetate in acetonitrile (ACN)/water (95:5, v/v) as solvent B, and ACN/water/formic acid (80:20:0.1, v/v) as solvent C, as described previously (Basu et al., Anal. Chem. 83, 1363–1369, 2011; Worth et al., J. Biol. Chem. 289, 26895–26903, 2014). A linear gradient was run as follows: 2% solvent B for 1.5 min, increased to 25% over 3.5 min, increased to 100% over 0.5 min, held for 8.5 min, and washed with 100% solvent C for 5 min before equilibration for 5 min. The flow rate was 200 ml/min. Samples were analyzed with an API 4000 triple-quadrupole mass spectrometer (Applied Biosystems) in the positive electrospray ionization (ESI) mode. Samples (10 ml) were injected with a LEAP autosampler (CTC Analytics AG) and maintained at 4°C. Data were

analyzed with Analyst Version 1.4.1 software (AB SCIEX). The column effluent was diverted to the mass spectrometer from 8–23 min and to waste for the remainder of the run. The mass spectrometer operating conditions were as follows: ion spray voltage (5.0 kV), nitrogen as curtain gas (15 U), ion source gas 1 (8 U), ion source gas 2 (15 U), and collision-induced dissociation gas (5 U). The ESI probe temperature was 450°C, the declustering potential was 105V, the entrance potential was 10 V, the collision energy was 45 V, and the collision exit potential was 15 V. A loss of 507 Da was monitored for each acyl-CoA.

Microscopy

Cells at different time points were stained with DiI, Mitotracker green and DAPI (Life Technologies) and fixed with 4% PFA before imaging on the Leica TSC SP8 confocal microscope. Captured images were analyzed with Fiji (ImageJ) and fluorescence emission was quantified as mean fluorescence intensity (MFI). For transmission electron microscopy, the cells were prepared by Penn's Electron Microscopy Resource Laboratory and imaged using the Jeol-1010 microscope.

Statistical analysis

Wherever indicated, all results are expressed as mean ± standard error of mean (SEM) or standard deviation (SD). Statistical comparisons were performed either by the student's t test or a two-way ANOVA model with factors being CAR group and time points of sample collection, using Prism (GraphPad software). The Wilcoxon signed-rank test (two-tailed) was performed on the population doublings between the two CAR T cell groups.

Results

BBz CAR T cells show increased expansion and survival ex vivo

This study initially compared two CD19 CAR designs (**Figure 32A**) specific for either CD19 or mesothelin. The CARs were equipped with signaling domains comprised of either CD28 (Kochenderfer et al., J. Immunother. 32, 689–702, 2009) or 4-1BB (Milone et al., Mol. Ther. 17, 1453–1464, 2009). These CARs were chosen because they have been tested extensively in clinical trials (Beatty et al., Cancer Immunol. Res. 2, 112–120, 2014; Kochenderfer et al., Blood 119, 2709–2720, 2012; Lee et al., Lancet 385, 517–528, 2015; Maude et al., N. Engl. J. Med. 371, 1507–1517, 2014; Maus et al., Cancer Immunol. Res. 1, 26–31, 2013; Porter et al., Sci. Transl. Med. 7, 303ra139, 2015). Both CAR constructs were expressed on >90% of CD4+ and CD8+ T cells at comparable mean fluorescence intensities

(MFIs) (**Figure 32B**). A schematic of the study design is shown in **Figure 32C**. The effects of the CD28 and 4-1BB (referred to as 28z and BBz) signaling domains on the differentiation and metabolic fate of T cells. CD4+ T cells were cultured medium supplemented with 30 U/ml of human IL2. CD8+ T cells were cultured in medium supplemented with either 100 U/ml of human IL2 or 10 ng/ml IL7 and 10 ng/ml IL15, as indicated in the Experimental Procedures. Approximately 24 hours after electroporation, CAR-T cells were stimulated with a bead-bound anti-idiotype-Fc to the FMC-63 scFv, which serves as a surrogate for cognate CD19 antigen. To ensure that the CAR T cells received uniform stimulation, the surface expression of the activation molecule CD69 was analyzed on day 1 after activation. CD69 is an inducible cell-surface glycoprotein that is a sensitive indication of lymphoid activation (Hara et al., J. Exp. Med. 164, 1988–2005, 1986). Cells that received CAR-specific stimulation showed elevated expression of CD69 on day 1 that was similar on 28z and BBz CAR T cells (Figure 33A). However, the proliferative potential of both CD4 and CD8 T cells bearing the BBz CAR was extended through to at least day 20. In contrast, the proliferative phase of 28z CAR T cells was limited to 14 days (**Figures 33B** and **37**, $p < 0.01$). CAR surface expression rapidly decreased following stimulation with cognate antigen (**Figure 41**). Importantly, cytokine receptor expression was comparable in both CAR groups (**Figure 41**), indicating that the proliferative differences between the different CAR T cells are not due to differences in cytokine receptor expression. In one donor, over ten population doublings in the BBz CAR T cell culture, expanding the starting culture of 4×10^6 cells to a calculated yield of over 5×10^9 in less than four weeks, were observed (Table 5). The BBz CAR T cells persisted in culture for over 4 weeks in cytokine-supplemented medium following a single stimulation. In contrast, the proliferation and/or survival of the 28z CAR T cells was lower. Although proliferative capacity varied among donors, the trend remained consistent, in that BBz CAR T cells displayed a higher proliferative capacity and persistence in comparison to the 28z CAR T cells (Figure 40, $p < 0.01$). Similar results were obtained with CARs directed against mesothelin (Figure 33C, **Figure 38**, Tables 5 and 7). The remainder of this Example focuses mainly on the effect of CAR design in CD8+ T cells.

Table 5: Population doublings and total yield for 3 independent human donor T cells. The BBz T cells continued to persist for longer durations as compared to 28z cells. Cultures were stopped after at least two consecutive decline in cell numbers were observed. BBz CAR T cells also showed higher population doublings in every donor tested. The last column shows the total number of cells obtained by the end of expansion, starting with $4x10^6$ cells in each group.

Donor #	CAR	Number of days in culture before two consecutive population declines	Total Population Doublings	Maximum cell yield in culture ($x 10^6$ cells)
1	28z	20	4.3	78.80
	BBz	22	5.0	128.00
2	28z	22	6.0	256.00
	BBz	28	7.2	588.13
3	28z	24	6.9	477.71
	BBz	30	10.3	5,042.77

BBζ CAR signaling promotes enhanced central memory T cell (TCM) subset

It was hypothesized that the enhanced persistence of BBz T cells was due to a relative preservation of cells with a more extensive proliferative capacity. To test the differentiation status of BBz and 28z CAR-T cells, a standard panel of cell-surface markers associated with T cell differentiation was used. Expression of CD45RO and CCR7, which are associated with Tcm cells was assessed. All cultures contained the same heterogeneous population of T cell subsets at day 0. After stimulation through the CAR, the proportion of CD45RO+CCR7+ cells was progressively enriched (**Figure 33D**). Notably, the enrichment of this Tcm cell population was higher in the BBz CAR group in comparison to the 28z group ($p < 0.01$), and persisted through the end of culture (**Figure 33E**). In contrast, the 28z CAR cultures consistently yielded a higher proportion of effector-memory phenotype (Tem), identified as CD45RO+CCR7- cells. The partitioning/differentiation of cells into memory phenotypic pools could potentially be attributed with the difference in longevity of the cells stimulated with a BBz CAR versus a 28z CAR.

Table 6: Absolute cell counts showing proportion of T_E and T_M cells in culture for 3 donors. 28z CAR T cells show a higher percentage and a higher number of cells that are decorated with markers characteristic of T_E cells. On the other hand BBz CAR T cells had higher numbers with the T_M phenotype.

Donor #	CAR	Absolute counts (# of cells per 26,500 beads counted)					
		Day 0		Day 20		Day 27	
		CD62L-CCR7-	CD62L+CCR7+	CD62L-CCR7-	CD62L+CCR7+	CD62L-CCR7-	CD62L+CCR7+
1	28z	13827	12318	52168	32908	83217	28801
	BBz	9473	10237	41498	39928	72570	31474
2	28z	46596	32002	124638	19398	81519	9725
	BBz	40388	29813	86700	31259	48066	14058
3	28z	61969	43819	28461	43849	53213	23418
	BBz	62743	46127	18256	79659	4136	24459

Table 7: Population doublings and total yield for 3 independent human donor T cells stimulated through meso CAR. The last column shows the total number of cells obtained by the end of expansion, starting with $4x10^6$ cells in each group. Data is from 3 representative donors (out of at least 6 independent donor T cells tested).

Donor #	SS1 CAR	Number of days in culture before two consecutive declines	Total Population Doublings	Maximum number of cells reached in culture (x 10^6 cells)
1	28z	12	5.8	222.86
	BBz	24	8.8	1,782.89
2	28z	16	6.9	477.71
	BBz	24	8.4	1,351.18
3	28z	14	6.0	256.00
	BBz	22	8.4	1,351.18

CAR signaling domains reprogram T cell metabolism (BBζ CAR T cells demonstrate distinct oxidative features)

Upon stimulation, CD8+ T cells undergo an ordered process involving proliferation and differentiation into effector and memory cells. Activation is associated with a biosynthetic and bioenergetics flux required to support T cell proliferation and function (Pearce and Pearce, Immunity 38, 633–643, 2013; Wang and Green, Nat. Immunol. 13, 907–915, 2012). For example, naïve and memory T cells rely primarily on the mitochondrial oxidation of free fatty acids for development and persistence (Pearce et al., Nature 460, 103–107, 2009; van der Windt et al., Immunity 36, 68–78, 2012). In contrast, activated effector T cells shift to glycolysis (or concurrently upregulate oxidative phosphorylation and aerobic glycolysis) to fulfill the metabolic demands of proliferation (van der Windt et al., Immunity 36, 68–78, 2012). Among other factors including signaling events, cell death and immunological functions, that regulate T cell differentiation and survival, this Example investigates the interconnection of cellular metabolism to the observations seen above.

Based on the distinct growth rates and differentiation of 28z and BBz CAR T cells, we sought to explore the interconnection of cellular metabolism and CAR signaling. First, the metabolic profiles of T cells expressing the two CARs at different time points after stimulation were examined. Cell volume, a surrogate for cell mass, was found to be comparable after cognate antigen stimulation (**Figure 34A**). The oxygen consumption rate (OCR) of 28z and BBz CAR T cells before and 7 and 21 days after antigenic stimulation during log-phase proliferation was measured. Basal OCR was measured, followed by serial additions of oligomycin (an inhibitor of ATP synthesis), carbonyl cyanide-ptrifluoromethoxyphenylhydrazone (FCCP; an uncoupling ionophore), and rotenone with antimycin A (blocking agents for complex I and III of the electron transport chain, respectively) (van der Windt et al., Immunity 36, 68–78, 2012). The OCR profiles were similar before antigen stimulation on day 0 (**Figure 34B**). After antigen stimulation, there was a ~10-fold increase in basal OCR in both groups of T cells on days 7 and 21 (**Figure 34C**). However, there was a robust increase in maximal respiratory capacity that was specific to the BBz CAR T cells , following decoupling of the mitochondrial membrane using FCCP on both days 7 and 21 (**Figure 34F**). In contrast the maximal respiratory capacity of the 28z CAR T cells on days 7 and 21 was similar to what it was on day 0. To confirm that these differences in OCR were due to the signaling domains of the receptor, similar experiments were performed with mesothelin-

specific CAR T cells. The mesothelin-BBz CAR T cells exhibited an elevated basal and maximal respiratory capacity compared to the 28z CAR T cells on days 7 and 21 after stimulation with mesothelin (**Figure 39**). The extracellular acidification rate (ECAR) was also measured as a measurable surrogate for lactic acid production during glycolysis. Glycolysis involves a series of enzyme-catalyzed reactions culminating in the production of lactic acid. At physiologic pH, lactic acid dissociates into lactate and H+ which are exported extracellularly. ECAR levels were elevated in 28z cells in comparison to BBz CAR T cells on days 7 and 21 (**Figures 34D** and **34G**).

Several reports have shown that natural central memory differentiated T cells display elevated basal OCR and SRC in comparison to effector memory and terminally differentiated effector cells. These oxidative features suggest that an increased reliance on fatty acid oxidation (FAO) may be necessary for central memory differentiation and survival (Pearce et al., Nature 460, 103–107, 2009; van der Windt et al., Immunity 36, 68–78, 2012). Because a differential enrichment of memory phenotypes was seen in the two CAR T cell groups in culture, the analysis was extended to uncover how individual memory subsets contribute to the metabolic properties of CART cells. Again, usingCCR7 and CD45RO as phenotypic markers, the populations were sorted into CCR7+CD45RO-, CCR7+CD45RO+, and CCR7-CD45RO+ to define naive-like, Tcm cell, and Tem cell subpopulations, respectively. Metabolic flux revealed higher basal OCR and maximum respiratory capacity of the BBz in the Tcm and Tn memory sub-types ascompared to 28z CART cells (**Figures 34H** and **34I**). As observed in past reports concerning effector cells, the basal OCR as well as the maximum respiratory levels remained low for the Tem cell subpopulations for both CAR groups (**Figure 34J**). On the other hand, the ECAR levels remained higher for Tcm and Tem cell subpopulations of cells obtained from the 28z CAR T cell culture (**Figure 34K**). In aggregate, these studies show that BBz CAR T cells are metabolically distinct from 28z CAR T cells with the former displaying greater capacity for oxidative metabolism that might contribute to the enhanced central memory differentiation and persistence of BBz CAR T cells.

28z and BBz CAR T cells have distinct glycolytic and fatty acid metabolism

To investigate whether the differences in the basal OCR in CAR T cells altered the fuel sources by which these cells satisfy their bioenergetic appetite, glucose uptake and fatty acid utilization rates were measured in CAR T cells. At day 7 after stimulation, the cells were

replated in fresh media. At different points (as indicated in **Figure 34L**), the amount of residual glucose in the media and the lactate produced were measured. 28z CAR T cells consumed glucose at a relatively quicker rate along with production of lactic acid. This is consistent with the greater ECAR we observed in 28z CAR T cells (**Figures 34G** and **34K**).

The increased OCR in BBz CAR T cells prompted us to examine the fatty acid consumption rate in these cells. Using a heavy-carbon-labeled long-chain fatty acid (palmitic acid), its uptake rate was analyzed by measuring the levels of heavy-carbon- labeled acetyl-CoA. The catabolic process of b oxidation breaks down fatty acid molecules into acetyl-CoA in the mitochondria to feed the citric-acid cycle. It was found that BBz showed a higher percentage of labeled acetyl-CoA pool as compared to 28z CAR T cells (**Figure 34M**). This data suggest that BBz CAR T cells, similar to CD8+ Tcm cells, extensively rely on catabolic pathways such as FAO to fuel their bioenergetic demands.

To gain insight into the mechanism leading to the metabolic differences conferred by distinct CAR signaling domains expression of candidate genes that are implicated in glycolytic and lipid metabolism were measured. Two main enzymes implicated in glucose metabolism, Glut1 and PDK1, were initially focused on. The cell-surface expression of Glut1, the transporter involved in glucose uptake, is induced following CD28 activation (Frauwirth et al., Immunity 16, 769–777, 2002). In certain contexts, including hypoxia, PDK1 inhibits the decarboxylation of pyruvate and entry of glucose derivatives into the tricarboxylic acid (TCA) cycle (Duvel et al., Mol. Cell 39, 171–183, 2010). Both Glut1 and PDK1 are induced to significantly higher levels in 28z cells relative to BBz cells at day 7 (**Figure 34E**). Increased expression levels of Glut1 and PDK1, coupled with the earlier finding of increased ECAR, is consistent with enhanced glycolysis in 28z CAR T cells in comparison to their BBz counterparts.

Two important enzymes involved in the breakdown of glucose during the ATP-generating step of the glycolytic pathway are phosphoglycerate kinase (PGK) and glucose-6-phosphate dehydrogenase (G6PD). PGK transfers a phosphate group to ADP in order to facilitate ATP generation, whereas G6PD, an NADP+-dependent enzyme, catalyzes the oxidative phase of the pentose phosphate pathway (PPP). Given that these enzymes have an important role in glycolysis, their expression levels in CAR T cells were investigated on Day 7. Their levels were elevated in 28z CAR T cells. Finally, the levels of solute carrier family 16 (SLC16A3), an exporter of the glycolysis byproducts, lactic acid and pyruvate, were also

examined. 28z CAR T cells showed higher levels of SLC16A3 mRNA in comparison to BBz T cells, consistent with the hypothesis that 28z CAR T cells use increased glycolysis as a means to meet their metabolic demands. Increased expression of VEGFA was also detected in 28z CAR T cells, which is an established target of the hypoxiainducible factors (HIF). Several genes involved in glycolysis are targets of HIF1a (Finlay et al., J. Exp. Med. 209, 2441–2453, 2012), including Glut1 and PFK. Others have shown that HIF1A-/- T cells display impaired autoreactivity (Dang et al., Cell 146, 772–784, 2011). The findings shown in this Example add to the growing body of evidence implicating costimulation through CD28 and glycolytic reprogramming in effector differentiation. Next, genes associated with mitochondrial FAO were investigated. Increasing evidence has demonstrated a role for carnitine palmitoyl transferase (CPT1A) in regulating oxidative metabolism in CD8+ cells (van der Windt et al., Immunity 36, 68–78, 2012). CPT1A is a metabolic enzyme that controls a rate-limiting step in mitochondrial FAO and promotes mitochondrial biogenesis. Significantly higher levels of CPT1A mRNA were observed in BBz CAR T cells in comparison to 28z CAR T cells. Additionally, mRNA levels of fatty acid binding protein (FABP5), which plays a critical role in long-chain fatty acid uptake, transport and metabolism were significantly upregulated in BBz CAR T cells in comparison to 28z (**Figure 34E**). These findings suggest that 28z CAR T cells rely more on a glycolytic-based metabolism whereas BBz programs T cells to use fatty acids as the predominant energy source, which are characteristics of natural effector and memory T cells, respectively.

BBζ CAR T cells have increased Spare Respiratory Capacity

Mitochondrial spare respiratory capacity (SRC) is a measure of how effectively protons can be shuttled into the mitochondrial intermembrane space upon cellular or mitochondrial stress (Mookerjee et al., Mech. Ageing Dev. 131, 463–472, 2010; Nicholls, Biochem. Soc. Trans. 37, 1385–1388, 2009). SRC enhances survival and function of memory T cells by providing a contingency source of energy for cells exposed to metabolic stress including nutrient depletion, oxygen deprivation or under conditions of increased cellular activity. Increased SRC likely supports T cell function in a hostile tumor environment (Ferrick et al., Drug Discov. Today 13, 268–274, 2008; Nicholls, Biochem. Soc. Trans. 37, 1385–1388, 2009; Yadava and Nicholls, J. Neurosci. 27, 7310–7317, 2007). Memory CD8 T cells, unlike effectors, maintain a substantial SRC (van der Windt et al., Immunity 36, 68–78, 2012). When

comparing the SRC of the two CAR groups, it was observed that BBz CAR T cells maintained higher levels of SRC in comparison to 28z CAR T cells at Day 7 and Day 21 post stimulation (Figure 35A). This is consistent with the metabolic characteristics of long-lived CD8+ memory cells, lending additional support to the hypothesis that BBz signals support a metabolic reprogramming that contributes to long-lived memory-like T cells.

Given the role of mitochondrial density in oxidative metabolism (van der Windt et al., Immunity 36, 68–78, 2012), the possibility that the increased SRC in BBz CAR T cells was associated with an increase in mitochondrial mass was explored. Using electron microscopy, similar mitochondrial density between 28z and BBz CAR-T cells was measured at day 7 (**Figures 35B** and **35C**). However, there was a substantial increase in mitochondrial mass in BBz CAR T cells at days 14 (**Figure 35B**) and 21 (**Figure 42**) after antigen stimulation. Despite similar cell volumes (**Figure 34A**), a significantly ($p < 0.001$) increased density of mitochondria in BBz CAR-T cells. To confirm that BBz CAR T cells have enhanced mitochondrial content, we also measured mitochondrial density using confocal microscopy (Figure 36A). BBz CAR T cells showed an increased ratio of mitochondrial mass to total cell mass on days 14 and 21 (**Figure 36B**).

BBz CAR T show enhanced mitochondrial biogenesis

It was contemplated that specific signals from the 4-1BB signaling domain in the CAR structure supported mitochondrial biogenesis, thus endowing these cells with greater mitochondrial mass. However, in addition to quantitative differences in mitochondrial content, it was examined whether qualitative differences in mitochondria might contribute to the differences in metabolic profiles between these CAR cells. Level of certain mitochondrial genes encoded by the nuclear the mitochondrial genome, namely mitochondrial transcription factor A (TFAM) and MTCO-1, respectively, was examined. Notably, BBz cells had significantly enhanced mRNA expression of mitochondrial TFAM and mitochondrially encoded cytochrome c oxidase 1, the main subunit of the cytochrome c oxidase complex (**Figure 36C**).

To explore the role of 28z and BBz costimulatory domains on the mitochondrial function in the context of CAR T cells, we measured gene expression of two transcription factors of mitochondrial genes, namely nuclear respiratory factor 1 (NRF1) and GA-binding protein (also known as NRF2). Whereas NRF1 regulates the expression of TFAM and

coordinates mtDNA replication and expression, NRF2 has a role in the transcription of the OXPHOS components, mitochondrial import, and TFAM. Consistent with its enhanced oxidative features as seen by metabolic flux analyses and mitochondrial density, we found that BBz CAR T cells had significantly higher expression of NRF1 and NRF2 in comparison to the 28z CAR T cell group (**Figure 36D**).

Taken together, these findings suggest increased mitochondrial content in BBz CAR T cells in comparison to 28z CAR T cells, which strongly correlates with the increased SRC observed in these cells. These findings are consistent with a model in which BBz signaling reprograms transcriptional networks supporting mitochondrial biogenesis and oxidative metabolism. Given the role of metabolic adaptation in allowing for T cell memory and effector functions, the aforementioned oxidative features in BBz CAR T cells most likely support central memory differentiation and T cell persistence.

Discussion

These studies uncover significant differences in the differentiation and metabolic profiles of CAR T cells using CD28 or 4-1BB signaling domains. The predominant metabolic program in 28z CAR T cells is aerobic glycolysis, and, in BBz CAR T cells, it is oxidative breakdown of fatty acids. The studies provide evidence for plasticity in T cell metabolic reprogramming and, further, that the choice of CAR signaling domain can impact the subsequent fate of the T cells. The enhanced proliferation and persistence of BBz over 28z CAR T cells observed in the studies mirrors the outcomes of CAR persistence observed in clinical studies (Brentjens et al., Sci. Transl. Med. 5, 177ra38, 2013; Brentjens et al., Blood 118, 4817–4828, 2011; Lee et al., Lancet 385, 517–528, 2015; Porter et al., Sci. Transl. Med. 7, 303ra139, 2015). The studies suggest that one mechanism for the differential persistence may be the metabolic reprograming of the CART cells to enhance either oxidative phosphorylation that is characteristic of memory cells or aerobic glycolysis that is characteristic of effector cells (MacIver et al., Annu. Rev. Immunol. 31, 259–283, 2013; van der Windt et al., Immunity 36, 68–78, 2012).

Previous studies have shown that CD28 signaling initiates a cascade leading to enhanced surface expression of Glut1 and increased reliance on aerobic glycolysis (Frauwirth et al., Immunity 16, 769–777, 2002). In contrast, a TNFR pathway is required for the initiation of mitochondrial FAO and T cell memory development (Pearce et al., Nature 460, 103–107,

2009). Although IL2 promotes effector differentiation and glycolysis in CD8+ T cells (Finlay et al., J. Exp. Med. 209, 2441–2453, 2012; Liao et al., Immunity 38, 13–25, 2013; Pipkin et al., Immunity 32, 79–90, 2010), IL7 and IL15 have been implicated in the maintenance of memory T cells and increased mitochondrial biogenesis (Ku et al., 2000; Schluns and Lefranc¸ ois, 2003; van der Windt et al., Immunity 36, 68–78, 2012). Given that human CD8+ T survival is impaired in the absence of exogenous cytokines, IL7 and IL15 are necessarily present in the culture system. Although these extrinsic factors may play a significant role in stabilizing the metabolic profiles of T cells, it was hypothesized that the system described in this example is largely governed by cell-intrinsic factors influenced by the two unique intracellular CAR signaling domains. This is further corroborated by the lack of differences in the cell-surface expression of these cytokine receptors, suggesting that the relative distinction in metabolic reprogramming between the two CARs cannot be solely mediated by the supplemented cytokines. Thus, the studies suggest that the ectopic expression of CD28 or 4-1BB signaling domains in CARs leads to a phenocopy of the natural T cell activation process. By extension, the studies suggest that the incorporation of various signaling modules may biosynthetically reprogram T cells to desired effector or regulatory functions. For example, it was found that the incorporation of the ICOS signaling domain in CARs promotes a Th17 cell differentiation program (Guedan et al., Blood 124, 1070–1080, 2014).

One clinical application of the findings is that short-lived or long-lived CAR T cells can be created ''at will.'' This could extend the range of targets, depending on certain surface molecules where long-term CAR effects may not be tolerable due to potential off-tumor toxicity. In this case, a CD28 signaling domain would be expected to be superior. Another implication from the studies is that a mixture of CAR T cells expressing 4-1BB and CD28 domains may be superior to either CAR as a single population. This was contemplated because the combination of CAR T cells would be expected to more completely mimic a natural immune response comprised of an early dominance of T effector cells, achieved with CD28 CARs having enhanced aerobic glycolysis in the cytoplasm, and T memory cells, achieved with 4-1BB CARs having enhanced mitochondrial oxidative phosphorylation.

Apart from cell intrinsic factors, there has been substantial interest in understanding the effects of nutrient consumption on T cell survival in the tumor microenvironment. T cells have substantial bioenergetics and biosynthetic challenges to survive and conduct effector functions. The results that BBz CAR T cells have an increased capacity to generate mitochondrial mass.

This increase in mitochondrial mass provides a survival advantage (van der Windt et al., 2013). A higher SRC was consistently seen in BBz CAR T cells, and this mitochondrial respiratory capacity has been shown to be an important characteristic of natural CD8+ T cell memory development (van der Windt et al., Immunity 36, 68–78, 2012). The increased basal oxygen consumption of BBz cells also suggests a preferential reliance on oxidative phosphorylation as the predominant energy generating mechanism to account for the metabolic demands required for enhanced CAR T cell proliferation Furthermore, the data suggest that metabolism is an important mediator of CAR T cell survival and is influenced by the signaling induced by the costimulatory domain included in the CAR. In summary, these results reveal a new role for CAR T cell engineering to control T cell metabolism as a key determinant of T cell effector and memory responses. Using synthetic biology, it is possible to shape the immune response to a desired balance of long-lived memory cells and short-lived effector cells. By extension, the studies should influence the design of engineered T effector or engineered T regulatory cells that resist exhaustion or have enhanced survival in hostile tumor and inflammatory microenvironments.

Example 7: Activation and Expansion of T cells via Transiently Expressed CARs

In this protocol, complete activation and robust expansion of T cells is achieved by stimulation of a transiently expressed Chimeric Antigen Receptor (CAR) on the cell surface. The stimulation is carried out with an antigenic recombinant protein, instead of using antibodies. The antigen specificity of CARs is conferred by antibody fragments, also known as single-chain variable fragments (scFv). This scFv is held up on the surface of the T cell by a hinge, and is linked to signaling domains through a trans-membrane domain. The signaling domain could either be just a CD3z signaling tail (1st generation CAR) or intra-cellular segments of CD28, 4-1BB, and/or ICOSz in addition to CD3z. This obviates the need for a TCR to stimulate the cell. The recombinant protein can be manufactured in-house and coated on culture plates or cross-linked to microbeads to stimulate lymphocytes. Also, since the CAR is transiently expressed on the cell surface, and is then internalized post a single antigen-engagement, the cells do not receive repeated stimulations. This protocol can be customized to any CAR model. By adjusting the CAR-surface density as well the affinity of the scFv domain, the strength of the stimulations can be fine-tuned to desired levels. Cutting around the caveats

of the conventional TCR-stimulated expansion protocol, this new protocol shows comparable and in most cases more superior proliferation profiles and cell number yields.

RNA Manufacture and expression

In vitro transcribed (IVT) RNA coding for the CAR is prepared in-house using the T7 mScript™ RNA system (Cellscript, Madison WI), as per the manufacturer's instructions and as described previously (Zhao et al., Cancer Res. 70, 9053–9061, 2010). The IVT products are purified using a RNeasy® Mini Kit (Qiagen Inc, Valencia, CA) and the purified RNA is eluted into RNase-free water.

To obtain high expression of CAR on the cell surface, the IVT RNA is electroporated into primary human T cells (Zhao et al., Cancer Res. 70, 9053–9061, 2010). After letting the cells rest over-night and to allow for CAR-protein translation, surface expression of the CAR is examined by flow cytometry. The electroporation-based gene transfer technique allows for 95%+ CAR-positive T cells.

CAR T cell stimulation

After confirming CAR expression, the T cells are stimulated with a recombinant antigenic protein coupled to Dynabeads M-450 (Invitrogen, USA). Protein-bead coupling is carried out according to the manufacturer's protocol. Briefly, every 1mL aliquot of $400e^6$ beads in incubated with 150ug of protein overnight in sterile Borate solution (0.1M Boric acid, pH 9.5). After at least three washes, these beads are finally resuspended in R10 media (RPMI supplemented with 10% FCS, 100U/mL penicillin, 100ug/mL streptomycin sulfate). These beads are then used to stimulate the CAR T cells in media at a bead-to-cell ratio of 3:1.

Culture maintenance

The cell culture is started at a concentration of $7.5x10^5$ cells/mL of R10 media, supplemented with either IL2 (100 units/mL) or IL7 and IL15 (10 ng/mL each). Cell counts are measured every 48 hours, when they are fed with fresh media and re-plated at $7.5x10^5$ cells/mL. This culture is maintained until two consecutive drops in cell-population doublings are noticed.

The CAR T cells incubated with the cognate antigen receive the initial stimulus to activate the T cells and proliferate in culture. Use of different CAR co-stimulatory domains show different effects on the growth profiles and differentiation of T cells when expanding in culture. Up to 9 total population doublings have been recorded, which corresponds to every cell

multiplying to over 500 cells. These yields are comparable, and in some case, superior to the ones obtained using the traditional CD3/28 based stimulation system.

EQUIVALENTS

The disclosures of each and every patent, patent application, and publication cited herein are hereby incorporated herein by reference in their entirety. While this invention has been disclosed with reference to specific aspects, it is apparent that other aspects and variations of this invention may be devised by others skilled in the art without departing from the true spirit and scope of the invention. The appended claims are intended to be construed to include all such aspects and equivalent variations.

The reference in this specification to any prior publication (or information derived from it), or to any matter which is known, is not, and should not be taken as an acknowledgment or admission or any form of suggestion that that prior publication (or information derived from it) or known matter forms part of the common general knowledge in the field of endeavour to which this specification relates.

Throughout this specification and the claims which follow, unless the context requires otherwise, the word "comprise", and variations such as "comprises" and "comprising", will be understood to imply the inclusion of a stated integer or step or group of integers or steps but not the exclusion of any other integer or step or group of integers or steps.

THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. A method of expanding and/or activating a population of immune cells, e.g., immune effector cells, comprising:

providing a first Chimeric Antigen Receptor (CAR)-expressing cell population, said first CAR-expressing cell population comprising a transiently expressed first CAR molecule, and wherein said CAR molecule comprises an antigen binding domain of an antibody molecule;

contacting said first CAR-expressing cell population with a ligand of the CAR molecule chosen from a cognate antigen molecule, or an anti-antigen idiotypic antibody molecule, under conditions such that immune cell expansion and/or activation occurs, thereby producing an expanded and/or activated immune cell population; and

contacting the expanded and/or activated immune cell population with a nucleic acid encoding a second CAR molecule, wherein the second CAR molecule is stably expressed, thereby producing a second CAR-expressing cell population.

2. The method of claim 1, wherein providing the first CAR-expressing cell population comprises introducing a nucleic acid encoding a first CAR molecule into an immune cell population, thereby producing a first CAR-expressing cell population comprising a transiently expressed first CAR molecule.

3. The method of claim 1 or 2, wherein the expansion and/or activation of the population of immune cells is carried out *in vitro*, *ex vivo* or *in vivo*.

4. The method of any one of claims 1-3, wherein the population of immune cells:

(a) is acquired from a blood sample from a subject;

(b) comprises immune effector cells chosen from T cells, B cells, natural killer (NK) cells, natural killer T (NKT) cells, mast cells, myeloid-derived phagocytes, or a combination thereof;

(c) comprises primary T cells or a subset of lymphocytes chosen from anergized T cells, naïve T cells, T-regulatory cells, Th-17 cells, stem T cells, or a combination thereof;

(d) comprises peripheral blood mononucleated cells (PBMCs), cord blood cells, or a combination thereof; and/or

(e) comprises cells that express a low level of, substantially impaired, or do not have, a functional T cell receptor or that express a mutated or truncated form of one or more of a subunit of the TCR.

5. The method of any one of claims 1-3, wherein the ligand is a cognate antigen molecule.

6. The method of any one of claims 1-3, wherein the ligand is an anti-antigen idiotypic antibody molecule.

7. The method of any one of claims 1-6, wherein the ligand of the CAR molecule is immobilized or attached to a non-naturally occurring substrate.

8. The method of claim 7, wherein:

(a) the non-naturally occurring substrate is a solid support chosen from a plate, a membrane, a matrix, a chip or a bead; and/or

(b) the T cells are expanded *in vivo* by lymph node injection, or by injection of the tumor-infiltrating lymphocytes (TIL) into a tumor.

9. The method of any one of claims 1-8, wherein:

(a) the nucleic acid encoding the first CAR molecule is an RNA molecule;

(b) the first CAR molecule is transiently expressed in the immune cell population for a finite period of time or number of cell replications;

(c) the first CAR-expressing immune cells are cultured in the presence of the ligand of the CAR molecule for about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 18, 21, 22, 23, or 24 hours, or about 1, 5, 10, 15, 20, 25, 30, 35, 40, 45, or 50 days;

(d) the CAR-expressing cells shows at least 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12 or higher population doublings;

(e) the first CAR-expressing immune cell population expands to a total of 400-600, or about 500 cells, wherein the cell expansion is measured between 10 and 25 days after stimulation with the ligand; and/or

(f) the expanded and/or activated immune cell population comprises immune effector cells having a less differentiated phenotype.

10. The method of any one of claims 1-9, wherein:

(a) the first CAR molecule is internalized post a single ligand stimulation;

(b) the immune cell does not receive repeated ligand stimulation; or

(c) the strength of the immune cell stimulation is customized to a desired level by adjusting one or both of: the first CAR-surface density, or the affinity of the CAR antigen binding domain to the ligand.

11. The method of claim 9, wherein:

(a) the first CAR-expressing cells are cultured for a period of 8 days or less; and/or

(b) the cells having a less differentiated phenotype are younger T cells chosen from a naïve T cell (T_N), a memory stem cell (T_{SCM}), a central memory T cell (T_{CM}), or a combination thereof.

12. The method of claim 2, wherein:

(a) the nucleic acid encoding the second CAR molecule is selected from the group consisting of a DNA, an RNA, a plasmid, a lentivirus vector, adenoviral vector, and a retrovirus vector;

(b) the first and second CAR molecules are directed to the same antigen or different antigens;

(c) wherein the first and second CAR molecules are the same or different CAR molecules;

(d) the immune cell population transiently expressing the first CAR is expanded and/or activated *in vitro* or *ex vivo*, and the immune cell population expressing the second CAR is administered to a subject as part of a therapeutic protocol; and/or

(e) the method further comprises storing the expanded and/or activated immune cell population after the appropriate expansion period.

13. The method of claim 12, wherein the cancer associated antigen is chosen from CD19, CD123, CD22, CD30, CD171, CS-1, CLL-1 (CLECL1), CD33, EGFRvIII , GD2, GD3, BCMA, Tn Ag, PSMA, ROR1, FLT3, TAG72, CD38, CD44v6, CEA, EPCAM, B7H3, KIT, IL-13Ra2, Mesothelin, IL-11Ra, PSCA, PRSS21, VEGFR2, LewisY, CD24, PDGFR-beta, SSEA-4, CD20, Folate receptor alpha, ERBB2 (Her2/neu), MUC1, EGFR, NCAM, Prostase, PAP, ELF2M, Ephrin B2, FAP, IGF-I receptor, CAIX, LMP2, gp100, bcr-abl, tyrosinase, EphA2, Fucosyl GM1, sLe, GM3, TGS5, HMWMAA, o-acetyl-GD2, Folate receptor beta, TEM1/CD248, TEM7R, CLDN6, TSHR, GPRC5D, CXORF61, CD97, CD179a, ALK, Polysialic acid, PLAC1, GloboH, NY-BR-1, UPK2, HAVCR1, ADRB3, PANX3, GPR20, LY6K, OR51E2, TARP, WT1, NY-ESO-1, LAGE-1a, MAGE-A1, MAGE A1, ETV6-AML, sperm protein 17, XAGE1, Tie 2, MAD-CT-1, MAD-CT-2, Fos-related antigen 1, p53, p53 mutant, prostein, survivin and telomerase, PCTA-1/Galectin 8, MelanA/MART1, Ras mutant, hTERT, sarcoma translocation breakpoints, ML-IAP, ERG (TMPRSS2 ETS fusion gene), NA17, PAX3, Androgen receptor, Cyclin B1, MYCN, RhoC, TRP-2, CYP1B1, BORIS, SART3, PAX5, OY-TES1, LCK, AKAP-4, SSX2, RAGE-1, human telomerase reverse transcriptase, RU1, RU2, legumain, HPV E6, E7, intestinal carboxyl esterase, mut hsp70-2, CD79a, CD79b, CD72, LAIR1, FCAR, LILRA2, CD300LF, CLEC12A, BST2, EMR2, LY75, GPC3, FCRL5, or IGLL1.

14. The method of any one of claims 1-13, wherein the first and second CAR molecules are each independently chosen from a CD19 CAR, a BCMA CAR, a CD33 CAR, a CLL-1 CAR, EGFRvIII CAR, a GFR alpha 4 CAR, an ROR1 CAR, a CD20 CAR, a CD22 CAR, a CD123 CAR, a CD10 CAR, a CD34 CAR, a FLT-3 CAR, a CD79b CAR, a CD179b CAR, a mesothelin CAR or a CD79a CAR, or any combination thereof.

15. A method of treating a cancer, or providing anti-tumor immunity, in a subject, comprising administering to the subject an expanded and/or activated immune cell population

made according to the method of any one or more of claims 1-14, alone or in combination with an additional therapy, thereby treating or providing anti-tumor immunity to the subject.

16. Use of an expanded and/or activated immune cell population that expresses a first and/or second CAR molecule made according to the method of any one or more of claims 1-14 in the manufacture of a medicament for treating, or providing anti-tumor immunity to, a subject having a cancer, wherein said medicament is administered to the subject alone or in combination with an additional therapy.

17. A method of treating, or providing anti-tumor immunity to, a subject having a cancer, comprising:

administering to the subject an effective amount of an immune cell population expressing a second CAR molecule, wherein the immune cell population was previously obtained by expanding and/or activating *in vitro* or *ex vivo* an immune cell population transiently expressing a first CAR molecule, said first CAR molecule comprising an antigen binding domain of an antibody molecule.

18. The method of claim 17, wherein the *in vitro* or *ex vivo* expansion and/or activation of the immune cell population comprises contacting said immune cell population with a ligand of the first CAR molecule chosen from a cognate antigen molecule, or an anti-antigen idiotypic antibody against the first CAR binding domain.

19. The method of claim 18, wherein the ligand of the first CAR molecule is immobilized onto a non-cellular substrate.

20. The method or use of any one of claims 15-19, wherein:

(a) the second CAR-expressing cell population comprises a nucleic acid encoding the second CAR molecule selected from the group consisting of a DNA, a RNA, a plasmid, a lentivirus vector, adenoviral vector, or a retrovirus vector;

(b) the first and second CAR molecules are directed to the same or different cancer associated antigen; or

(c) the first and second CAR molecules are the same CAR molecule, or different CAR molecules.

21. The method or use of claim 20, wherein:

(a) the cancer associated antigen is chosen from CD19, CD123, CD22, CD30, CD171, CS-1, CLL-1 (CLECL1), CD33, EGFRvIII , GD2, GD3, BCMA, Tn Ag, PSMA, ROR1, FLT3, TAG72, CD38, CD44v6, CEA, EPCAM, B7H3, KIT, IL-13Ra2, Mesothelin, IL-11Ra, PSCA, PRSS21, VEGFR2, LewisY, CD24, PDGFR-beta, SSEA-4, CD20, Folate receptor alpha, ERBB2 (Her2/neu), MUC1, EGFR, NCAM, Prostase, PAP, ELF2M, Ephrin B2, FAP, IGF-I receptor, CAIX, LMP2, gp100, bcr-abl, tyrosinase, EphA2, Fucosyl GM1, sLe, GM3, TGS5, HMWMAA, o-acetyl-GD2, Folate receptor beta, TEM1/CD248, TEM7R, CLDN6, TSHR, GPRC5D, CXORF61, CD97, CD179a, ALK, Polysialic acid, PLAC1, GloboH, NY-BR-1, UPK2, HAVCR1, ADRB3, PANX3, GPR20, LY6K, OR51E2, TARP, WT1, NY-ESO-1, LAGE-1a, MAGE-A1, MAGE A1, ETV6-AML, sperm protein 17, XAGE1, Tie 2, MAD-CT-1, MAD-CT-2, Fos-related antigen 1, p53, p53 mutant, prostein, survivin and telomerase, PCTA-1/Galectin 8, MelanA/MART1, Ras mutant, hTERT, sarcoma translocation breakpoints, ML-IAP, ERG (TMPRSS2 ETS fusion gene), NA17, PAX3, Androgen receptor, Cyclin B1, MYCN, RhoC, TRP-2, CYP1B1, BORIS, SART3, PAX5, OY-TES1, LCK, AKAP-4, SSX2, RAGE-1, human telomerase reverse transcriptase, RU1, RU2, legumain, HPV E6, E7, intestinal carboxyl esterase, mut hsp70-2, CD79a, CD79b, CD72, LAIR1, FCAR, LILRA2, CD300LF, CLEC12A, BST2, EMR2, LY75, GPC3, FCRL5, or IGLL1;

(b) the first and/or second CAR molecules are each independently chosen from a CD19 CAR, a BCMA CAR, a CD33 CAR, a CLL-1 CAR, EGFRvIII CAR, a GFR alpha 4 CAR, an ROR1 CAR, a CD20 CAR, a CD22 CAR, a CD123 CAR, a CD10 CAR, a CD34 CAR, a FLT-3 CAR, a CD79b CAR, a CD179b CAR, a mesothelin CAR or a CD79a CAR, or any combination thereof; or

(c) the first and second CAR molecules are mesothelin CAR and CD19 CAR molecules, respectively.

22. The method or use of any one of claims 1-21, wherein:

(a) the first and/or second CAR-expressing immune effector cell comprises a CD19 CAR, a BCMA CAR, a CD33 CAR, a CLL-1 CAR, EGFRvIII CAR, a GFR alpha 4 CAR, an ROR1 CAR, a CD19 CAR, a CD20 CAR, a CD22 CAR, a CD123 CAR, a CD10 CAR, a CD34 CAR, a FLT-3 CAR, a CD79b CAR, a CD179b CAR, a mesothelin CAR or a CD79a CAR;

(b) the first and/or second CAR-expressing immune effector cell comprises a CD19 CAR;

(c) the CD19 CAR comprises a sequence according to any of SEQ ID NOs: 39-102 or 107-12;

(d) the CD19 CAR comprises the amino acid sequence of the antigen binding domain of CTL019; and/or

(e) the CD19 CAR comprises the amino acid sequence of CTL019, with or without the signal sequence, or an amino acid sequence substantially identical thereto.

23. The method or use of any one of claims 1-22, wherein:

(a) at least 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96 %, 97%, 98%, 99% or 100% of the immune effector cells in the immune effector cell population express the first and/or the second CAR molecule on their cell surface;

(b) the subject from which immune effector cells are acquired and/or the subject to be treated, is a human cancer patient;

(c) the cancer is a hematological cancer chosen from one or more of: a B-cell acute lymphocytic leukemia (B-ALL), T-cell acute lymphocytic leukemia (T-ALL), acute lymphocytic leukemia (ALL), chronic myelogenous leukemia (CML), chronic lymphocytic leukemia (CLL), B cell promyelocytic leukemia, blastic plasmacytoid dendritic cell neoplasm, Burkitt's lymphoma, diffuse large B cell lymphoma, follicular lymphoma, hairy cell leukemia, small cell- or a large cell-follicular lymphoma, malignant lymphoproliferative conditions, MALT lymphoma, mantle cell lymphoma (MCL), marginal zone lymphoma, multiple myeloma, myelodysplasia and myelodysplastic syndrome, non-Hodgkin's lymphoma (NHL), Hodgkin's lymphoma (HL), plasmablastic lymphoma, plasmacytoid dendritic cell neoplasm, and Waldenstrom macroglobulinemia;

(d) the population of immune effector cells are from a subject having a haematological cancer chosen from a leukemia or a lymphoma;

(e) the population of cells is expanded in the presence a cytokine;

(f) the method further comprises removing T regulatory cells from the immune cell population, to thereby provide a population of T regulatory-depleted cells;

(g) the acquired immune effector cell population are cells of a subject having a CD25 expressing cancer;

(h) the acquired immune effector cell population has been selected based upon the expression of one or more markers; and/or

(i) the population of the immune cells is cryopreserved after the appropriate expansion period.

24. The method or use of claim 23, wherein:

(a) the leukemia is a chronic lymphocytic leukemia (CLL) or an acute lymphocytic leukemia (ALL);

(b) the lymphoma is a mantle cell lymphoma (MCL);

(c) the cytokine is IL-2 or IL-15 and IL-7;

(d) population of T regulatory-depleted cells contains less than 30%, 25%, 20%, 15%, 10%, 5%, 4%, 3%, 2%, 1% of CD25+ cells; and/or

(e) the CD25-expressing cancer is a chronic lymphocytic leukemia (CLL).

25. The method or use of claim 24, wherein the population of T regulatory-depleted cells contains less than 30%, 25%, 20%, 15%, 10%, 5%, 4%, 3%, 2%, 1% of the leukemia cells.

26. The method or use of any one of claims 1-25, further comprising:

(a) removing cells from the immune effector cell population which express a tumor antigen, to thereby provide a population of T regulatory-depleted and tumor antigen depleted cells that are suitable for expression of a CAR; and/or

(b) removing cells from the acquired immune effector cell population which express a checkpoint inhibitor to thereby provide a population of T regulatory-depleted cells and checkpoint inhibitor depleted cells.

27. The method or use of claim 26, wherein the checkpoint inhibitor is one or more of PD-1, LAG-3, and TIM-3.

28. The method or use of claim 27, wherein:

(a) the one or more markers are one or more of CD3, CD28, CD4, CD8, CD45RA, and CD45RO; and/or

(b) the provided population of immune effector cells are CD3+ and/or CD28+.

29. The method or use of any one of claims 1-28, further comprising:

(a) activating the population of T regulatory-depleted cells; and/or

(b) transducing a cell from the population of T regulatory-depleted cells with a vector comprising a nucleic acid encoding a CAR.

30. The method or use of claim 29, further comprising expanding the population of T regulatory-depleted cells.

31. The method or use of any one of claims 1-30 further comprising contacting the population of immune effector cells with a nucleic acid encoding a telomerase subunit.

32. A reaction mixture comprising:

(a) a population of immune effector cells, wherein a plurality of the cells of the population comprise a nucleic acid encoding a first CAR molecule and a nucleic acid encoding a second CAR molecule, wherein nucleic acid encoding the first CAR molecule is not integrated into the cellular genome, further wherein the nucleic acid encoding the first CAR molecule is an in vitro transcribed RNA or a synthetic RNA and the nucleic acid encoding the second CAR molecule is integrated into the genome of the cells; and

(b) a ligand of the first CAR molecule chosen from a cognate antigen molecule or an anti-antigen idiotypic antibody molecule.

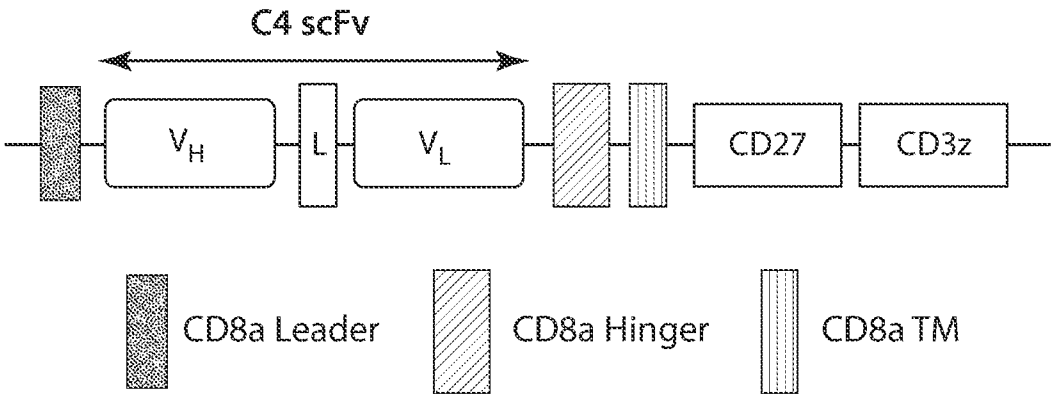

C4 scFv
V_H
L
V_L
CD27
CD3z
CD8a Leader
CD8a Hinger
CD8a TM

FIG. 1A

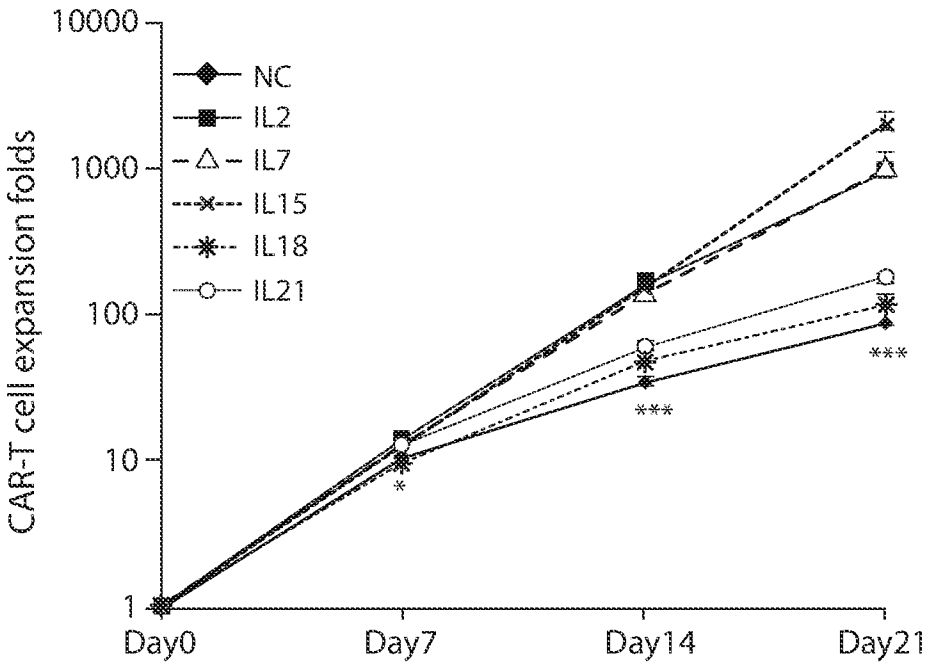

10000
1000
100
10
1
CAR-T cell expansion folds
NC
IL2
IL7
IL15
IL18
IL21
*
***
***
Day0
Day7
Day14
Day21

FIG. 1B

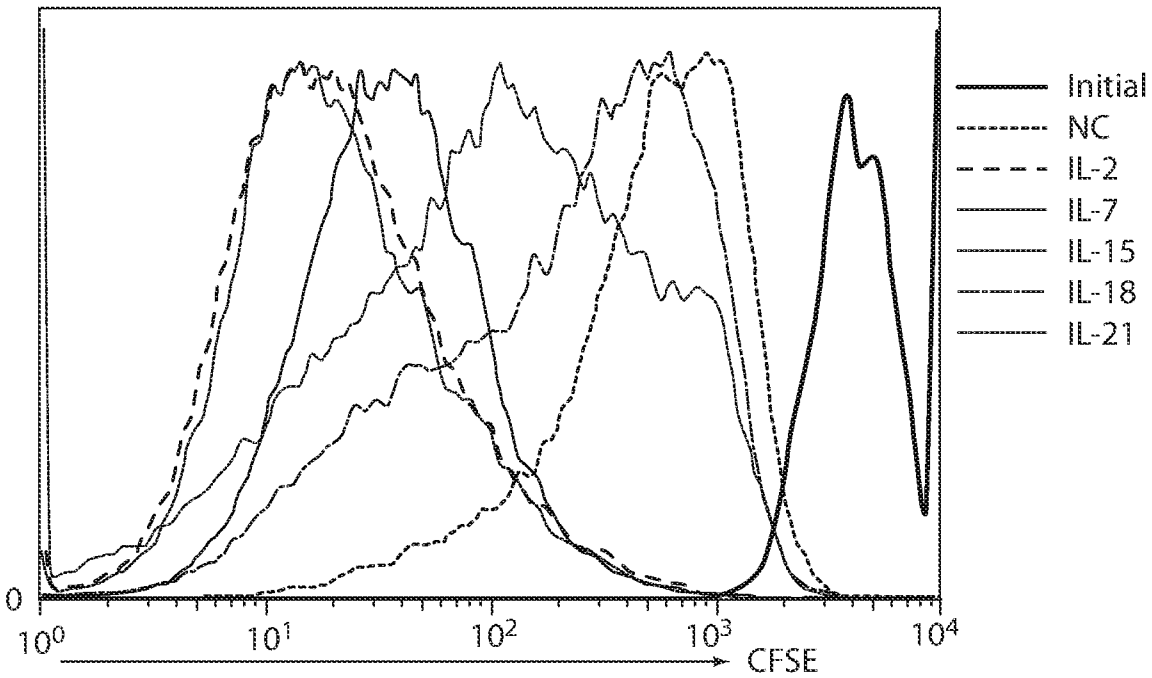

Initial
NC
IL-2
IL-7
IL-15
IL-18
IL-21
0
10^0
10^1
10^2
10^3
10^4
CFSE

FIG. 1C

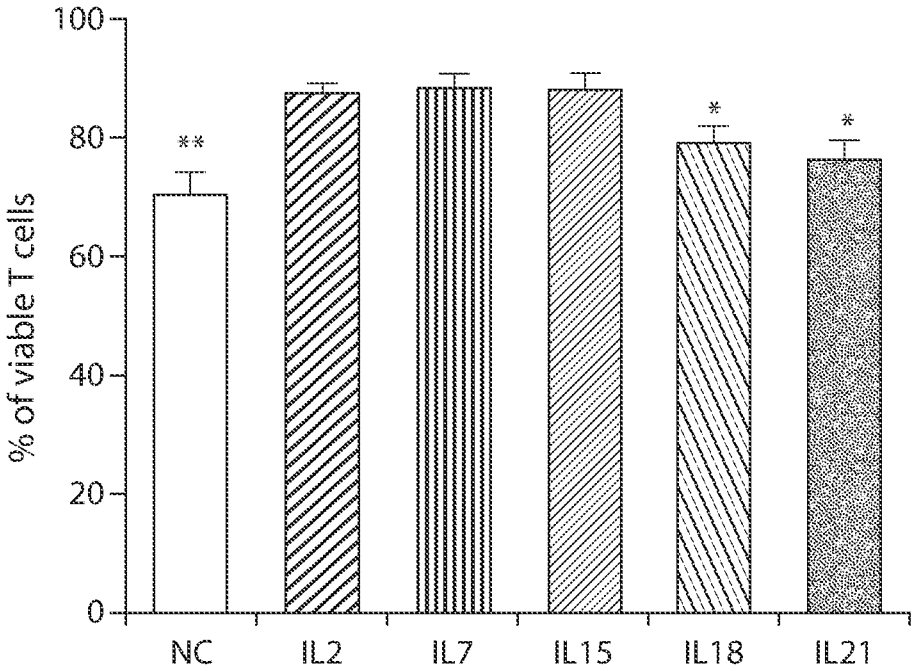

100
80
60
40
20
0
% of viable T cells
**
*
*
NC
IL2
IL7
IL15
IL18
IL21

FIG. 1D

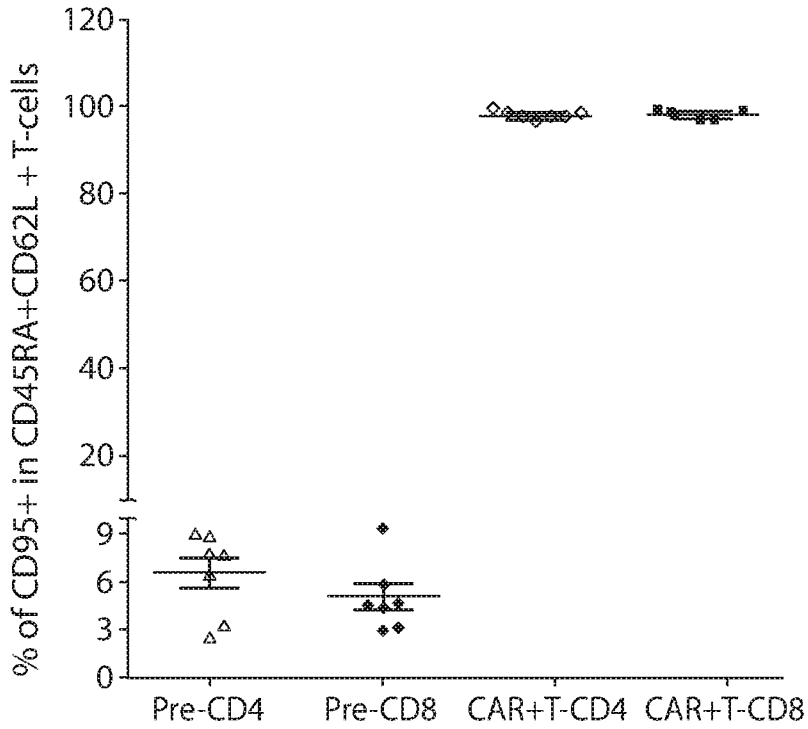

% of CD95+ in CD45RA+CD62L + T-cells
120
100
80
60
40
20
9
6
3
0
Pre-CD4
Pre-CD8
CAR+T-CD4
CAR+T-CD8

FIG. 2A

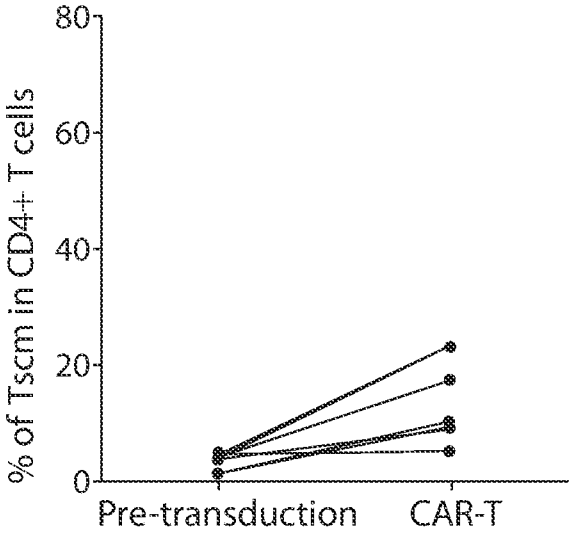


FIG. 2B

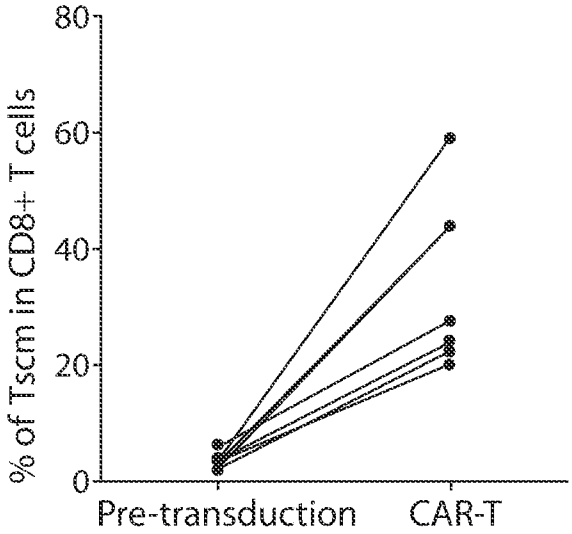


FIG. 2C

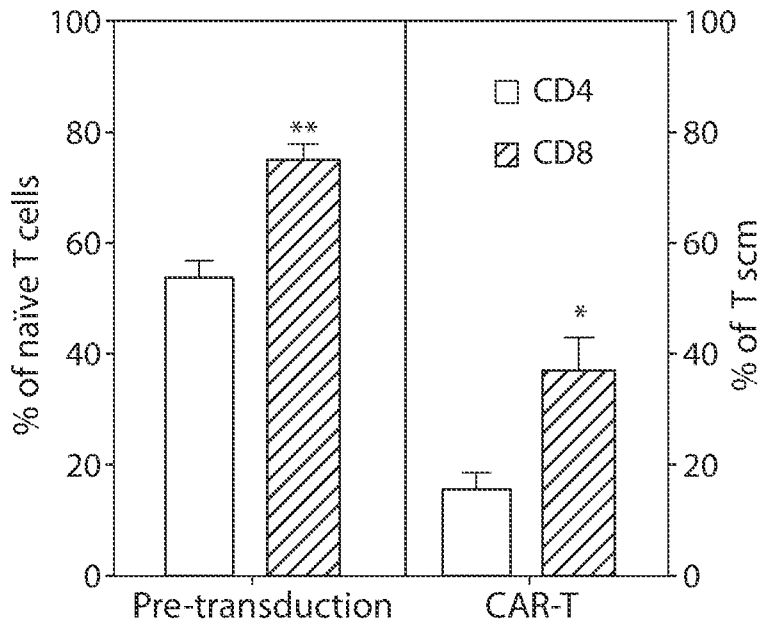


FIG. 2D

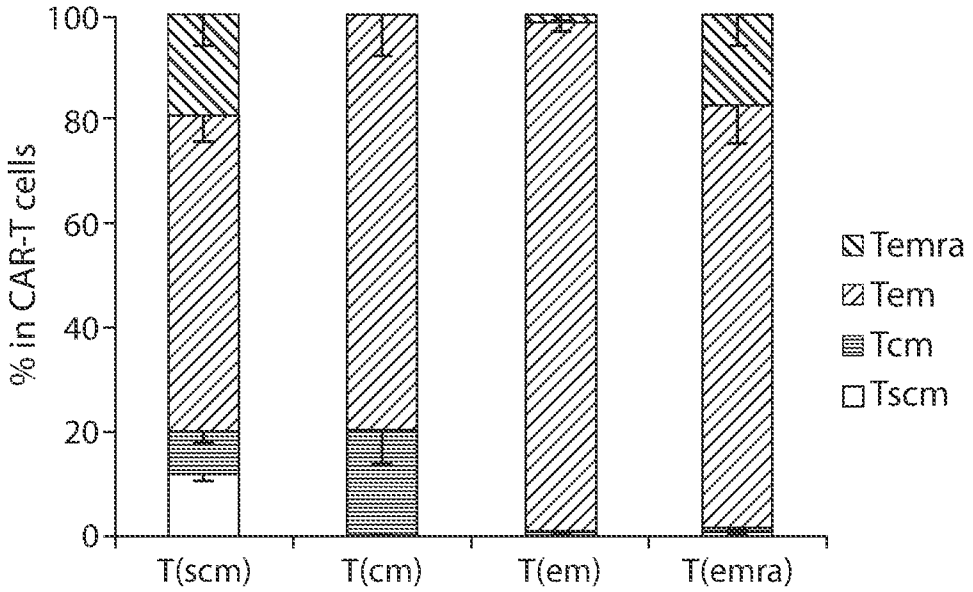

100
80
60
40
20
0
% in CAR-T cells
T(scm)
T(cm)
T(em)
T(emra)
Temra
Tem
Tcm
Tscm

FIG. 2E

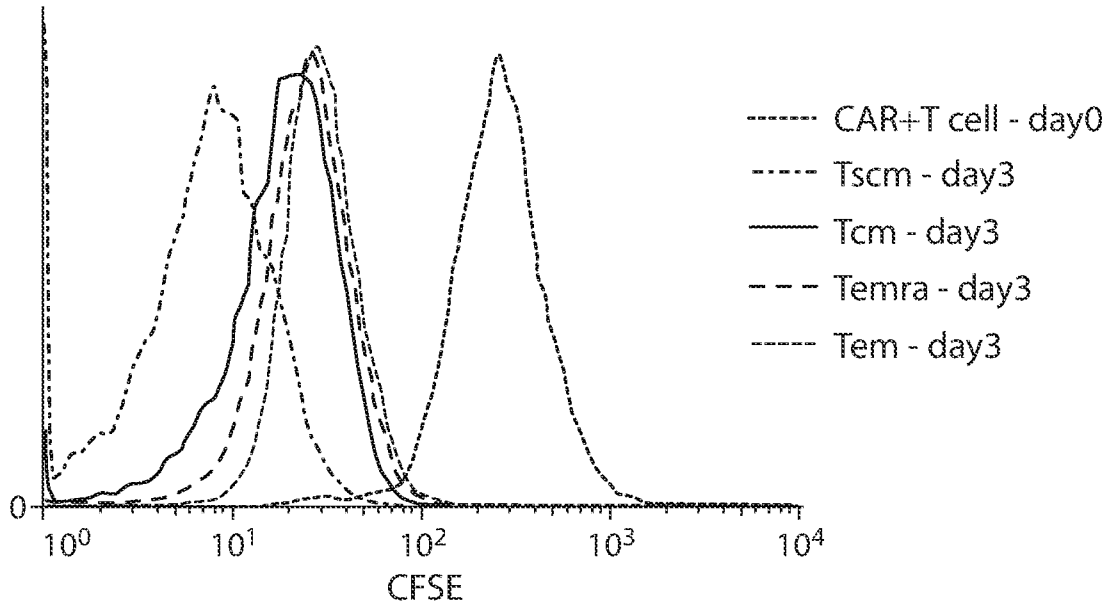

CAR+T cell - day0
Tscm - day3
Tcm - day3
Temra - day3
Tem - day3
0
10^0
10^1
10^2
10^3
10^4
CFSE

FIG. 2F

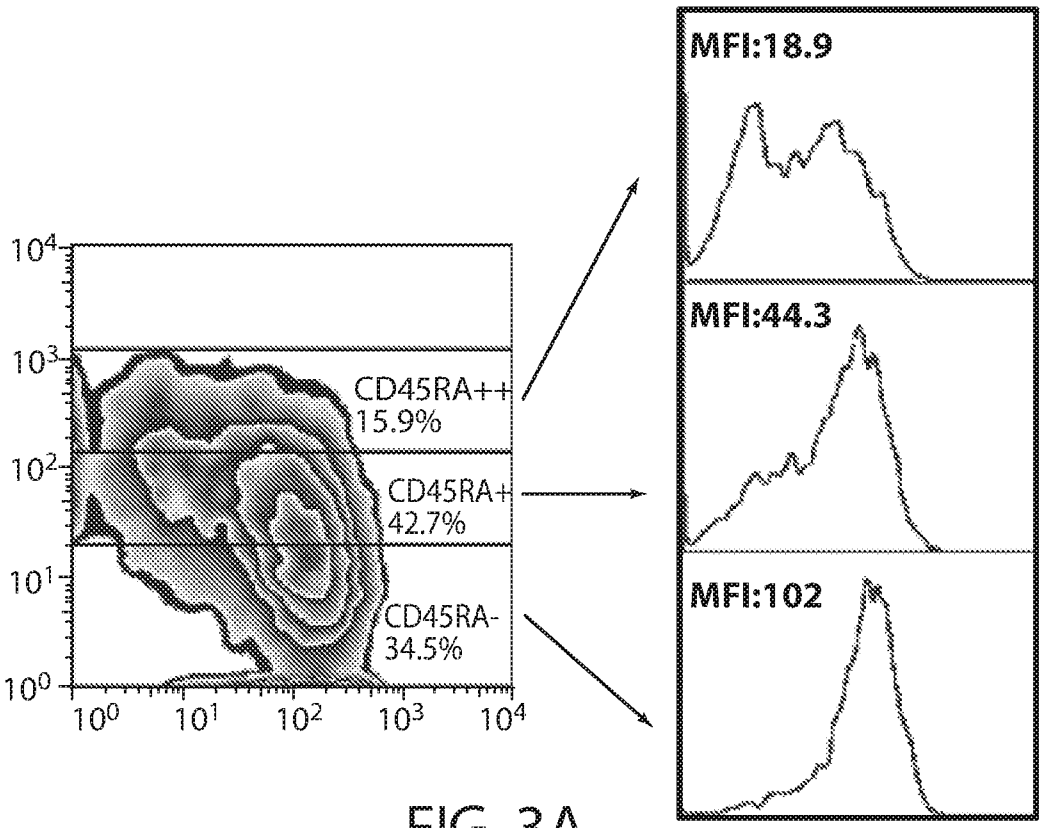

MFI:18.9
MFI:44.3
MFI:102
CD45RA++
15.9%
CD45RA+
42.7%
CD45RA-
34.5%
10^4
10^3
10^2
10^1
10^0
10^0 10^1 10^2 10^3 10^4

FIG. 3A

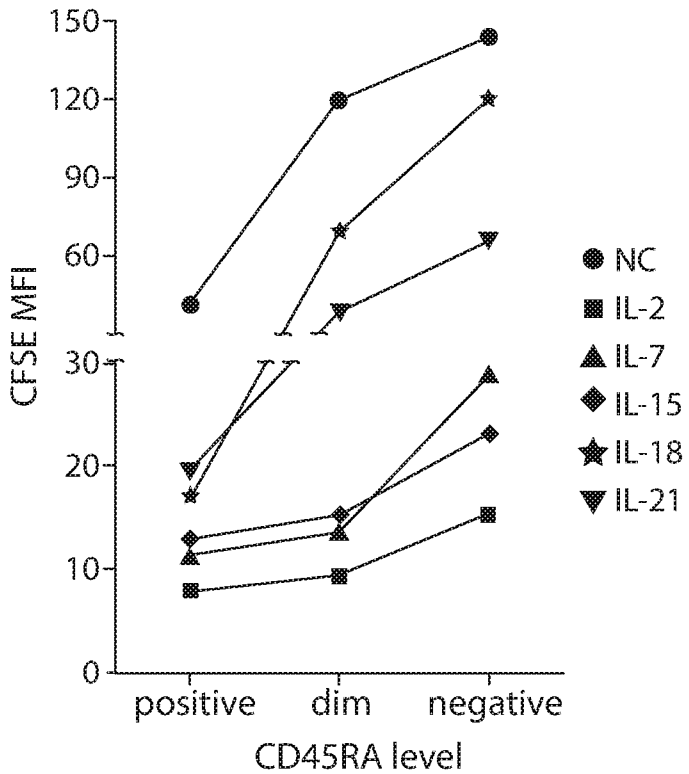

150
120
90
60
30
20
10
0
CFSE MFI
positive
dim
negative
CD45RA level
NC
IL-2
IL-7
IL-15
IL-18
IL-21

FIG. 3B

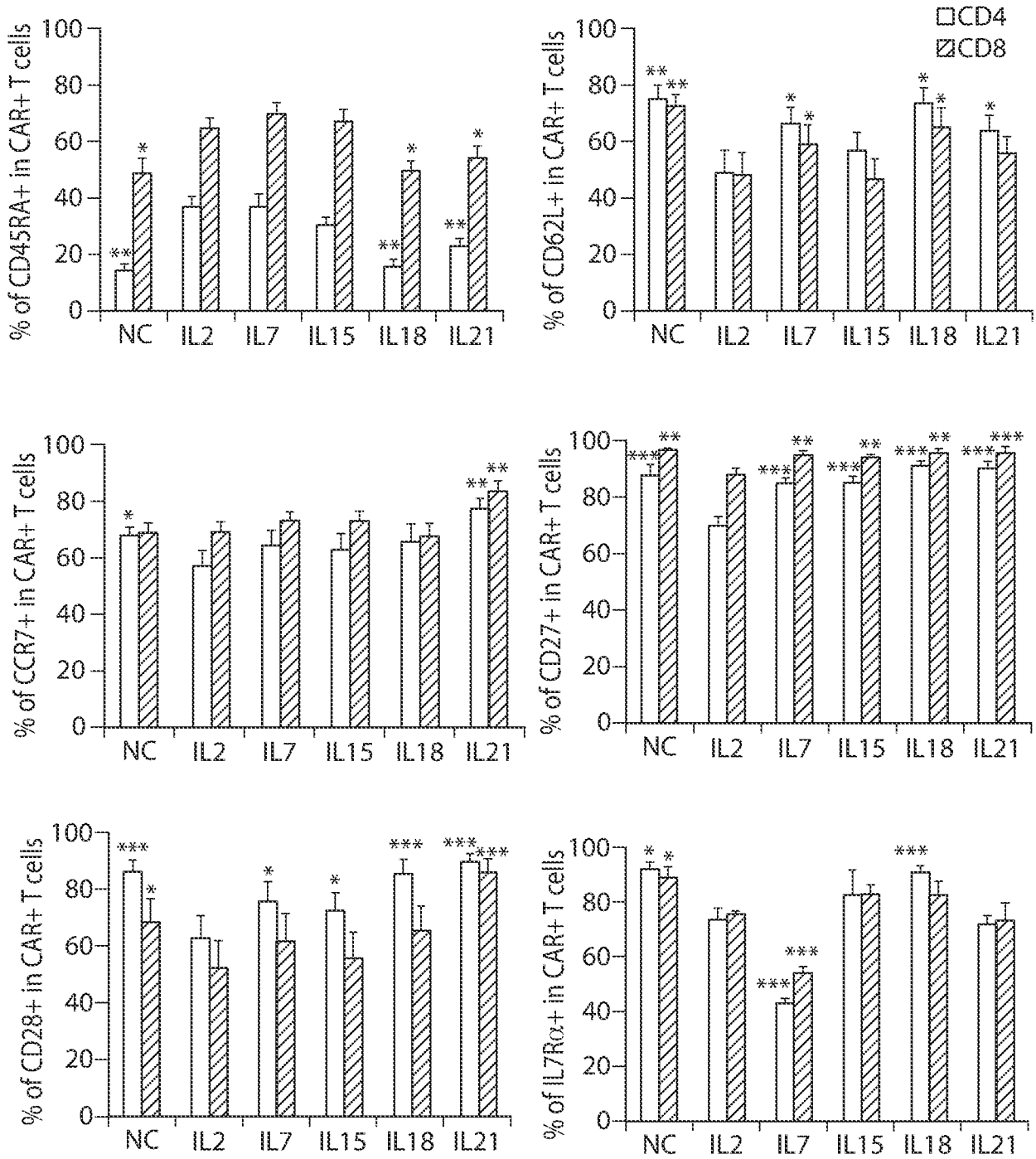

% of CD45RA+ in CAR+ T cells
% of CD62L+ in CAR+ T cells
% of CCR7+ in CAR+ T cells
% of CD27+ in CAR+ T cells
% of CD28+ in CAR+ T cells
% of IL7Rα+ in CAR+ T cells
CD4
CD8
NC
IL2
IL7
IL15
IL18
IL21

FIG. 4

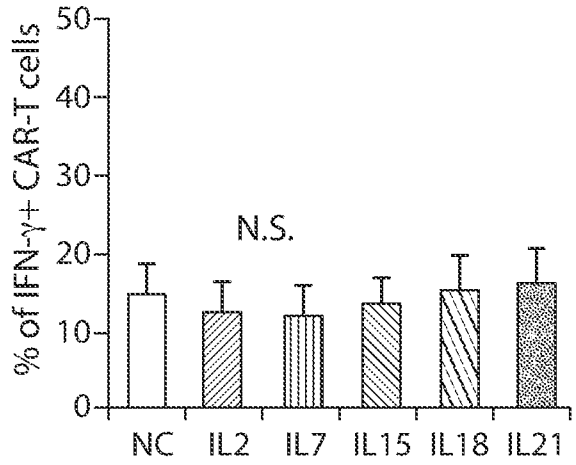


FIG. 5A

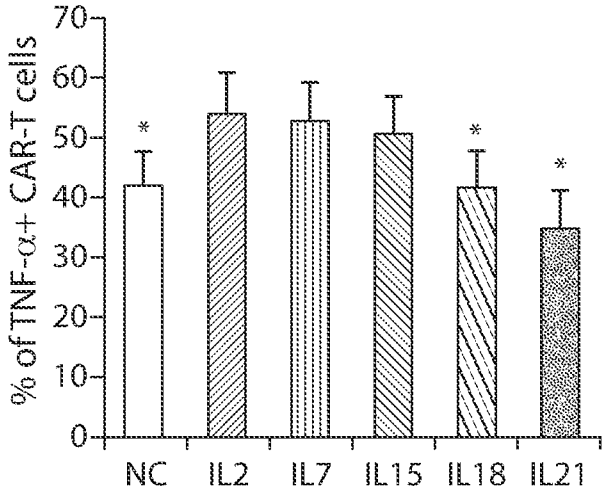


FIG. 5B

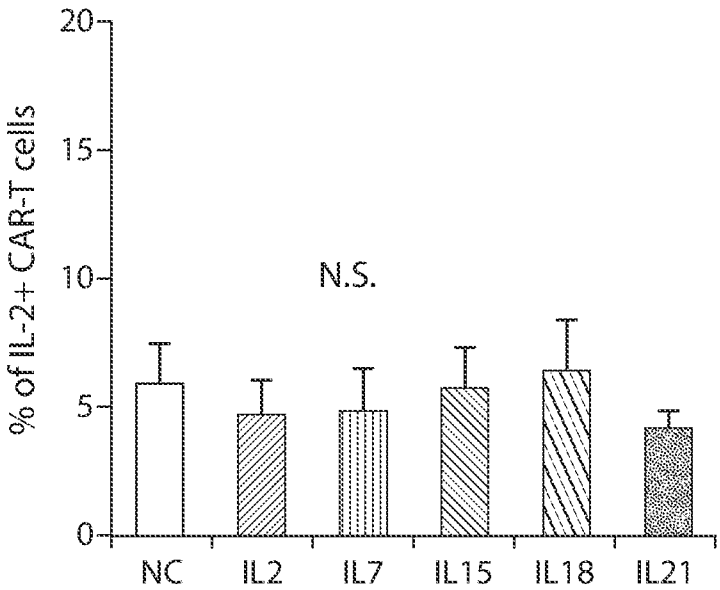


FIG. 5C

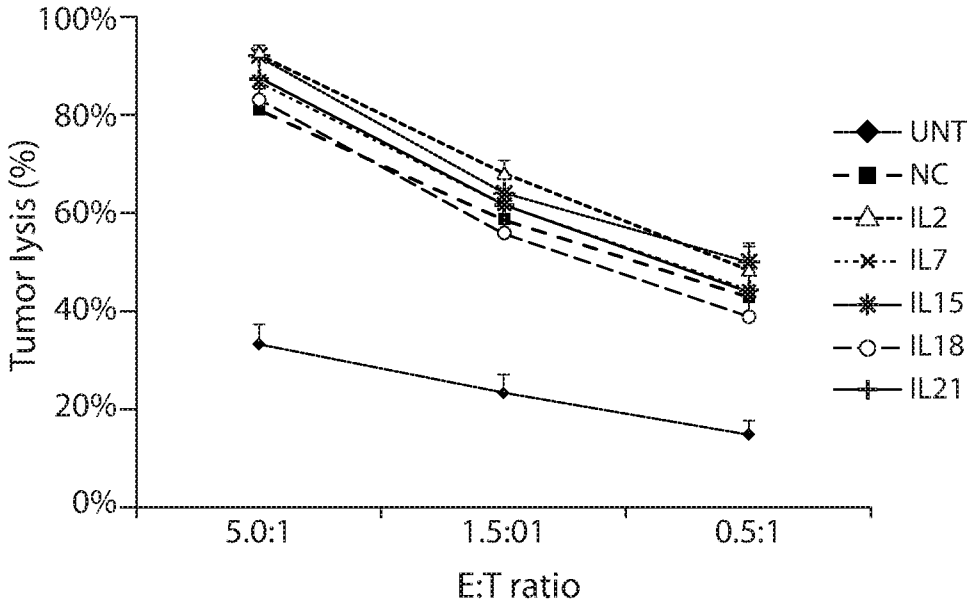

100%
80%
60%
40%
20%
0%
Tumor lysis (%)
5.0:1
1.5:01
0.5:1
E:T ratio
UNT
NC
IL2
IL7
IL15
IL18
IL21

FIG. 5D

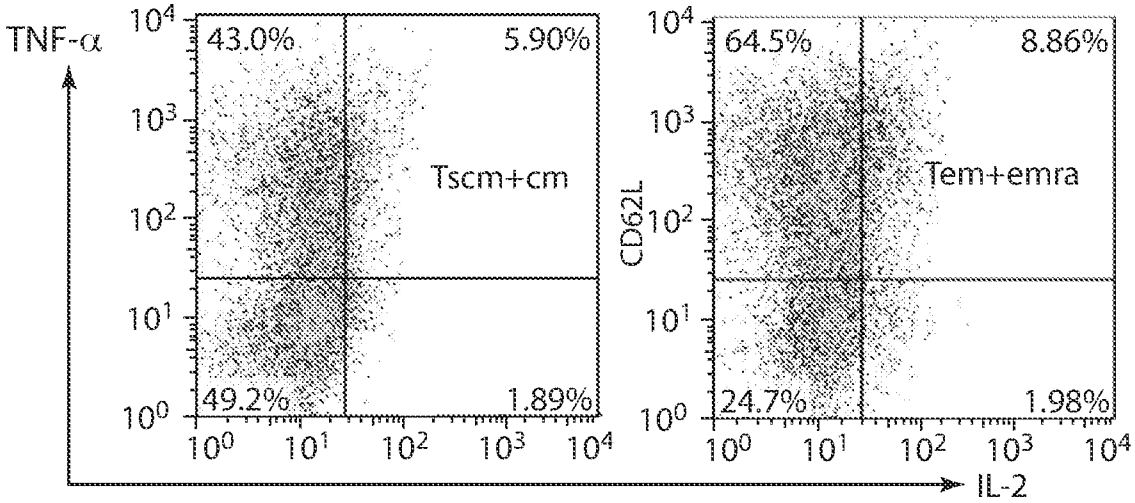


FIG. 6A

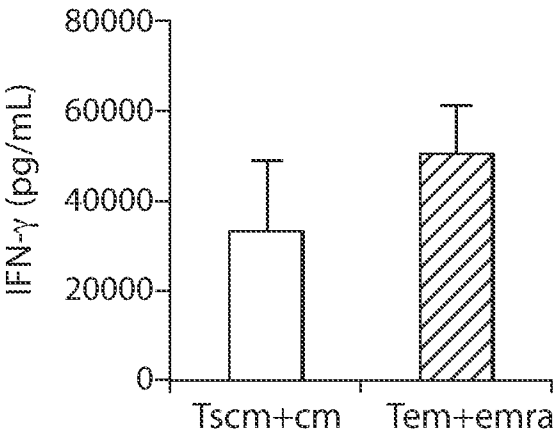


FIG. 6B

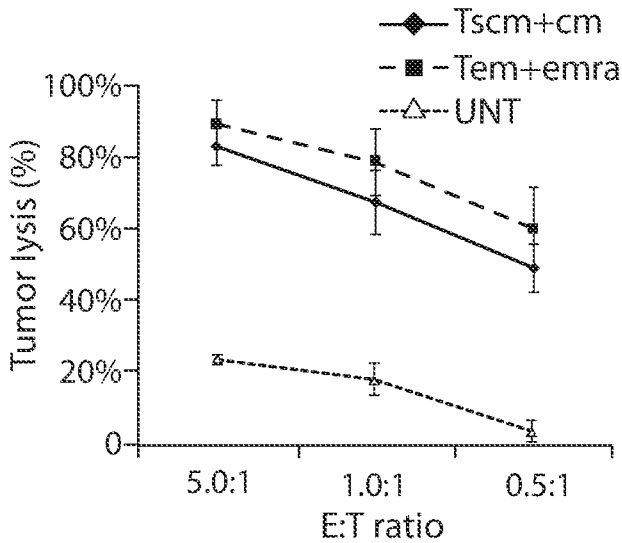


FIG. 6C

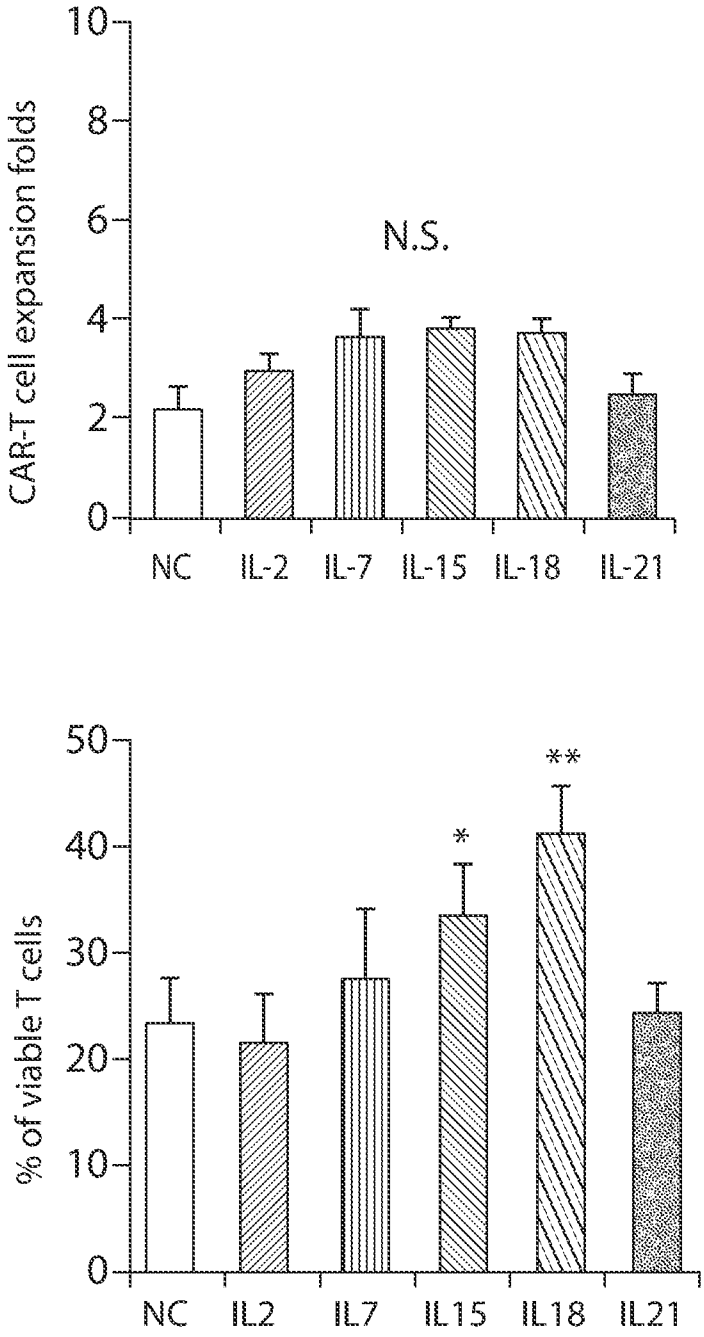

CAR-T cell expansion folds
10
8
6
4
2
0
N.S.
NC
IL-2
IL-7
IL-15
IL-18
IL-21
% of viable T cells
50
40
30
20
10
0
*
**
NC
IL2
IL7
IL15
IL18
IL21

FIG. 7A

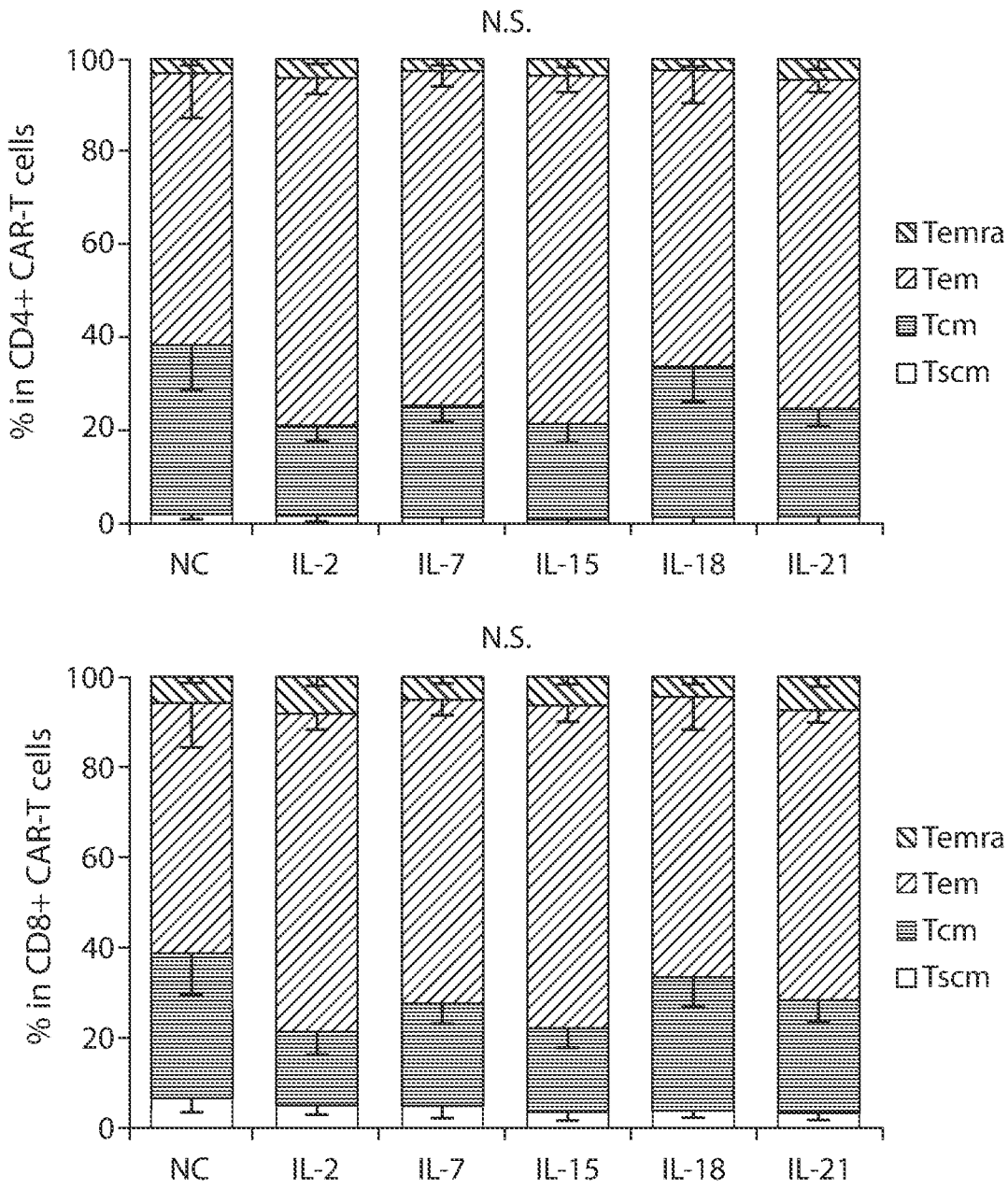

N.S.
% in CD4+ CAR-T cells
100
80
60
40
20
0
NC
IL-2
IL-7
IL-15
IL-18
IL-21
Temra
Tem
Tcm
Tscm
N.S.
% in CD8+ CAR-T cells
100
80
60
40
20
0
NC
IL-2
IL-7
IL-15
IL-18
IL-21
Temra
Tem
Tcm
Tscm

FIG. 7B

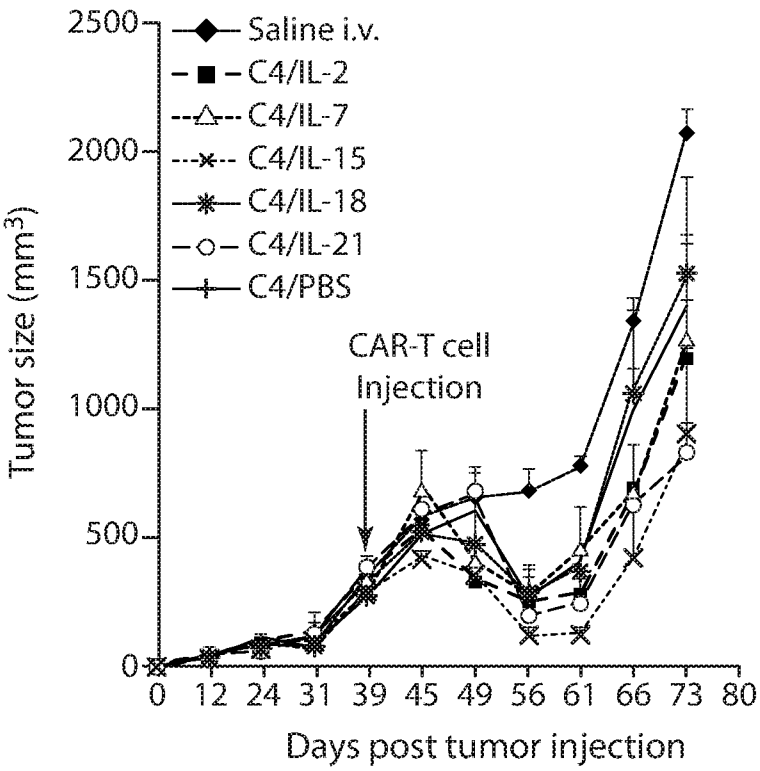

2500
2000
1500
1000
500
0
Tumor size (mm3)
Saline i.v.
C4/IL-2
C4/IL-7
C4/IL-15
C4/IL-18
C4/IL-21
C4/PBS
CAR-T cell Injection
0 12 24 31 39 45 49 56 61 66 73 80
Days post tumor injection

Fig. 8A

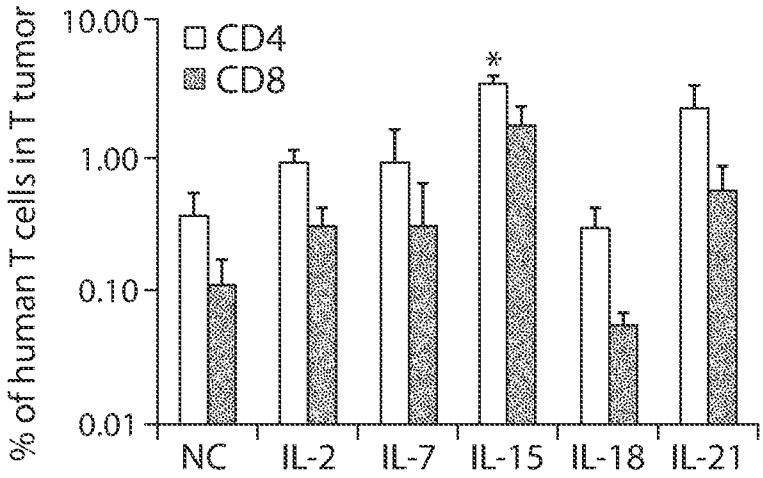

% of human T cells in T tumor
10.00
1.00
0.10
0.01
CD4
CD8
*
NC
IL-2
IL-7
IL-15
IL-18
IL-21

FIG. 8B

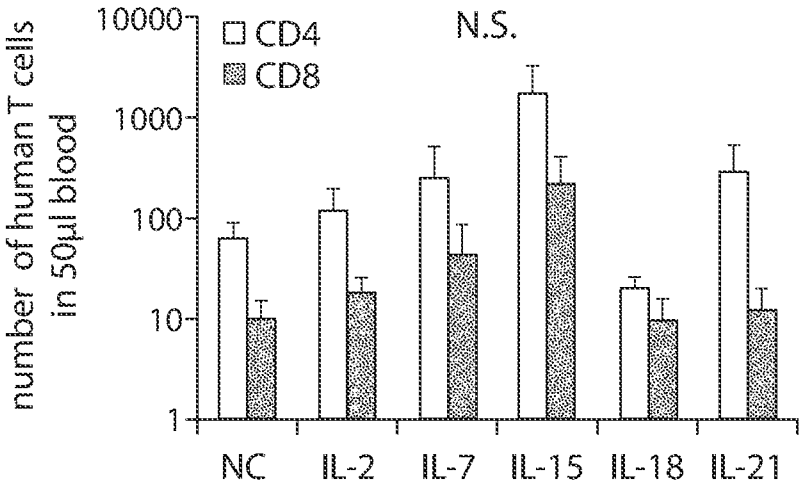

number of human T cells in 50µl blood
10000
1000
100
10
1
CD4
CD8
N.S.
NC
IL-2
IL-7
IL-15
IL-18
IL-21

FIG. 8C

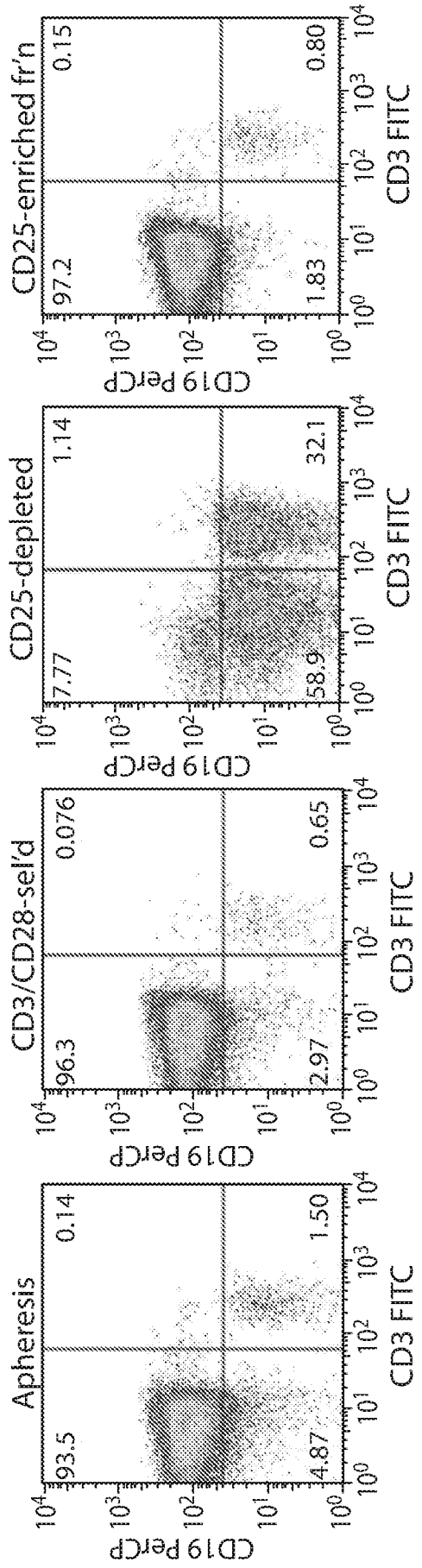

Apheresis
93.5
0.14
4.87
1.50
CD3/CD28-sel'd
96.3
0.076
2.97
0.65
CD25-depleted
7.77
1.14
58.9
32.1
CD25-enriched fr'n
97.2
0.15
1.83
0.80
CD19 PerCP
CD3 FITC

FIG. 9

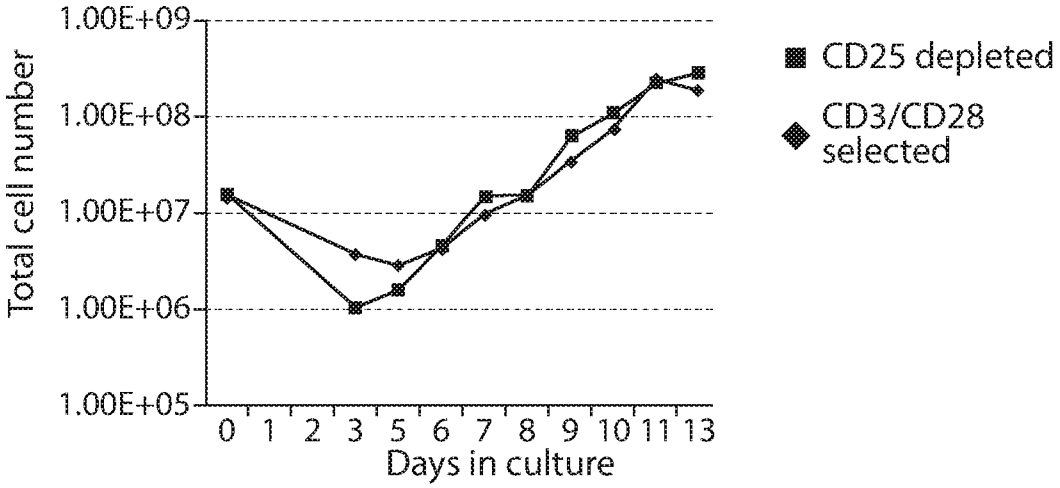


FIG. 10A

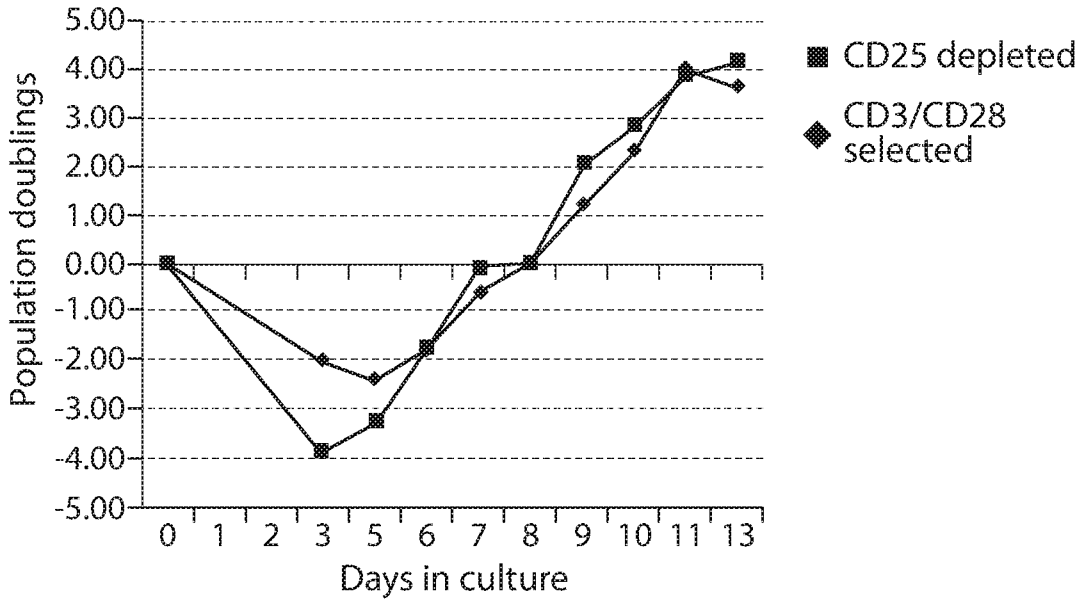


FIG. 10B

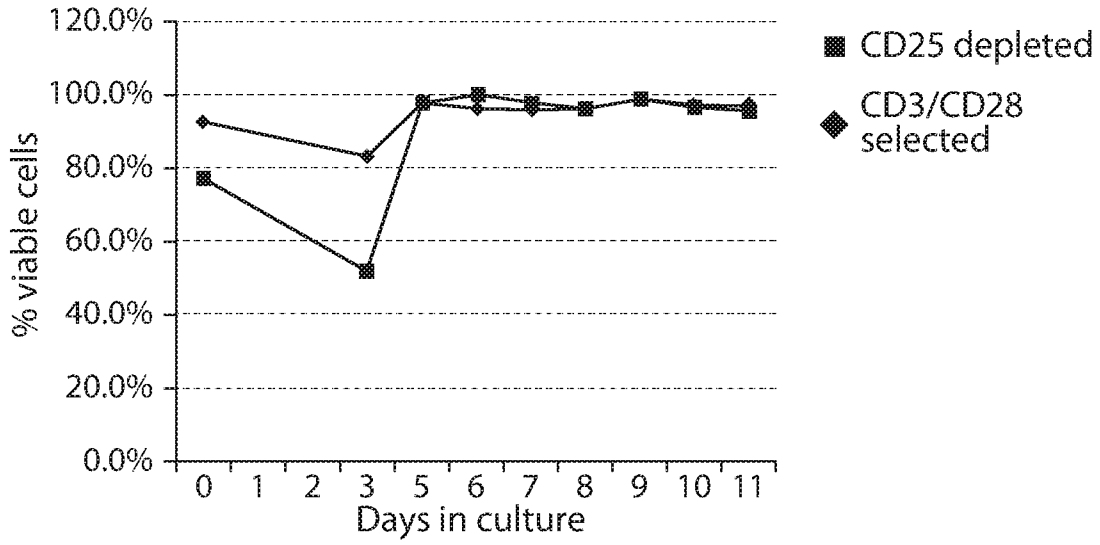


FIG. 10C

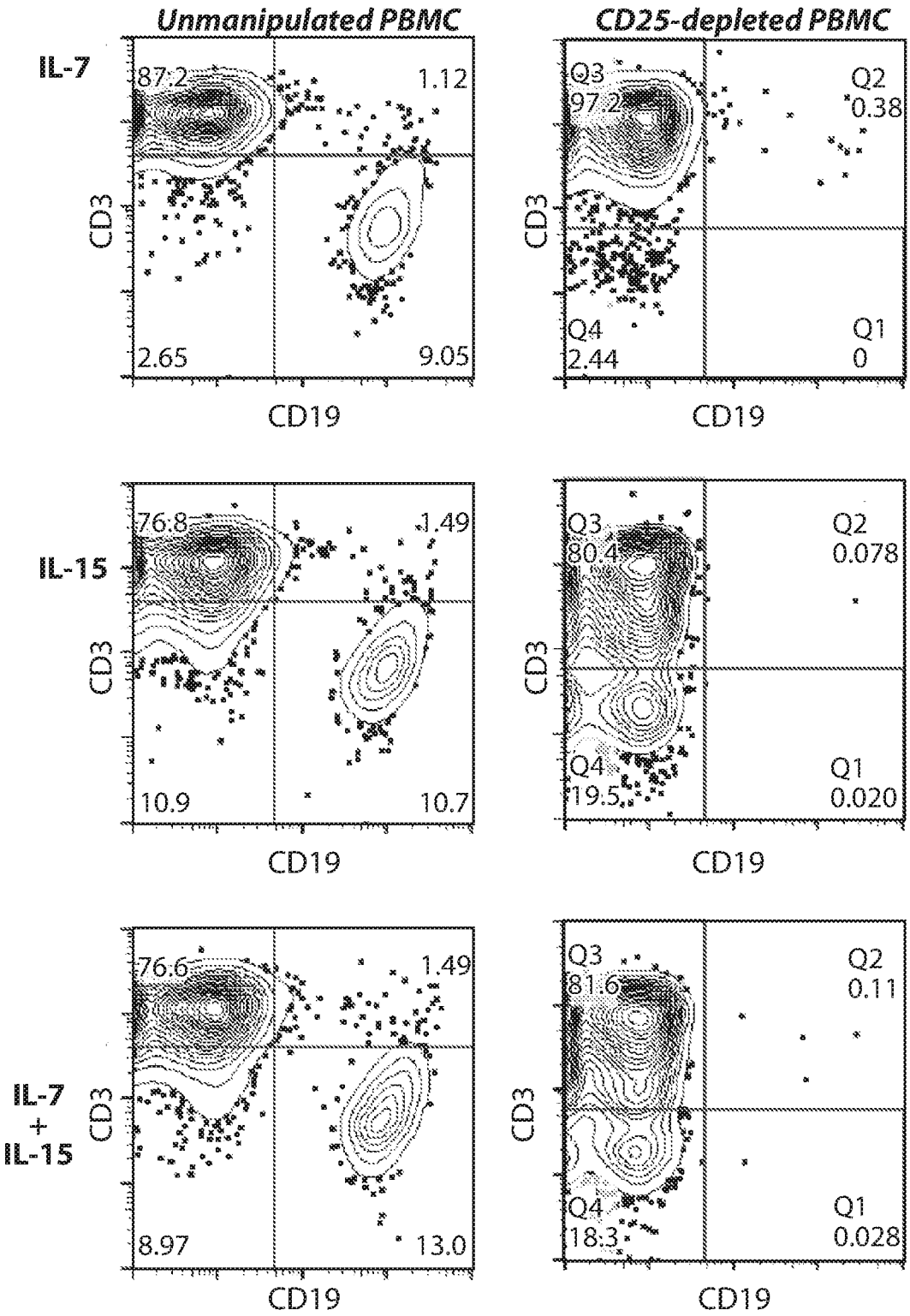

Unmanipulated PBMC
CD25-depleted PBMC
IL-7
87.2
1.12
2.65
9.05
Q3
97.2
Q2
0.38
Q4
2.44
Q1
0
IL-15
76.8
1.49
10.9
10.7
Q3
80.4
Q2
0.078
Q4
19.5
Q1
0.020
IL-7
+
IL-15
76.6
1.49
8.97
13.0
Q3
81.6
Q2
0.11
Q4
18.3
Q1
0.028
CD3
CD19

FIG. 11

ND447 PBMCs activated, transduced, de-beaded, and harvested at Day 5 and D9 for comparative performance in vitro and in vivo

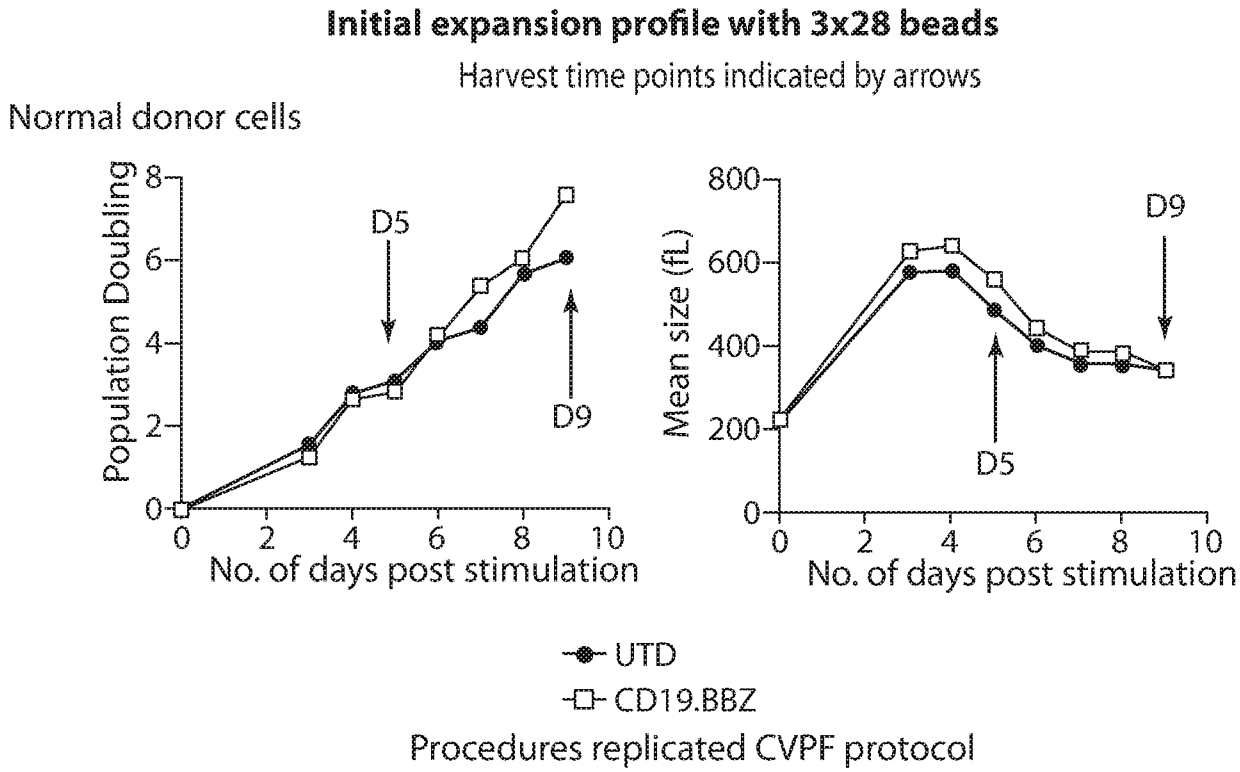


FIG. 12

There is no difference in CART19 cell killing from cells isolated at day 5 and day 9 from expansion

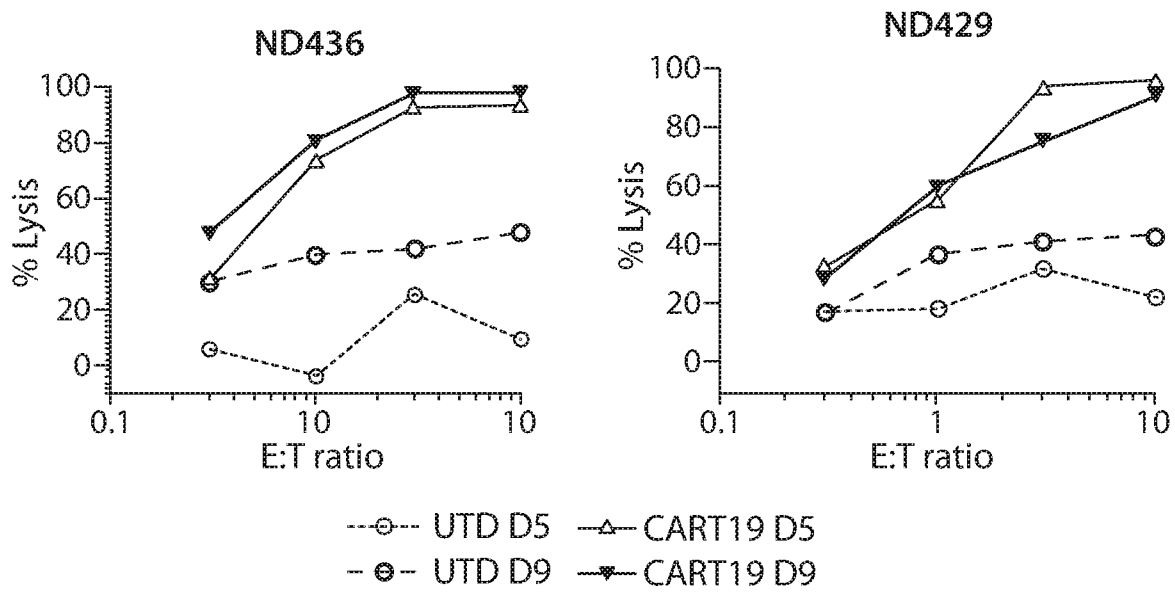


FIG. 13

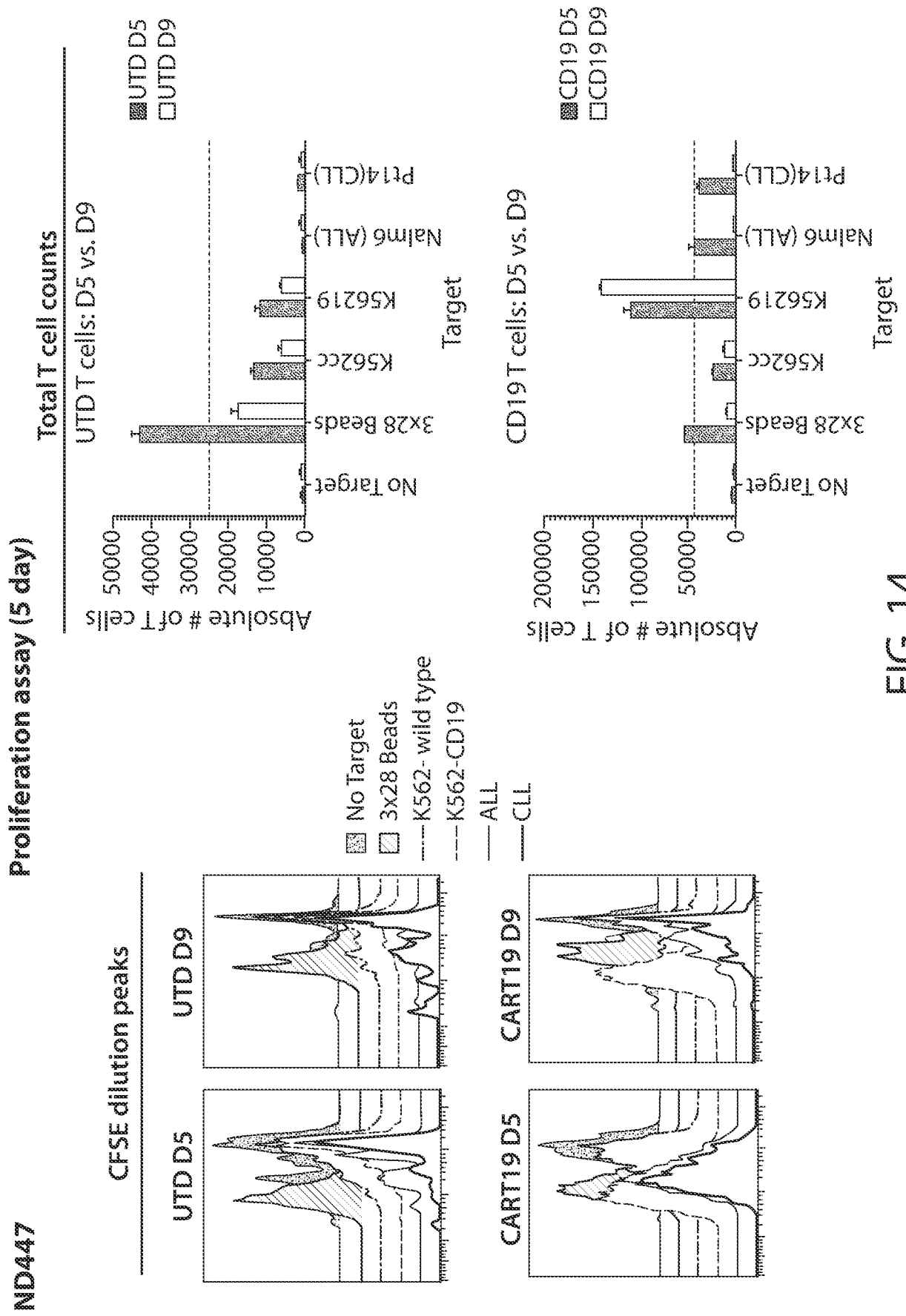

ND447
Proliferation assay (5 day)
CFSE dilution peaks
UTD D5
UTD D9
CART19 D5
CART19 D9
No Target
3x28 Beads
K562- wild type
K562-CD19
ALL
CLL
Total T cell counts
UTD T cells: D5 vs. D9
UTD D5
UTD D9
Absolute # of T cells
50000
40000
30000
20000
10000
0
No Target
3x28 Beads
K562cc
K56219
Nalm6 (ALL)
Pt14(CLL)
Target
CD19 T cells: D5 vs. D9
CD19 D5
CD19 D9
Absolute # of T cells
200000
150000
100000
50000
0
No Target
3x28 Beads
K562cc
K56219
Nalm6 (ALL)
Pt14(CLL)
Target

FIG. 14

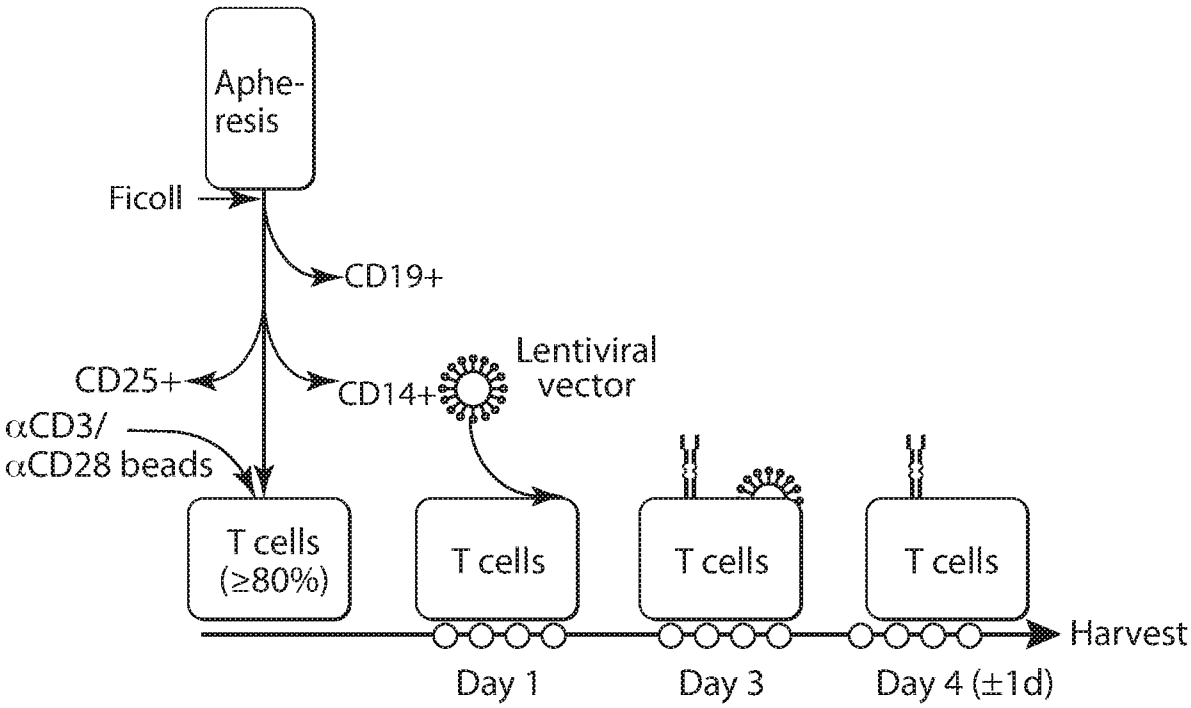

Aphe-
resis
Ficoll
CD19+
CD25+
CD14+
Lentiviral
vector
αCD3/
αCD28 beads
T cells
(≥80%)
T cells
T cells
T cells
Harvest
Day 1
Day 3
Day 4 (±1d)

FIG. 15

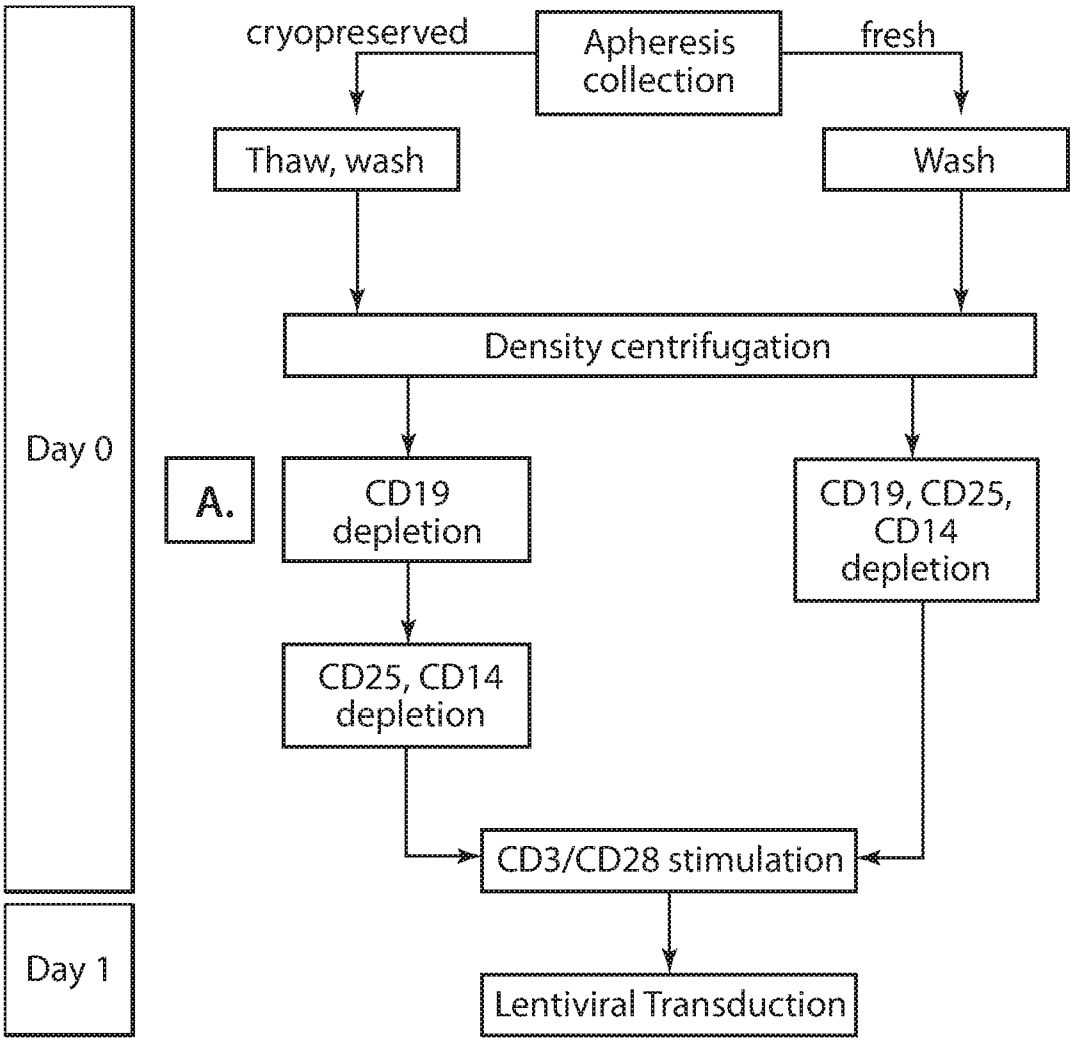

Day 0
Day 1
A.
cryopreserved
Apheresis collection
fresh
Thaw, wash
Wash
Density centrifugation
CD19 depletion
CD19, CD25, CD14 depletion
CD25, CD14 depletion
CD3/CD28 stimulation
Lentiviral Transduction

FIG. 16

Cells harvested on D5 proliferated better than cells harvested on D9 over 7 days of stimulation with K562s expressing CD19.

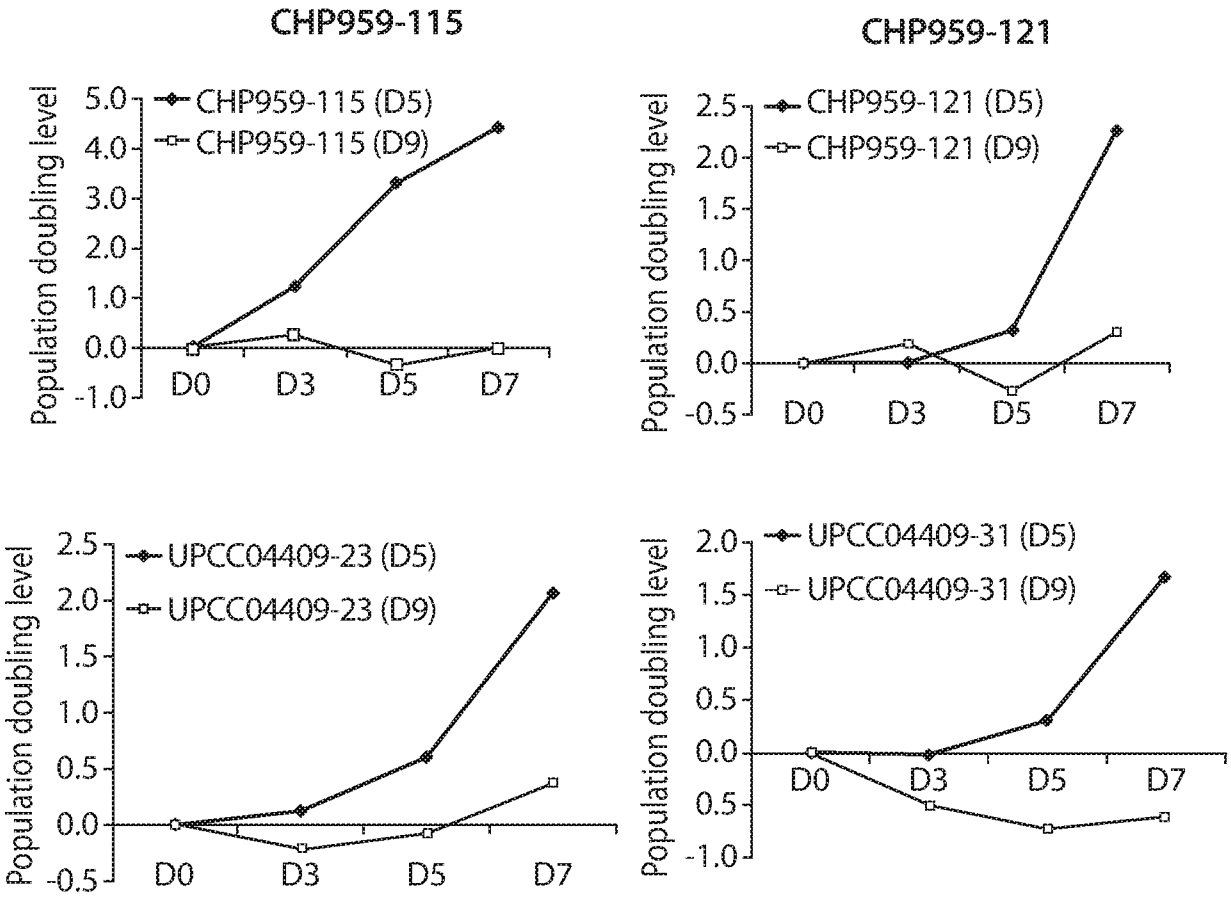


FIG. 17

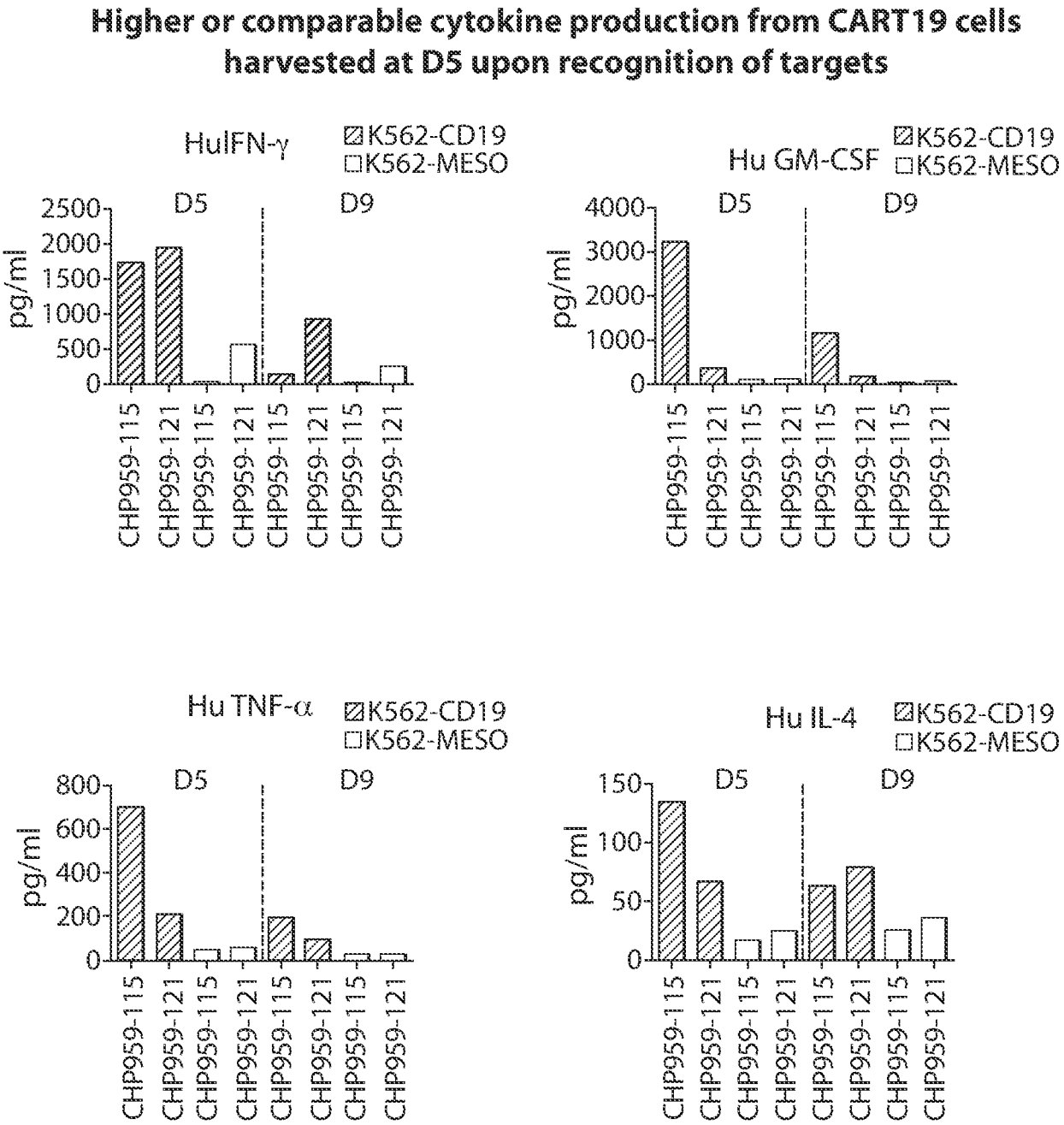
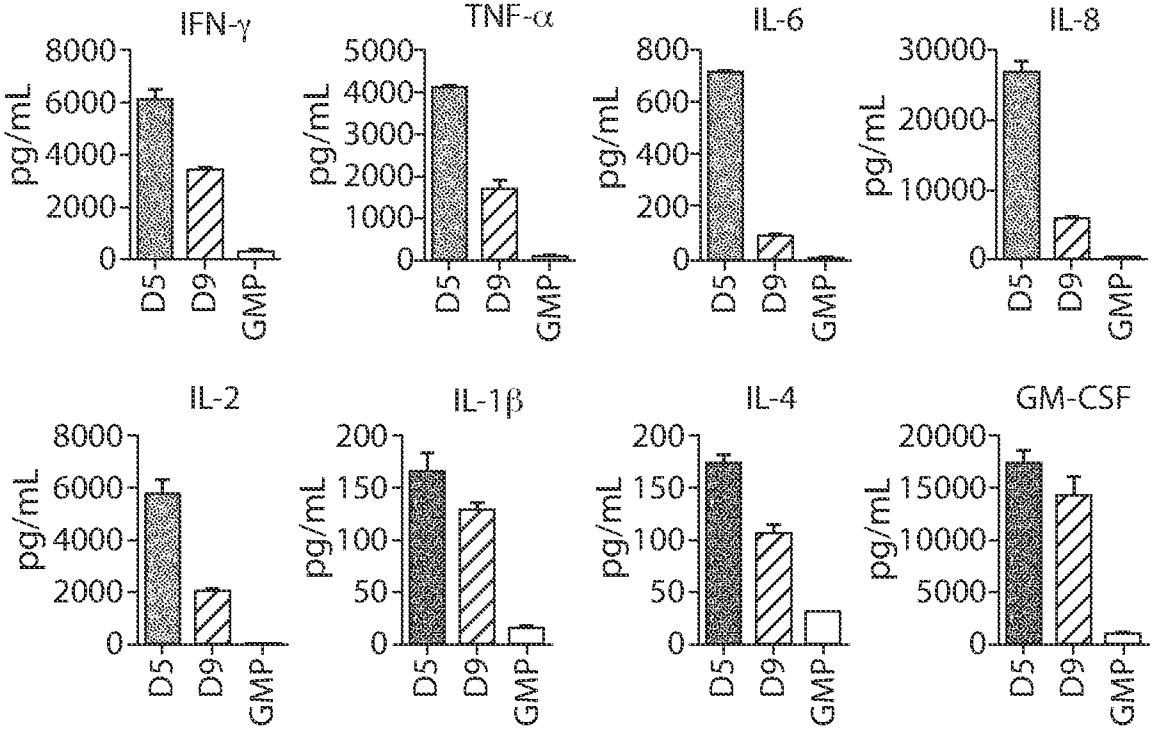

Higher or comparable cytokine production from CART19 cells harvested at D5 upon recognition of targets
HuIFN-γ
K562-CD19
K562-MESO
pg/ml
2500
2000
1500
1000
500
0
D5
D9
CHP959-115
CHP959-121
CHP959-115
CHP959-121
CHP959-115
CHP959-121
CHP959-115
CHP959-121
Hu GM-CSF
K562-CD19
K562-MESO
pg/ml
4000
3000
2000
1000
0
D5
D9
CHP959-115
CHP959-121
CHP959-115
CHP959-121
CHP959-115
CHP959-121
CHP959-115
CHP959-121
Hu TNF-α
K562-CD19
K562-MESO
pg/ml
800
600
400
200
0
D5
D9
CHP959-115
CHP959-121
CHP959-115
CHP959-121
CHP959-115
CHP959-121
CHP959-115
CHP959-121
Hu IL-4
K562-CD19
K562-MESO
pg/ml
150
100
50
0
D5
D9
CHP959-115
CHP959-121
CHP959-115
CHP959-121
CHP959-115
CHP959-121
CHP959-115
CHP959-121

FIG. 18

Increased levels of multiple cytokines are produced in CART19 cells harvested at day 5 upon recognition of targets

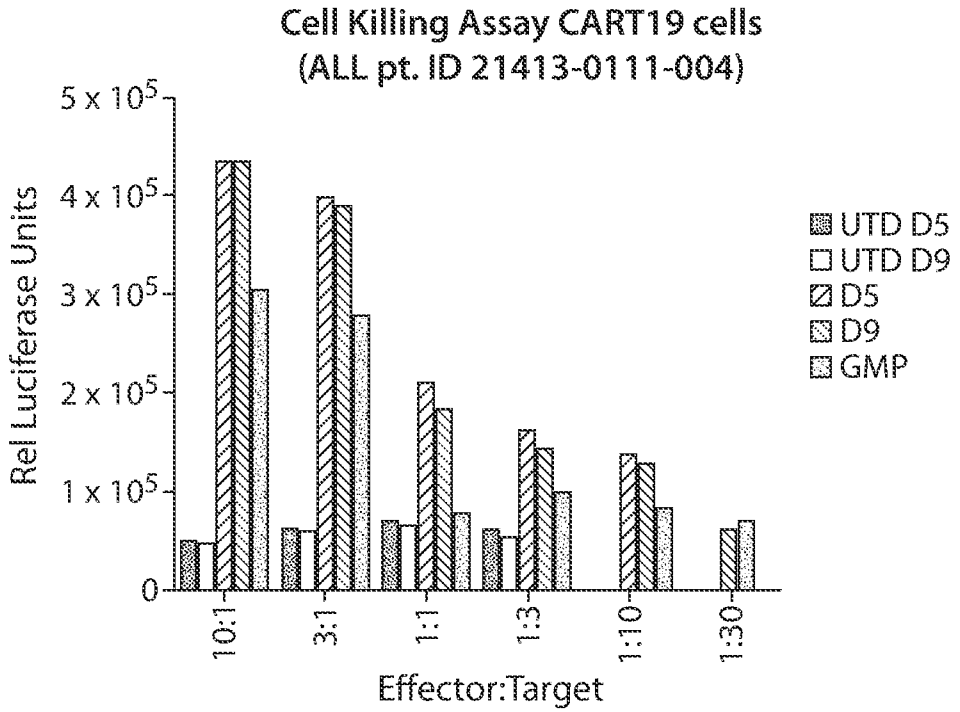
ALL pt. ID 21413_0111_004



- CART19 cells were stimulated with anti-CAR19-idiotype-Ab-coated or control beads for 24h.
- No cytokine or low levels (<200 pg/ml) of cytokine were detected with control beads.

FIG. 19

CART19 cells harvested at day 5 possess a better cell-killing capacity



- CART19 cells were co-cultured with NALM6-Luc cells at increasing E:T ratios for 16h.
- Total cell lysates were examined by luciferase assay.

FIG. 20

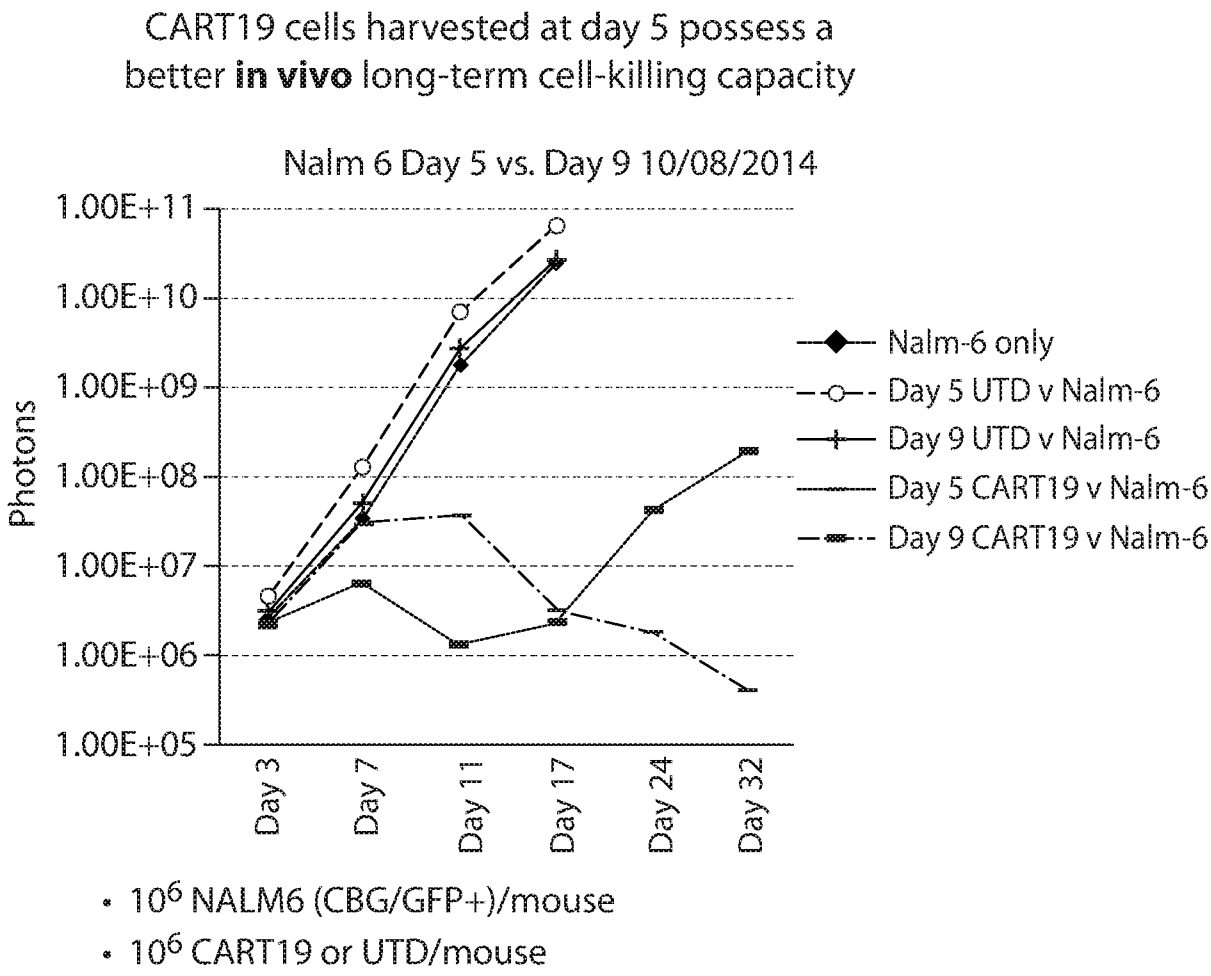

CART19 cells harvested at day 5 possess a
better in vivo long-term cell-killing capacity
Nalm 6 Day 5 vs. Day 9 10/08/2014
Photons
1.00E+11
1.00E+10
1.00E+09
1.00E+08
1.00E+07
1.00E+06
1.00E+05
Day 3
Day 7
Day 11
Day 17
Day 24
Day 32
Nalm-6 only
Day 5 UTD v Nalm-6
Day 9 UTD v Nalm-6
Day 5 CART19 v Nalm-6
Day 9 CART19 v Nalm-6
• 10^6 NALM6 (CBG/GFP+)/mouse
• 10^6 CART19 or UTD/mouse

FIG. 21

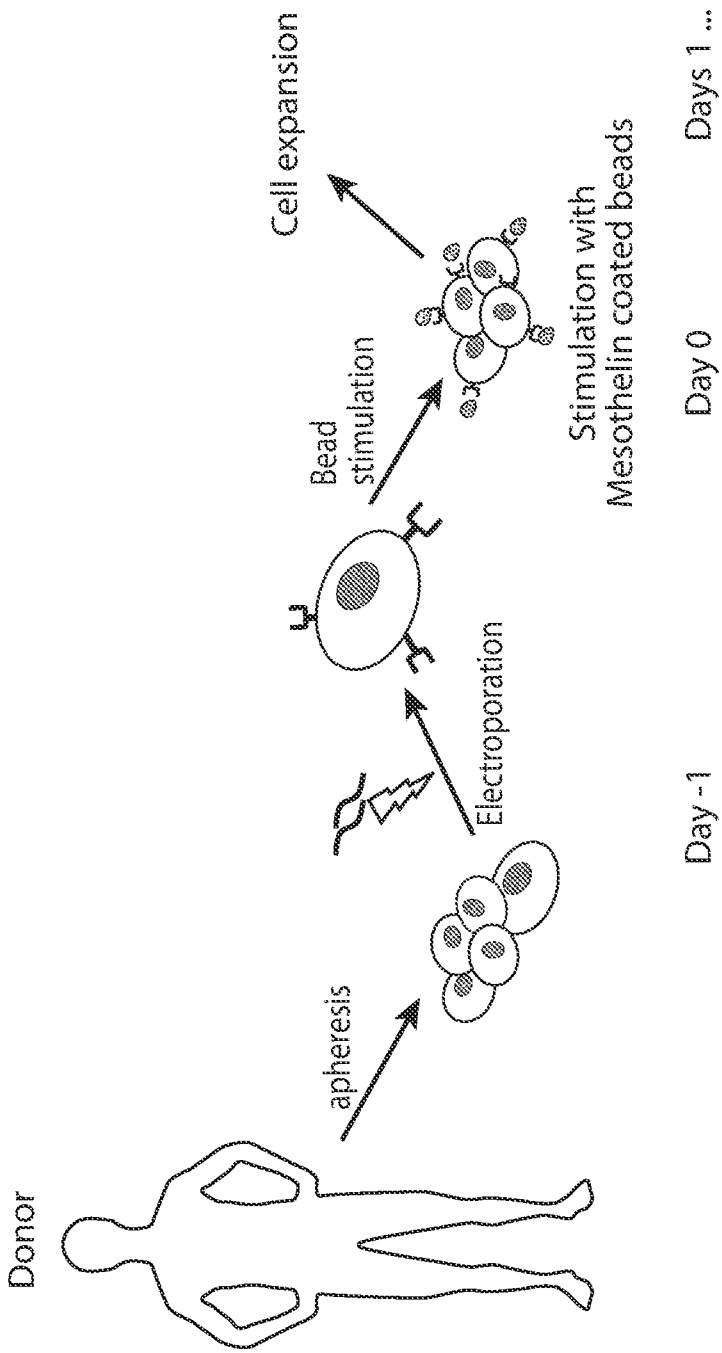

Donor
apheresis
Electroporation
Bead stimulation
Cell expansion
Stimulation with Mesothelin coated beads
Day -1
Day 0
Days 1 ...

FIG. 22

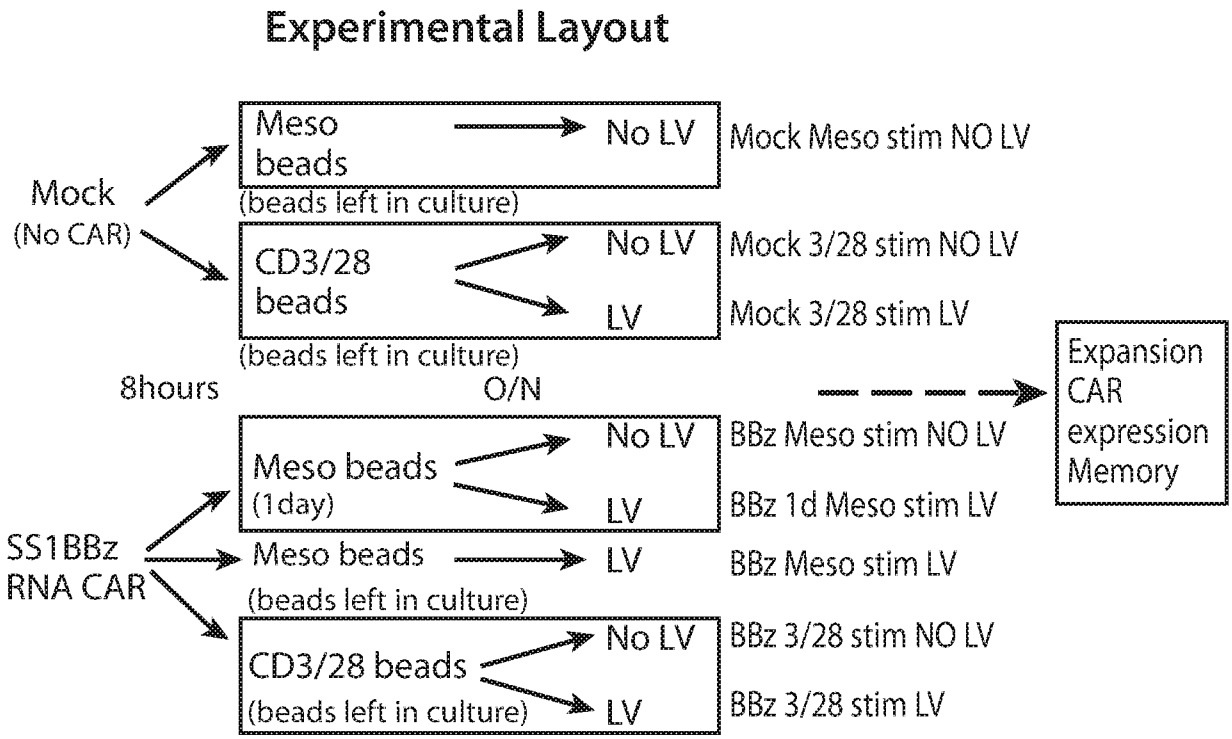

Experimental Layout
Mock
(No CAR)
Meso beads
No LV
Mock Meso stim NO LV
(beads left in culture)
CD3/28 beads
No LV
Mock 3/28 stim NO LV
LV
Mock 3/28 stim LV
(beads left in culture)
8hours
O/N
Expansion CAR expression Memory
SS1BBz RNA CAR
Meso beads (1day)
No LV
BBz Meso stim NO LV
LV
BBz 1d Meso stim LV
Meso beads
LV
BBz Meso stim LV
(beads left in culture)
CD3/28 beads
(beads left in culture)
No LV
BBz 3/28 stim NO LV
LV
BBz 3/28 stim LV

FIG. 23

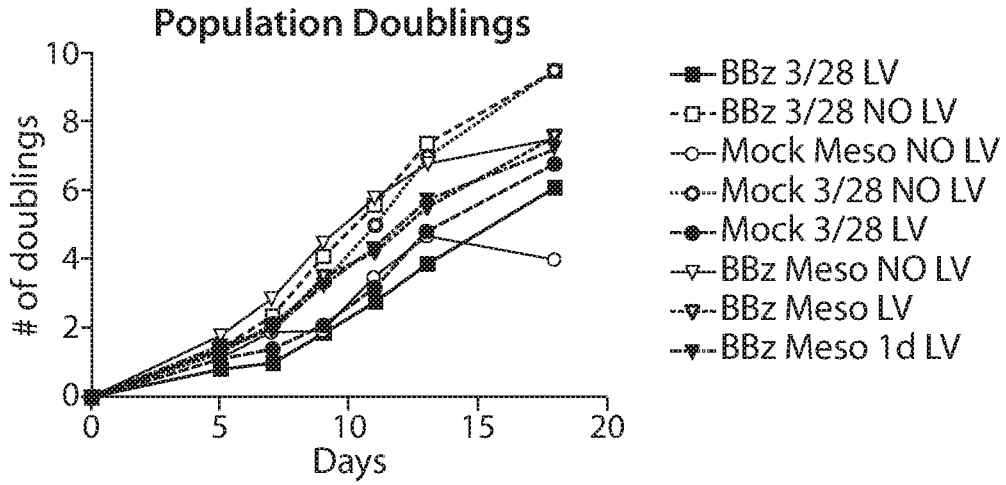


FIG. 24A

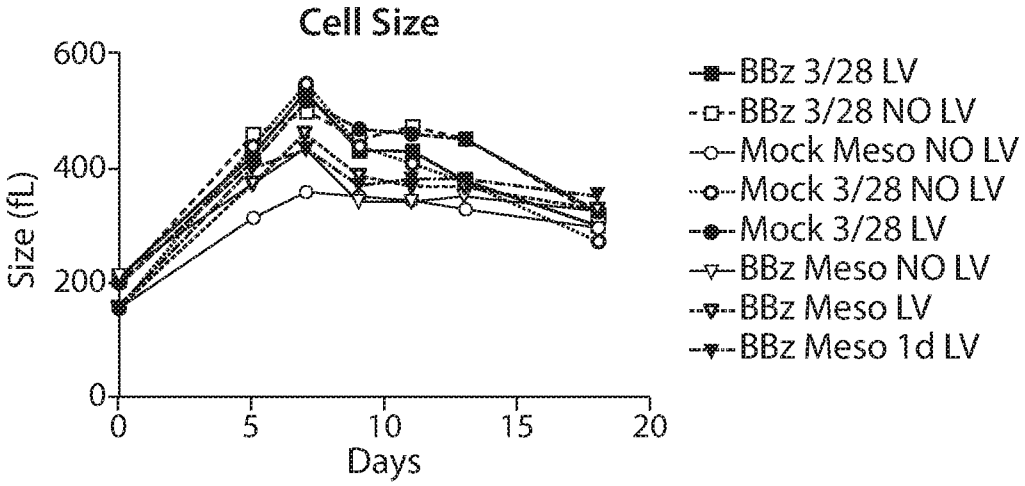


FIG. 24B

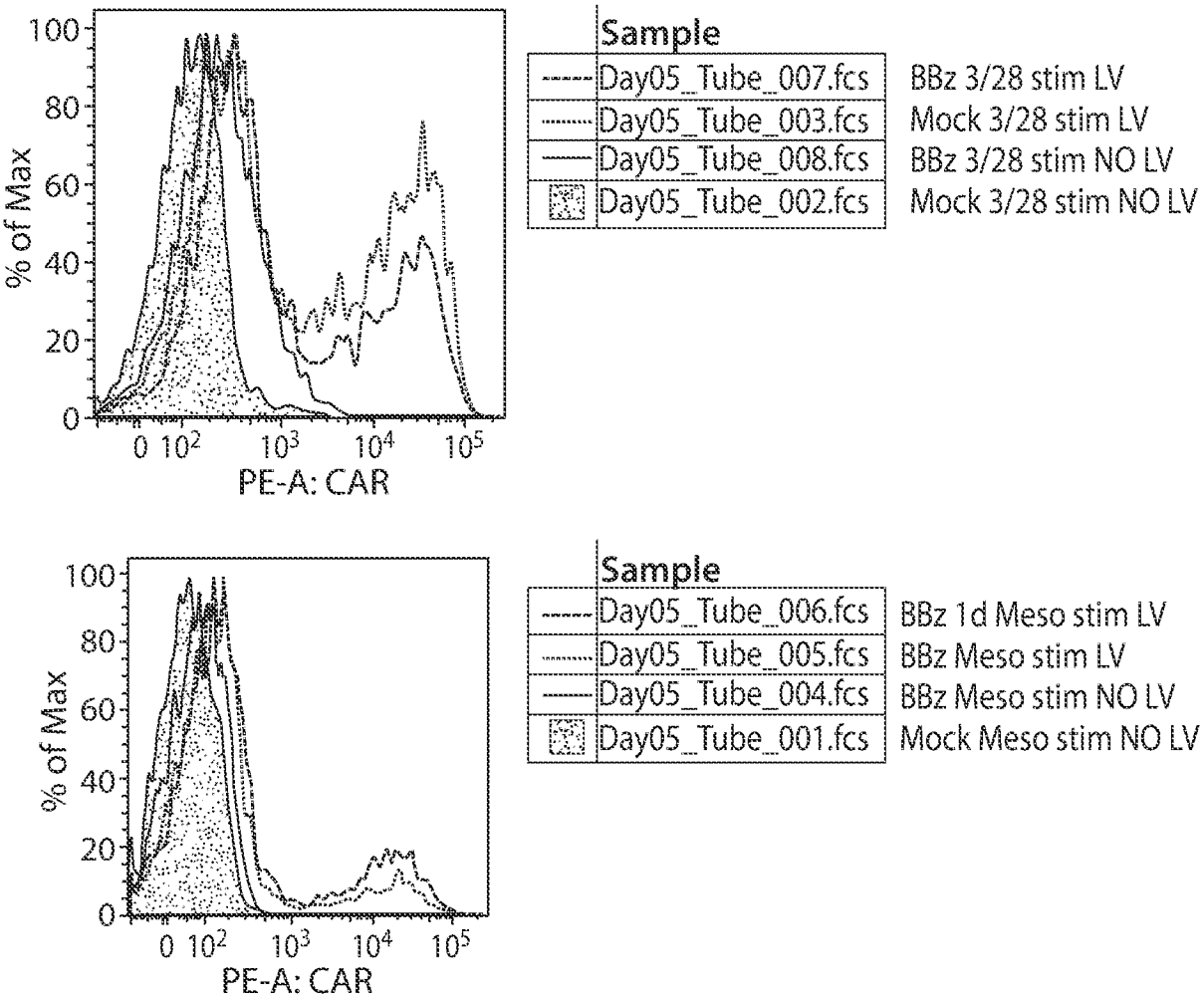
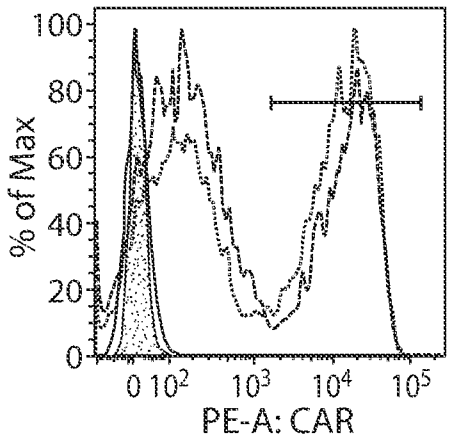
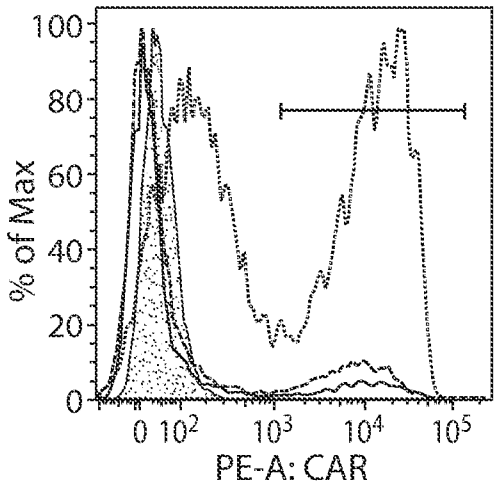

100
80
60
40
20
0
% of Max
0 10^2 10^3 10^4 10^5
PE-A: CAR
Sample
Day05_Tube_007.fcs
Day05_Tube_003.fcs
Day05_Tube_008.fcs
Day05_Tube_002.fcs
BBz 3/28 stim LV
Mock 3/28 stim LV
BBz 3/28 stim NO LV
Mock 3/28 stim NO LV
100
80
60
40
20
0
% of Max
0 10^2 10^3 10^4 10^5
PE-A: CAR
Sample
Day05_Tube_006.fcs
Day05_Tube_005.fcs
Day05_Tube_004.fcs
Day05_Tube_001.fcs
BBz 1d Meso stim LV
BBz Meso stim LV
BBz Meso stim NO LV
Mock Meso stim NO LV

FIG. 25A



	Sample	% CAR-ve	
-----	Day11_Tube_007.fcs	37	BBz 3/28 stim LV
.....	Day11_Tube_003.fcs	50.3	Mock 3/28 stim LV
——	Day11_Tube_008.fcs	0.197	BBz 3/28 stim NO LV
▒	Day11_Tube_002.fcs	0.0591	Mock 3/28 stim NO LV

Comparable transduction efficiency with both cell stimulation conditions



	Sample	%	
----	Day11_Tube_006.fcs	17	BBz 1d Meso stim LV
.....	Day11_Tube_005.fcs	50.4	BBz Meso stim LV
——	Day11_Tube_004.fcs	9.98	BBz Meso stim NO LV
▒	Day11_Tube_001.fcs	0.151	Mock Meso stim NO LV

FIG. 25B

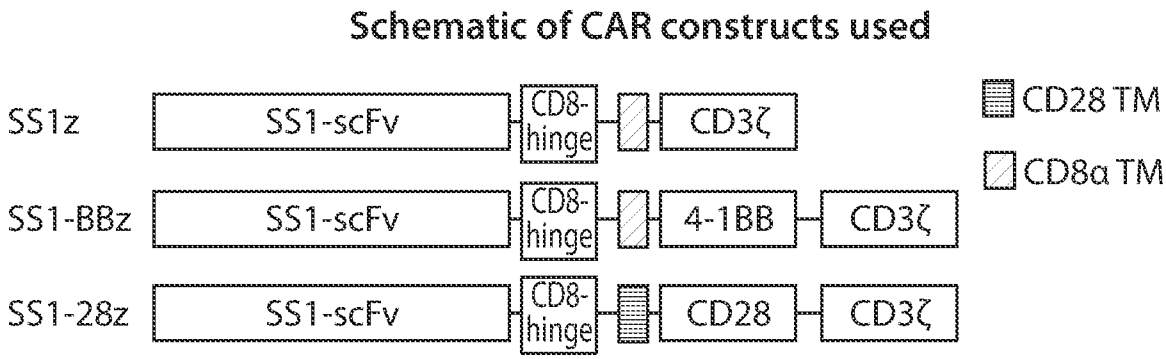


FIG. 26A

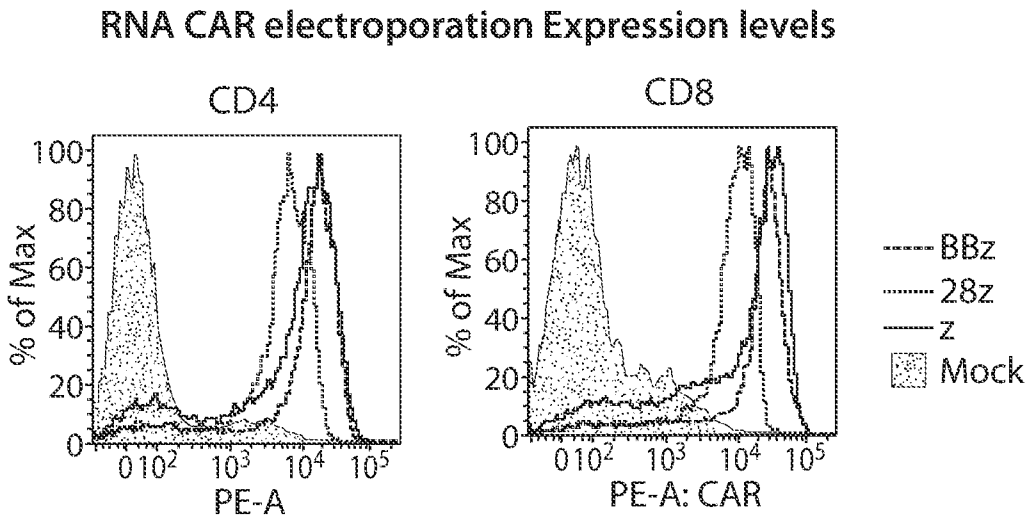


FIG. 26B

Expansion of CAR-grafted peripheral blood T cells

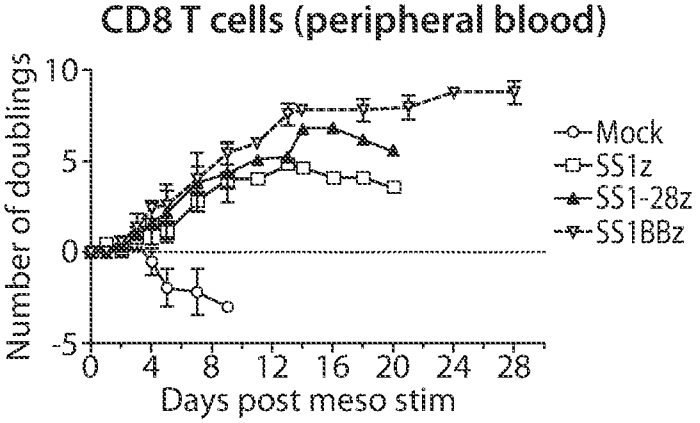


FIG. 27A

Expansion of CAR-grafted peripheral blood T cells

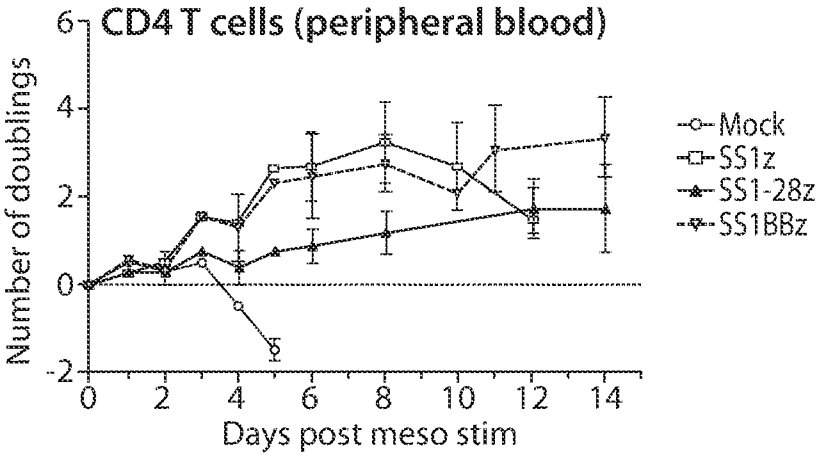


FIG. 27B

Expansion of CAR-grafted cord blood T cells

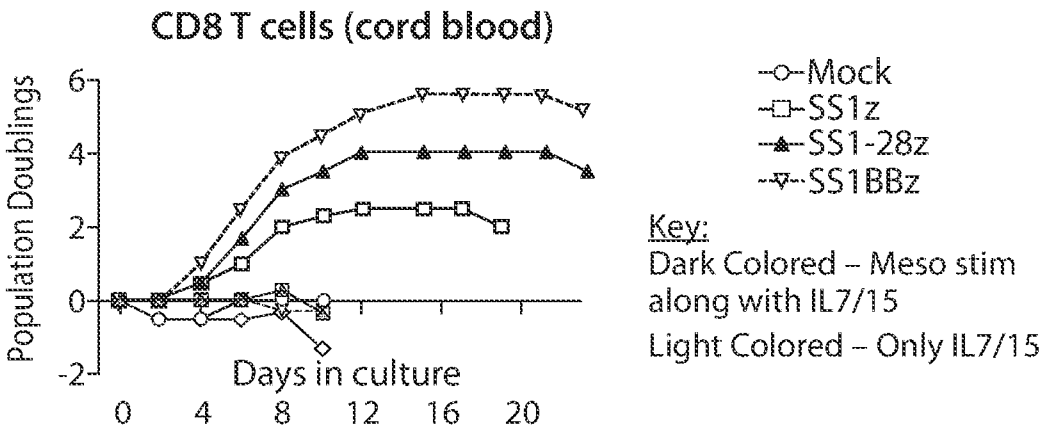


FIG. 27C

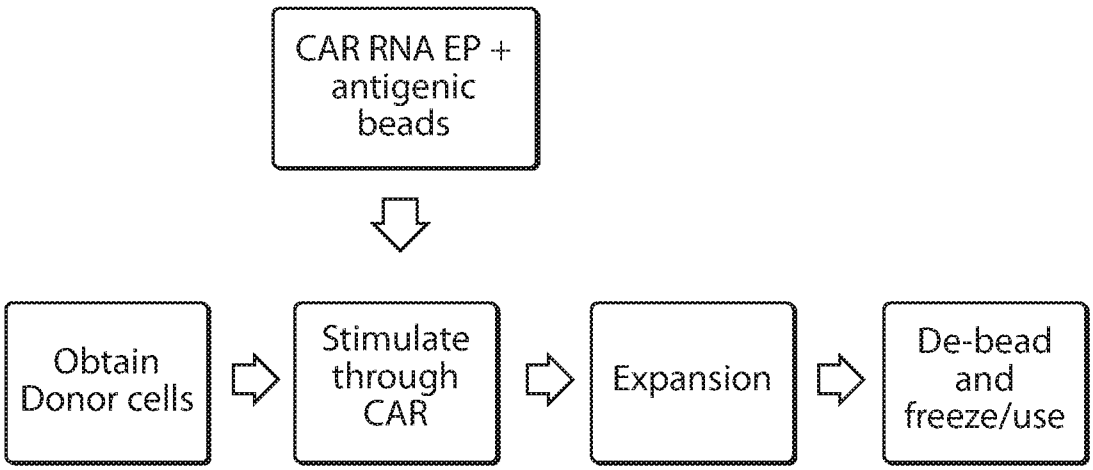

CAR RNA EP + antigenic beads
Obtain Donor cells
Stimulate through CAR
Expansion
De-bead and freeze/use

FIG. 28

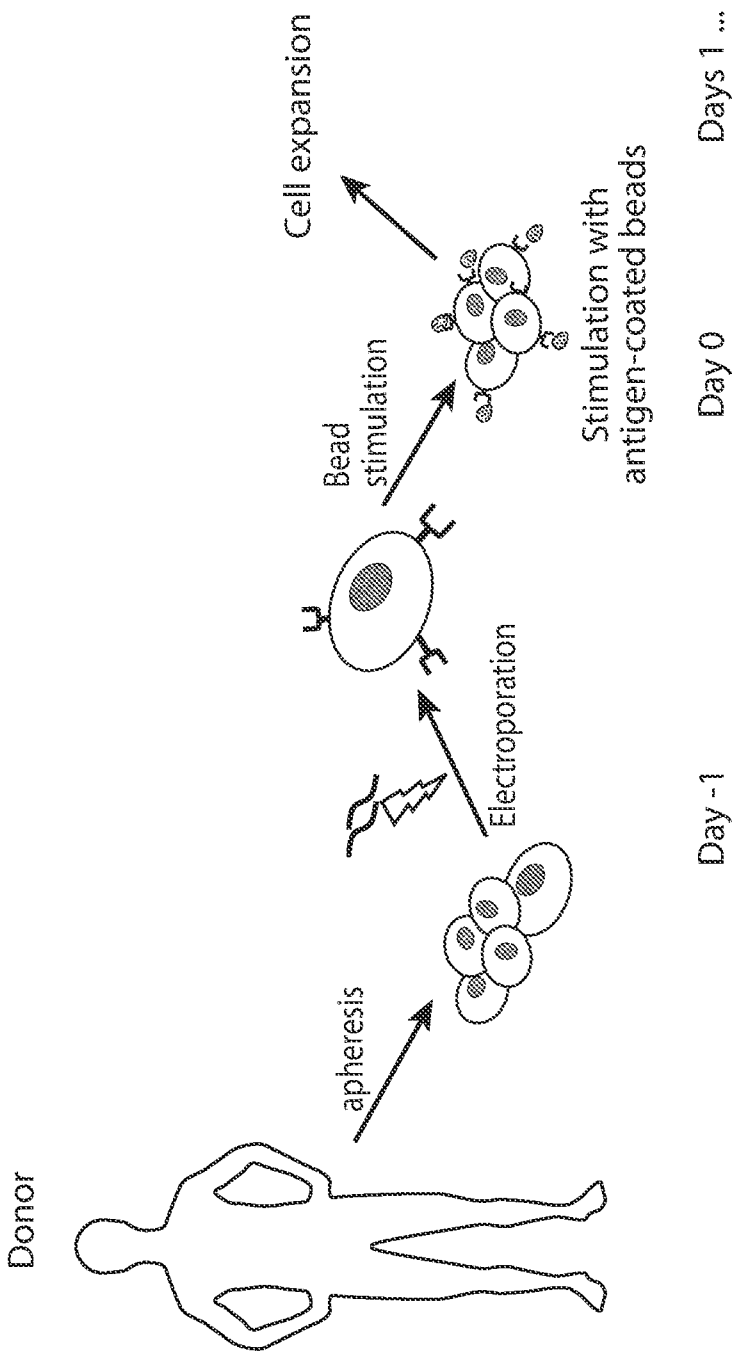

Donor
apheresis
Electroporation
Bead stimulation
Cell expansion
Stimulation with antigen-coated beads
Day -1
Day 0
Days 1 ...

FIG. 29

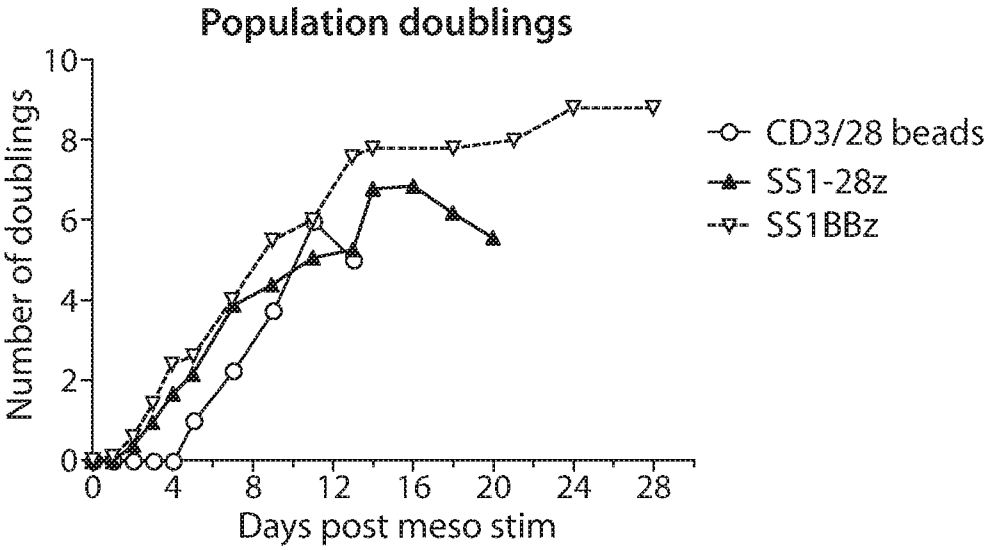


FIG. 30A

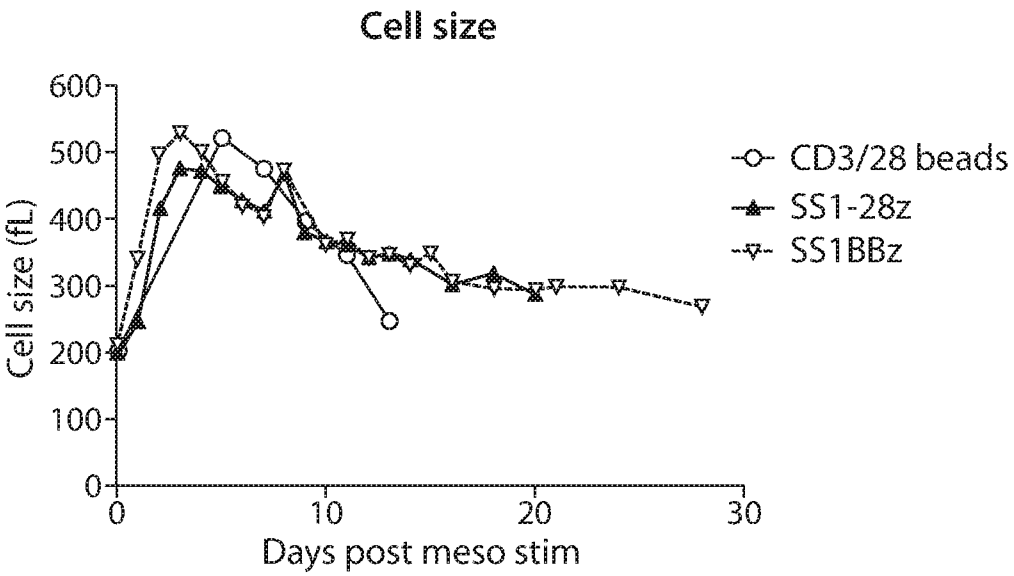


FIG. 30B

Expansion of CAR-grafted peripheral blood T cells

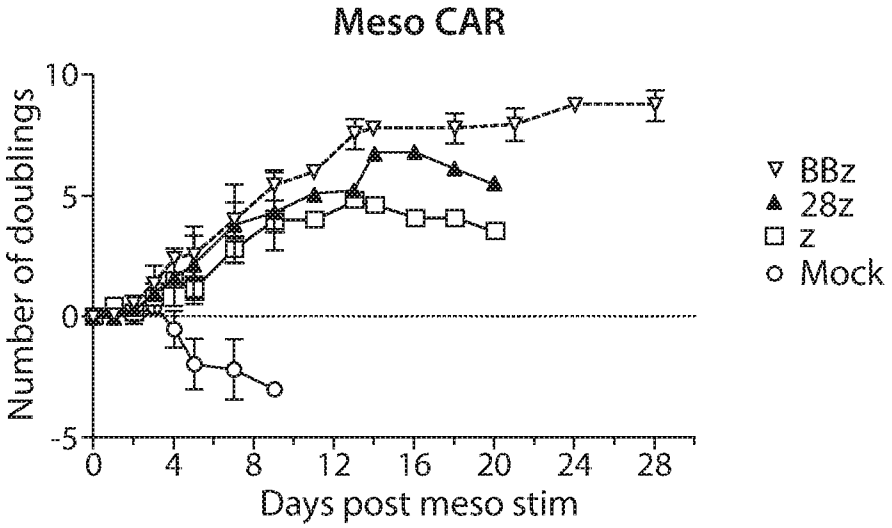


FIG. 31A

Expansion of CAR-grafted peripheral blood T cells

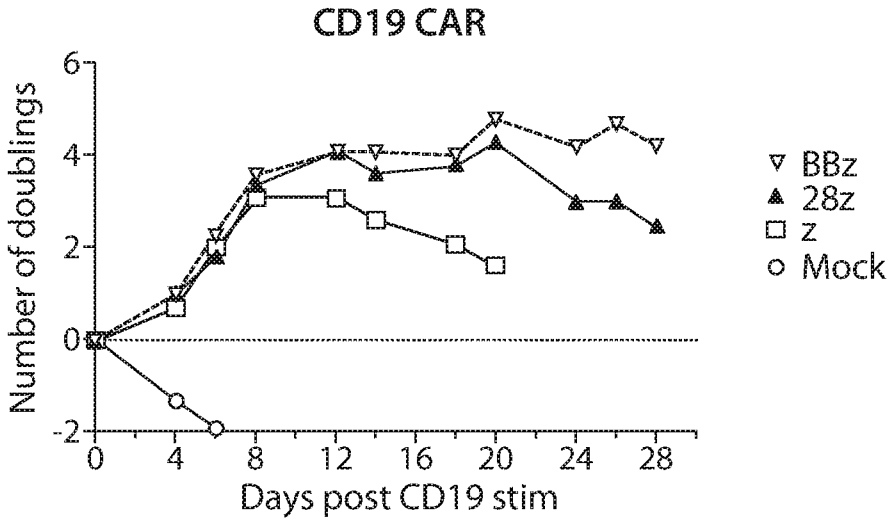


FIG. 31B

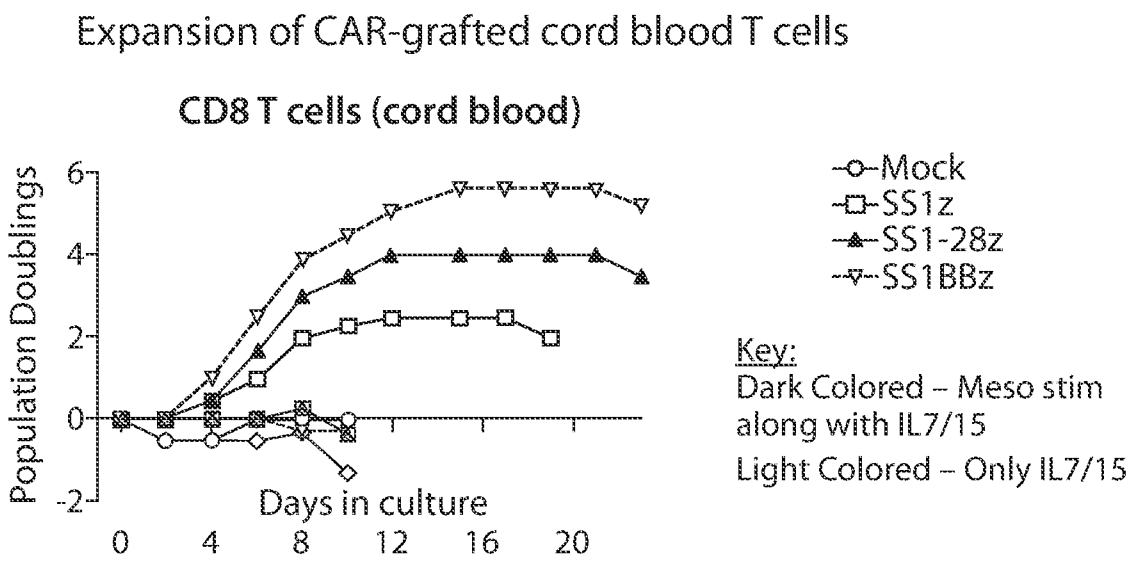

Expansion of CAR-grafted cord blood T cells
CD8 T cells (cord blood)
Population Doublings
6
4
2
0
-2
Days in culture
0
4
8
12
16
20
Mock
SS1z
SS1-28z
SS1BBz
Key:
Dark Colored – Meso stim along with IL7/15
Light Colored – Only IL7/15

FIG. 31C

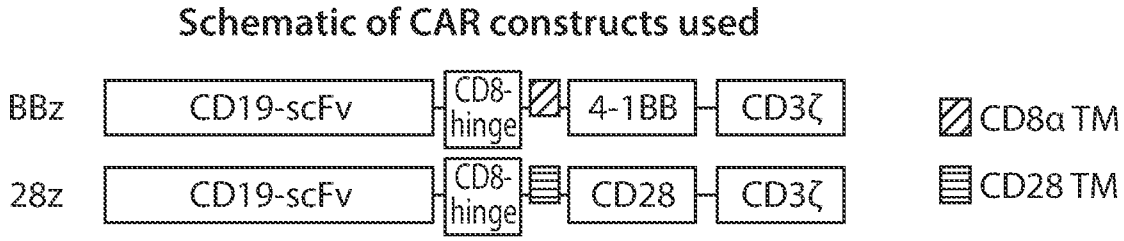


FIG. 32A

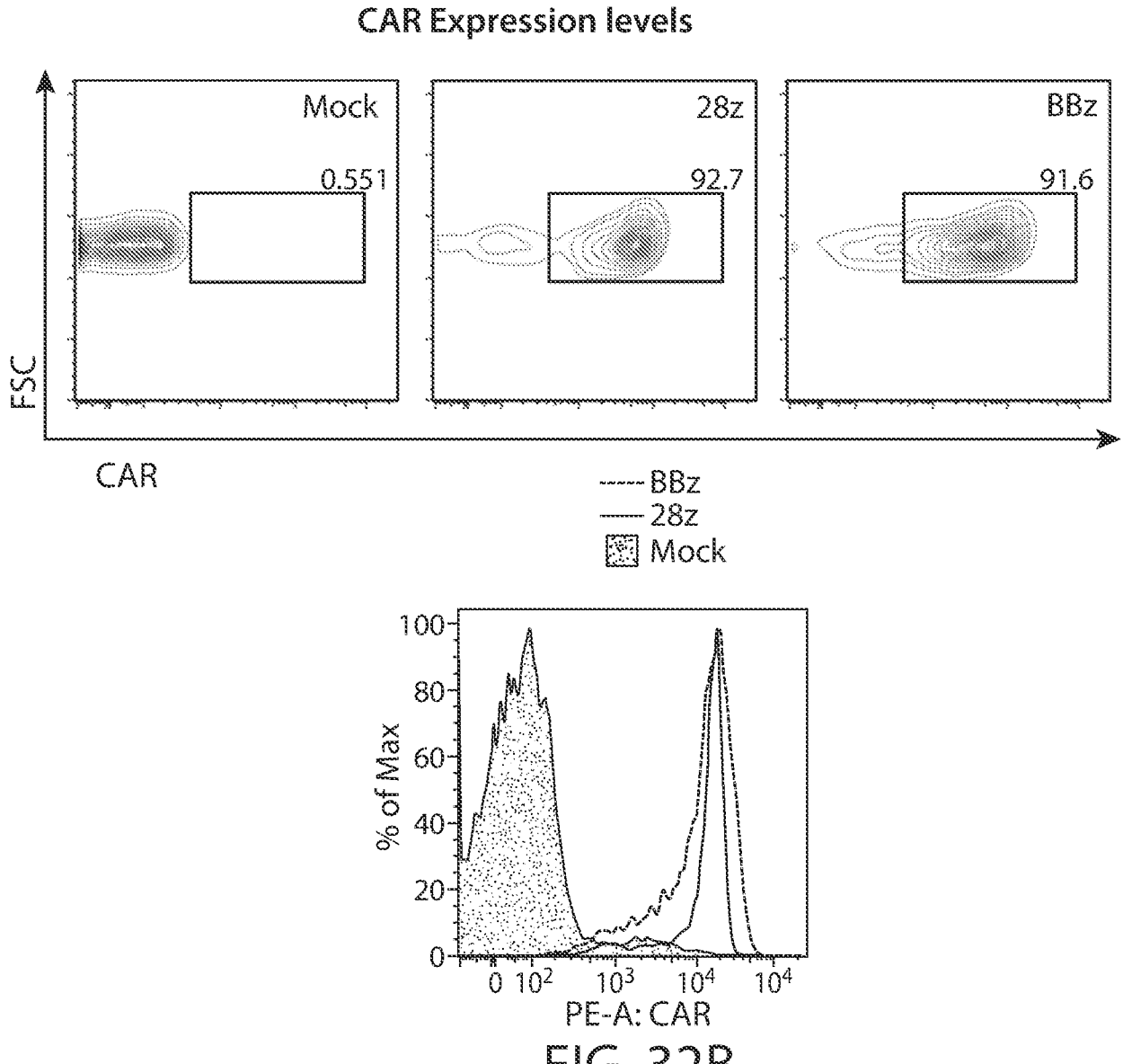


FIG. 32B

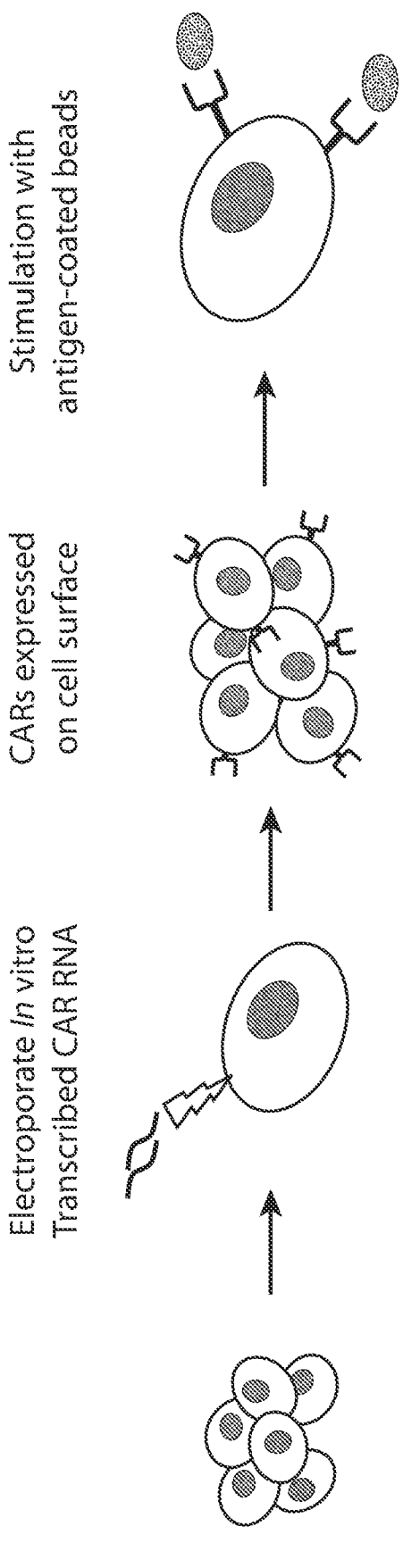

Freshly isolated T cells
Day -1
Electroporate *In vitro* Transcribed CAR RNA
CARs expressed on cell surface
Day 0
Stimulation with antigen-coated beads

FIG. 32C

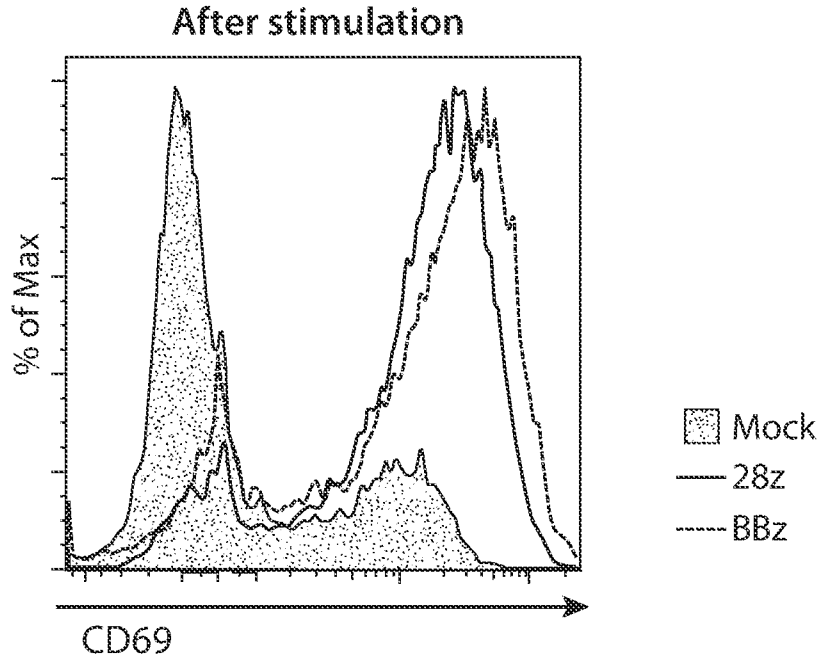


FIG. 33A

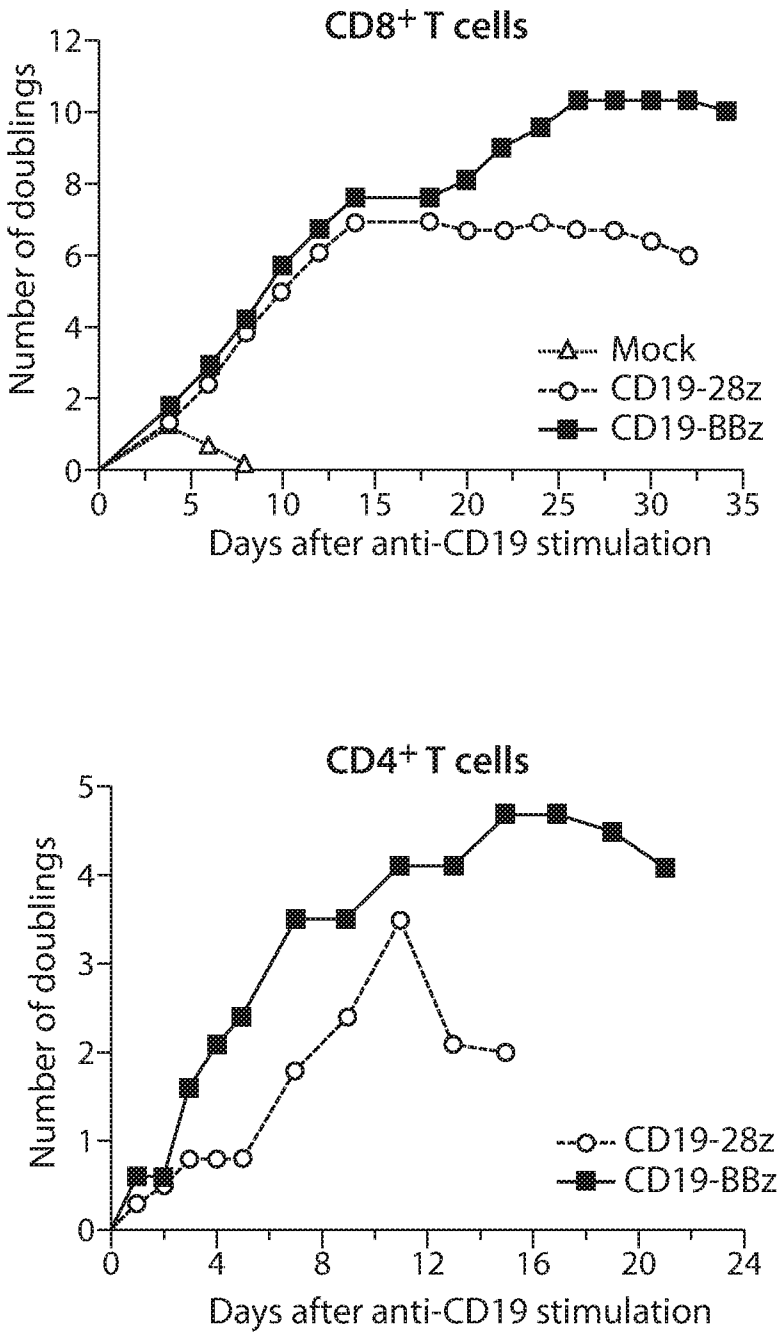
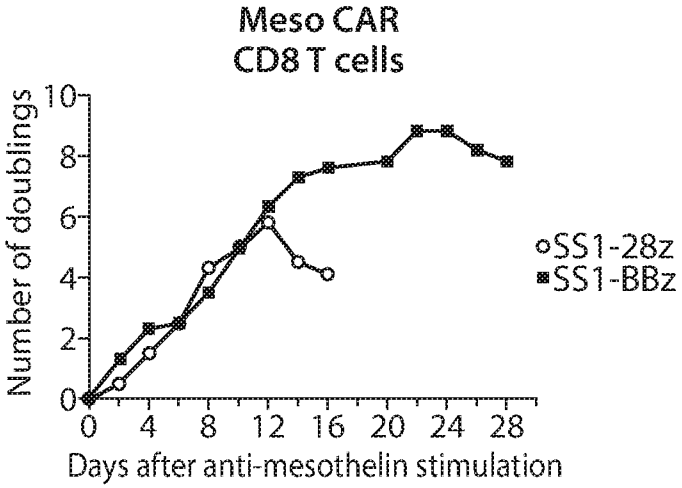

CD8+ T cells
Number of doublings
0
2
4
6
8
10
12
0
5
10
15
20
25
30
35
Days after anti-CD19 stimulation
Mock
CD19-28z
CD19-BBz
CD4+ T cells
Number of doublings
0
1
2
3
4
5
0
4
8
12
16
20
24
Days after anti-CD19 stimulation
CD19-28z
CD19-BBz

FIG. 33B


Meso CAR
CD8 T cells
Number of doublings
0
2
4
6
8
10
0 4 8 12 16 20 24 28
Days after anti-mesothelin stimulation
SS1-28z
SS1-BBz

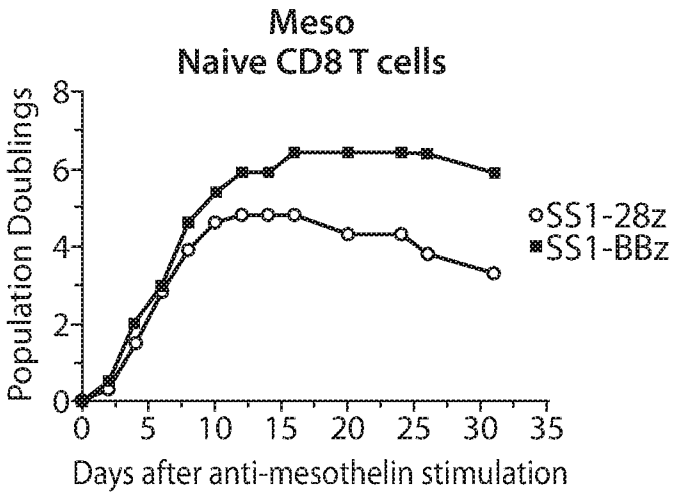

Meso
Naive CD8 T cells
Population Doublings
0
2
4
6
8
0 5 10 15 20 25 30 35
Days after anti-mesothelin stimulation
SS1-28z
SS1-BBz

FIG. 33C

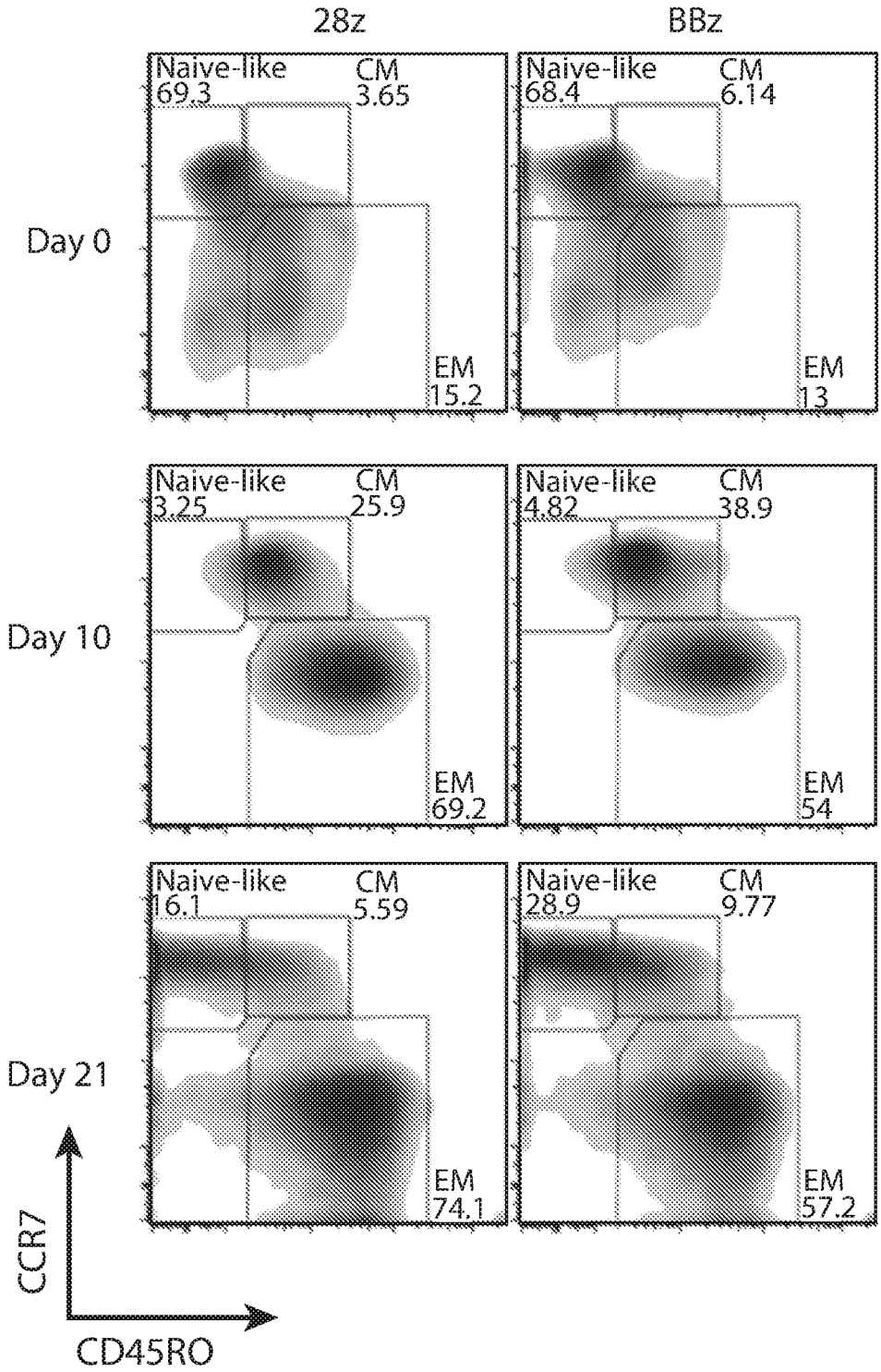

28z
BBz
Day 0
Day 10
Day 21
Naive-like
69.3
CM
3.65
EM
15.2
Naive-like
68.4
CM
6.14
EM
13
Naive-like
3.25
CM
25.9
EM
69.2
Naive-like
4.82
CM
38.9
EM
54
Naive-like
16.1
CM
5.59
EM
74.1
Naive-like
28.9
CM
9.77
EM
57.2
CCR7
CD45RO

FIG. 33D

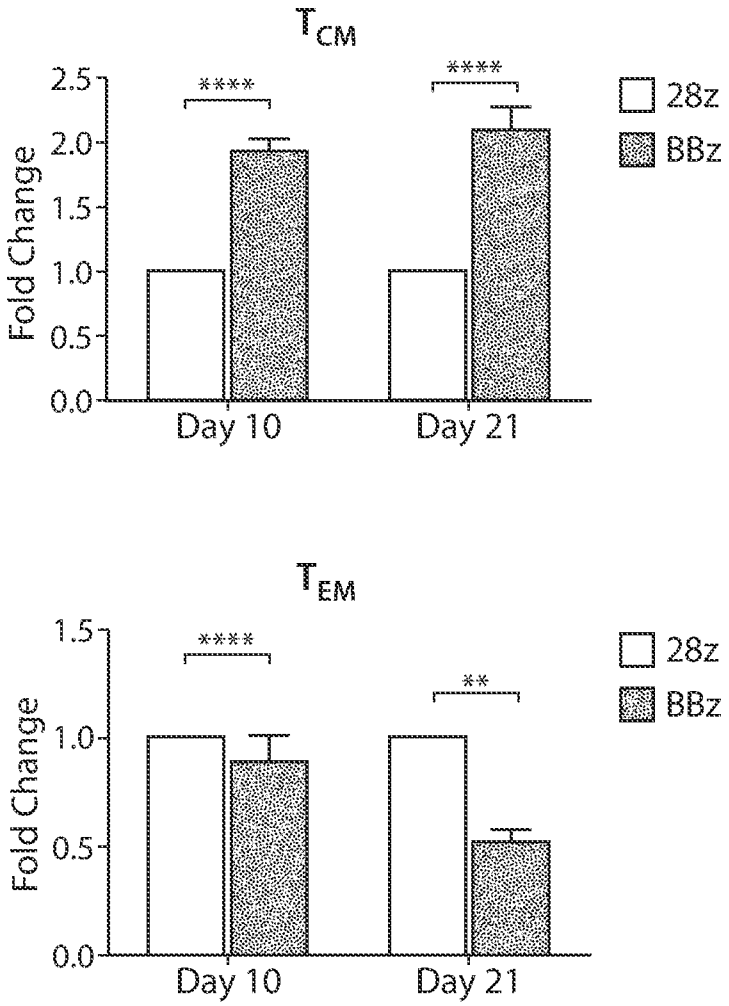

T CM
Fold Change
2.5
2.0
1.5
1.0
0.5
0.0
****
****
Day 10
Day 21
28z
BBz
T EM
Fold Change
1.5
1.0
0.5
0.0
****
**
Day 10
Day 21
28z
BBz

FIG. 33E

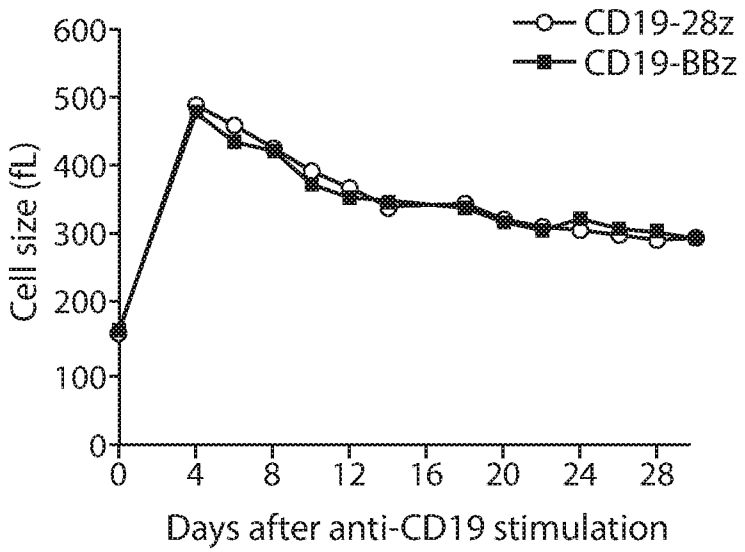

CD19-28z
CD19-BBz
Cell size (fL)
600
500
400
300
200
100
0
0
4
8
12
16
20
24
28
Days after anti-CD19 stimulation

FIG. 34A

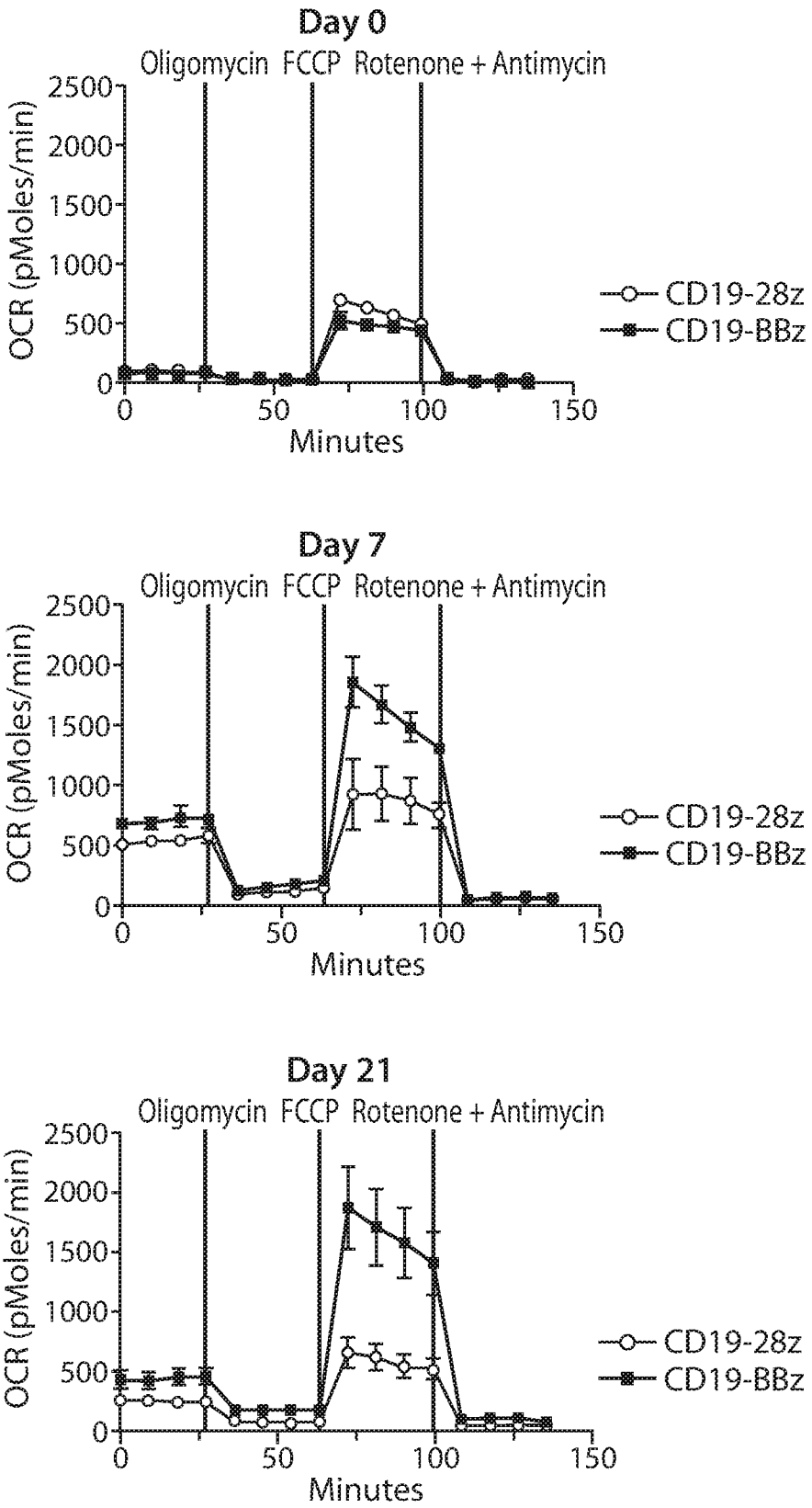

Day 0
Oligomycin FCCP Rotenone + Antimycin
OCR (pMoles/min)
2500
2000
1500
1000
500
0
0
50
100
150
Minutes
CD19-28z
CD19-BBz
Day 7
Oligomycin FCCP Rotenone + Antimycin
OCR (pMoles/min)
Minutes
CD19-28z
CD19-BBz
Day 21
Oligomycin FCCP Rotenone + Antimycin
OCR (pMoles/min)
Minutes
CD19-28z
CD19-BBz

FIG. 34B

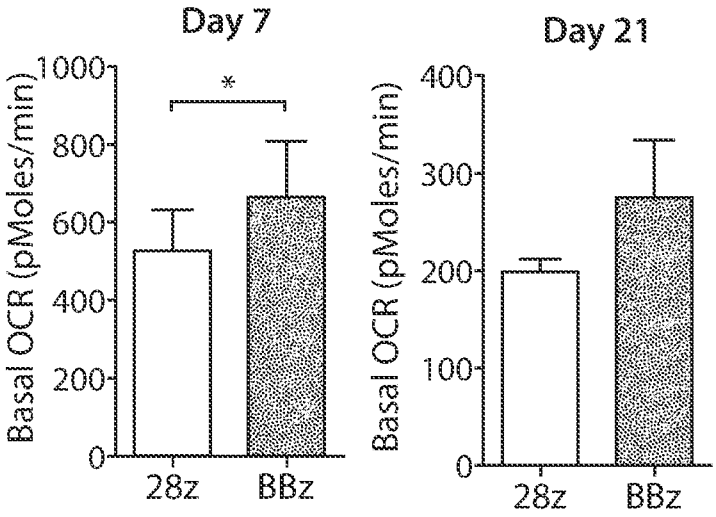


FIG. 34C

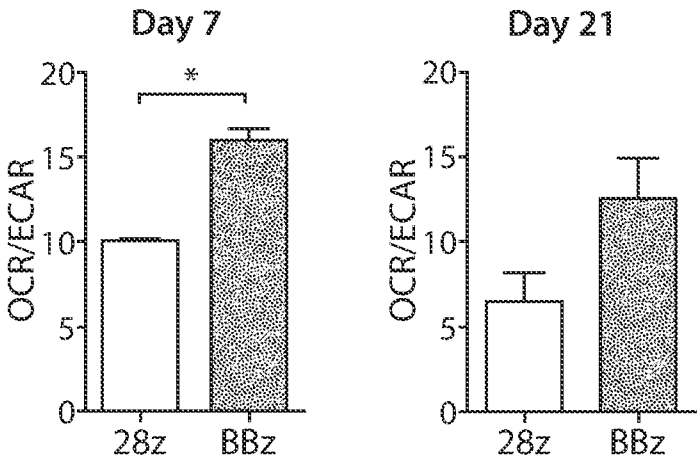


FIG. 34D

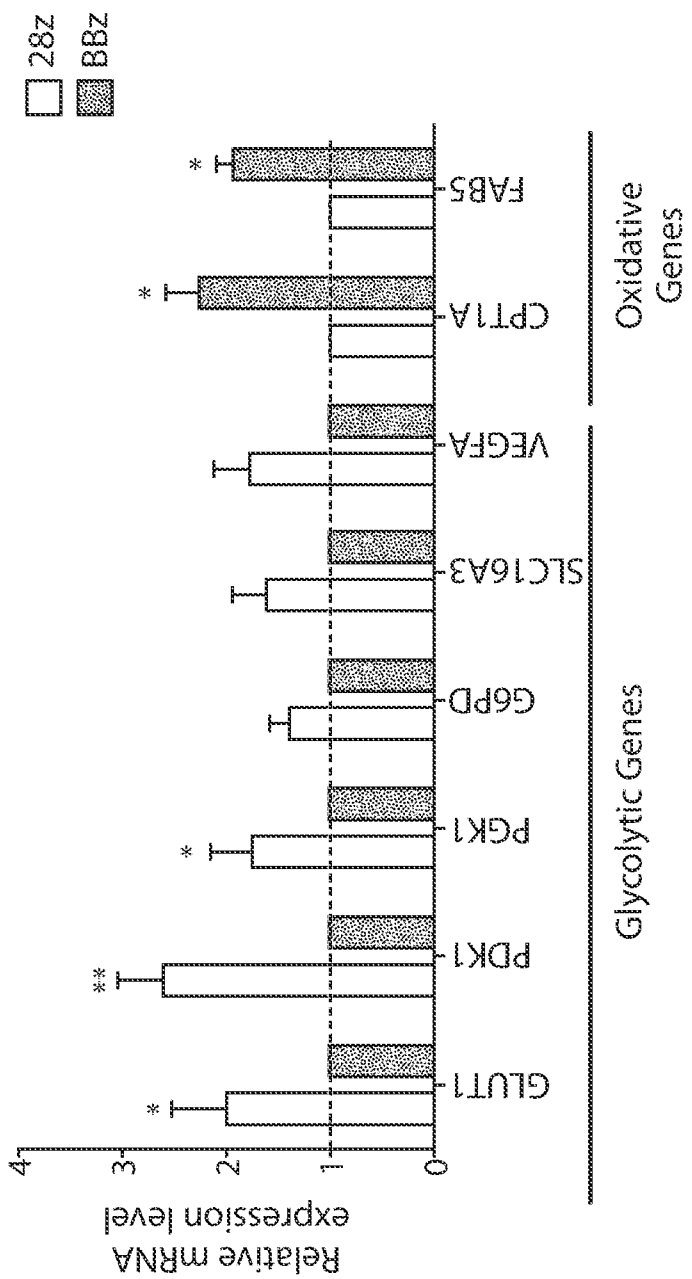

28z
BBz
Relative mRNA expression level
0
1
2
3
4
GLUT1
PDK1
PGK1
G6PD
SLC16A3
VEGFA
CPT1A
FAB5
Glycolytic Genes
Oxidative Genes
*
**

FIG. 34E

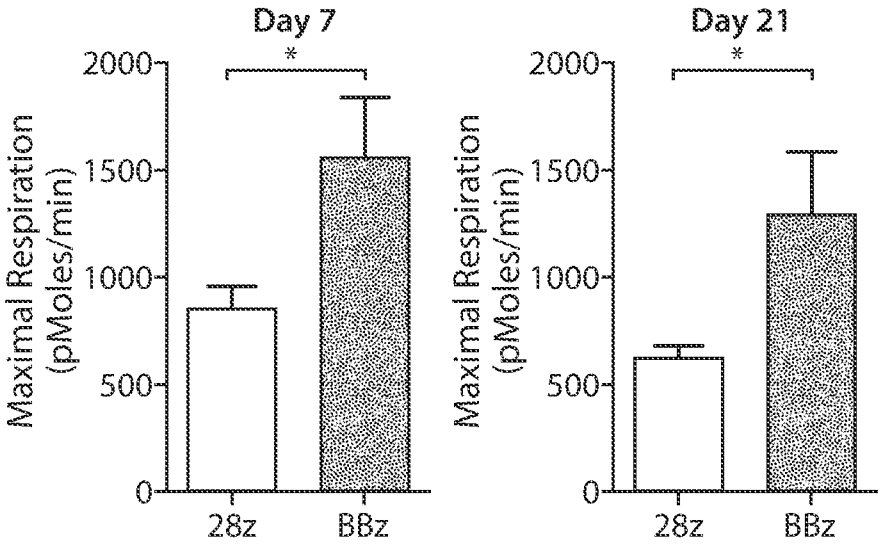


FIG. 34F

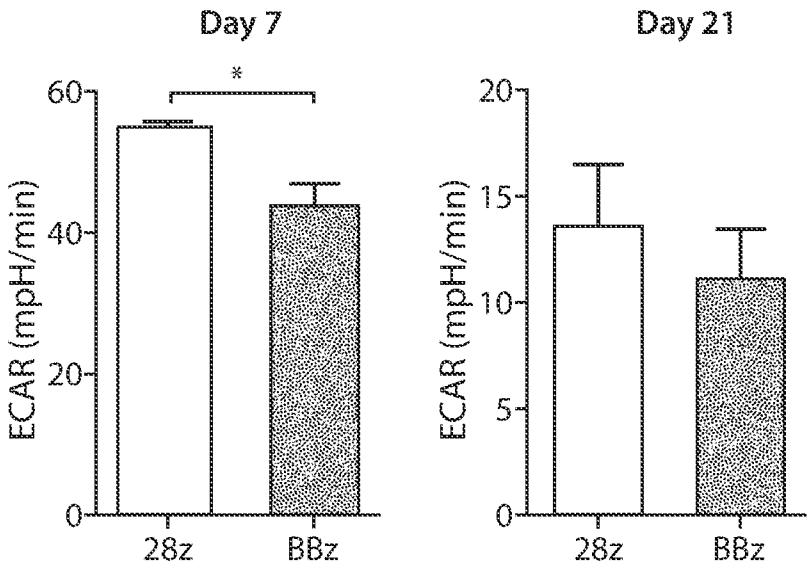


FIG. 34G

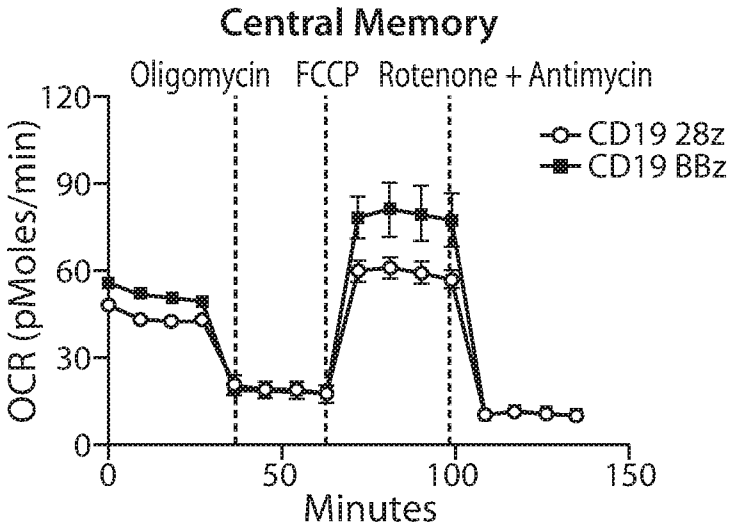


FIG. 34H

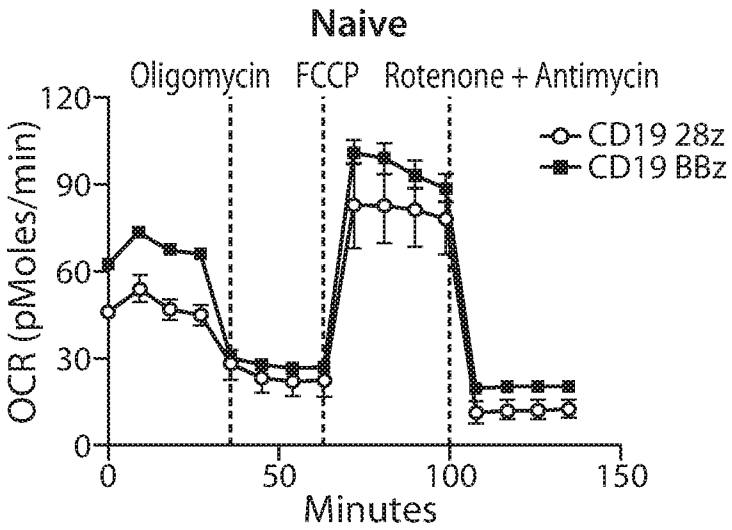


FIG. 34I

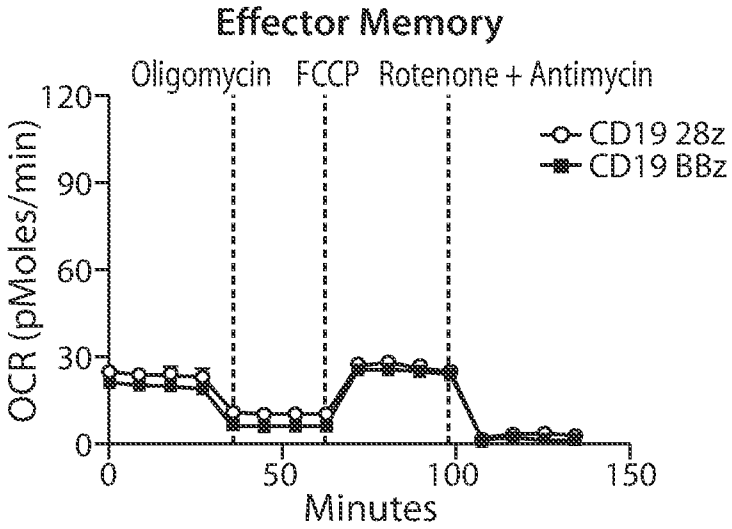


FIG. 34J

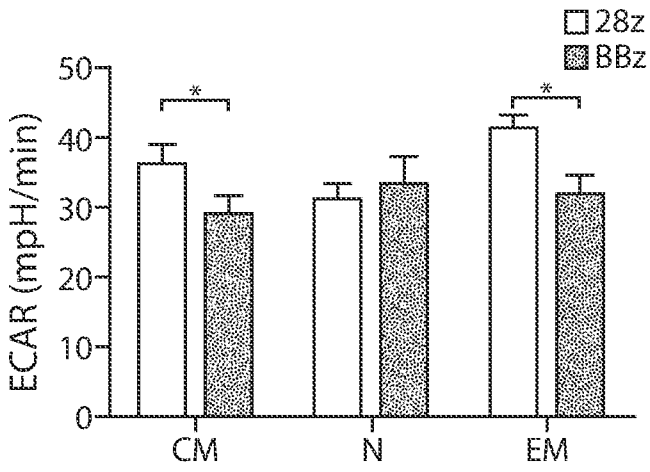


FIG. 34K

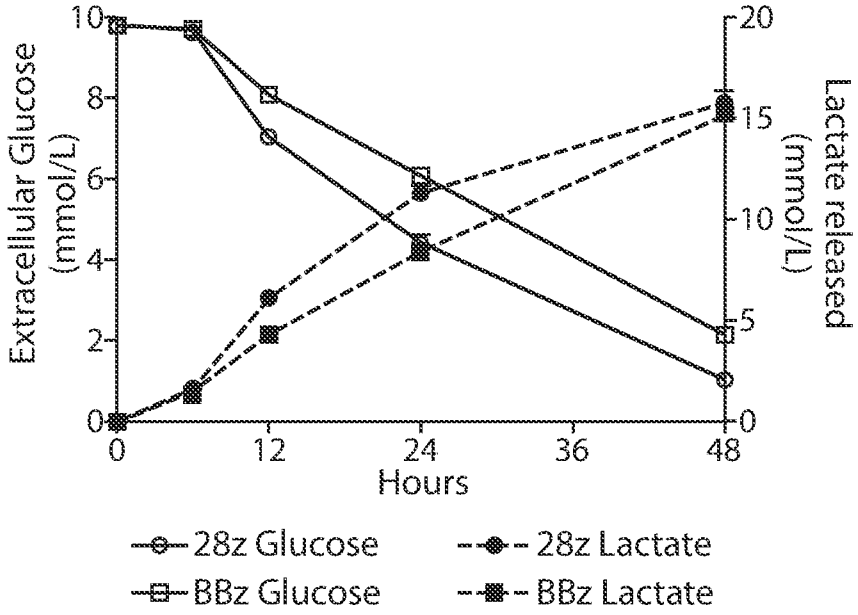


FIG. 34L

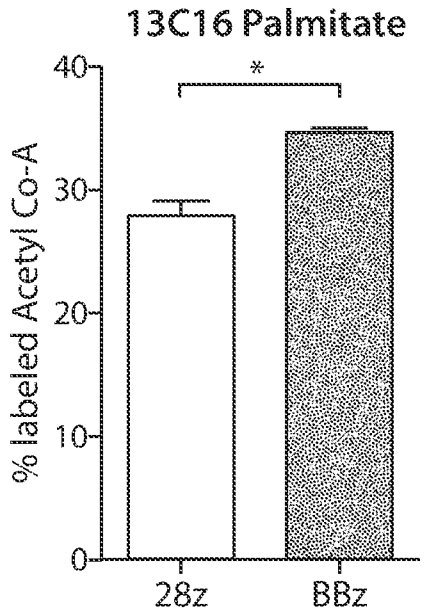


FIG. 34M

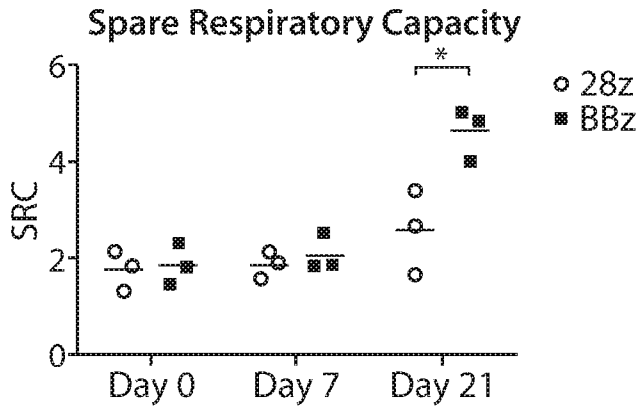


FIG. 35A

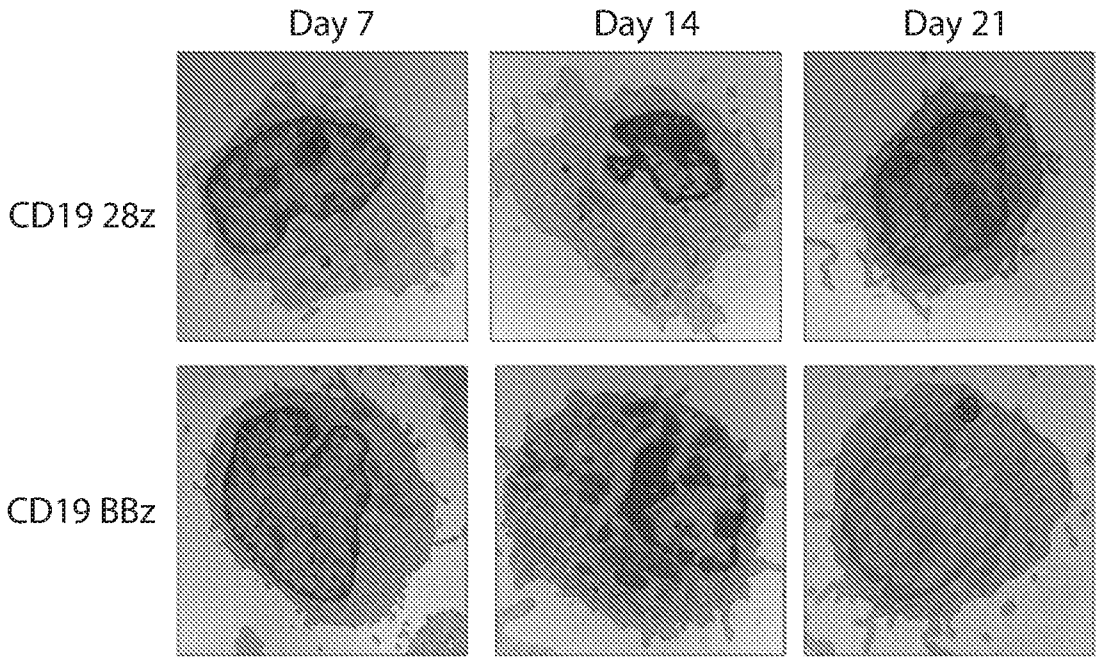


FIG. 35B

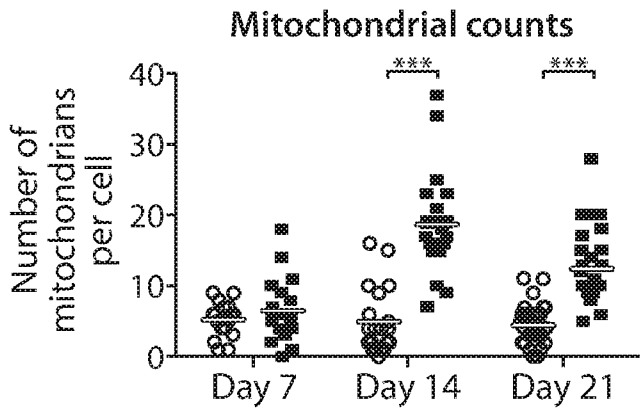


FIG. 35C

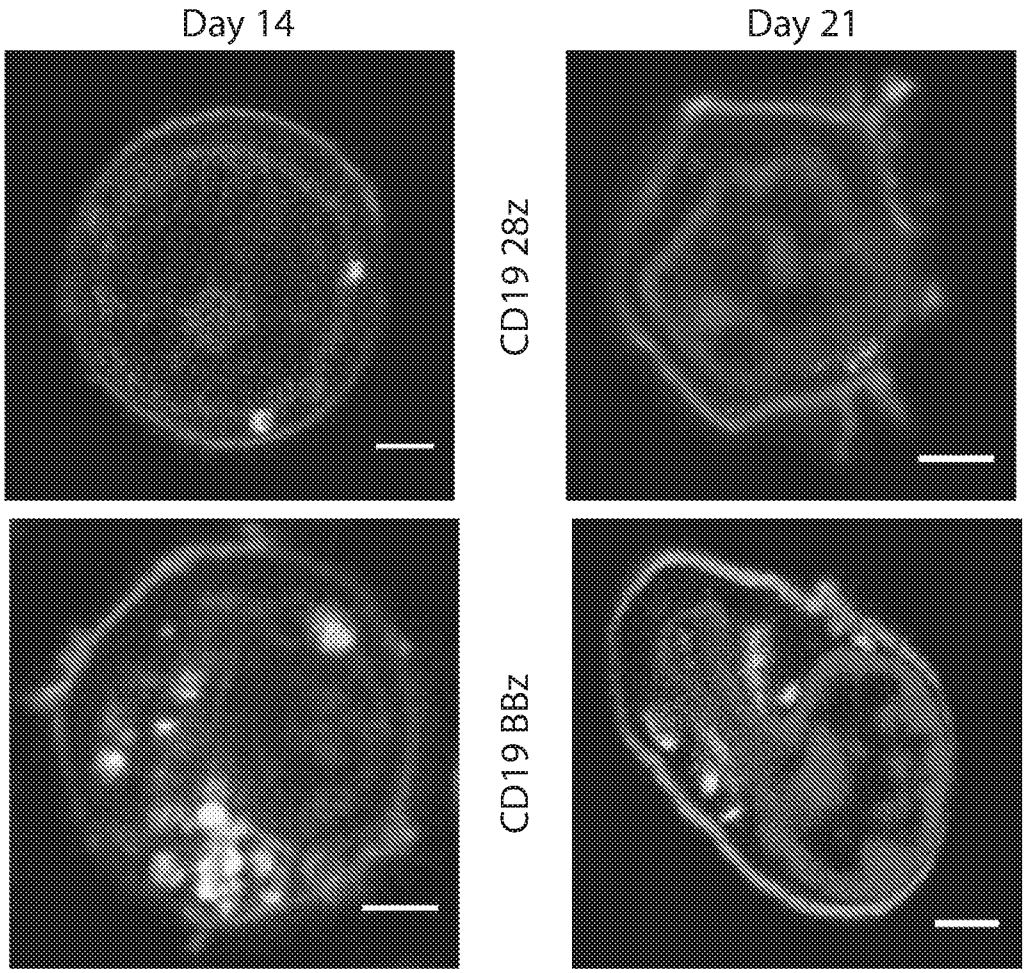


FIG. 36A

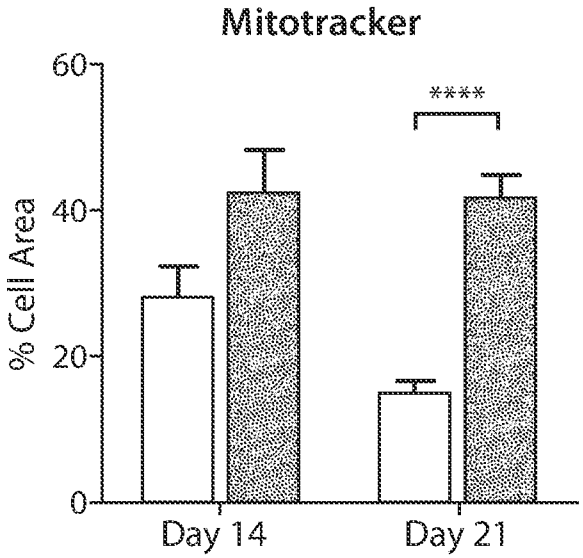


FIG. 36B

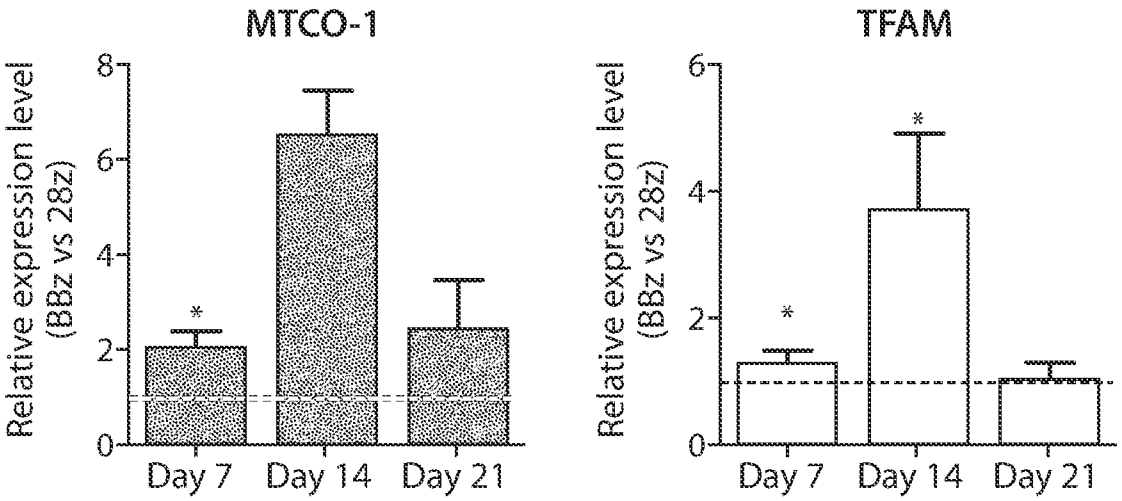


FIG. 36C

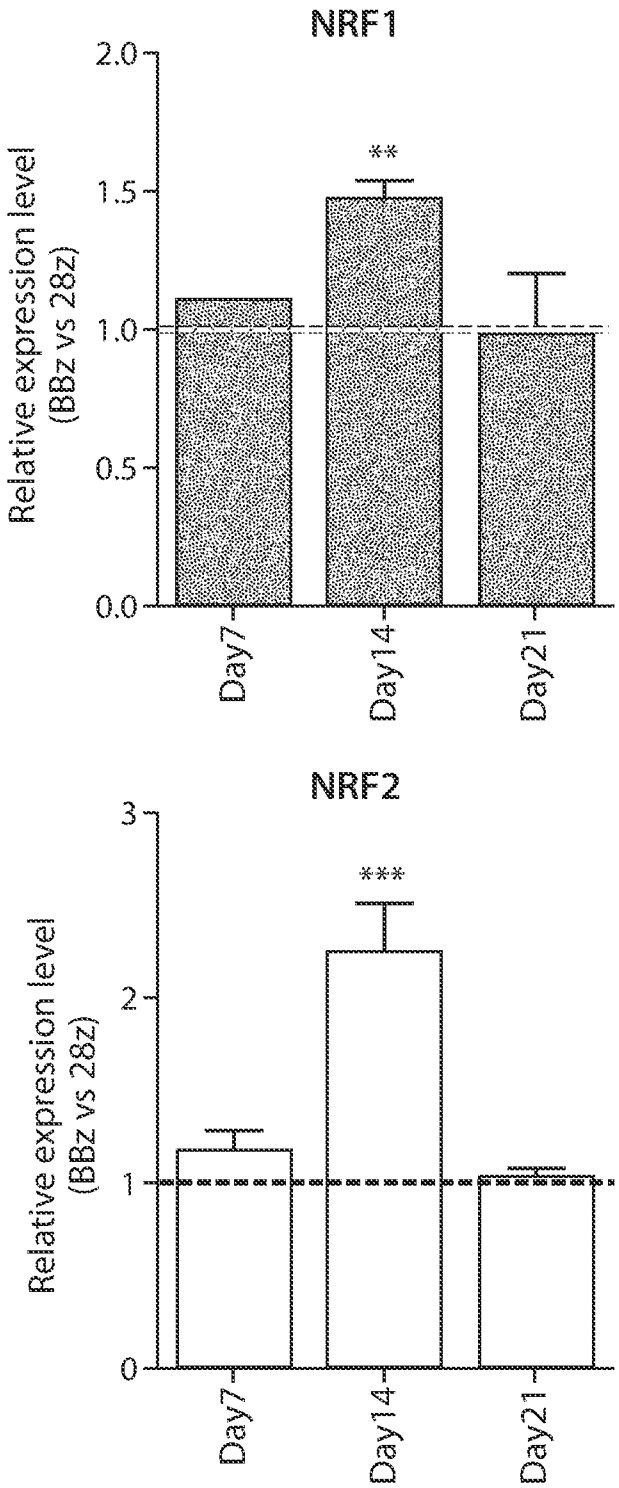

NRF1
Relative expression level
(BBz vs 28z)
2.0
1.5
1.0
0.5
0.0
**
Day7
Day14
Day21
NRF2
Relative expression level
(BBz vs 28z)
3
2
1
0
***
Day7
Day14
Day21

FIG. 36D

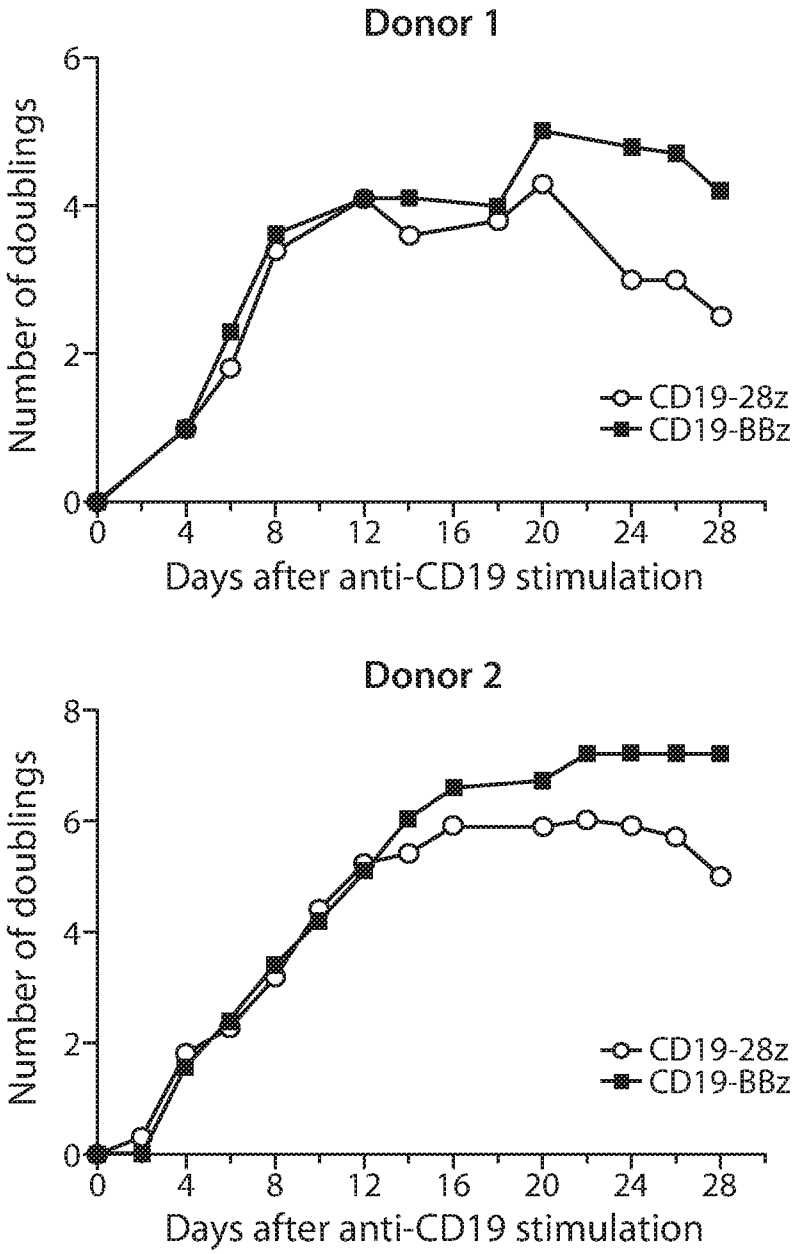

Donor 1
Number of doublings
0
2
4
6
0
4
8
12
16
20
24
28
Days after anti-CD19 stimulation
CD19-28z
CD19-BBz
Donor 2
Number of doublings
0
2
4
6
8
0
4
8
12
16
20
24
28
Days after anti-CD19 stimulation
CD19-28z
CD19-BBz

FIG. 37

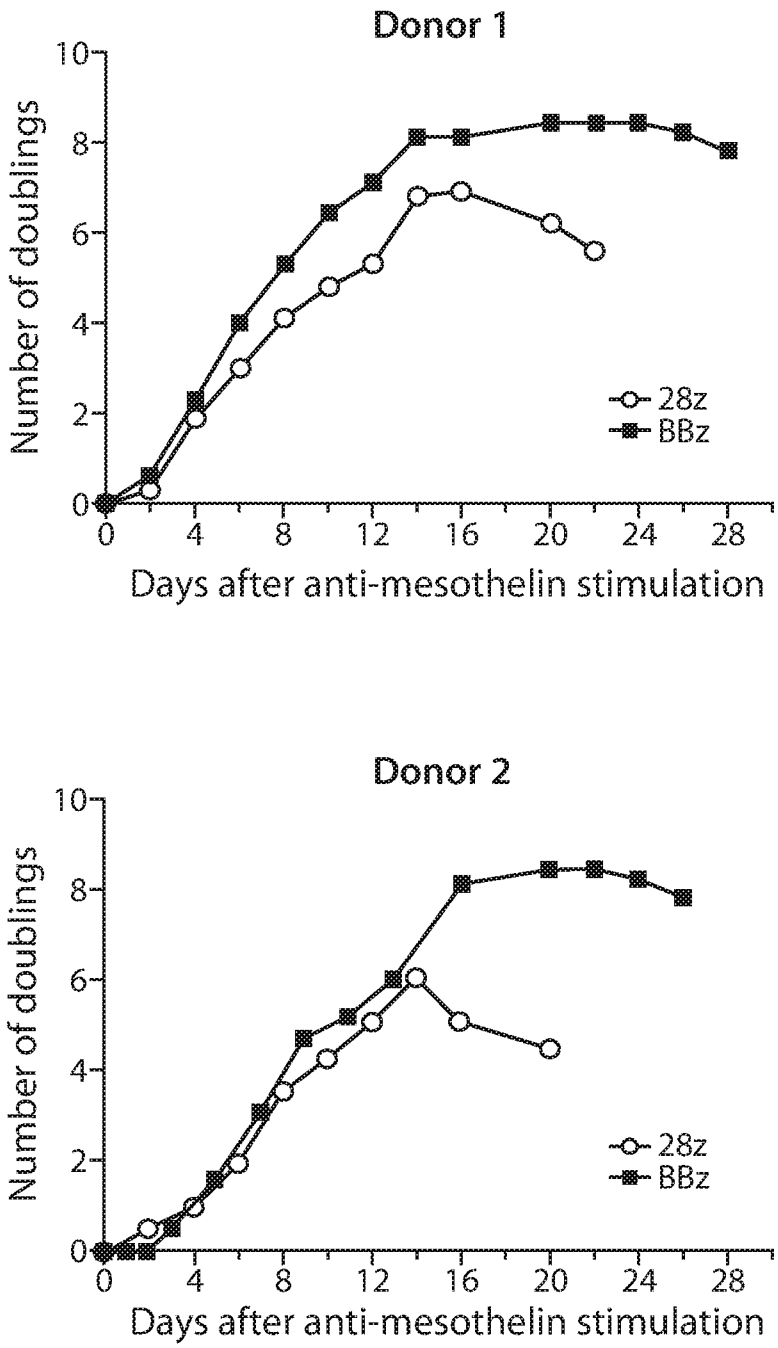

Donor 1
Number of doublings
0
2
4
6
8
10
0
4
8
12
16
20
24
28
Days after anti-mesothelin stimulation
28z
BBz
Donor 2
Number of doublings
0
2
4
6
8
10
0
4
8
12
16
20
24
28
Days after anti-mesothelin stimulation
28z
BBz

FIG. 38

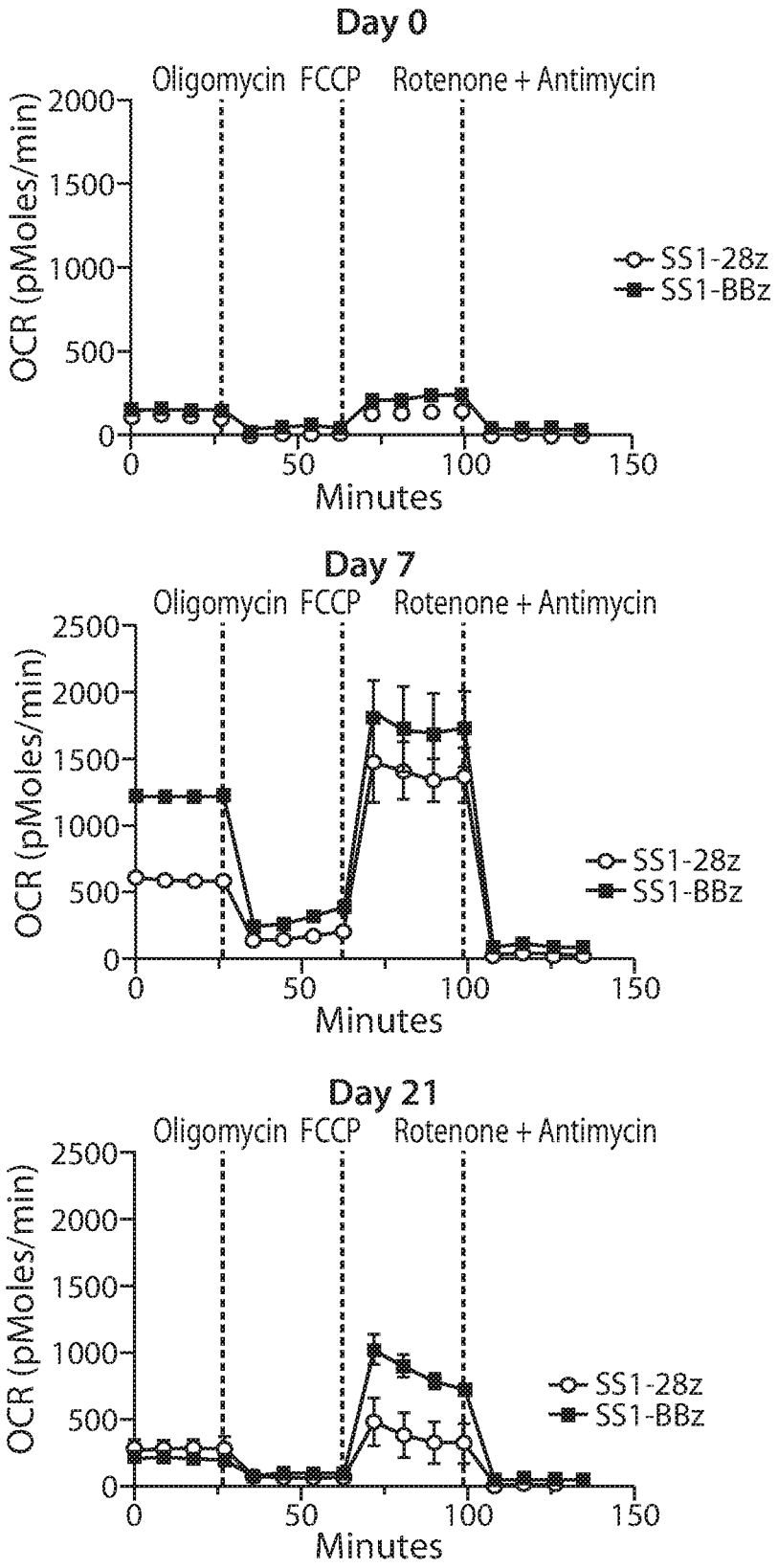

Day 0
Oligomycin
FCCP
Rotenone + Antimycin
OCR (pMoles/min)
2000
1500
1000
500
0
0
50
100
150
Minutes
SS1-28z
SS1-BBz
Day 7
Oligomycin
FCCP
Rotenone + Antimycin
OCR (pMoles/min)
2500
2000
1500
1000
500
0
0
50
100
150
Minutes
SS1-28z
SS1-BBz
Day 21
Oligomycin
FCCP
Rotenone + Antimycin
OCR (pMoles/min)
2500
2000
1500
1000
500
0
0
50
100
150
Minutes
SS1-28z
SS1-BBz

FIG. 39

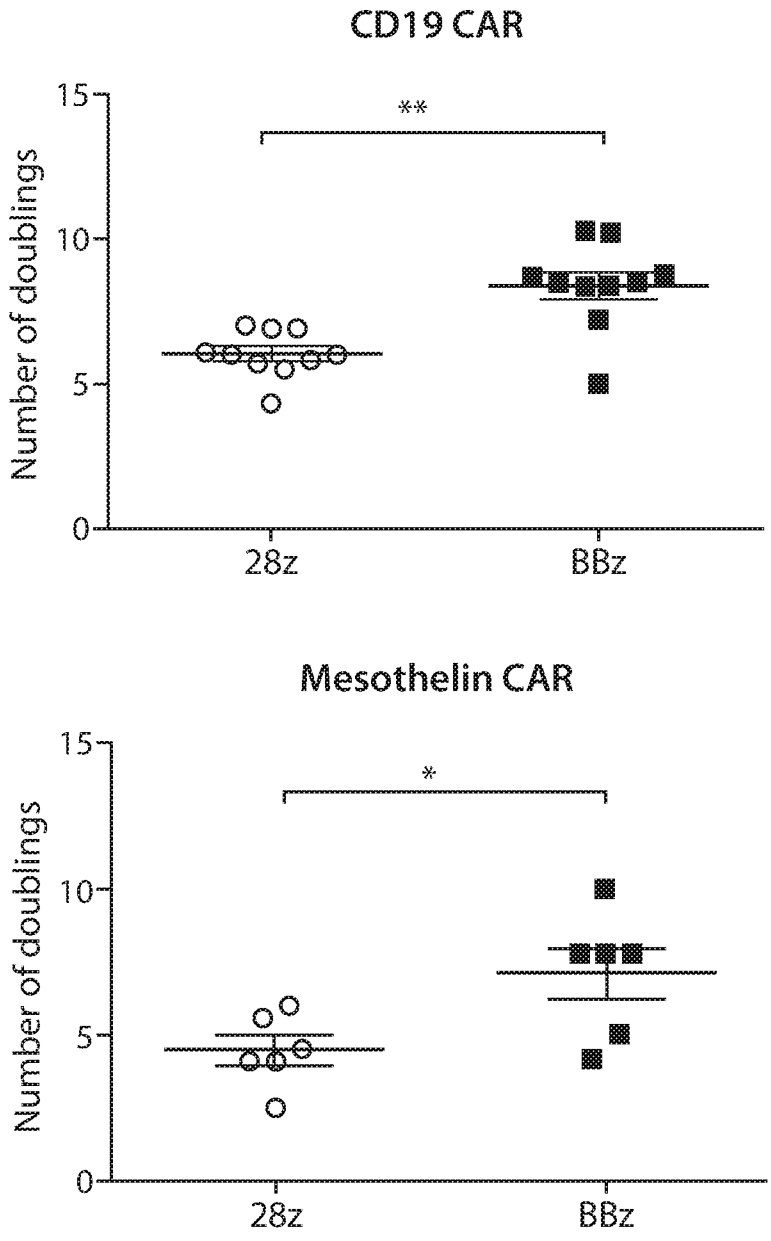

CD19 CAR
**
Number of doublings
15
10
5
0
28z
BBz
Mesothelin CAR
*
Number of doublings
15
10
5
0
28z
BBz

FIG. 40

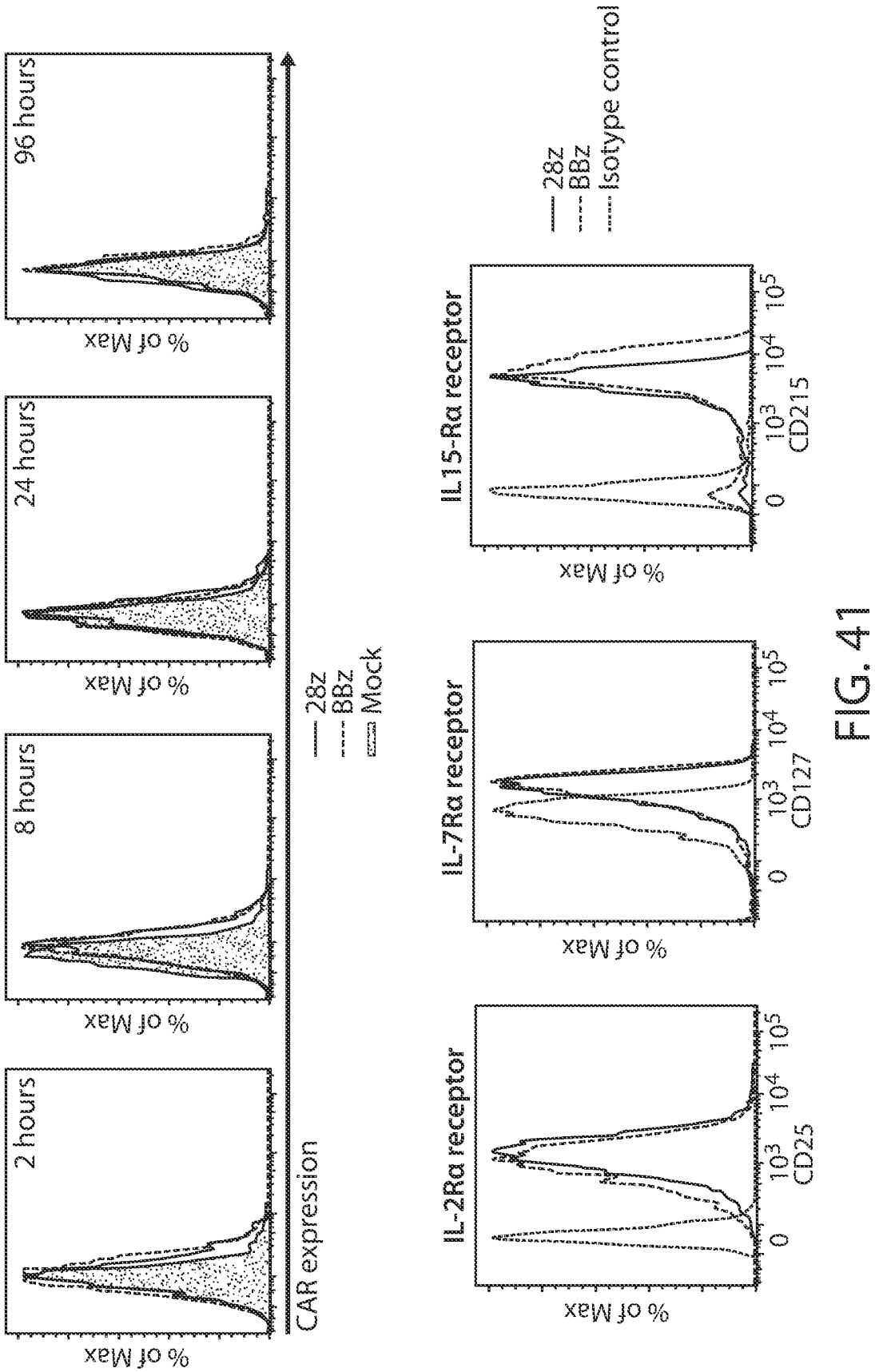

2 hours
8 hours
24 hours
96 hours
% of Max
CAR expression
28z
BBz
Mock
IL-2Rα receptor
IL-7Rα receptor
IL15-Rα receptor
CD25
CD127
CD215
0
10^3
10^4
10^5
28z
BBz
Isotype control

FIG. 41

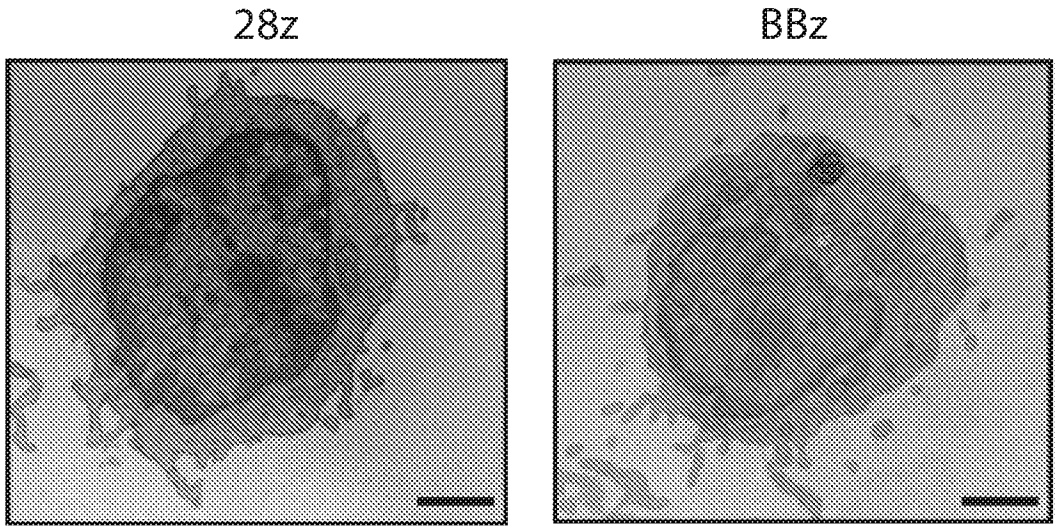


FIG. 42

_SL
SEQUENCE LISTING

<110> BEDOYA, FELIPE
GHASSEMI, SABA
JUNE, CARL H.
LEVINE, BRUCE L.
KAWALEKAR, OMKAR U.
MELENHORST, JAN J.
MILONE, MICHAEL C.
POWELL, JR., DANIEL J.
ZHENG, ZOE

<120> METHODS FOR IMPROVING THE EFFICACY AND EXPANSION OF IMMUNE CELLS

<130> N2067-7081WO

<140>
<141>

<150> 62/195,056
<151> 2015-07-21

<160> 986

<170> PatentIn version 3.5

<210> 1
<211> 21
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro
20

<210> 2
<211> 45
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 2
Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala
1 5 10 15

Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly
20 25 30

Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp
35 40 45

<210> 3
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic primer"

<400> 3
ataggatccc agctggtgga gtctggggga ggc 33

<210> 4
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic primer"

<400> 4
atagctagca cctaggacgg tcagcttggt ccc 33

<210> 5
<211> 1132
<212> PRT
<213> Homo sapiens

<400> 5
Met Pro Arg Ala Pro Arg Cys Arg Ala Val Arg Ser Leu Leu Arg Ser
1 5 10 15

His Tyr Arg Glu Val Leu Pro Leu Ala Thr Phe Val Arg Arg Leu Gly
20 25 30

Pro Gln Gly Trp Arg Leu Val Gln Arg Gly Asp Pro Ala Ala Phe Arg
35 40 45

Ala Leu Val Ala Gln Cys Leu Val Cys Val Pro Trp Asp Ala Arg Pro
50 55 60

Pro Pro Ala Ala Pro Ser Phe Arg Gln Val Ser Cys Leu Lys Glu Leu
65 70 75 80

Val Ala Arg Val Leu Gln Arg Leu Cys Glu Arg Gly Ala Lys Asn Val
85 90 95

```
                                                    _SL
Leu Ala Phe Gly Phe Ala Leu Leu Asp Gly Ala Arg Gly Gly Pro Pro
            100                 105                 110

Glu Ala Phe Thr Thr Ser Val Arg Ser Tyr Leu Pro Asn Thr Val Thr
        115                 120                 125

Asp Ala Leu Arg Gly Ser Gly Ala Trp Gly Leu Leu Leu Arg Arg Val
    130                 135                 140

Gly Asp Asp Val Leu Val His Leu Leu Ala Arg Cys Ala Leu Phe Val
145                 150                 155                 160

Leu Val Ala Pro Ser Cys Ala Tyr Gln Val Cys Gly Pro Pro Leu Tyr
                165                 170                 175

Gln Leu Gly Ala Ala Thr Gln Ala Arg Pro Pro Pro His Ala Ser Gly
            180                 185                 190

Pro Arg Arg Arg Leu Gly Cys Glu Arg Ala Trp Asn His Ser Val Arg
        195                 200                 205

Glu Ala Gly Val Pro Leu Gly Leu Pro Ala Pro Gly Ala Arg Arg Arg
    210                 215                 220

Gly Gly Ser Ala Ser Arg Ser Leu Pro Leu Pro Lys Arg Pro Arg Arg
225                 230                 235                 240

Gly Ala Ala Pro Glu Pro Glu Arg Thr Pro Val Gly Gln Gly Ser Trp
                245                 250                 255

Ala His Pro Gly Arg Thr Arg Gly Pro Ser Asp Arg Gly Phe Cys Val
            260                 265                 270

Val Ser Pro Ala Arg Pro Ala Glu Glu Ala Thr Ser Leu Glu Gly Ala
        275                 280                 285

Leu Ser Gly Thr Arg His Ser His Pro Ser Val Gly Arg Gln His His
    290                 295                 300

Ala Gly Pro Pro Ser Thr Ser Arg Pro Pro Arg Pro Trp Asp Thr Pro
305                 310                 315                 320

Cys Pro Pro Val Tyr Ala Glu Thr Lys His Phe Leu Tyr Ser Ser Gly
                325                 330                 335

Asp Lys Glu Gln Leu Arg Pro Ser Phe Leu Leu Ser Ser Leu Arg Pro
            340                 345                 350
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Ser Leu Thr Gly Ala Arg Arg Leu Val Glu Thr Ile Phe Leu Gly Ser
        355                 360                 365

Arg Pro Trp Met Pro Gly Thr Pro Arg Arg Leu Pro Arg Leu Pro Gln
    370                 375                 380

Arg Tyr Trp Gln Met Arg Pro Leu Phe Leu Glu Leu Leu Gly Asn His
385                 390                 395                 400

Ala Gln Cys Pro Tyr Gly Val Leu Leu Lys Thr His Cys Pro Leu Arg
                405                 410                 415

Ala Ala Val Thr Pro Ala Ala Gly Val Cys Ala Arg Glu Lys Pro Gln
            420                 425                 430

Gly Ser Val Ala Ala Pro Glu Glu Glu Asp Thr Asp Pro Arg Arg Leu
        435                 440                 445

Val Gln Leu Leu Arg Gln His Ser Ser Pro Trp Gln Val Tyr Gly Phe
    450                 455                 460

Val Arg Ala Cys Leu Arg Arg Leu Val Pro Pro Gly Leu Trp Gly Ser
465                 470                 475                 480

Arg His Asn Glu Arg Arg Phe Leu Arg Asn Thr Lys Lys Phe Ile Ser
                485                 490                 495

Leu Gly Lys His Ala Lys Leu Ser Leu Gln Glu Leu Thr Trp Lys Met
            500                 505                 510

Ser Val Arg Gly Cys Ala Trp Leu Arg Arg Ser Pro Gly Val Gly Cys
        515                 520                 525

Val Pro Ala Ala Glu His Arg Leu Arg Glu Glu Ile Leu Ala Lys Phe
    530                 535                 540

Leu His Trp Leu Met Ser Val Tyr Val Val Glu Leu Leu Arg Ser Phe
545                 550                 555                 560

Phe Tyr Val Thr Glu Thr Thr Phe Gln Lys Asn Arg Leu Phe Phe Tyr
                565                 570                 575

Arg Lys Ser Val Trp Ser Lys Leu Gln Ser Ile Gly Ile Arg Gln His
            580                 585                 590

Leu Lys Arg Val Gln Leu Arg Glu Leu Ser Glu Ala Glu Val Arg Gln
        595                 600                 605
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His Arg Glu Ala Arg Pro Ala Leu Leu Thr Ser Arg Leu Arg Phe Ile
    610                 615                 620

Pro Lys Pro Asp Gly Leu Arg Pro Ile Val Asn Met Asp Tyr Val Val
625                 630                 635                 640

Gly Ala Arg Thr Phe Arg Arg Glu Lys Arg Ala Glu Arg Leu Thr Ser
                645                 650                 655

Arg Val Lys Ala Leu Phe Ser Val Leu Asn Tyr Glu Arg Ala Arg Arg
            660                 665                 670

Pro Gly Leu Leu Gly Ala Ser Val Leu Gly Leu Asp Asp Ile His Arg
        675                 680                 685

Ala Trp Arg Thr Phe Val Leu Arg Val Arg Ala Gln Asp Pro Pro Pro
    690                 695                 700

Glu Leu Tyr Phe Val Lys Val Asp Val Thr Gly Ala Tyr Asp Thr Ile
705                 710                 715                 720

Pro Gln Asp Arg Leu Thr Glu Val Ile Ala Ser Ile Ile Lys Pro Gln
                725                 730                 735

Asn Thr Tyr Cys Val Arg Arg Tyr Ala Val Val Gln Lys Ala Ala His
            740                 745                 750

Gly His Val Arg Lys Ala Phe Lys Ser His Val Ser Thr Leu Thr Asp
        755                 760                 765

Leu Gln Pro Tyr Met Arg Gln Phe Val Ala His Leu Gln Glu Thr Ser
    770                 775                 780

Pro Leu Arg Asp Ala Val Val Ile Glu Gln Ser Ser Ser Leu Asn Glu
785                 790                 795                 800

Ala Ser Ser Gly Leu Phe Asp Val Phe Leu Arg Phe Met Cys His His
                805                 810                 815

Ala Val Arg Ile Arg Gly Lys Ser Tyr Val Gln Cys Gln Gly Ile Pro
            820                 825                 830

Gln Gly Ser Ile Leu Ser Thr Leu Leu Cys Ser Leu Cys Tyr Gly Asp
        835                 840                 845

Met Glu Asn Lys Leu Phe Ala Gly Ile Arg Arg Asp Gly Leu Leu Leu
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    850                 855                 860

Arg Leu Val Asp Asp Phe Leu Leu Val Thr Pro His Leu Thr His Ala
865                 870                 875                 880

Lys Thr Phe Leu Arg Thr Leu Val Arg Gly Val Pro Glu Tyr Gly Cys
                885                 890                 895

Val Val Asn Leu Arg Lys Thr Val Val Asn Phe Pro Val Glu Asp Glu
            900                 905                 910

Ala Leu Gly Gly Thr Ala Phe Val Gln Met Pro Ala His Gly Leu Phe
        915                 920                 925

Pro Trp Cys Gly Leu Leu Leu Asp Thr Arg Thr Leu Glu Val Gln Ser
    930                 935                 940

Asp Tyr Ser Ser Tyr Ala Arg Thr Ser Ile Arg Ala Ser Leu Thr Phe
945                 950                 955                 960

Asn Arg Gly Phe Lys Ala Gly Arg Asn Met Arg Arg Lys Leu Phe Gly
                965                 970                 975

Val Leu Arg Leu Lys Cys His Ser Leu Phe Leu Asp Leu Gln Val Asn
            980                 985                 990

Ser Leu Gln Thr Val Cys Thr Asn  Ile Tyr Lys Ile Leu  Leu Leu Gln
        995                 1000                1005

Ala Tyr  Arg Phe His Ala Cys  Val Leu Gln Leu Pro  Phe His Gln
    1010                1015                1020

Gln Val  Trp Lys Asn Pro Thr  Phe Phe Leu Arg Val  Ile Ser Asp
    1025                1030                1035

Thr Ala  Ser Leu Cys Tyr Ser  Ile Leu Lys Ala Lys  Asn Ala Gly
    1040                1045                1050

Met Ser  Leu Gly Ala Lys Gly  Ala Ala Gly Pro Leu  Pro Ser Glu
    1055                1060                1065

Ala Val  Gln Trp Leu Cys His  Gln Ala Phe Leu Leu  Lys Leu Thr
    1070                1075                1080

Arg His  Arg Val Thr Tyr Val  Pro Leu Leu Gly Ser  Leu Arg Thr
    1085                1090                1095
```

_SL

Ala Gln Thr Gln Leu Ser Arg Lys Leu Pro Gly Thr Thr Leu Thr
    1100   1105   1110

Ala Leu Glu Ala Ala Ala Asn Pro Ala Leu Pro Ser Asp Phe Lys
    1115   1120   1125

Thr Ile Leu Asp
    1130

<210> 6
<211> 24
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 6
Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu
1   5   10   15

Ser Leu Val Ile Thr Leu Tyr Cys
            20

<210> 7
<211> 42
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 7
Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met
1   5   10   15

Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe
            20   25   30

Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu
        35   40

<210> 8
<211> 4027
<212> DNA
<213> Homo sapiens

<400> 8
caggcagcgt ggtcctgctg cgcacgtggg aagccctggc cccggccacc cccgcgatgc   60

cgcgcgctcc ccgctgccga gccgtgcgct ccctgctgcg cagccactac cgcgaggtgc   120

tgccgctggc cacgttcgtg cggcgcctgg ggccccaggg ctggcggctg gtgcagcgcg 180

gggacccggc ggctttccgc gcgctggtgg cccagtgcct ggtgtgcgtg ccctgggacg 240

cacggccgcc ccccgccgcc ccctccttcc gccaggtgtc ctgcctgaag gagctggtgg 300

cccgagtgct gcagaggctg tgcgagcgcg gcgcgaagaa cgtgctggcc ttcggcttcg 360

cgctgctgga cggggcccgc gggggccccc ccgaggcctt caccaccagc gtgcgcagct 420

acctgcccaa cacggtgacc gacgcactgc gggggagcgg ggcgtggggg ctgctgttgc 480

gccgcgtggg cgacgacgtg ctggttcacc tgctggcacg ctgcgcgctc tttgtgctgg 540

tggctcccag ctgcgcctac caggtgtgcg ggccgccgct gtaccagctc ggcgctgcca 600

ctcaggcccg gcccccgcca cacgctagtg gaccccgaag gcgtctggga tgcgaacggg 660

cctggaacca tagcgtcagg gaggccgggg tccccctggg cctgccagcc ccgggtgcga 720

ggaggcgcgg gggcagtgcc agccgaagtc tgccgttgcc caagaggccc aggcgtggcg 780

ctgcccctga gccggagcgg acgcccgttg ggcaggggtc ctgggcccac ccgggcagga 840

cgcgtggacc gagtgaccgt ggtttctgtg tggtgtcacc tgccagaccc gccgaagaag 900

ccacctcttt ggagggtgcg ctctctggca cgcgccactc ccacccatcc gtgggccgcc 960

agcaccacgc gggccccccа tccacatcgc ggccaccacg tccctgggac acgccttgtc 1020

ccccggtgta cgccgagacc aagcacttcc tctactcctc aggcgacaag gagcagctgc 1080

ggccctcctt cctactcagc tctctgaggc ccagcctgac tggcgctcgg aggctcgtgg 1140

agaccatctt tctgggttcc aggccctgga tgccagggac tccccgcagg ttgccccgcc 1200

tgccccagcg ctactggcaa atgcggcccc tgtttctgga gctgcttggg aaccacgcgc 1260

agtgccccta cggggtgctc ctcaagacgc actgcccgct gcgagctgcg gtcaccccag 1320

cagccggtgt ctgtgcccgg gagaagcccc agggctctgt ggcggccccc gaggaggagg 1380

acacagaccc ccgtcgcctg gtgcagctgc tccgccagca cagcagcccc tggcaggtgt 1440

acggcttcgt gcgggcctgc ctgcgccggc tggtgccccc aggcctctgg ggctccaggc 1500

acaacgaacg ccgcttcctc aggaacacca agaagttcat ctccctgggg aagcatgcca 1560

agctctcgct gcaggagctg acgtggaaga tgagcgtgcg gggctgcgct tggctgcgca 1620

ggagcccagg ggttggctgt gttccggccg cagagcaccg tctgcgtgag gagatcctgg 1680

ccaagttcct gcactggctg atgagtgtgt acgtcgtcga gctgctcagg tctttctttt 1740

atgtcacgga gaccacgttt caaaagaaca ggctcttttt ctaccggaag agtgtctgga 1800

gcaagttgca aagcattgga atcagacagc acttgaagag ggtgcagctg cgggagctgt 1860

cggaagcaga ggtcaggcag catcgggaag ccaggcccgc cctgctgacg tccagactcc 1920

gcttcatccc caagcctgac gggctgcggc cgattgtgaa catggactac gtcgtgggag 1980

ccagaacgtt ccgcagagaa aagagggccg agcgtctcac ctcgagggtg aaggcactgt 2040

tcagcgtgct caactacgag cgggcgcggc gccccggcct cctgggcgcc tctgtgctgg 2100

gcctggacga tatccacagg gcctggcgca ccttcgtgct gcgtgtgcgg gcccaggacc 2160

cgccgcctga gctgtacttt gtcaaggtgg atgtgacggg cgcgtacgac accatccccc 2220

aggacaggct cacggaggtc atcgccagca tcatcaaacc ccagaacacg tactgcgtgc 2280

gtcggtatgc cgtggtccag aaggccgccc atgggcacgt ccgcaaggcc ttcaagagcc 2340

acgtctctac cttgacagac ctccagccgt acatgcgaca gttcgtggct cacctgcagg 2400

agaccagccc gctgagggat gccgtcgtca tcgagcagag ctcctccctg aatgaggcca 2460

gcagtggcct cttcgacgtc ttcctacgct tcatgtgcca ccacgccgtg cgcatcaggg 2520

gcaagtccta cgtccagtgc caggggatcc cgcagggctc catcctctcc acgctgctct 2580

gcagcctgtg ctacggcgac atggagaaca agctgtttgc ggggattcgg cgggacgggc 2640

tgctcctgcg tttggtggat gatttcttgt tggtgacacc tcacctcacc cacgcgaaaa 2700

ccttcctcag gaccctggtc cgaggtgtcc ctgagtatgg ctgcgtggtg aacttgcgga 2760

agacagtggt gaacttccct gtagaagacg aggccctggg tggcacggct tttgttcaga 2820

tgccggccca cggcctattc ccctggtgcg gcctgctgct ggatacccgg accctggagg 2880

tgcagagcga ctactccagc tatgcccgga cctccatcag agccagtctc accttcaacc 2940

gcggcttcaa ggctgggagg aacatgcgtc gcaaactctt tggggtcttg cggctgaagt 3000

gtcacagcct gtttctggat ttgcaggtga acagcctcca gacggtgtgc accaacatct 3060

acaagatcct cctgctgcag gcgtacaggt ttcacgcatg tgtgctgcag ctcccatttc 3120

atcagcaagt ttggaagaac cccacatttt tcctgcgcgt catctctgac acggcctccc 3180

tctgctactc catcctgaaa gccaagaacg cagggatgtc gctgggggcc aagggcgccg 3240

ccggccctct gccctccgag gccgtgcagt ggctgtgcca ccaagcattc ctgctcaagc 3300

tgactcgaca ccgtgtcacc tacgtgccac tcctggggtc actcaggaca gcccagacgc 3360

agctgagtcg gaagctcccg gggacgacgc tgactgccct ggaggccgca gccaacccgg 3420

cactgccctc agacttcaag accatcctgg actgatggcc acccgcccac agccaggccg 3480

agagcagaca ccagcagccc tgtcacgccg ggctctacgt cccagggagg gaggggcggc 3540

ccacacccag gcccgcaccg ctgggagtct gaggcctgag tgagtgtttg gccgaggcct 3600

gcatgtccgg ctgaaggctg agtgtccggc tgaggcctga gcgagtgtcc agccaagggc 3660

tgagtgtcca gcacacctgc cgtcttcact tccccacagg ctggcgctcg gctccacccc 3720

agggccagct tttcctcacc aggagcccgg cttccactcc ccacatagga atagtccatc 3780

cccagattcg ccattgttca cccctcgccc tgccctcctt tgccttccac ccccaccatc 3840

caggtggaga ccctgagaag gaccctggga gctctgggaa tttggagtga ccaaaggtgt 3900

gccctgtaca caggcgagga ccctgcacct ggatgggggt ccctgtgggt caaattgggg 3960

ggaggtgctg tgggagtaaa atactgaata tatgagtttt tcagttttga aaaaaaaaaa 4020

aaaaaaa 4027

<210> 9
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 9
Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly
1 5 10 15

Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr
20 25 30

Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys
35 40 45

Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys
50 55 60

Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg
65 70 75 80

Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala
85 90 95

Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
100 105 110

<210> 10
<211> 112
<212> PRT
<213> Homo sapiens

<400> 10
Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly
1 5 10 15

Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr
20 25 30

Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys
35 40 45

Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys
50 55 60

Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg
65 70 75 80

Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala
85 90 95

Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
100 105 110

<210> 11
<211> 1184
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 11
cgtgaggctc cggtgcccgt cagtgggcag agcgcacatc gcccacagtc cccgagaagt 60

tgggggggagg ggtcggcaat tgaaccggtg cctagagaag gtggcgcggg gtaaactggg 120

aaagtgatgt cgtgtactgg ctccgccttt ttcccgaggg tgggggagaa ccgtatataa 180

gtgcagtagt cgccgtgaac gttctttttc gcaacgggtt tgccgccaga acacaggtaa 240

gtgccgtgtg tggttcccgc gggcctggcc tctttacggg ttatggccct tgcgtgcctt 300

gaattacttc cacctggctg cagtacgtga ttcttgatcc cgagcttcgg gttggaagtg 360

ggtgggagag ttcgaggcct tgcgcttaag gagcccttc gcctcgtgct tgagttgagg 420

cctggcctgg gcgctggggc cgccgcgtgc gaatctggtg gcaccttcgc gcctgtctcg 480

ctgctttcga taagtctcta gccatttaaa atttttgatg acctgctgcg acgcttttt 540

tctggcaaga tagtcttgta aatgcgggcc aagatctgca cactggtatt tcggtttttg 600

gggccgcggg cggcgacggg gcccgtgcgt cccagcgcac atgttcggcg aggcggggcc 660

tgcgagcgcg gccaccgaga atcggacggg ggtagtctca agctggccgg cctgctctgg 720

tgcctggcct cgcgccgccg tgtatcgccc cgccctgggc ggcaaggctg gcccggtcgg 780

caccagttgc gtgagcggaa agatggccgc ttcccggccc tgctgcaggg agctcaaaat 840

ggaggacgcg gcgctcggga gagcgggcgg gtgagtcacc cacacaaagg aaaagggcct 900

ttccgtcctc agccgtcgct tcatgtgact ccacggagta ccgggcgccg tccaggcacc 960

tcgattagtt ctcgagcttt tggagtacgt cgtctttagg ttgggggggag gggttttatg 1020

cgatggagtt tccccacact gagtgggtgg agactgaagt taggccagct tggcacttga 1080

tgtaattctc cttggaattt gccctttttg agtttggatc ttggttcatt ctcaagcctc 1140

agacagtggt tcaaagtttt tttcttccat ttcaggtgtc gtga 1184

<210> 12
<211> 63
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic oligonucleotide"

<400> 12
atggccctgc ctgtgacagc cctgctgctg cctctggctc tgctgctgca tgccgctaga 60

ccc 63

<210> 13
<211> 135
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 13
accacgacgc cagcgccgcg accaccaaca ccggcgccca ccatcgcgtc gcagcccctg 60

tccctgcgcc cagaggcgtg ccggccagcg gcgggggcg cagtgcacac gagggggctg 120

gacttcgcct gtgat 135

<210> 14
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 14
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
1 5 10

<210> 15
<211> 123
<212> DNA
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 15
aggagtaaga ggagcaggct cctgcacagt gactacatga acatgactcc ccgccgcccc 60

gggcccaccc gcaagcatta ccagccctat gccccaccac gcgacttcgc agcctatcgc 120

tcc 123

<210> 16
<211> 48
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 16
Gln Arg Arg Lys Tyr Arg Ser Asn Lys Gly Glu Ser Pro Val Glu Pro
1 5 10 15

Ala Glu Pro Cys Arg Tyr Ser Cys Pro Arg Glu Glu Glu Gly Ser Thr
20 25 30

Ile Pro Ile Gln Glu Asp Tyr Arg Lys Pro Glu Pro Ala Cys Ser Pro
35 40 45

<210> 17
<211> 72
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic oligonucleotide"

<400> 17
atctacatct gggcgccctt ggccgggact tgtggggtcc ttctcctgtc actggttatc 60

acccttttact gc 72

<210> 18
<211> 126
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 18
aaacggggca gaaagaaact cctgtatata ttcaaacaac catttatgag accagtacaa 60

actactcaag aggaagatgg ctgtagctgc cgatttccag aagaagaaga aggaggatgt 120

gaactg 126

<210> 19
<211> 30
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic oligonucleotide"

<400> 19
ggtggcggag gttctggagg tggaggttcc 30

<210> 20
<211> 336
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 20
agagtgaagt tcagcaggag cgcagacgcc cccgcgtaca agcagggcca gaaccagctc 60

tataacgagc tcaatctagg acgaagagag gagtacgatg ttttggacaa gagacgtggc 120

cgggaccctg agatgggggg aaagccgaga aggaagaacc ctcaggaagg cctgtacaat 180

gaactgcaga aagataagat ggcggaggcc tacagtgaga ttgggatgaa aggcgagcgc 240

cggaggggca aggggcacga tggcctttac cagggtctca gtacagccac caaggacacc 300

tacgacgccc ttcacatgca ggccctgccc cctcgc 336

<210> 21
<211> 336
<212> DNA
<213> Homo sapiens

<400> 21
agagtgaagt tcagcaggag cgcagacgcc cccgcgtacc agcagggcca gaaccagctc 60

tataacgagc tcaatctagg acgaagagag gagtacgatg ttttggacaa gagacgtggc 120

cgggaccctg agatgggggg aaagccgaga aggaagaacc ctcaggaagg cctgtacaat 180

gaactgcaga aagataagat ggcggaggcc tacagtgaga ttgggatgaa aggcgagcgc 240

cggaggggca aggggcacga tggcctttac cagggtctca gtacagccac caaggacacc 300

tacgacgccc ttcacatgca ggccctgccc cctcgc 336

<210> 22

<211> 40
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<220>
<221> MISC_FEATURE
<222> (1)..(40)
<223> /note="This sequence may encompass 1-10 'Gly Gly Gly Ser' repeating units"

<400> 22
Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser
1 5 10 15

Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser
20 25 30

Gly Gly Gly Ser Gly Gly Gly Ser
35 40

<210> 23
<211> 282
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 23
Arg Trp Pro Glu Ser Pro Lys Ala Gln Ala Ser Ser Val Pro Thr Ala
1 5 10 15

Gln Pro Gln Ala Glu Gly Ser Leu Ala Lys Ala Thr Thr Ala Pro Ala
20 25 30

Thr Thr Arg Asn Thr Gly Arg Gly Gly Glu Glu Lys Lys Lys Glu Lys
35 40 45

Glu Lys Glu Glu Gln Glu Glu Arg Glu Thr Lys Thr Pro Glu Cys Pro
50 55 60

Ser His Thr Gln Pro Leu Gly Val Tyr Leu Leu Thr Pro Ala Val Gln
65 70 75 80

Asp Leu Trp Leu Arg Asp Lys Ala Thr Phe Thr Cys Phe Val Val Gly
85 90 95

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Ser Asp Leu Lys Asp Ala His Leu Thr Trp Glu Val Ala Gly Lys Val
            100                 105                 110

Pro Thr Gly Gly Val Glu Glu Gly Leu Leu Glu Arg His Ser Asn Gly
        115                 120                 125

Ser Gln Ser Gln His Ser Arg Leu Thr Leu Pro Arg Ser Leu Trp Asn
    130                 135                 140

Ala Gly Thr Ser Val Thr Cys Thr Leu Asn His Pro Ser Leu Pro Pro
145                 150                 155                 160

Gln Arg Leu Met Ala Leu Arg Glu Pro Ala Ala Gln Ala Pro Val Lys
                165                 170                 175

Leu Ser Leu Asn Leu Leu Ala Ser Ser Asp Pro Pro Glu Ala Ala Ser
            180                 185                 190

Trp Leu Leu Cys Glu Val Ser Gly Phe Ser Pro Pro Asn Ile Leu Leu
        195                 200                 205

Met Trp Leu Glu Asp Gln Arg Glu Val Asn Thr Ser Gly Phe Ala Pro
    210                 215                 220

Ala Arg Pro Pro Pro Gln Pro Gly Ser Thr Thr Phe Trp Ala Trp Ser
225                 230                 235                 240

Val Leu Arg Val Pro Ala Pro Pro Ser Pro Gln Pro Ala Thr Tyr Thr
                245                 250                 255

Cys Val Val Ser His Glu Asp Ser Arg Thr Leu Leu Asn Ala Ser Arg
            260                 265                 270

Ser Leu Glu Val Ser Tyr Val Thr Asp His
        275                 280
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<210> 24
<211> 847
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 24
aggtggcccg aaagtcccaa ggcccaggca tctagtgttc ctactgcaca gccccaggca 60

gaaggcagcc tagccaaagc tactactgca cctgccacta cgcgcaatac tggccgtggc 120

ggggaggaga agaaaaagga gaaagagaaa gaagaacagg aagagaggga gaccaagacc 180

cctgaatgtc catcccatac ccagccgctg ggcgtctatc tcttgactcc cgcagtacag 240

gacttgtggc ttagagataa ggccaccttt acatgtttcg tcgtgggctc tgacctgaag 300

gatgcccatt tgacttggga ggttgccgga aaggtaccca cagggggggt tgaggaaggg 360

ttgctggagc gccattccaa tggctctcag agccagcact caagactcac ccttccgaga 420

tccctgtgga acgccgggac ctctgtcaca tgtactctaa atcatcctag cctgccccca 480

cagcgtctga tggcccttag agagccagcc gcccaggcac cagttaagct tagcctgaat 540

ctgctcgcca gtagtgatcc cccagaggcc gccagctggc tcttatgcga agtgtccggc 600

tttagcccgc ccaacatctt gctcatgtgg ctggaggacc agcgagaagt gaacaccagc 660

ggcttcgctc cagcccggcc cccaccccag ccgggttcta ccacattctg ggcctggagt 720

gtcttaaggg tcccagcacc acctagcccc cagccagcca catacacctg tgttgtgtcc 780

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<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 25
Gly Gly Gly Gly Ser
1 5

<210> 26
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<220>
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<222> (1)..(30)
<223> /note="This sequence may encompass 1-6 'Gly Gly Gly Gly Ser' repeating units"

<400> 26
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1 5 10 15

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
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<210> 27
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
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<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 27
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1 5 10 15

Gly Gly Gly Ser
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<210> 28
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
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<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 28
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
1 5 10 15

<210> 29
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
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<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 29
Gly Gly Gly Ser
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<210> 30
<211> 5000
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

polynucleotide"

<220>
<221> misc_feature
<222> (1)..(5000)
<223> /note="This sequence may encompass 50-5000 nucleotides"

<400> 30
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aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 120

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 180

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 240

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 300

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 360

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 420

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 480

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 540

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 600

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 660

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 720

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 780

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 840

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 900

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aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1080

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1140

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1200

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<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

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<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<220>
<221> misc_feature
<222> (1)..(5000)
<223> /note="This sequence may encompass 50-5000 nucleotides"

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<211> 5000
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
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<220>
<221> misc_feature
<222> (1)..(5000)
<223> /note="This sequence may encompass 100-5000 nucleotides"

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aaaaaaaaaa aaaaaaaaaa 5000

<210> 34

<211> 400
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<220>
<221> misc_feature
<222> (1)..(400)
<223> /note="This sequence may encompass 100-400 nucleotides"

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aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 300

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aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 400

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<211> 2000
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<220>
<221> misc_feature
<222> (1)..(2000)
<223> /note="This sequence may encompass 50-2000 nucleotides"

<400> 35
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 60

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 120

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 180

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 240

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 300

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 360

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 420

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 480

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 540

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 600

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 660

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 720

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 780

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 840

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 900

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 960

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1020

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1080

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1140

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1200

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1260

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1320

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1380

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1440

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1500

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1560

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1620

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1680

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1740

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1800

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1860

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1920

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1980

aaaaaaaaaa aaaaaaaaaa 2000

<210> 36
<211> 230
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 36

```
Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe
1               5                  10                  15

Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
            20                  25                  30

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
        35                  40                  45

Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val
    50                  55                  60

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser
65                  70                  75                  80

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
                85                  90                  95

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser
            100                 105                 110

Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
        115                 120                 125

Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln
    130                 135                 140

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
145                 150                 155                 160

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
                165                 170                 175

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu
            180                 185                 190

Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser
        195                 200                 205

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
    210                 215                 220

Leu Ser Leu Gly Lys Met
225                 230
```

<210> 37

<211> 690
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 37
gagagcaagt acggccctcc ctgcccccct tgccctgccc ccgagttcct gggcggaccc 60

agcgtgttcc tgttcccccc caagcccaag gacaccctga tgatcagccg gacccccgag 120

gtgacctgtg tggtggtgga cgtgtcccag gaggaccccg aggtccagtt caactggtac 180

gtggacggcg tggaggtgca caacgccaag accaagcccc gggaggagca gttcaatagc 240

acctaccggg tggtgtccgt gctgaccgtg ctgcaccagg actggctgaa cggcaaggaa 300

tacaagtgta aggtgtccaa caagggcctg cccagcagca tcgagaaaac catcagcaag 360

gccaagggcc agcctcggga gccccaggtg tacaccctgc cccctagcca agaggagatg 420

accaagaacc aggtgtccct gacctgcctg gtgaagggct tctaccccag cgacatcgcc 480

gtggagtggg agagcaacgg ccagcccgag aacaactaca agaccacccc ccctgtgctg 540

gacagcgacg gcagcttctt cctgtacagc cggctgaccg tggacaagag ccggtggcag 600

gagggcaacg tctttagctg ctccgtgatg cacgaggccc tgcacaacca ctacacccag 660

aagagcctga gcctgtccct gggcaagatg 690

<210> 38
<211> 40
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<220>
<221> MISC_FEATURE
<222> (1)..(40)
<223> /note="This sequence may encompass 1-10 'Gly Gly Gly Ser' repeating units"

<400> 38
Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser
1 5 10 15

Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser
20 25 30

Gly Gly Gly Ser Gly Gly Gly Ser
35 40

<210> 39
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 39

```
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1               5                  10                  15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr
            20                  25                  30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
        35                  40                  45

Tyr His Thr Ser Arg Leu His Ser Gly Ile Pro Ala Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser
            100                 105                 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Glu
        115                 120                 125

Ser Gly Pro Gly Leu Val Lys Pro Ser Glu Thr Leu Ser Leu Thr Cys
    130                 135                 140

Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg
145                 150                 155                 160

Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly Val Ile Trp Gly Ser
                165                 170                 175

Glu Thr Thr Tyr Tyr Ser Ser Ser Leu Lys Ser Arg Val Thr Ile Ser
            180                 185                 190

Lys Asp Asn Ser Lys Asn Gln Val Ser Leu Lys Leu Ser Ser Val Thr
        195                 200                 205
```

Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly
210 215 220

Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val
225 230 235 240

Ser Ser

<210> 40
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 40
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45

Tyr His Thr Ser Arg Leu His Ser Gly Ile Pro Ala Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser
100 105 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Glu
115 120 125

Ser Gly Pro Gly Leu Val Lys Pro Ser Glu Thr Leu Ser Leu Thr Cys
130 135 140

Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg
145 150 155 160

```
Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly Val Ile Trp Gly Ser
                165                 170                 175

Glu Thr Thr Tyr Tyr Gln Ser Ser Leu Lys Ser Arg Val Thr Ile Ser
            180                 185                 190

Lys Asp Asn Ser Lys Asn Gln Val Ser Leu Lys Leu Ser Ser Val Thr
        195                 200                 205

Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly
    210                 215                 220

Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val
225                 230                 235                 240

Ser Ser
```

<210> 41
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 41

```
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1               5                   10                  15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr
            20                  25                  30

Gly Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
        35                  40                  45

Gly Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Ser Ser Ser Leu Lys
    50                  55                  60

Ser Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn Gln Val Ser Leu
65                  70                  75                  80

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
                85                  90                  95

Lys His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln
            100                 105                 110
```

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Met Thr Gln Ser Pro Ala
130 135 140

Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala
145 150 155 160

Ser Gln Asp Ile Ser Lys Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly
165 170 175

Gln Ala Pro Arg Leu Leu Ile Tyr His Thr Ser Arg Leu His Ser Gly
180 185 190

Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu
195 200 205

Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Val Tyr Phe Cys Gln
210 215 220

Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu
225 230 235 240

Ile Lys

<210> 42
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 42
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr
20 25 30

Gly Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Gln Ser Ser Leu Lys
50 55 60

```
Ser Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn Gln Val Ser Leu
65                  70                  75                  80

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
                85                  90                  95

Lys His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115                 120                 125

Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Met Thr Gln Ser Pro Ala
    130                 135                 140

Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala
145                 150                 155                 160

Ser Gln Asp Ile Ser Lys Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly
                165                 170                 175

Gln Ala Pro Arg Leu Leu Ile Tyr His Thr Ser Arg Leu His Ser Gly
            180                 185                 190

Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu
        195                 200                 205

Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Val Tyr Phe Cys Gln
    210                 215                 220

Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu
225                 230                 235                 240

Ile Lys
```

<210> 43
<211> 247
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 43

```
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1               5                  10                  15
```

```
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr
            20                  25                  30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
        35                  40                  45

Tyr His Thr Ser Arg Leu His Ser Gly Ile Pro Ala Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser
            100                 105                 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln
        115                 120                 125

Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu Thr
    130                 135                 140

Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly
145                 150                 155                 160

Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly
                165                 170                 175

Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Ser Ser Ser Leu Lys Ser
            180                 185                 190

Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn Gln Val Ser Leu Lys
        195                 200                 205

Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Lys
    210                 215                 220

His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly
225                 230                 235                 240

Thr Leu Val Thr Val Ser Ser
                245
```

<210> 44

<211> 247
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 44

```
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1               5                  10                  15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr
            20                  25                  30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
        35                  40                  45

Tyr His Thr Ser Arg Leu His Ser Gly Ile Pro Ala Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser
            100                 105                 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln
        115                 120                 125

Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu Thr
    130                 135                 140

Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly
145                 150                 155                 160

Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly
                165                 170                 175

Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Gln Ser Ser Leu Lys Ser
            180                 185                 190

Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn Gln Val Ser Leu Lys
        195                 200                 205

Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Lys
```

_SL
210 215 220

His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly
225 230 235 240

Thr Leu Val Thr Val Ser Ser
245

<210> 45
<211> 247
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 45
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr
20 25 30

Gly Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Ser Ser Ser Leu Lys
50 55 60

Ser Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn Gln Val Ser Leu
65 70 75 80

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Lys His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Met
130 135 140

Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr
145 150 155 160

Leu Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr Leu Asn Trp Tyr

_SL
165 170 175

Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr His Thr Ser
180 185 190

Arg Leu His Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly
195 200 205

Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
210 215 220

Val Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
225 230 235 240

Gly Thr Lys Leu Glu Ile Lys
245

<210> 46
<211> 247
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 46
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr
20 25 30

Gly Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Gln Ser Ser Leu Lys
50 55 60

Ser Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn Gln Val Ser Leu
65 70 75 80

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Lys His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly

_SL
115 120 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Met
130 135 140

Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr
145 150 155 160

Leu Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr Leu Asn Trp Tyr
165 170 175

Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr His Thr Ser
180 185 190

Arg Leu His Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly
195 200 205

Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
210 215 220

Val Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
225 230 235 240

Gly Thr Lys Leu Glu Ile Lys
245

<210> 47
<211> 247
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 47
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45

Tyr His Thr Ser Arg Leu His Ser Gly Ile Pro Ala Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro

_SL
65 70 75 80

Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser
100 105 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln
115 120 125

Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu Thr
130 135 140

Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly
145 150 155 160

Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly
165 170 175

Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Asn Ser Ser Leu Lys Ser
180 185 190

Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn Gln Val Ser Leu Lys
195 200 205

Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Lys
210 215 220

His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly
225 230 235 240

Thr Leu Val Thr Val Ser Ser
245

<210> 48
<211> 247
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 48
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr

_SL

20 25 30

Gly Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Asn Ser Ser Leu Lys
50 55 60

Ser Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn Gln Val Ser Leu
65 70 75 80

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Lys His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Met
130 135 140

Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr
145 150 155 160

Leu Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr Leu Asn Trp Tyr
165 170 175

Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr His Thr Ser
180 185 190

Arg Leu His Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly
195 200 205

Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
210 215 220

Val Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
225 230 235 240

Gly Thr Lys Leu Glu Ile Lys
245

<210> 49
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 49

```
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1               5                  10                  15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr
            20                  25                  30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
        35                  40                  45

Tyr His Thr Ser Arg Leu His Ser Gly Ile Pro Ala Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser
            100                 105                 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Glu
        115                 120                 125

Ser Gly Pro Gly Leu Val Lys Pro Ser Glu Thr Leu Ser Leu Thr Cys
    130                 135                 140

Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg
145                 150                 155                 160

Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly Val Ile Trp Gly Ser
                165                 170                 175

Glu Thr Thr Tyr Tyr Asn Ser Ser Leu Lys Ser Arg Val Thr Ile Ser
            180                 185                 190

Lys Asp Asn Ser Lys Asn Gln Val Ser Leu Lys Leu Ser Ser Val Thr
        195                 200                 205

Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly
    210                 215                 220
```

_SL
Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val
225 230 235 240

Ser Ser

<210> 50
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 50
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr
20 25 30

Gly Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Asn Ser Ser Leu Lys
50 55 60

Ser Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn Gln Val Ser Leu
65 70 75 80

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Lys His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Met Thr Gln Ser Pro Ala
130 135 140

Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala
145 150 155 160

Ser Gln Asp Ile Ser Lys Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly
165 170 175

_SL
Gln Ala Pro Arg Leu Leu Ile Tyr His Thr Ser Arg Leu His Ser Gly
180 185 190

Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu
195 200 205

Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Val Tyr Phe Cys Gln
210 215 220

Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu
225 230 235 240

Ile Lys

<210> 51
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 51
Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly
1 5 10 15

Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Val Lys Leu Leu Ile
35 40 45

Tyr His Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Gln
65 70 75 80

Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Thr Gly Gly Gly Gly Ser
100 105 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Lys Leu Gln Glu
115 120 125

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                                                _SL
Ser Gly Pro Gly Leu Val Ala Pro Ser Gln Ser Leu Ser Val Thr Cys
    130                 135                 140

Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg
145                 150                 155                 160

Gln Pro Pro Arg Lys Gly Leu Glu Trp Leu Gly Val Ile Trp Gly Ser
                165                 170                 175

Glu Thr Thr Tyr Tyr Asn Ser Ala Leu Lys Ser Arg Leu Thr Ile Ile
            180                 185                 190

Lys Asp Asn Ser Lys Ser Gln Val Phe Leu Lys Met Asn Ser Leu Gln
        195                 200                 205

Thr Asp Asp Thr Ala Ile Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly
    210                 215                 220

Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser Val Thr Val
225                 230                 235                 240

Ser Ser
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<210> 52
<211> 813
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 52
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaaattg tgatgaccca gtcacccgcc actcttagcc tttcacccgg tgagcgcgca 120

accctgtctt gcagagcctc ccaagacatc tcaaaatacc ttaattggta tcaacagaag 180

cccggacagg ctcctcgcct tctgatctac cacaccagcc ggctccattc tggaatccct 240

gccaggttca gcggtagcgg atctgggacc gactacaccc tcactatcag ctcactgcag 300

ccagaggact tcgctgtcta tttctgtcag caagggaaca ccctgcccta cacctttgga 360

cagggcacca agctcgagat taaaggtgga ggtggcagcg gaggaggtgg gtccggcggt 420

ggaggaagcc aggtccaact ccaagaaagc ggaccgggtc ttgtgaagcc atcagaaact 480

ctttcactga cttgtactgt gagcggagtg tctctccccg attacggggt gtcttggatc 540

agacagccac cggggaaggg tctggaatgg attggagtga tttggggctc tgagactact 600

tactactctt catccctcaa gtcacgcgtc accatctcaa aggacaactc taagaatcag 660

gtgtcactga aactgtcatc tgtgaccgca gccgacaccg ccgtgtacta ttgcgctaag 720

cattactatt atggcgggag ctacgcaatg gattactggg gacagggtac tctggtcacc 780

gtgtccagcc accaccatca tcaccatcac cat 813

<210> 53
<211> 813
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 53
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaaattg tgatgaccca gtcacccgcc actcttagcc tttcacccgg tgagcgcgca 120

accctgtctt gcagagcctc ccaagacatc tcaaaatacc ttaattggta tcaacagaag 180

cccggacagg ctcctcgcct tctgatctac cacaccagcc ggctccattc tggaatccct 240

gccaggttca gcggtagcgg atctgggacc gactacaccc tcactatcag ctcactgcag 300

ccagaggact tcgctgtcta tttctgtcag caagggaaca ccctgcccta caccttgga 360

cagggcacca agctcgagat taaaggtgga ggtggcagcg gaggaggtgg gtccggcggt 420

ggaggaagcc aggtccaact ccaagaaagc ggaccgggtc ttgtgaagcc atcagaaact 480

ctttcactga cttgtactgt gagcggagtg tctctccccg attacggggt gtcttggatc 540

agacagccac cggggaaggg tctggaatgg attggagtga tttggggctc tgagactact 600

tactaccaat catccctcaa gtcacgcgtc accatctcaa aggacaactc taagaatcag 660

gtgtcactga aactgtcatc tgtgaccgca gccgacaccg ccgtgtacta ttgcgctaag 720

cattactatt atggcgggag ctacgcaatg gattactggg gacagggtac tctggtcacc 780

gtgtccagcc accaccatca tcaccatcac cat 813

<210> 54
<211> 813
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 54
atggctctgc ccgtgaccgc actcctcctg ccactggctc tgctgcttca cgccgctcgc 60

ccacaagtcc agcttcaaga atcagggcct ggtctggtga agccatctga gactctgtcc 120

ctcacttgca ccgtgagcgg agtgtccctc ccagactacg gagtgagctg gattagacag 180

cctcccggaa agggactgga gtggatcgga gtgatttggg gtagcgaaac cacttactat 240

tcatcttccc tgaagtcacg ggtcaccatt tcaaaggata actcaaagaa tcaagtgagc 300

ctcaagctct catcagtcac cgccgctgac accgccgtgt attactgtgc caagcattac 360

tactatggag ggtcctacgc catggactac tggggccagg gaactctggt cactgtgtca 420

tctggtggag gaggtagcgg aggaggcggg agcggtggag gtggctccga aatcgtgatg 480

acccagagcc ctgcaaccct gtccctttct cccggggaac gggctaccct ttcttgtcgg 540

gcatcacaag atatctcaaa atacctcaat tggtatcaac agaagccggg acaggcccct 600

aggcttctta tctaccacac ctctcgcctg catagcggga ttcccgcacg ctttagcggg 660

tctggaagcg ggaccgacta cactctgacc atctcatctc tccagcccga ggacttcgcc 720

gtctacttct gccagcaggg taacaccctg ccgtacacct tcggccaggg caccaagctt 780

gagatcaaac atcaccacca tcatcaccat cac 813

<210> 55
<211> 813
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 55
atggctctgc ccgtgaccgc actcctcctg ccactggctc tgctgcttca cgccgctcgc 60

ccacaagtcc agcttcaaga atcagggcct ggtctggtga agccatctga gactctgtcc 120

ctcacttgca ccgtgagcgg agtgtccctc ccagactacg gagtgagctg gattagacag 180

cctcccggaa agggactgga gtggatcgga gtgatttggg gtagcgaaac cacttactat 240

caatcttccc tgaagtcacg ggtcaccatt tcaaaggata actcaaagaa tcaagtgagc 300

ctcaagctct catcagtcac cgccgctgac accgccgtgt attactgtgc caagcattac 360

tactatggag ggtcctacgc catggactac tggggccagg gaactctggt cactgtgtca 420

tctggtggag gaggtagcgg aggaggcggg agcggtggag gtggctccga aatcgtgatg 480

acccagagcc ctgcaaccct gtccctttct cccggggaac gggctaccct ttcttgtcgg 540

gcatcacaag atatctcaaa atacctcaat tggtatcaac agaagccggg acaggcccct 600

aggcttctta tctaccacac ctctcgcctg catagcggga ttcccgcacg ctttagcggg 660

tctggaagcg ggaccgacta cactctgacc atctcatctc tccagcccga ggacttcgcc 720

gtctacttct gccagcaggg taacaccctg ccgtacacct tcggccaggg caccaagctt 780

gagatcaaac atcaccacca tcatcaccat cac 813

<210> 56
<211> 828
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 56
atggccctcc cagtgaccgc tctgctgctg cctctcgcac ttcttctcca tgccgctcgg 60

cctgagatcg tcatgaccca aagccccgct accctgtccc tgtcacccgg cgagagggca 120

acccttttcat gcagggccag ccaggacatt tctaagtacc tcaactggta tcagcagaag 180

ccagggcagg ctcctcgcct gctgatctac cacaccagcc gcctccacag cggtatcccc 240

gccagatttt ccgggagcgg gtctggaacc gactacaccc tcaccatctc ttctctgcag 300

cccgaggatt tcgccgtcta tttctgccag caggggaata ctctgccgta caccttcggt 360

caaggtacca agctggaaat caagggaggc ggaggatcag gcggtggcgg aagcggagga 420

ggtggctccg gaggaggagg ttcccaagtg cagcttcaag aatcaggacc cggacttgtg 480

aagccatcag aaaccctctc cctgacttgt accgtgtccg gtgtgagcct ccccgactac 540

ggagtctctt ggattcgcca gcctccgggg aagggtcttg aatggattgg ggtgatttgg 600

ggatcagaga ctacttacta ctcttcatca cttaagtcac gggtcaccat cagcaaagat 660

aatagcaaga accaagtgtc acttaagctg tcatctgtga ccgccgctga caccgccgtg 720

tactattgtg ccaaacatta ctattacgga gggtcttatg ctatggacta ctggggacag 780

gggaccctgg tgactgtctc tagccatcac catcaccacc atcatcac 828

<210> 57
<211> 828
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 57
atggccctcc cagtgaccgc tctgctgctg cctctcgcac ttcttctcca tgccgctcgg 60

cctgagatcg tcatgaccca aagccccgct accctgtccc tgtcacccgg cgagagggca 120

acccttttcat gcagggccag ccaggacatt tctaagtacc tcaactggta tcagcagaag 180

ccagggcagg ctcctcgcct gctgatctac cacaccagcc gcctccacag cggtatcccc 240

gccagatttt ccgggagcgg gtctggaacc gactacaccc tcaccatctc ttctctgcag 300

cccgaggatt tcgccgtcta tttctgccag caggggaata ctctgccgta caccttcggt 360

caaggtacca agctggaaat caagggaggc ggaggatcag gcggtggcgg aagcggagga 420

ggtggctccg gaggaggagg ttcccaagtg cagcttcaag aatcaggacc cggacttgtg 480

aagccatcag aaaccctctc cctgacttgt accgtgtccg gtgtgagcct ccccgactac 540

ggagtctctt ggattcgcca gcctccgggg aagggtcttg aatggattgg ggtgatttgg 600

ggatcagaga ctacttacta ccagtcatca cttaagtcac gggtcaccat cagcaaagat 660

aatagcaaga accaagtgtc acttaagctg tcatctgtga ccgccgctga caccgccgtg 720

tactattgtg ccaaacatta ctattacgga gggtcttatg ctatggacta ctggggacag 780

gggaccctgg tgactgtctc tagccatcac catcaccacc atcatcac 828

<210> 58
<211> 828
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 58
atggcactgc ctgtcactgc cctcctgctg cctctggccc tccttctgca tgccgccagg 60

ccccaagtcc agctgcaaga gtcaggaccc ggactggtga agccgtctga gactctctca 120

ctgacttgta ccgtcagcgg cgtgtccctc cccgactacg gagtgtcatg gatccgccaa 180

cctcccggga aagggcttga atggattggt gtcatctggg gttctgaaac cacctactac 240

tcatcttccc tgaagtccag ggtgaccatc agcaaggata attccaagaa ccaggtcagc 300

cttaagctgt catctgtgac cgctgctgac accgccgtgt attactgcgc caagcactac 360

tattacggag gaagctacgc tatggactat tggggacagg gcactctcgt gactgtgagc 420

agcggcggtg gagggtctgg aggtggagga tccggtggtg gtgggtcagg cggaggaggg 480

agcgagattg tgatgactca gtcaccagcc acccttctc tttcacccgg cgagagagca 540

accctgagct gtagagccag ccaggacatt tctaagtacc tcaactggta tcagcaaaaa 600

ccggggcagg cccctcgcct cctgatctac catacctcac gccttcactc tggtatcccc 660

gctcggttta gcggatcagg atctggtacc gactacactc tgaccatttc cagcctgcag 720

ccagaagatt tcgcagtgta tttctgccag cagggcaata cccttcctta caccttcggt 780

cagggaacca agctcgaaat caagcaccat caccatcatc accaccat 828

<210> 59
<211> 828
<212> DNA

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 59
atggcactgc ctgtcactgc cctcctgctg cctctggccc tccttctgca tgccgccagg 60

ccccaagtcc agctgcaaga gtcaggaccc ggactggtga agccgtctga gactctctca 120

ctgacttgta ccgtcagcgg cgtgtccctc cccgactacg gagtgtcatg gatccgccaa 180

cctcccggga aagggcttga atggattggt gtcatctggg gttctgaaac cacctactac 240

cagtcttccc tgaagtccag ggtgaccatc agcaaggata attccaagaa ccaggtcagc 300

cttaagctgt catctgtgac cgctgctgac accgccgtgt attactgcgc caagcactac 360

tattacggag gaagctacgc tatggactat tggggacagg gcactctcgt gactgtgagc 420

agcggcggtg gagggtctgg aggtggagga tccggtggtg gtgggtcagg cggaggaggg 480

agcgagattg tgatgactca gtcaccagcc acccttctc tttcacccgg cgagagagca 540

accctgagct gtagagccag ccaggacatt tctaagtacc tcaactggta tcagcaaaaa 600

ccggggcagg cccctcgcct cctgatctac catacctcac gccttcactc tggtatcccc 660

gctcggttta gcggatcagg atctggtacc gactacactc tgaccatttc cagcctgcag 720

ccagaagatt tcgcagtgta tttctgccag cagggcaata cccttcctta caccttcggt 780

cagggaacca agctcgaaat caagcaccat caccatcatc atcaccac 828

<210> 60
<211> 828
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 60
atggccctcc cagtgaccgc tctgctgctg cctctcgcac ttcttctcca tgccgctcgg 60

cctgagatcg tcatgaccca aagccccgct accctgtccc tgtcacccgg cgagagggca 120

acccttttcat gcagggccag ccaggacatt tctaagtacc tcaactggta tcagcagaag 180

ccagggcagg ctcctcgcct gctgatctac cacaccagcc gcctccacag cggtatcccc 240

gccagatttt ccgggagcgg gtctggaacc gactacaccc tcaccatctc ttctctgcag 300

cccgaggatt tcgccgtcta tttctgccag caggggaata ctctgccgta caccttcggt 360

caaggtacca agctggaaat caagggaggc ggaggatcag gcggtggcgg aagcggagga 420

ggtggctccg gaggaggagg ttcccaagtg cagcttcaag aatcaggacc cggacttgtg 480

aagccatcag aaaccctctc cctgacttgt accgtgtccg gtgtgagcct ccccgactac 540

ggagtctctt ggattcgcca gcctccgggg aagggtcttg aatggattgg ggtgatttgg 600

ggatcagaga ctacttacta caattcatca cttaagtcac gggtcaccat cagcaaagat 660

aatagcaaga accaagtgtc acttaagctg tcatctgtga ccgccgctga caccgccgtg 720

tactattgtg ccaaacatta ctattacgga gggtcttatg ctatggacta ctggggacag 780

gggaccctgg tgactgtctc tagccatcac catcaccacc atcatcac 828

<210> 61
<211> 828
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 61
atggcactgc ctgtcactgc cctcctgctg cctctggccc tccttctgca tgccgccagg 60

ccccaagtcc agctgcaaga gtcaggaccc ggactggtga agccgtctga gactctctca 120

ctgacttgta ccgtcagcgg cgtgtccctc cccgactacg gagtgtcatg gatccgccaa 180

cctcccggga aagggcttga atggattggt gtcatctggg gttctgaaac cacctactac 240

aactcttccc tgaagtccag ggtgaccatc agcaaggata attccaagaa ccaggtcagc 300

cttaagctgt catctgtgac cgctgctgac accgccgtgt attactgcgc caagcactac 360

tattacggag gaagctacgc tatggactat tggggacagg gcactctcgt gactgtgagc 420

agcggcggtg gagggtctgg aggtggagga tccggtggtg gtgggtcagg cggaggaggg 480

agcgagattg tgatgactca gtcaccagcc acccttctc tttcacccgg cgagagagca 540

accctgagct gtagagccag ccaggacatt tctaagtacc tcaactggta tcagcaaaaa 600

ccggggcagg cccctcgcct cctgatctac catacctcac gccttcactc tggtatcccc 660

gctcggttta gcggatcagg atctggtacc gactacactc tgaccatttc cagcctgcag 720

ccagaagatt tcgcagtgta tttctgccag cagggcaata cccttcctta caccttcggt 780

cagggaacca agctcgaaat caagcaccat caccatcatc accaccat 828

<210> 62
<211> 813
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 62
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaaattg tgatgaccca gtcacccgcc actcttagcc tttcacccgg tgagcgcgca 120

accctgtctt gcagagcctc ccaagacatc tcaaaatacc ttaattggta tcaacagaag 180

cccggacagg ctcctcgcct tctgatctac cacaccagcc ggctccattc tggaatccct 240

gccaggttca gcggtagcgg atctgggacc gactacaccc tcactatcag ctcactgcag 300

ccagaggact tcgctgtcta tttctgtcag caagggaaca ccctgcccta caccttgga 360

cagggcacca agctcgagat taaaggtgga ggtggcagcg gaggaggtgg gtccggcggt 420

ggaggaagcc aggtccaact ccaagaaagc ggaccgggtc ttgtgaagcc atcagaaact 480

ctttcactga cttgtactgt gagcggagtg tctctccccg attacggggt gtcttggatc 540

agacagccac cggggaaggg tctggaatgg attggagtga tttggggctc tgagactact 600

tactacaatt catccctcaa gtcacgcgtc accatctcaa aggacaactc taagaatcag 660

gtgtcactga aactgtcatc tgtgaccgca gccgacaccg ccgtgtacta ttgcgctaag 720

cattactatt atggcgggag ctacgcaatg gattactggg gacagggtac tctggtcacc 780

gtgtccagcc accaccatca tcaccatcac cat 813

<210> 63
<211> 813
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 63
atggctctgc ccgtgaccgc actcctcctg ccactggctc tgctgcttca cgccgctcgc 60

ccacaagtcc agcttcaaga atcagggcct ggtctggtga agccatctga gactctgtcc 120

ctcacttgca ccgtgagcgg agtgtccctc ccagactacg gagtgagctg gattagacag 180

cctcccggaa agggactgga gtggatcgga gtgatttggg gtagcgaaac cacttactat 240

aactcttccc tgaagtcacg ggtcaccatt tcaaaggata actcaaagaa tcaagtgagc 300

ctcaagctct catcagtcac cgccgctgac accgccgtgt attactgtgc caagcattac 360

tactatggag ggtcctacgc catggactac tggggccagg gaactctggt cactgtgtca 420

tctggtggag gaggtagcgg aggaggcggg agcggtggag gtggctccga aatcgtgatg 480

acccagagcc ctgcaaccct gtccctttct cccggggaac gggctaccct ttcttgtcgg 540

gcatcacaag atatctcaaa atacctcaat tggtatcaac agaagccggg acaggcccct 600

aggcttctta tctaccacac ctctcgcctg catagcggga ttcccgcacg ctttagcggg 660

tctggaagcg ggaccgacta cactctgacc atctcatctc tccagcccga ggacttcgcc 720

gtctacttct gccagcaggg taacaccctg ccgtacacct tcggccaggg caccaagctt 780

gagatcaaac atcaccacca tcatcaccat cac 813

<210> 64
<211> 271
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 64
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu
20 25 30

Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln
35 40 45

Asp Ile Ser Lys Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala
50 55 60

Pro Arg Leu Leu Ile Tyr His Thr Ser Arg Leu His Ser Gly Ile Pro
65 70 75 80

Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile
85 90 95

Ser Ser Leu Gln Pro Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Gly
100 105 110

Asn Thr Leu Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln
130 135 140

Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu Thr
145 150 155 160

Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly
165 170 175

_SL
Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly
180 185 190

Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Ser Ser Ser Leu Lys Ser
195 200 205

Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn Gln Val Ser Leu Lys
210 215 220

Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Lys
225 230 235 240

His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly
245 250 255

Thr Leu Val Thr Val Ser Ser His His His His His His His His
260 265 270

<210> 65
<211> 271
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 65
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu
20 25 30

Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln
35 40 45

Asp Ile Ser Lys Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala
50 55 60

Pro Arg Leu Leu Ile Tyr His Thr Ser Arg Leu His Ser Gly Ile Pro
65 70 75 80

Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile
85 90 95

Ser Ser Leu Gln Pro Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Gly
100 105 110

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                                                    _SL
Asn Thr Leu Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
        115                 120                 125


Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln
    130                 135                 140


Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu Thr
145                 150                 155                 160


Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly
                165                 170                 175


Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly
            180                 185                 190


Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Gln Ser Ser Leu Lys Ser
        195                 200                 205


Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn Gln Val Ser Leu Lys
    210                 215                 220


Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Lys
225                 230                 235                 240


His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly
                245                 250                 255


Thr Leu Val Thr Val Ser Ser His His His His His His His His
            260                 265                 270


<210> 66
<211> 271
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 66
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15


His Ala Ala Arg Pro Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu
            20                  25                  30


Val Lys Pro Ser Glu Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Val
        35                  40                  45
```

_SL
Ser Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg Gln Pro Pro Gly Lys
50 55 60

Gly Leu Glu Trp Ile Gly Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr
65 70 75 80

Ser Ser Ser Leu Lys Ser Arg Val Thr Ile Ser Lys Asp Asn Ser Lys
85 90 95

Asn Gln Val Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala
100 105 110

Val Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met
115 120 125

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
130 135 140

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Met
145 150 155 160

Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr
165 170 175

Leu Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr Leu Asn Trp Tyr
180 185 190

Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr His Thr Ser
195 200 205

Arg Leu His Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly
210 215 220

Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
225 230 235 240

Val Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
245 250 255

Gly Thr Lys Leu Glu Ile Lys His His His His His His His His
260 265 270

<210> 67
<211> 271
<212> PRT
<213> Artificial Sequence

<220>
<221> source

_SL
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 67

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15

His Ala Ala Arg Pro Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu
            20                  25                  30

Val Lys Pro Ser Glu Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Val
        35                  40                  45

Ser Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg Gln Pro Pro Gly Lys
    50                  55                  60

Gly Leu Glu Trp Ile Gly Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr
65                  70                  75                  80

Gln Ser Ser Leu Lys Ser Arg Val Thr Ile Ser Lys Asp Asn Ser Lys
                85                  90                  95

Asn Gln Val Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala
            100                 105                 110

Val Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met
        115                 120                 125

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
    130                 135                 140

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Met
145                 150                 155                 160

Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr
                165                 170                 175

Leu Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr Leu Asn Trp Tyr
            180                 185                 190

Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr His Thr Ser
        195                 200                 205

Arg Leu His Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly
    210                 215                 220

Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
225                 230                 235                 240
```

Val Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
245 250 255

Gly Thr Lys Leu Glu Ile Lys His His His His His His His His
260 265 270

<210> 68
<211> 276
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 68
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu
20 25 30

Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln
35 40 45

Asp Ile Ser Lys Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala
50 55 60

Pro Arg Leu Leu Ile Tyr His Thr Ser Arg Leu His Ser Gly Ile Pro
65 70 75 80

Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile
85 90 95

Ser Ser Leu Gln Pro Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Gly
100 105 110

Asn Thr Leu Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
130 135 140

Gly Gly Gly Ser Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val
145 150 155 160

Lys Pro Ser Glu Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser
165 170 175

Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly
180 185 190

Leu Glu Trp Ile Gly Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Ser
195 200 205

Ser Ser Leu Lys Ser Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn
210 215 220

Gln Val Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val
225 230 235 240

Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp
245 250 255

Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser His His His His
260 265 270

His His His His
275

<210> 69
<211> 276
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 69
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu
20 25 30

Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln
35 40 45

Asp Ile Ser Lys Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala
50 55 60

Pro Arg Leu Leu Ile Tyr His Thr Ser Arg Leu His Ser Gly Ile Pro
65 70 75 80

Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile
85 90 95

```
Ser Ser Leu Gln Pro Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Gly
            100                 105                 110

Asn Thr Leu Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val
145                 150                 155                 160

Lys Pro Ser Glu Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser
                165                 170                 175

Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly
            180                 185                 190

Leu Glu Trp Ile Gly Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Gln
        195                 200                 205

Ser Ser Leu Lys Ser Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn
    210                 215                 220

Gln Val Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val
225                 230                 235                 240

Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp
                245                 250                 255

Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser His His His His
            260                 265                 270

His His His His
        275
```

<210> 70
<211> 276
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 70

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15
```

```
His Ala Ala Arg Pro Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu
            20                  25                  30

Val Lys Pro Ser Glu Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Val
        35                  40                  45

Ser Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg Gln Pro Pro Gly Lys
    50                  55                  60

Gly Leu Glu Trp Ile Gly Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr
65                  70                  75                  80

Ser Ser Ser Leu Lys Ser Arg Val Thr Ile Ser Lys Asp Asn Ser Lys
                85                  90                  95

Asn Gln Val Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala
            100                 105                 110

Val Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met
        115                 120                 125

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
    130                 135                 140

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
145                 150                 155                 160

Ser Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro
                165                 170                 175

Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys
            180                 185                 190

Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
        195                 200                 205

Ile Tyr His Thr Ser Arg Leu His Ser Gly Ile Pro Ala Arg Phe Ser
    210                 215                 220

Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln
225                 230                 235                 240

Pro Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro
                245                 250                 255

Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys His His His His
            260                 265                 270
```

His His His His
275

<210> 71
<211> 276
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 71
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu
20 25 30

Val Lys Pro Ser Glu Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Val
35 40 45

Ser Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg Gln Pro Pro Gly Lys
50 55 60

Gly Leu Glu Trp Ile Gly Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr
65 70 75 80

Gln Ser Ser Leu Lys Ser Arg Val Thr Ile Ser Lys Asp Asn Ser Lys
85 90 95

Asn Gln Val Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala
100 105 110

Val Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met
115 120 125

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
130 135 140

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
145 150 155 160

Ser Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro
165 170 175

Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys
180 185 190

Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
195 200 205

Ile Tyr His Thr Ser Arg Leu His Ser Gly Ile Pro Ala Arg Phe Ser
210 215 220

Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln
225 230 235 240

Pro Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro
245 250 255

Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys His His His His
260 265 270

His His His His
275

<210> 72
<211> 276
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 72
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu
20 25 30

Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln
35 40 45

Asp Ile Ser Lys Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala
50 55 60

Pro Arg Leu Leu Ile Tyr His Thr Ser Arg Leu His Ser Gly Ile Pro
65 70 75 80

Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile
85 90 95

Ser Ser Leu Gln Pro Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Gly
100 105 110

```
Asn Thr Leu Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val
145                 150                 155                 160

Lys Pro Ser Glu Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser
                165                 170                 175

Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly
            180                 185                 190

Leu Glu Trp Ile Gly Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Asn
        195                 200                 205

Ser Ser Leu Lys Ser Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn
    210                 215                 220

Gln Val Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val
225                 230                 235                 240

Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp
                245                 250                 255

Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser His His His His
            260                 265                 270

His His His His
        275


<210> 73
<211> 276
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 73
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15

His Ala Ala Arg Pro Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu
            20                  25                  30
```

```
Val Lys Pro Ser Glu Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Val
        35                  40                  45

Ser Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg Gln Pro Pro Gly Lys
    50                  55                  60

Gly Leu Glu Trp Ile Gly Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr
65                  70                  75                  80

Asn Ser Ser Leu Lys Ser Arg Val Thr Ile Ser Lys Asp Asn Ser Lys
                85                  90                  95

Asn Gln Val Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala
            100                 105                 110

Val Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met
        115                 120                 125

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
    130                 135                 140

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
145                 150                 155                 160

Ser Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro
                165                 170                 175

Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys
            180                 185                 190

Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
        195                 200                 205

Ile Tyr His Thr Ser Arg Leu His Ser Gly Ile Pro Ala Arg Phe Ser
    210                 215                 220

Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln
225                 230                 235                 240

Pro Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro
                245                 250                 255

Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys His His His His
            260                 265                 270

His His His His
```

275

<210> 74
<211> 271
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 74
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu
20 25 30

Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln
35 40 45

Asp Ile Ser Lys Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala
50 55 60

Pro Arg Leu Leu Ile Tyr His Thr Ser Arg Leu His Ser Gly Ile Pro
65 70 75 80

Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile
85 90 95

Ser Ser Leu Gln Pro Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Gly
100 105 110

Asn Thr Leu Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln
130 135 140

Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu Thr
145 150 155 160

Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly
165 170 175

Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly
180 185 190

Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Asn Ser Ser Leu Lys Ser

_SL
195 200 205

Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn Gln Val Ser Leu Lys
210 215 220

Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Lys
225 230 235 240

His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly
245 250 255

Thr Leu Val Thr Val Ser Ser His His His His His His His His
260 265 270

<210> 75
<211> 271
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 75
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu
20 25 30

Val Lys Pro Ser Glu Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Val
35 40 45

Ser Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg Gln Pro Pro Gly Lys
50 55 60

Gly Leu Glu Trp Ile Gly Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr
65 70 75 80

Asn Ser Ser Leu Lys Ser Arg Val Thr Ile Ser Lys Asp Asn Ser Lys
85 90 95

Asn Gln Val Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala
100 105 110

Val Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met
115 120 125

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly

_SL
130 135 140

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Met
145 150 155 160

Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr
165 170 175

Leu Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr Leu Asn Trp Tyr
180 185 190

Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr His Thr Ser
195 200 205

Arg Leu His Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly
210 215 220

Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
225 230 235 240

Val Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
245 250 255

Gly Thr Lys Leu Glu Ile Lys His His His His His His His His
260 265 270

<210> 76
<211> 271
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 76
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu
20 25 30

Ser Ala Ser Leu Gly Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln
35 40 45

Asp Ile Ser Lys Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr
50 55 60

Val Lys Leu Leu Ile Tyr His Thr Ser Arg Leu His Ser Gly Val Pro

65 70 _SL 75 80

Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile
85 90 95

Ser Asn Leu Glu Gln Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly
100 105 110

Asn Thr Leu Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Thr
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu
130 135 140

Val Lys Leu Gln Glu Ser Gly Pro Gly Leu Val Ala Pro Ser Gln Ser
145 150 155 160

Leu Ser Val Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly
165 170 175

Val Ser Trp Ile Arg Gln Pro Pro Arg Lys Gly Leu Glu Trp Leu Gly
180 185 190

Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Asn Ser Ala Leu Lys Ser
195 200 205

Arg Leu Thr Ile Ile Lys Asp Asn Ser Lys Ser Gln Val Phe Leu Lys
210 215 220

Met Asn Ser Leu Gln Thr Asp Asp Thr Ala Ile Tyr Tyr Cys Ala Lys
225 230 235 240

His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly
245 250 255

Thr Ser Val Thr Val Ser Ser His His His His His His His His
260 265 270

<210> 77
<211> 486
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 77
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu

```
                                                _SL
1               5                   10                  15

His Ala Ala Arg Pro Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu
            20                  25                  30

Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln
        35                  40                  45

Asp Ile Ser Lys Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala
    50                  55                  60

Pro Arg Leu Leu Ile Tyr His Thr Ser Arg Leu His Ser Gly Ile Pro
65                  70                  75                  80

Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile
                85                  90                  95

Ser Ser Leu Gln Pro Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Gly
            100                 105                 110

Asn Thr Leu Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln
    130                 135                 140

Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu Thr
145                 150                 155                 160

Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly
                165                 170                 175

Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly
            180                 185                 190

Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Ser Ser Ser Leu Lys Ser
        195                 200                 205

Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn Gln Val Ser Leu Lys
    210                 215                 220

Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Lys
225                 230                 235                 240

His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly
                245                 250                 255
```

_SL
Thr Leu Val Thr Val Ser Ser Thr Thr Thr Pro Ala Pro Arg Pro Pro
260 265 270

Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu
275 280 285

Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
290 295 300

Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly
305 310 315 320

Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg
325 330 335

Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln
340 345 350

Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu
355 360 365

Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
370 375 380

Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
385 390 395 400

Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
405 410 415

Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
420 425 430

Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
435 440 445

Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
450 455 460

Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
465 470 475 480

Gln Ala Leu Pro Pro Arg
485

<210> 78
<211> 486
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 78

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15

His Ala Ala Arg Pro Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu
            20                  25                  30

Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln
        35                  40                  45

Asp Ile Ser Lys Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala
    50                  55                  60

Pro Arg Leu Leu Ile Tyr His Thr Ser Arg Leu His Ser Gly Ile Pro
65                  70                  75                  80

Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile
                85                  90                  95

Ser Ser Leu Gln Pro Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Gly
            100                 105                 110

Asn Thr Leu Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln
    130                 135                 140

Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu Thr
145                 150                 155                 160

Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly
                165                 170                 175

Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly
            180                 185                 190

Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Gln Ser Ser Leu Lys Ser
        195                 200                 205

Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn Gln Val Ser Leu Lys
    210                 215                 220
```

```
Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Lys
225                 230                 235                 240

His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly
                245                 250                 255

Thr Leu Val Thr Val Ser Ser Thr Thr Thr Pro Ala Pro Arg Pro Pro
            260                 265                 270

Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu
        275                 280                 285

Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
    290                 295                 300

Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly
305                 310                 315                 320

Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg
                325                 330                 335

Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln
            340                 345                 350

Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu
        355                 360                 365

Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
    370                 375                 380

Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
385                 390                 395                 400

Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
                405                 410                 415

Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
            420                 425                 430

Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
        435                 440                 445

Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
    450                 455                 460

Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
465                 470                 475                 480
```

Gln Ala Leu Pro Pro Arg
485

<210> 79
<211> 486
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 79
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu
20 25 30

Val Lys Pro Ser Glu Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Val
35 40 45

Ser Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg Gln Pro Pro Gly Lys
50 55 60

Gly Leu Glu Trp Ile Gly Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr
65 70 75 80

Ser Ser Ser Leu Lys Ser Arg Val Thr Ile Ser Lys Asp Asn Ser Lys
85 90 95

Asn Gln Val Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala
100 105 110

Val Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met
115 120 125

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
130 135 140

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Met
145 150 155 160

Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr
165 170 175

Leu Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr Leu Asn Trp Tyr
180 185 190

```
Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr His Thr Ser
        195                 200                 205

Arg Leu His Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly
    210                 215                 220

Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
225                 230                 235                 240

Val Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
                245                 250                 255

Gly Thr Lys Leu Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro
            260                 265                 270

Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu
        275                 280                 285

Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
    290                 295                 300

Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly
305                 310                 315                 320

Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg
                325                 330                 335

Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln
            340                 345                 350

Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu
        355                 360                 365

Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
    370                 375                 380

Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
385                 390                 395                 400

Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
                405                 410                 415

Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
            420                 425                 430

Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
```

_SL
435 440 445

Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
450 455 460

Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
465 470 475 480

Gln Ala Leu Pro Pro Arg
485

<210> 80
<211> 486
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 80
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu
20 25 30

Val Lys Pro Ser Glu Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Val
35 40 45

Ser Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg Gln Pro Pro Gly Lys
50 55 60

Gly Leu Glu Trp Ile Gly Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr
65 70 75 80

Gln Ser Ser Leu Lys Ser Arg Val Thr Ile Ser Lys Asp Asn Ser Lys
85 90 95

Asn Gln Val Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala
100 105 110

Val Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met
115 120 125

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
130 135 140

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Met

```
                                                _SL
145                 150                 155                 160

Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr
                165                 170                 175

Leu Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr Leu Asn Trp Tyr
            180                 185                 190

Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr His Thr Ser
        195                 200                 205

Arg Leu His Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly
    210                 215                 220

Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
225                 230                 235                 240

Val Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
                245                 250                 255

Gly Thr Lys Leu Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro
            260                 265                 270

Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu
        275                 280                 285

Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
    290                 295                 300

Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly
305                 310                 315                 320

Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg
                325                 330                 335

Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln
            340                 345                 350

Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu
        355                 360                 365

Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
    370                 375                 380

Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
385                 390                 395                 400
```

_SL
Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
405 410 415

Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
420 425 430

Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
435 440 445

Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
450 455 460

Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
465 470 475 480

Gln Ala Leu Pro Pro Arg
485

<210> 81
<211> 491
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 81
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu
20 25 30

Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln
35 40 45

Asp Ile Ser Lys Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala
50 55 60

Pro Arg Leu Leu Ile Tyr His Thr Ser Arg Leu His Ser Gly Ile Pro
65 70 75 80

Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile
85 90 95

Ser Ser Leu Gln Pro Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Gly
100 105 110

```
                                                  _SL
Asn Thr Leu Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val
145                 150                 155                 160

Lys Pro Ser Glu Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser
                165                 170                 175

Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly
            180                 185                 190

Leu Glu Trp Ile Gly Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Ser
        195                 200                 205

Ser Ser Leu Lys Ser Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn
    210                 215                 220

Gln Val Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val
225                 230                 235                 240

Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp
                245                 250                 255

Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Thr Thr Thr Pro
            260                 265                 270

Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu
        275                 280                 285

Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His
    290                 295                 300

Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu
305                 310                 315                 320

Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr
                325                 330                 335

Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe
            340                 345                 350

Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg
        355                 360                 365
```

```
Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser
    370                 375                 380

Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr
385                 390                 395                 400

Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys
                405                 410                 415

Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn
            420                 425                 430

Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu
        435                 440                 445

Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly
    450                 455                 460

His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr
465                 470                 475                 480

Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
                485                 490
```

<210> 82
<211> 491
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 82

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15

His Ala Ala Arg Pro Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu
            20                  25                  30

Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln
        35                  40                  45

Asp Ile Ser Lys Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala
    50                  55                  60

Pro Arg Leu Leu Ile Tyr His Thr Ser Arg Leu His Ser Gly Ile Pro
65                  70                  75                  80
```

```
Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile
                85                  90                  95

Ser Ser Leu Gln Pro Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Gly
            100                 105                 110

Asn Thr Leu Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val
145                 150                 155                 160

Lys Pro Ser Glu Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser
                165                 170                 175

Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly
            180                 185                 190

Leu Glu Trp Ile Gly Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Gln
        195                 200                 205

Ser Ser Leu Lys Ser Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn
    210                 215                 220

Gln Val Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val
225                 230                 235                 240

Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp
                245                 250                 255

Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Thr Thr Thr Pro
            260                 265                 270

Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu
        275                 280                 285

Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His
    290                 295                 300

Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu
305                 310                 315                 320

Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr
                325                 330                 335
```

```
Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe
            340                 345                 350

Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg
        355                 360                 365

Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser
    370                 375                 380

Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr
385                 390                 395                 400

Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys
                405                 410                 415

Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn
            420                 425                 430

Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu
        435                 440                 445

Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly
    450                 455                 460

His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr
465                 470                 475                 480

Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
                485                 490
```

<210> 83
<211> 491
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 83

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15

His Ala Ala Arg Pro Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu
            20                  25                  30

Val Lys Pro Ser Glu Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Val
        35                  40                  45
```

```
Ser Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg Gln Pro Pro Gly Lys
    50                  55                  60

Gly Leu Glu Trp Ile Gly Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr
65                  70                  75                  80

Ser Ser Ser Leu Lys Ser Arg Val Thr Ile Ser Lys Asp Asn Ser Lys
                85                  90                  95

Asn Gln Val Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala
            100                 105                 110

Val Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met
        115                 120                 125

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
    130                 135                 140

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
145                 150                 155                 160

Ser Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro
                165                 170                 175

Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys
            180                 185                 190

Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
        195                 200                 205

Ile Tyr His Thr Ser Arg Leu His Ser Gly Ile Pro Ala Arg Phe Ser
    210                 215                 220

Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln
225                 230                 235                 240

Pro Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro
                245                 250                 255

Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Thr Thr Thr Pro
            260                 265                 270

Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu
        275                 280                 285

Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His
```

_SL
290 295 300

Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu
305 310 315 320

Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr
325 330 335

Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe
340 345 350

Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg
355 360 365

Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser
370 375 380

Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr
385 390 395 400

Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys
405 410 415

Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn
420 425 430

Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu
435 440 445

Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly
450 455 460

His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr
465 470 475 480

Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 84
<211> 491
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 84
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu

```
                                                _SL
1               5                   10                  15

His Ala Ala Arg Pro Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu
            20                  25                  30

Val Lys Pro Ser Glu Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Val
        35                  40                  45

Ser Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg Gln Pro Pro Gly Lys
    50                  55                  60

Gly Leu Glu Trp Ile Gly Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr
65                  70                  75                  80

Gln Ser Ser Leu Lys Ser Arg Val Thr Ile Ser Lys Asp Asn Ser Lys
                85                  90                  95

Asn Gln Val Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala
            100                 105                 110

Val Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met
        115                 120                 125

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
    130                 135                 140

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
145                 150                 155                 160

Ser Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro
                165                 170                 175

Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys
            180                 185                 190

Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
        195                 200                 205

Ile Tyr His Thr Ser Arg Leu His Ser Gly Ile Pro Ala Arg Phe Ser
    210                 215                 220

Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln
225                 230                 235                 240

Pro Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro
                245                 250                 255
```

_SL
Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Thr Thr Thr Pro
260 265 270

Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu
275 280 285

Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His
290 295 300

Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu
305 310 315 320

Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr
325 330 335

Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe
340 345 350

Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg
355 360 365

Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser
370 375 380

Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr
385 390 395 400

Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys
405 410 415

Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn
420 425 430

Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu
435 440 445

Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly
450 455 460

His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr
465 470 475 480

Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 85
<211> 491
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 85

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15

His Ala Ala Arg Pro Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu
            20                  25                  30

Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln
        35                  40                  45

Asp Ile Ser Lys Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala
    50                  55                  60

Pro Arg Leu Leu Ile Tyr His Thr Ser Arg Leu His Ser Gly Ile Pro
65                  70                  75                  80

Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile
                85                  90                  95

Ser Ser Leu Gln Pro Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Gly
            100                 105                 110

Asn Thr Leu Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val
145                 150                 155                 160

Lys Pro Ser Glu Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser
                165                 170                 175

Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly
            180                 185                 190

Leu Glu Trp Ile Gly Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Asn
        195                 200                 205

Ser Ser Leu Lys Ser Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn
    210                 215                 220
```

```
Gln Val Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val
225                 230                 235                 240

Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp
                245                 250                 255

Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Thr Thr Thr Pro
            260                 265                 270

Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu
        275                 280                 285

Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His
    290                 295                 300

Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu
305                 310                 315                 320

Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr
                325                 330                 335

Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe
            340                 345                 350

Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg
        355                 360                 365

Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser
    370                 375                 380

Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr
385                 390                 395                 400

Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys
                405                 410                 415

Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn
            420                 425                 430

Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu
        435                 440                 445

Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly
    450                 455                 460

His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr
465                 470                 475                 480
```

Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 86
<211> 491
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 86
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu
20 25 30

Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln
35 40 45

Asp Ile Ser Lys Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala
50 55 60

Pro Arg Leu Leu Ile Tyr His Thr Ser Arg Leu His Ser Gly Ile Pro
65 70 75 80

Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile
85 90 95

Ser Ser Leu Gln Pro Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Gly
100 105 110

Asn Thr Leu Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
130 135 140

Gly Gly Gly Ser Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val
145 150 155 160

Lys Pro Ser Glu Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser
165 170 175

Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly
180 185 190

```
Leu Glu Trp Ile Gly Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Asn
        195                 200                 205

Ser Ser Leu Lys Ser Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn
    210                 215                 220

Gln Val Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val
225                 230                 235                 240

Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp
                245                 250                 255

Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Thr Thr Thr Pro
            260                 265                 270

Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu
        275                 280                 285

Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His
    290                 295                 300

Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu
305                 310                 315                 320

Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr
                325                 330                 335

Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe
            340                 345                 350

Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg
        355                 360                 365

Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser
    370                 375                 380

Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr
385                 390                 395                 400

Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys
                405                 410                 415

Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn
            420                 425                 430

Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu
```

_SL
435 440 445

Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly
450 455 460

His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr
465 470 475 480

Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 87
<211> 491
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 87
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu
20 25 30

Val Lys Pro Ser Glu Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Val
35 40 45

Ser Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg Gln Pro Pro Gly Lys
50 55 60

Gly Leu Glu Trp Ile Gly Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr
65 70 75 80

Asn Ser Ser Leu Lys Ser Arg Val Thr Ile Ser Lys Asp Asn Ser Lys
85 90 95

Asn Gln Val Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala
100 105 110

Val Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met
115 120 125

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
130 135 140

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly

```
                                                _SL
145                 150                 155                 160

Ser Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro
                165                 170                 175

Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys
            180                 185                 190

Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
        195                 200                 205

Ile Tyr His Thr Ser Arg Leu His Ser Gly Ile Pro Ala Arg Phe Ser
    210                 215                 220

Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln
225                 230                 235                 240

Pro Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro
                245                 250                 255

Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Thr Thr Thr Pro
            260                 265                 270

Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu
        275                 280                 285

Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His
    290                 295                 300

Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu
305                 310                 315                 320

Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr
                325                 330                 335

Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe
            340                 345                 350

Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg
        355                 360                 365

Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser
    370                 375                 380

Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr
385                 390                 395                 400
```

```
                                                _SL
Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys
                405                 410                 415

Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn
            420                 425                 430

Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu
        435                 440                 445

Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly
    450                 455                 460

His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr
465                 470                 475                 480

Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
                485                 490


<210> 88
<211> 486
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 88
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15

His Ala Ala Arg Pro Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu
            20                  25                  30

Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln
        35                  40                  45

Asp Ile Ser Lys Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala
    50                  55                  60

Pro Arg Leu Leu Ile Tyr His Thr Ser Arg Leu His Ser Gly Ile Pro
65                  70                  75                  80

Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile
                85                  90                  95

Ser Ser Leu Gln Pro Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Gly
            100                 105                 110
```

```
                                                 _SL
Asn Thr Leu Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln
    130                 135                 140

Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu Thr
145                 150                 155                 160

Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly
                165                 170                 175

Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly
            180                 185                 190

Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Asn Ser Ser Leu Lys Ser
        195                 200                 205

Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn Gln Val Ser Leu Lys
    210                 215                 220

Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Lys
225                 230                 235                 240

His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly
                245                 250                 255

Thr Leu Val Thr Val Ser Ser Thr Thr Thr Pro Ala Pro Arg Pro Pro
            260                 265                 270

Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu
        275                 280                 285

Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
    290                 295                 300

Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly
305                 310                 315                 320

Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg
                325                 330                 335

Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln
            340                 345                 350

Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu
        355                 360                 365
```

```
Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
    370                 375                 380

Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
385                 390                 395                 400

Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
                405                 410                 415

Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
            420                 425                 430

Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
        435                 440                 445

Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
    450                 455                 460

Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
465                 470                 475                 480

Gln Ala Leu Pro Pro Arg
                485
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<210> 89
<211> 486
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 89

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Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15

His Ala Ala Arg Pro Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu
            20                  25                  30

Ser Ala Ser Leu Gly Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln
        35                  40                  45

Asp Ile Ser Lys Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr
    50                  55                  60

Val Lys Leu Leu Ile Tyr His Thr Ser Arg Leu His Ser Gly Val Pro
65                  70                  75                  80
```

```
Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile
                85                  90                  95

Ser Asn Leu Glu Gln Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly
            100                 105                 110

Asn Thr Leu Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Thr
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu
    130                 135                 140

Val Lys Leu Gln Glu Ser Gly Pro Gly Leu Val Ala Pro Ser Gln Ser
145                 150                 155                 160

Leu Ser Val Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly
                165                 170                 175

Val Ser Trp Ile Arg Gln Pro Pro Arg Lys Gly Leu Glu Trp Leu Gly
            180                 185                 190

Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Asn Ser Ala Leu Lys Ser
        195                 200                 205

Arg Leu Thr Ile Ile Lys Asp Asn Ser Lys Ser Gln Val Phe Leu Lys
    210                 215                 220

Met Asn Ser Leu Gln Thr Asp Asp Thr Ala Ile Tyr Tyr Cys Ala Lys
225                 230                 235                 240

His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly
                245                 250                 255

Thr Ser Val Thr Val Ser Ser Thr Thr Thr Pro Ala Pro Arg Pro Pro
            260                 265                 270

Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu
        275                 280                 285

Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
    290                 295                 300

Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly
305                 310                 315                 320

Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg
                325                 330                 335
```

```
Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln
            340                 345                 350

Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu
        355                 360                 365

Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
    370                 375                 380

Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
385                 390                 395                 400

Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
                405                 410                 415

Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
            420                 425                 430

Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
        435                 440                 445

Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
    450                 455                 460

Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
465                 470                 475                 480

Gln Ala Leu Pro Pro Arg
                485
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<210> 90
<211> 1458
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 90
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaaattg tgatgaccca gtcacccgcc actcttagcc tttcacccgg tgagcgcgca 120

accctgtctt gcagagcctc ccaagacatc tcaaaatacc ttaattggta tcaacagaag 180

cccggacagg ctcctcgcct tctgatctac cacaccagcc ggctccattc tggaatccct 240

gccaggttca gcggtagcgg atctgggacc gactacaccc tcactatcag ctcactgcag 300

ccagaggact tcgctgtcta tttctgtcag caagggaaca ccctgcccta cacctttgga 360

cagggcacca agctcgagat taaaggtgga ggtggcagcg gaggaggtgg gtccggcggt 420

ggaggaagcc aggtccaact ccaagaaagc ggaccgggtc ttgtgaagcc atcagaaact 480

ctttcactga cttgtactgt gagcggagtg tctctccccg attacggggt gtcttggatc 540

agacagccac cggggaaggg tctggaatgg attggagtga tttggggctc tgagactact 600

tactactctt catccctcaa gtcacgcgtc accatctcaa aggacaactc taagaatcag 660

gtgtcactga aactgtcatc tgtgaccgca gccgacaccg ccgtgtacta ttgcgctaag 720

cattactatt atggcgggag ctacgcaatg gattactggg gacagggtac tctggtcacc 780

gtgtccagca ccactacccc agcaccgagg ccacccaccc cggctcctac catcgcctcc 840

cagcctctgt ccctgcgtcc ggaggcatgt agacccgcag ctggtggggc cgtgcatacc 900

cggggtcttg acttcgcctg cgatatctac atttgggccc ctctggctgg tacttgcggg 960

gtcctgctgc tttcactcgt gatcactctt tactgtaagc gcggtcggaa gaagctgctg 1020

tacatcttta agcaaccctt catgaggcct gtgcagacta ctcaagagga ggacggctgt 1080

tcatgccggt tcccagagga ggaggaaggc ggctgcgaac tgcgcgtgaa attcagccgc 1140

agcgcagatg ctccagccta caagcagggg cagaaccagc tctacaacga actcaatctt 1200

ggtcggagag aggagtacga cgtgctggac aagcggagag gacgggaccc agaaatgggc 1260

gggaagccgc gcagaaagaa tccccaagag ggcctgtaca acgagctcca aaaggataag 1320

atggcagaag cctatagcga gattggtatg aaaggggaac gcagaagagg caaaggccac 1380

gacggactgt accagggact cagcaccgcc accaaggaca cctatgacgc tcttcacatg 1440

caggccctgc cgcctcgg 1458

<210> 91
<211> 1458
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 91
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaaattg tgatgaccca gtcacccgcc actcttagcc tttcacccgg tgagcgcgca 120

accctgtctt gcagagcctc ccaagacatc tcaaaatacc ttaattggta tcaacagaag 180

cccggacagg ctcctcgcct tctgatctac cacaccagcc ggctccattc tggaatccct 240

gccaggttca gcggtagcgg atctgggacc gactacaccc tcactatcag ctcactgcag 300

ccagaggact tcgctgtcta tttctgtcag caagggaaca ccctgcccta cacctttgga 360

cagggcacca agctcgagat taaaggtgga ggtggcagcg gaggaggtgg gtccggcggt 420

ggaggaagcc aggtccaact ccaagaaagc ggaccgggtc ttgtgaagcc atcagaaact 480

ctttcactga cttgtactgt gagcggagtg tctctccccg attacggggt gtcttggatc 540

agacagccac cggggaaggg tctggaatgg attggagtga tttggggctc tgagactact 600

tactaccaat catccctcaa gtcacgcgtc accatctcaa aggacaactc taagaatcag 660

gtgtcactga aactgtcatc tgtgaccgca gccgacaccg ccgtgtacta ttgcgctaag 720

cattactatt atggcgggag ctacgcaatg gattactggg gacagggtac tctggtcacc 780

gtgtccagca ccactacccc agcaccgagg ccacccaccc cggctcctac catcgcctcc 840

cagcctctgt ccctgcgtcc ggaggcatgt agacccgcag ctggtggggc cgtgcatacc 900

cggggtcttg acttcgcctg cgatatctac atttgggccc ctctggctgg tacttgcggg 960

gtcctgctgc tttcactcgt gatcactctt tactgtaagc gcggtcggaa gaagctgctg 1020

tacatcttta agcaaccctt catgaggcct gtgcagacta ctcaagagga ggacggctgt 1080

tcatgccggt tcccagagga ggaggaaggc ggctgcgaac tgcgcgtgaa attcagccgc 1140

agcgcagatg ctccagccta caagcagggg cagaaccagc tctacaacga actcaatctt 1200

ggtcggagag aggagtacga cgtgctggac aagcggagag gacgggaccc agaaatgggc 1260

gggaagccgc gcagaaagaa tccccaagag ggcctgtaca acgagctcca aaaggataag 1320

atggcagaag cctatagcga gattggtatg aaaggggaac gcagaagagg caaaggccac 1380

gacggactgt accagggact cagcaccgcc accaaggaca cctatgacgc tcttcacatg 1440

caggccctgc cgcctcgg 1458

<210> 92
<211> 1458
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 92
atggctctgc ccgtgaccgc actcctcctg ccactggctc tgctgcttca cgccgctcgc 60

ccacaagtcc agcttcaaga atcagggcct ggtctggtga agccatctga gactctgtcc 120

ctcacttgca ccgtgagcgg agtgtccctc ccagactacg gagtgagctg gattagacag 180

cctcccggaa agggactgga gtggatcgga gtgatttggg gtagcgaaac cacttactat 240

tcatcttccc tgaagtcacg ggtcaccatt tcaaaggata actcaaagaa tcaagtgagc 300

ctcaagctct catcagtcac cgccgctgac accgccgtgt attactgtgc caagcattac 360

tactatggag ggtcctacgc catggactac tggggccagg gaactctggt cactgtgtca 420

tctggtggag gaggtagcgg aggaggcggg agcggtggag gtggctccga aatcgtgatg 480

acccagagcc ctgcaaccct gtccctttct cccggggaac gggctaccct ttcttgtcgg 540

gcatcacaag atatctcaaa atacctcaat tggtatcaac agaagccggg acaggcccct 600

aggcttctta tctaccacac ctctcgcctg catagcggga ttcccgcacg ctttagcggg 660

tctggaagcg ggaccgacta cactctgacc atctcatctc tccagcccga ggacttcgcc 720

gtctacttct gccagcaggg taacaccctg ccgtacacct tcggccaggg caccaagctt 780

gagatcaaaa ccactactcc cgctccaagg ccacccaccc ctgccccgac catcgcctct 840

cagccgcttt ccctgcgtcc ggaggcatgt agacccgcag ctggtggggc cgtgcatacc 900

cggggtcttg acttcgcctg cgatatctac atttgggccc ctctggctgg tacttgcggg 960

gtcctgctgc tttcactcgt gatcactctt tactgtaagc gcggtcggaa gaagctgctg 1020

tacatcttta agcaaccctt catgaggcct gtgcagacta ctcaagagga ggacggctgt 1080

tcatgccggt tcccagagga ggaggaaggc ggctgcgaac tgcgcgtgaa attcagccgc 1140

agcgcagatg ctccagccta caagcagggg cagaaccagc tctacaacga actcaatctt 1200

ggtcggagag aggagtacga cgtgctggac aagcggagag gacgggaccc agaaatgggc 1260

gggaagccgc gcagaaagaa tccccaagag ggcctgtaca acgagctcca aaaggataag 1320

atggcagaag cctatagcga gattggtatg aaaggggaac gcagaagagg caaaggccac 1380

gacggactgt accagggact cagcaccgcc accaaggaca cctatgacgc tcttcacatg 1440

caggccctgc cgcctcgg 1458

<210> 93
<211> 1458
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 93
atggctctgc ccgtgaccgc actcctcctg ccactggctc tgctgcttca cgccgctcgc 60

ccacaagtcc agcttcaaga atcagggcct ggtctggtga agccatctga gactctgtcc 120

ctcacttgca ccgtgagcgg agtgtccctc ccagactacg gagtgagctg gattagacag 180

cctcccggaa agggactgga gtggatcgga gtgatttggg gtagcgaaac cacttactat 240

caatcttccc tgaagtcacg ggtcaccatt tcaaaggata actcaaagaa tcaagtgagc 300

ctcaagctct catcagtcac cgccgctgac accgccgtgt attactgtgc caagcattac 360

tactatggag ggtcctacgc catggactac tggggccagg gaactctggt cactgtgtca 420

tctggtggag gaggtagcgg aggaggcggg agcggtggag gtggctccga aatcgtgatg 480

acccagagcc ctgcaaccct gtccctttct cccggggaac gggctaccct ttcttgtcgg 540

gcatcacaag atatctcaaa atacctcaat tggtatcaac agaagccggg acaggcccct 600

aggcttctta tctaccacac ctctcgcctg catagcggga ttcccgcacg ctttagcggg 660

tctggaagcg ggaccgacta cactctgacc atctcatctc tccagcccga ggacttcgcc 720

gtctacttct gccagcaggg taacaccctg ccgtacacct tcggccaggg caccaagctt 780

gagatcaaaa ccactactcc cgctccaagg ccacccaccc ctgccccgac catcgcctct 840

cagccgcttt ccctgcgtcc ggaggcatgt agacccgcag ctggtggggc cgtgcatacc 900

cggggtcttg acttcgcctg cgatatctac atttgggccc ctctggctgg tacttgcggg 960

gtcctgctgc tttcactcgt gatcactctt tactgtaagc gcggtcggaa gaagctgctg 1020

tacatcttta agcaaccctt catgaggcct gtgcagacta ctcaagagga ggacggctgt 1080

tcatgccggt tcccagagga ggaggaaggc ggctgcgaac tgcgcgtgaa attcagccgc 1140

agcgcagatg ctccagccta caagcagggg cagaaccagc tctacaacga actcaatctt 1200

ggtcggagag aggagtacga cgtgctggac aagcggagag gacgggaccc agaaatgggc 1260

gggaagccgc gcagaaagaa tccccaagag ggcctgtaca acgagctcca aaaggataag 1320

atggcagaag cctatagcga gattggtatg aaaggggaac gcagaagagg caaaggccac 1380

gacggactgt accagggact cagcaccgcc accaaggaca cctatgacgc tcttcacatg 1440

caggccctgc cgcctcgg 1458

<210> 94
<211> 1473
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 94
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaaattg tgatgaccca gtcacccgcc actcttagcc tttcacccgg tgagcgcgca 120

accctgtctt gcagagcctc ccaagacatc tcaaaatacc ttaattggta tcaacagaag 180

cccggacagg ctcctcgcct tctgatctac cacaccagcc ggctccattc tggaatccct 240

gccaggttca gcggtagcgg atctgggacc gactacaccc tcactatcag ctcactgcag 300

ccagaggact tcgctgtcta tttctgtcag caagggaaca ccctgcccta caccttgga 360

cagggcacca agctcgagat taaaggtgga ggtggcagcg gaggaggtgg gtccggcggt 420

ggaggaagcg gcggaggcgg gagccaggtc caactccaag aaagcggacc gggtcttgtg 480

aagccatcag aaactctttc actgacttgt actgtgagcg gagtgtctct ccccgattac 540

ggggtgtctt ggatcagaca gccaccgggg aagggtctgg aatggattgg agtgatttgg 600

ggctctgaga ctacttacta ctcttcatcc ctcaagtcac gcgtcaccat ctcaaaggac 660

aactctaaga atcaggtgtc actgaaactg tcatctgtga ccgcagccga caccgccgtg 720

tactattgcg ctaagcatta ctattatggc gggagctacg caatggatta ctggggacag 780

ggtactctgg tcaccgtgtc agcaccact accccagcac cgaggccacc caccccggct 840

cctaccatcg cctcccagcc tctgtccctg cgtccggagg catgtagacc cgcagctggt 900

ggggccgtgc atacccgggg tcttgacttc gcctgcgata tctacatttg ggcccctctg 960

gctggtactt gcggggtcct gctgctttca ctcgtgatca ctctttactg taagcgcggt 1020

cggaagaagc tgctgtacat ctttaagcaa cccttcatga ggcctgtgca gactactcaa 1080

gaggaggacg gctgttcatg ccggttccca gaggaggagg aaggcggctg cgaactgcgc 1140

gtgaaattca gccgcagcgc agatgctcca gcctacaagc aggggcagaa ccagctctac 1200

aacgaactca atcttggtcg gagagaggag tacgacgtgc tggacaagcg gagaggacgg 1260

gacccagaaa tgggcgggaa gccgcgcaga aagaatcccc aagagggcct gtacaacgag 1320

ctccaaaagg ataagatggc agaagcctat agcgagattg gtatgaaagg ggaacgcaga 1380

agaggcaaag gccacgacgg actgtaccag ggactcagca ccgccaccaa ggacacctat 1440

gacgctcttc acatgcaggc cctgccgcct cgg 1473

<210> 95
<211> 1473
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 95
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cccgaaattg tgatgaccca gtcacccgcc actcttagcc tttcacccgg tgagcgcgca 120

accctgtctt gcagagcctc ccaagacatc tcaaaatacc ttaattggta tcaacagaag 180

cccggacagg ctcctcgcct tctgatctac cacaccagcc ggctccattc tggaatccct 240

gccaggttca gcggtagcgg atctgggacc gactacaccc tcactatcag ctcactgcag 300

ccagaggact tcgctgtcta tttctgtcag caagggaaca ccctgcccta caccttgga 360

cagggcacca agctcgagat taaaggtgga ggtggcagcg gaggaggtgg gtccggcggt 420

ggaggaagcg gaggcggagg gagccaggtc caactccaag aaagcggacc gggtcttgtg 480

aagccatcag aaactctttc actgacttgt actgtgagcg gagtgtctct ccccgattac 540

ggggtgtctt ggatcagaca gccaccgggg aagggtctgg aatggattgg agtgatttgg 600

ggctctgaga ctacttacta ccaatcatcc ctcaagtcac gcgtcaccat ctcaaaggac 660

aactctaaga atcaggtgtc actgaaactg tcatctgtga ccgcagccga caccgccgtg 720

tactattgcg ctaagcatta ctattatggc gggagctacg caatggatta ctggggacag 780

ggtactctgg tcaccgtgtc cagcaccact accccagcac cgaggccacc caccccggct 840

cctaccatcg cctcccagcc tctgtccctg cgtccggagg catgtagacc cgcagctggt 900

ggggccgtgc atacccgggg tcttgacttc gcctgcgata tctacatttg ggcccctctg 960

gctggtactt gcggggtcct gctgctttca ctcgtgatca ctctttactg taagcgcggt 1020

cggaagaagc tgctgtacat ctttaagcaa cccttcatga ggcctgtgca gactactcaa 1080

gaggaggacg gctgttcatg ccggttccca gaggaggagg aaggcggctg cgaactgcgc 1140

gtgaaattca gccgcagcgc agatgctcca gcctacaagc aggggcagaa ccagctctac 1200

aacgaactca atcttggtcg gagagaggag tacgacgtgc tggacaagcg gagaggacgg 1260

gacccagaaa tgggcgggaa gccgcgcaga aagaatcccc aagagggcct gtacaacgag 1320

ctccaaaagg ataagatggc agaagcctat agcgagattg gtatgaaagg ggaacgcaga 1380

agaggcaaag gccacgacgg actgtaccag ggactcagca ccgccaccaa ggacacctat 1440

gacgctcttc acatgcaggc cctgccgcct cgg 1473

<210> 96
<211> 1473
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 96
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ccacaagtcc agcttcaaga atcagggcct ggtctggtga agccatctga gactctgtcc 120

ctcacttgca ccgtgagcgg agtgtccctc ccagactacg gagtgagctg gattagacag 180

cctcccggaa agggactgga gtggatcgga gtgatttggg gtagcgaaac cacttactat 240

tcatcttccc tgaagtcacg ggtcaccatt tcaaaggata actcaaagaa tcaagtgagc 300

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tactatggag ggtcctacgc catggactac tggggccagg gaactctggt cactgtgtca 420

tctggtggag gaggtagcgg aggaggcggg agcggtggag gtggctccgg aggtggcgga 480

agcgaaatcg tgatgaccca gagccctgca accctgtccc tttctcccgg ggaacgggct 540

acccтttctt gtcgggcatc acaagatatc tcaaaatacc tcaattggta tcaacagaag 600

ccgggacagg cccctaggct tcttatctac cacacctctc gcctgcatag cgggattccc 660

gcacgcttta gcgggtctgg aagcgggacc gactacactc tgaccatctc atctctccag 720

cccgaggact tcgccgtcta cttctgccag cagggtaaca ccctgccgta caccttcggc 780

cagggcacca agcttgagat caaaaccact actcccgctc caaggccacc cacccctgcc 840

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ggggccgtgc atacccgggg tcttgacttc gcctgcgata tctacatttg ggcccctctg 960

gctggtactt gcggggtcct gctgctttca ctcgtgatca ctctttactg taagcgcggt 1020

cggaagaagc tgctgtacat ctttaagcaa cccttcatga ggcctgtgca gactactcaa 1080

gaggaggacg gctgttcatg ccggttccca gaggaggagg aaggcggctg cgaactgcgc 1140

gtgaaattca gccgcagcgc agatgctcca gcctacaagc aggggcagaa ccagctctac 1200

aacgaactca atcttggtcg gagagaggag tacgacgtgc tggacaagcg gagaggacgg 1260

gacccagaaa tgggcgggaa gccgcgcaga aagaatcccc aagagggcct gtacaacgag 1320

ctccaaaagg ataagatggc agaagcctat agcgagattg gtatgaaagg ggaacgcaga 1380

agaggcaaag gccacgacgg actgtaccag ggactcagca ccgccaccaa ggacacctat 1440

gacgctcttc acatgcaggc cctgccgcct cgg 1473

<210> 97
<211> 1473
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 97
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ccacaagtcc agcttcaaga atcagggcct ggtctggtga agccatctga gactctgtcc 120

ctcacttgca ccgtgagcgg agtgtccctc ccagactacg gagtgagctg gattagacag 180

cctcccggaa agggactgga gtggatcgga gtgatttggg gtagcgaaac cacttactat 240

caatcttccc tgaagtcacg ggtcaccatt tcaaaggata actcaaagaa tcaagtgagc 300

ctcaagctct catcagtcac cgccgctgac accgccgtgt attactgtgc caagcattac 360

tactatggag ggtcctacgc catggactac tggggccagg gaactctggt cactgtgtca 420

tctggtggag gaggtagcgg aggaggcggg agcggtggag gtggctccgg aggcggtggg 480

tcagaaatcg tgatgaccca gagccctgca accctgtccc tttctcccgg ggaacgggct 540

acccttttctt gtcgggcatc acaagatatc tcaaaatacc tcaattggta tcaacagaag 600

ccgggacagg cccctaggct tcttatctac cacacctctc gcctgcatag cgggattccc 660

gcacgcttta gcgggtctgg aagcgggacc gactacactc tgaccatctc atctctccag 720

cccgaggact tcgccgtcta cttctgccag cagggtaaca ccctgccgta caccttcggc 780

cagggcacca agcttgagat caaaaccact actcccgctc caaggccacc cacccctgcc 840

ccgaccatcg cctctcagcc gctttccctg cgtccggagg catgtagacc cgcagctggt 900

ggggccgtgc atacccgggg tcttgacttc gcctgcgata tctacatttg ggcccctctg 960

gctggtactt gcggggtcct gctgctttca ctcgtgatca ctctttactg taagcgcggt 1020

cggaagaagc tgctgtacat ctttaagcaa cccttcatga ggcctgtgca gactactcaa 1080

gaggaggacg gctgttcatg ccggttccca gaggaggagg aaggcggctg cgaactgcgc 1140

gtgaaattca gccgcagcgc agatgctcca gcctacaagc aggggcagaa ccagctctac 1200

aacgaactca atcttggtcg gagagaggag tacgacgtgc tggacaagcg gagaggacgg 1260

gacccagaaa tgggcgggaa gccgcgcaga aagaatcccc aagagggcct gtacaacgag 1320

ctccaaaagg ataagatggc agaagcctat agcgagattg gtatgaaagg ggaacgcaga 1380

agaggcaaag gccacgacgg actgtaccag ggactcagca ccgccaccaa ggacacctat 1440

gacgctcttc acatgcaggc cctgccgcct cgg 1473

<210> 98
<211> 1473
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 98
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accctgtctt gcagagcctc ccaagacatc tcaaaatacc ttaattggta tcaacagaag 180

cccggacagg ctcctcgcct tctgatctac cacaccagcc ggctccattc tggaatccct 240

gccaggttca gcggtagcgg atctgggacc gactacaccc tcactatcag ctcactgcag 300

ccagaggact tcgctgtcta tttctgtcag caagggaaca ccctgcccta caccttgga 360

cagggcacca agctcgagat taaaggtgga ggtggcagcg gaggaggtgg gtccggcggt 420

ggaggaagcg gaggcggtgg gagccaggtc caactccaag aaagcggacc gggtcttgtg 480

aagccatcag aaactctttc actgacttgt actgtgagcg gagtgtctct ccccgattac 540

ggggtgtctt ggatcagaca gccaccgggg aagggtctgg aatggattgg agtgatttgg 600

ggctctgaga ctacttacta caactcatcc ctcaagtcac gcgtcaccat ctcaaaggac 660

aactctaaga atcaggtgtc actgaaactg tcatctgtga ccgcagccga caccgccgtg 720

tactattgcg ctaagcatta ctattatggc gggagctacg caatggatta ctggggacag 780

ggtactctgg tcaccgtgtc cagcaccact accccagcac cgaggccacc caccccggct 840

cctaccatcg cctcccagcc tctgtccctg cgtccggagg catgtagacc cgcagctggt 900

ggggccgtgc atacccgggg tcttgacttc gcctgcgata tctacatttg ggcccctctg 960

gctggtactt gcggggtcct gctgctttca ctcgtgatca ctctttactg taagcgcggt 1020

cggaagaagc tgctgtacat ctttaagcaa cccttcatga ggcctgtgca gactactcaa 1080

gaggaggacg gctgttcatg ccggttccca gaggaggagg aaggcggctg cgaactgcgc 1140

gtgaaattca gccgcagcgc agatgctcca gcctacaagc aggggcagaa ccagctctac 1200

aacgaactca atcttggtcg gagagaggag tacgacgtgc tggacaagcg gagaggacgg 1260

gacccagaaa tgggcgggaa gccgcgcaga aagaatcccc aagagggcct gtacaacgag 1320

ctccaaaagg ataagatggc agaagcctat agcgagattg gtatgaaagg ggaacgcaga 1380

agaggcaaag gccacgacgg actgtaccag ggactcagca ccgccaccaa ggacacctat 1440

gacgctcttc acatgcaggc cctgccgcct cgg 1473

<210> 99
<211> 1473
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 99
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accctgtctt gcagagcctc ccaagacatc tcaaaatacc ttaattggta tcaacagaag 180

cccggacagg ctcctcgcct tctgatctac cacaccagcc ggctccattc tggaatccct 240

gccaggttca gcggtagcgg atctgggacc gactacaccc tcactatcag ctcactgcag 300

ccagaggact tcgctgtcta tttctgtcag caagggaaca ccctgcccta caccttgga 360

cagggcacca agctcgagat taaaggtgga ggtggcagcg gaggaggtgg gtccggcggt 420

ggaggaagcg gaggcggtgg gagccaggtc caactccaag aaagcggacc gggtcttgtg 480

aagccatcag aaactctttc actgacttgt actgtgagcg gagtgtctct ccccgattac 540

ggggtgtctt ggatcagaca gccaccgggg aagggtctgg aatggattgg agtgatttgg 600

ggctctgaga ctacttacta caactcatcc ctcaagtcac gcgtcaccat ctcaaaggac 660

aactctaaga atcaggtgtc actgaaactg tcatctgtga ccgcagccga caccgccgtg 720

tactattgcg ctaagcatta ctattatggc gggagctacg caatggatta ctggggacag 780

ggtactctgg tcaccgtgtc cagcaccact accccagcac cgaggccacc caccccggct 840

cctaccatcg cctcccagcc tctgtccctg cgtccggagg catgtagacc cgcagctggt 900

ggggccgtgc atacccgggg tcttgacttc gcctgcgata tctacatttg ggcccctctg 960

gctggtactt gcggggtcct gctgctttca ctcgtgatca ctctttactg taagcgcggt 1020

cggaagaagc tgctgtacat ctttaagcaa cccttcatga ggcctgtgca gactactcaa 1080

gaggaggacg gctgttcatg ccggttccca gaggaggagg aaggcggctg cgaactgcgc 1140

gtgaaattca gccgcagcgc agatgctcca gcctacaagc aggggcagaa ccagctctac 1200

aacgaactca atcttggtcg gagagaggag tacgacgtgc tggacaagcg gagaggacgg 1260

gacccagaaa tgggcgggaa gccgcgcaga aagaatcccc aagagggcct gtacaacgag 1320

ctccaaaagg ataagatggc agaagcctat agcgagattg gtatgaaagg ggaacgcaga 1380

agaggcaaag gccacgacgg actgtaccag ggactcagca ccgccaccaa ggacacctat 1440

gacgctcttc acatgcaggc cctgccgcct cgg 1473

<210> 100
<211> 1473
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 100
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ctcacttgca ccgtgagcgg agtgtccctc ccagactacg gagtgagctg gattagacag 180

cctcccggaa agggactgga gtggatcgga gtgatttggg gtagcgaaac cacttactat 240

aactcttccc tgaagtcacg ggtcaccatt tcaaaggata actcaaagaa tcaagtgagc 300

ctcaagctct catcagtcac cgccgctgac accgccgtgt attactgtgc caagcattac 360

tactatggag ggtcctacgc catggactac tggggccagg gaactctggt cactgtgtca 420

tctggtggag gaggtagcgg aggaggcggg agcggtggag gtggctccgg aggtggcgga 480

agcgaaatcg tgatgaccca gagccctgca accctgtccc tttctcccgg ggaacgggct 540

acccttttctt gtcgggcatc acaagatatc tcaaaatacc tcaattggta tcaacagaag 600

ccgggacagg cccctaggct tcttatctac cacacctctc gcctgcatag cgggattccc 660

gcacgcttta gcgggtctgg aagcgggacc gactacactc tgaccatctc atctctccag 720

cccgaggact tcgccgtcta cttctgccag cagggtaaca ccctgccgta caccttcggc 780

cagggcacca agcttgagat caaaaccact actcccgctc caaggccacc cacccctgcc 840

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gaggaggacg gctgttcatg ccggttccca gaggaggagg aaggcggctg cgaactgcgc 1140

gtgaaattca gccgcagcgc agatgctcca gcctacaagc aggggcagaa ccagctctac 1200

aacgaactca atcttggtcg gagagaggag tacgacgtgc tggacaagcg gagaggacgg 1260

gacccagaaa tgggcgggaa gccgcgcaga aagaatcccc aagagggcct gtacaacgag 1320

ctccaaaagg ataagatggc agaagcctat agcgagattg gtatgaaagg ggaacgcaga 1380

agaggcaaag gccacgacgg actgtaccag ggactcagca ccgccaccaa ggacacctat 1440

gacgctcttc acatgcaggc cctgccgcct cgg 1473

<210> 101
<211> 1458
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 101
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaaattg tgatgaccca gtcacccgcc actcttagcc tttcacccgg tgagcgcgca 120

accctgtctt gcagagcctc ccaagacatc tcaaaatacc ttaattggta tcaacagaag 180

cccggacagg ctcctcgcct tctgatctac cacaccagcc ggctccattc tggaatccct 240

gccaggttca gcggtagcgg atctgggacc gactacaccc tcactatcag ctcactgcag 300

ccagaggact tcgctgtcta tttctgtcag caagggaaca ccctgcccta caccttgga 360

cagggcacca agctcgagat taaaggtgga ggtggcagcg gaggaggtgg gtccggcggt 420

ggaggaagcc aggtccaact ccaagaaagc ggaccgggtc ttgtgaagcc atcagaaact 480

ctttcactga cttgtactgt gagcggagtg tctctccccg attacggggt gtcttggatc 540

agacagccac cggggaaggg tctggaatgg attggagtga tttggggctc tgagactact 600

tactacaact catccctcaa gtcacgcgtc accatctcaa aggacaactc taagaatcag 660

gtgtcactga aactgtcatc tgtgaccgca gccgacaccg ccgtgtacta ttgcgctaag 720

cattactatt atggcgggag ctacgcaatg gattactggg gacagggtac tctggtcacc 780

gtgtccagca ccactacccc agcaccgagg ccacccaccc cggctcctac catcgcctcc 840

cagcctctgt ccctgcgtcc ggaggcatgt agacccgcag ctggtggggc cgtgcatacc 900

cggggtcttg acttcgcctg cgatatctac atttgggccc ctctggctgg tacttgcggg 960

gtcctgctgc tttcactcgt gatcactctt tactgtaagc gcggtcggaa gaagctgctg 1020

tacatcttta agcaaccctt catgaggcct gtgcagacta ctcaagagga ggacggctgt 1080

tcatgccggt tcccagagga ggaggaaggc ggctgcgaac tgcgcgtgaa attcagccgc 1140

agcgcagatg ctccagccta caagcagggg cagaaccagc tctacaacga actcaatctt 1200

ggtcggagag aggagtacga cgtgctggac aagcggagag gacgggaccc agaaatgggc 1260

gggaagccgc gcagaaagaa tccccaagag ggcctgtaca acgagctcca aaaggataag 1320

atggcagaag cctatagcga gattggtatg aaaggggaac gcagaagagg caaaggccac 1380

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caggccctgc cgcctcgg 1458

<210> 102
<211> 1458
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 102
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ccggacatcc agatgacaca gactacatcc tccctgtctg cctctctggg agacagagtc 120

accatcagtt gcagggcaag tcaggacatt agtaaatatt taaattggta tcagcagaaa 180

ccagatggaa ctgttaaact cctgatctac catacatcaa gattacactc aggagtccca 240

tcaaggttca gtggcagtgg gtctggaaca gattattctc tcaccattag caacctggag 300

caagaagata ttgccactta cttttgccaa cagggtaata cgcttccgta cacgttcgga 360

gggggggacca agctggagat cacaggtggc ggtggctcgg gcggtggtgg gtcgggtggc 420

ggcggatctg aggtgaaact gcaggagtca ggacctggcc tggtggcgcc ctcacagagc 480

ctgtccgtca catgcactgt ctcaggggtc tcattacccg actatggtgt aagctggatt 540

cgccagcctc cacgaaaggg tctggagtgg ctgggagtaa tatggggtag tgaaaccaca 600

tactataatt cagctctcaa atccagactg accatcatca aggacaactc caagagccaa 660

gttttcttaa aaatgaacag tctgcaaact gatgacacag ccatttacta ctgtgccaaa 720

cattattact acggtggtag ctatgctatg gactactggg gccaaggaac ctcagtcacc 780

gtctcctcaa ccacgacgcc agcgccgcga ccaccaacac cggcgcccac catcgcgtcg 840

cagcccctgt ccctgcgccc agaggcgtgc cggccagcgg cgggggcgc agtgcacacg 900

agggggctgg acttcgcctg tgatatctac atctgggcgc ccttggccgg gacttgtggg 960

gtccttctcc tgtcactggt tatcaccctt tactgcaaac ggggcagaaa gaaactcctg 1020

tatatattca aacaaccatt tatgagacca gtacaaacta ctcaagagga agatggctgt 1080

agctgccgat ttccagaaga agaagaagga ggatgtgaac tgagagtgaa gttcagcagg 1140

agcgcagacg cccccgcgta caagcagggc cagaaccagc tctataacga gctcaatcta 1200

ggacgaagag aggagtacga tgttttggac aagagacgtg gccgggaccc tgagatgggg 1260

ggaaagccga gaaggaagaa ccctcaggaa ggcctgtaca atgaactgca gaaagataag 1320

atggcggagg cctacagtga gattgggatg aaaggcgagc gccggagggg caaggggcac 1380

gatggccttt accagggtct cagtacagcc accaaggaca cctacgacgc ccttcacatg 1440

caggccctgc cccctcgc 1458

<210> 103
<211> 1182
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 103
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ccacccggat ggtttctgga ctctccggat cgcccgtgga atcccccaac cttctcaccg 120

gcactcttgg ttgtgactga gggcgataat gcgaccttca cgtgctcgtt ctccaacacc 180

tccgaatcat tcgtgctgaa ctggtaccgc atgagcccgt caaaccagac cgacaagctc 240

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gctcctctcg ccggaacttg tggcgtgctc cttctgtccc tggtcatcac cctgtactgc 720

aagcggggtc ggaaaaagct tctgtacatt ttcaagcagc ccttcatgag gcccgtgcaa 780

accacccagg aggaggacgg ttgctcctgc cggttccccg aagaggaaga aggaggttgc 840

gagctgcgcg tgaagttctc ccggagcgcc gacgcccccg cctataagca gggccagaac 900

cagctgtaca acgaactgaa cctgggacgg cgggaagagt acgatgtgct ggacaagcgg 960

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gagcggcgga ggggaaaggg gcacgacggc ctgtaccaag gactgtccac cgccaccaag 1140

gacacatacg atgccctgca catgcaggcc cttccccctc gc 1182

<210> 104
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 104
Gly Ser Thr Ser Gly Ser Gly Lys Pro Gly Ser Gly Glu Gly Ser Thr
1 5 10 15

Lys Gly

<210> 105
<211> 394
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 105
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Pro Gly Trp Phe Leu Asp Ser Pro Asp Arg Pro
20 25 30

Trp Asn Pro Pro Thr Phe Ser Pro Ala Leu Leu Val Val Thr Glu Gly
35 40 45

Asp Asn Ala Thr Phe Thr Cys Ser Phe Ser Asn Thr Ser Glu Ser Phe
50 55 60

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Val Leu Asn Trp Tyr Arg Met Ser Pro Ser Asn Gln Thr Asp Lys Leu
65                  70                  75                  80

Ala Ala Phe Pro Glu Asp Arg Ser Gln Pro Gly Gln Asp Cys Arg Phe
                85                  90                  95

Arg Val Thr Gln Leu Pro Asn Gly Arg Asp Phe His Met Ser Val Val
            100                 105                 110

Arg Ala Arg Arg Asn Asp Ser Gly Thr Tyr Leu Cys Gly Ala Ile Ser
        115                 120                 125

Leu Ala Pro Lys Ala Gln Ile Lys Glu Ser Leu Arg Ala Glu Leu Arg
    130                 135                 140

Val Thr Glu Arg Arg Ala Glu Val Pro Thr Ala His Pro Ser Pro Ser
145                 150                 155                 160

Pro Arg Pro Ala Gly Gln Phe Gln Thr Leu Val Thr Thr Thr Pro Ala
                165                 170                 175

Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser
            180                 185                 190

Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr
        195                 200                 205

Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala
    210                 215                 220

Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys
225                 230                 235                 240

Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met
                245                 250                 255

Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe
            260                 265                 270

Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg
        275                 280                 285

Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn
    290                 295                 300

Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg
305                 310                 315                 320
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Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro
                325                 330                 335

Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala
            340                 345                 350

Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His
        355                 360                 365

Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp
    370                 375                 380

Ala Leu His Met Gln Ala Leu Pro Pro Arg
385                 390
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<210> 106
<211> 373
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 106

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Pro Gly Trp Phe Leu Asp Ser Pro Asp Arg Pro Trp Asn Pro Pro Thr
1               5                   10                  15

Phe Ser Pro Ala Leu Leu Val Val Thr Glu Gly Asp Asn Ala Thr Phe
            20                  25                  30

Thr Cys Ser Phe Ser Asn Thr Ser Glu Ser Phe Val Leu Asn Trp Tyr
        35                  40                  45

Arg Met Ser Pro Ser Asn Gln Thr Asp Lys Leu Ala Ala Phe Pro Glu
    50                  55                  60

Asp Arg Ser Gln Pro Gly Gln Asp Cys Arg Phe Arg Val Thr Gln Leu
65                  70                  75                  80

Pro Asn Gly Arg Asp Phe His Met Ser Val Val Arg Ala Arg Arg Asn
                85                  90                  95

Asp Ser Gly Thr Tyr Leu Cys Gly Ala Ile Ser Leu Ala Pro Lys Ala
            100                 105                 110

Gln Ile Lys Glu Ser Leu Arg Ala Glu Leu Arg Val Thr Glu Arg Arg
        115                 120                 125
```

```
Ala Glu Val Pro Thr Ala His Pro Ser Pro Ser Pro Arg Pro Ala Gly
    130                 135                 140

Gln Phe Gln Thr Leu Val Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr
145                 150                 155                 160

Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala
                165                 170                 175

Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe
            180                 185                 190

Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val
        195                 200                 205

Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys
    210                 215                 220

Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr
225                 230                 235                 240

Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu
                245                 250                 255

Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro
            260                 265                 270

Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly
        275                 280                 285

Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro
    290                 295                 300

Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr
305                 310                 315                 320

Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly
                325                 330                 335

Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln
            340                 345                 350

Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln
        355                 360                 365

Ala Leu Pro Pro Arg
```

370

<210> 107
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 107
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45

Tyr His Thr Ser Arg Leu His Ser Gly Ile Pro Ala Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser
100 105 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Glu
115 120 125

Ser Gly Pro Gly Leu Val Lys Pro Ser Glu Thr Leu Ser Leu Thr Cys
130 135 140

Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg
145 150 155 160

Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly Val Ile Trp Gly Ser
165 170 175

Glu Thr Thr Tyr Tyr Ser Ser Ser Leu Lys Ser Arg Val Thr Ile Ser
180 185 190

Lys Asp Asn Ser Lys Asn Gln Val Ser Leu Lys Leu Ser Ser Val Thr

_SL
195 200 205

Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly
210 215 220

Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val
225 230 235 240

Ser Ser

<210> 108
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 108
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45

Tyr His Thr Ser Arg Leu His Ser Gly Ile Pro Ala Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser
100 105 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Glu
115 120 125

Ser Gly Pro Gly Leu Val Lys Pro Ser Glu Thr Leu Ser Leu Thr Cys
130 135 140

Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg

_SL
145 150 155 160

Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly Val Ile Trp Gly Ser
165 170 175

Glu Thr Thr Tyr Tyr Gln Ser Ser Leu Lys Ser Arg Val Thr Ile Ser
180 185 190

Lys Asp Asn Ser Lys Asn Gln Val Ser Leu Lys Leu Ser Ser Val Thr
195 200 205

Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly
210 215 220

Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val
225 230 235 240

Ser Ser

<210> 109
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 109
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr
20 25 30

Gly Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Ser Ser Ser Leu Lys
50 55 60

Ser Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn Gln Val Ser Leu
65 70 75 80

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Lys His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln

_SL
100 105 110

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Met Thr Gln Ser Pro Ala
130 135 140

Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala
145 150 155 160

Ser Gln Asp Ile Ser Lys Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly
165 170 175

Gln Ala Pro Arg Leu Leu Ile Tyr His Thr Ser Arg Leu His Ser Gly
180 185 190

Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu
195 200 205

Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Val Tyr Phe Cys Gln
210 215 220

Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu
225 230 235 240

Ile Lys

<210> 110
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 110
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr
20 25 30

Gly Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Gln Ser Ser Leu Lys

_SL
50 55 60

Ser Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn Gln Val Ser Leu
65 70 75 80

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Lys His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Met Thr Gln Ser Pro Ala
130 135 140

Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala
145 150 155 160

Ser Gln Asp Ile Ser Lys Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly
165 170 175

Gln Ala Pro Arg Leu Leu Ile Tyr His Thr Ser Arg Leu His Ser Gly
180 185 190

Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu
195 200 205

Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Val Tyr Phe Cys Gln
210 215 220

Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu
225 230 235 240

Ile Lys

<210> 111
<211> 247
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 111
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly

```
                                                _SL
1               5                   10                  15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr
            20                  25                  30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
        35                  40                  45

Tyr His Thr Ser Arg Leu His Ser Gly Ile Pro Ala Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser
            100                 105                 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln
        115                 120                 125

Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu Thr
    130                 135                 140

Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly
145                 150                 155                 160

Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly
                165                 170                 175

Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Ser Ser Ser Leu Lys Ser
            180                 185                 190

Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn Gln Val Ser Leu Lys
        195                 200                 205

Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Lys
    210                 215                 220

His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly
225                 230                 235                 240

Thr Leu Val Thr Val Ser Ser
                245
```

<210> 112
<211> 247
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 112

```
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1               5                  10                  15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr
            20                  25                  30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
        35                  40                  45

Tyr His Thr Ser Arg Leu His Ser Gly Ile Pro Ala Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser
            100                 105                 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln
        115                 120                 125

Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu Thr
    130                 135                 140

Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly
145                 150                 155                 160

Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly
                165                 170                 175

Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Gln Ser Ser Leu Lys Ser
            180                 185                 190

Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn Gln Val Ser Leu Lys
        195                 200                 205
```

_SL
Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Lys
210 215 220

His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly
225 230 235 240

Thr Leu Val Thr Val Ser Ser
245

<210> 113
<211> 247
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 113
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr
20 25 30

Gly Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Ser Ser Ser Leu Lys
50 55 60

Ser Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn Gln Val Ser Leu
65 70 75 80

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Lys His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Met
130 135 140

Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr
145 150 155 160

```
                                                _SL
Leu Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr Leu Asn Trp Tyr
                165                 170                 175


Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr His Thr Ser
            180                 185                 190


Arg Leu His Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly
        195                 200                 205


Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
    210                 215                 220


Val Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
225                 230                 235                 240


Gly Thr Lys Leu Glu Ile Lys
                245


<210> 114
<211> 247
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 114
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1               5                   10                  15


Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr
            20                  25                  30


Gly Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
        35                  40                  45


Gly Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Gln Ser Ser Leu Lys
    50                  55                  60


Ser Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn Gln Val Ser Leu
65                  70                  75                  80


Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
                85                  90                  95


Lys His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln
            100                 105                 110
```

_SL
Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115   120   125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Met
    130   135   140

Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr
145   150   155   160

Leu Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr Leu Asn Trp Tyr
                165   170   175

Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr His Thr Ser
            180   185   190

Arg Leu His Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly
        195   200   205

Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
    210   215   220

Val Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
225   230   235   240

Gly Thr Lys Leu Glu Ile Lys
                245

<210> 115
<211> 247
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 115
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1   5   10   15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr
            20   25   30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
        35   40   45

Tyr His Thr Ser Arg Leu His Ser Gly Ile Pro Ala Arg Phe Ser Gly
    50   55   60

_SL
Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser
100 105 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln
115 120 125

Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu Thr
130 135 140

Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly
145 150 155 160

Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly
165 170 175

Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Asn Ser Ser Leu Lys Ser
180 185 190

Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn Gln Val Ser Leu Lys
195 200 205

Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Lys
210 215 220

His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly
225 230 235 240

Thr Leu Val Thr Val Ser Ser
245

<210> 116
<211> 247
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 116
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15

_SL
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr
            20   25   30

Gly Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
        35   40   45

Gly Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Asn Ser Ser Leu Lys
    50   55   60

Ser Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn Gln Val Ser Leu
65   70   75   80

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
                85   90   95

Lys His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln
            100   105   110

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115   120   125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Met
    130   135   140

Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr
145   150   155   160

Leu Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr Leu Asn Trp Tyr
                165   170   175

Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr His Thr Ser
            180   185   190

Arg Leu His Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly
        195   200   205

Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
    210   215   220

Val Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
225   230   235   240

Gly Thr Lys Leu Glu Ile Lys
                245

<210> 117
<211> 242
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 117

```
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1               5                  10                  15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr
            20                  25                  30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
        35                  40                  45

Tyr His Thr Ser Arg Leu His Ser Gly Ile Pro Ala Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser
            100                 105                 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Glu
        115                 120                 125

Ser Gly Pro Gly Leu Val Lys Pro Ser Glu Thr Leu Ser Leu Thr Cys
    130                 135                 140

Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg
145                 150                 155                 160

Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly Val Ile Trp Gly Ser
                165                 170                 175

Glu Thr Thr Tyr Tyr Asn Ser Ser Leu Lys Ser Arg Val Thr Ile Ser
            180                 185                 190

Lys Asp Asn Ser Lys Asn Gln Val Ser Leu Lys Leu Ser Ser Val Thr
        195                 200                 205

Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly
    210                 215                 220
```

Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val
225 230 235 240

Ser Ser

<210> 118
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 118
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr
20 25 30

Gly Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Asn Ser Ser Leu Lys
50 55 60

Ser Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn Gln Val Ser Leu
65 70 75 80

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Lys His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Met Thr Gln Ser Pro Ala
130 135 140

Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala
145 150 155 160

Ser Gln Asp Ile Ser Lys Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly
165 170 175

```
Gln Ala Pro Arg Leu Leu Ile Tyr His Thr Ser Arg Leu His Ser Gly
            180                 185                 190

Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu
        195                 200                 205

Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Val Tyr Phe Cys Gln
    210                 215                 220

Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu
225                 230                 235                 240

Ile Lys
```

<210> 119
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 119

```
Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly
1               5                   10                  15

Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr
            20                  25                  30

Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Val Lys Leu Leu Ile
        35                  40                  45

Tyr His Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Gln
65                  70                  75                  80

Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr
                85                  90                  95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Thr Gly Gly Gly Gly Ser
            100                 105                 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Lys Leu Gln Glu
        115                 120                 125
```

```
Ser Gly Pro Gly Leu Val Ala Pro Ser Gln Ser Leu Ser Val Thr Cys
    130                 135                 140

Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg
145                 150                 155                 160

Gln Pro Pro Arg Lys Gly Leu Glu Trp Leu Gly Val Ile Trp Gly Ser
                165                 170                 175

Glu Thr Thr Tyr Tyr Asn Ser Ala Leu Lys Ser Arg Leu Thr Ile Ile
            180                 185                 190

Lys Asp Asn Ser Lys Ser Gln Val Phe Leu Lys Met Asn Ser Leu Gln
        195                 200                 205

Thr Asp Asp Thr Ala Ile Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly
    210                 215                 220

Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser Val Thr Val
225                 230                 235                 240

Ser Ser
```

<210> 120
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 120

```
Gln Val Gln Leu Leu Glu Ser Gly Ala Glu Leu Val Arg Pro Gly Ser
1               5                   10                  15

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr
            20                  25                  30

Trp Met Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
        35                  40                  45

Gly Gln Ile Tyr Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe
    50                  55                  60

Lys Gly Gln Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr
65                  70                  75                  80
```

Met Gln Leu Ser Gly Leu Thr Ser Glu Asp Ser Ala Val Tyr Ser Cys
85 90 95

Ala Arg Lys Thr Ile Ser Ser Val Val Asp Phe Tyr Phe Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr
115

<210> 121
<211> 111
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 121
Glu Leu Val Leu Thr Gln Ser Pro Lys Phe Met Ser Thr Ser Val Gly
1 5 10 15

Asp Arg Val Ser Val Thr Cys Lys Ala Ser Gln Asn Val Gly Thr Asn
20 25 30

Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Pro Leu Ile
35 40 45

Tyr Ser Ala Thr Tyr Arg Asn Ser Gly Val Pro Asp Arg Phe Thr Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Thr Asn Val Gln Ser
65 70 75 80

Lys Asp Leu Ala Asp Tyr Phe Tyr Phe Cys Gln Tyr Asn Arg Tyr Pro
85 90 95

Tyr Thr Ser Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Arg Ser
100 105 110

<210> 122
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 122

Asp Tyr Gly Val Ser
1 5

<210> 123
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 123
Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Asn Ser Ala Leu Lys Ser
1 5 10 15

<210> 124
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 124
Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Ser Ser Ser Leu Lys Ser
1 5 10 15

<210> 125
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 125
Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Gln Ser Ser Leu Lys Ser
1 5 10 15

<210> 126
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 126
Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Asn Ser Ser Leu Lys Ser
1 5 10 15

<210> 127
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 127
His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr
1 5 10

<210> 128
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 128
Arg Ala Ser Gln Asp Ile Ser Lys Tyr Leu Asn
1 5 10

<210> 129
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 129
His Thr Ser Arg Leu His Ser
1 5

<210> 130
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 130
Gln Gln Gly Asn Thr Leu Pro Tyr Thr
1 5

<210> 131
<211> 132

<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 131
Asp Val Pro Asp Tyr Ala Ser Leu Gly Gly Pro Ser Ser Pro Lys Lys
1 5 10 15

Lys Arg Lys Val Ser Arg Gly Val Gln Val Glu Thr Ile Ser Pro Gly
20 25 30

Asp Gly Arg Thr Phe Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr
35 40 45

Thr Gly Met Leu Glu Asp Gly Lys Lys Phe Asp Ser Ser Arg Asp Arg
50 55 60

Asn Lys Pro Phe Lys Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly
65 70 75 80

Trp Glu Glu Gly Val Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu
85 90 95

Thr Ile Ser Pro Asp Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile
100 105 110

Ile Pro Pro His Ala Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu
115 120 125

Glu Thr Ser Tyr
130

<210> 132
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 132
Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe Pro Lys
1 5 10 15

Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu Asp Gly
20 25 30

```
Lys Lys Phe Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys Phe Met
        35                  40                  45

Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val Ala Gln
    50                  55                  60

Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp Tyr Ala
65                  70                  75                  80

Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala Thr Leu
                85                  90                  95

Val Phe Asp Val Glu Leu Leu Lys Leu Glu Thr Ser
            100                 105
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<210> 133
<211> 93
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 133

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Ile Leu Trp His Glu Met Trp His Glu Gly Leu Glu Glu Ala Ser Arg
1               5                   10                  15

Leu Tyr Phe Gly Glu Arg Asn Val Lys Gly Met Phe Glu Val Leu Glu
            20                  25                  30

Pro Leu His Ala Met Met Glu Arg Gly Pro Gln Thr Leu Lys Glu Thr
        35                  40                  45

Ser Phe Asn Gln Ala Tyr Gly Arg Asp Leu Met Glu Ala Gln Glu Trp
    50                  55                  60

Cys Arg Lys Tyr Met Lys Ser Gly Asn Val Lys Asp Leu Thr Gln Ala
65                  70                  75                  80

Trp Asp Leu Tyr Tyr His Val Phe Arg Arg Ile Ser Lys
                85                  90
```

<210> 134
<211> 95
<212> PRT
<213> Artificial Sequence

<220>
<221> source

_SL
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 134
Ile Leu Trp His Glu Met Trp His Glu Gly Leu Ile Glu Ala Ser Arg
1 5 10 15

Leu Tyr Phe Gly Glu Arg Asn Val Lys Gly Met Phe Glu Val Leu Glu
20 25 30

Pro Leu His Ala Met Met Glu Arg Gly Pro Gln Thr Leu Lys Glu Thr
35 40 45

Ser Phe Asn Gln Ala Tyr Gly Arg Asp Leu Met Glu Ala Gln Glu Trp
50 55 60

Cys Arg Lys Tyr Met Lys Ser Gly Asn Val Lys Asp Leu Thr Gln Ala
65 70 75 80

Trp Asp Leu Tyr Tyr His Val Phe Arg Arg Ile Ser Lys Thr Ser
85 90 95

<210> 135
<211> 95
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 135
Ile Leu Trp His Glu Met Trp His Glu Gly Leu Leu Glu Ala Ser Arg
1 5 10 15

Leu Tyr Phe Gly Glu Arg Asn Val Lys Gly Met Phe Glu Val Leu Glu
20 25 30

Pro Leu His Ala Met Met Glu Arg Gly Pro Gln Thr Leu Lys Glu Thr
35 40 45

Ser Phe Asn Gln Ala Tyr Gly Arg Asp Leu Met Glu Ala Gln Glu Trp
50 55 60

Cys Arg Lys Tyr Met Lys Ser Gly Asn Val Lys Asp Leu Thr Gln Ala
65 70 75 80

Trp Asp Leu Tyr Tyr His Val Phe Arg Arg Ile Ser Lys Thr Ser
85 90 95

<210> 136
<211> 95
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 136
Ile Leu Trp His Glu Met Trp His Glu Gly Leu Glu Glu Ala Ser Arg
1 5 10 15

Leu Tyr Phe Gly Glu Arg Asn Val Lys Gly Met Phe Glu Val Leu Glu
20 25 30

Pro Leu His Ala Met Met Glu Arg Gly Pro Gln Thr Leu Lys Glu Thr
35 40 45

Ser Phe Asn Gln Ala Tyr Gly Arg Asp Leu Met Glu Ala Gln Glu Trp
50 55 60

Cys Arg Lys Tyr Met Lys Ser Gly Asn Val Lys Asp Leu Leu Gln Ala
65 70 75 80

Trp Asp Leu Tyr Tyr His Val Phe Arg Arg Ile Ser Lys Thr Ser
85 90 95

<210> 137
<211> 95
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<220>
<221> MOD_RES
<222> (12)..(12)
<223> Any amino acid

<220>
<221> MOD_RES
<222> (78)..(78)
<223> Any amino acid

<400> 137
Ile Leu Trp His Glu Met Trp His Glu Gly Leu Xaa Glu Ala Ser Arg
1 5 10 15

Leu Tyr Phe Gly Glu Arg Asn Val Lys Gly Met Phe Glu Val Leu Glu
20 25 30

Pro Leu His Ala Met Met Glu Arg Gly Pro Gln Thr Leu Lys Glu Thr
35 40 45

Ser Phe Asn Gln Ala Tyr Gly Arg Asp Leu Met Glu Ala Gln Glu Trp
50 55 60

Cys Arg Lys Tyr Met Lys Ser Gly Asn Val Lys Asp Leu Xaa Gln Ala
65 70 75 80

Trp Asp Leu Tyr Tyr His Val Phe Arg Arg Ile Ser Lys Thr Ser
85 90 95

<210> 138
<211> 95
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 138
Ile Leu Trp His Glu Met Trp His Glu Gly Leu Ile Glu Ala Ser Arg
1 5 10 15

Leu Tyr Phe Gly Glu Arg Asn Val Lys Gly Met Phe Glu Val Leu Glu
20 25 30

Pro Leu His Ala Met Met Glu Arg Gly Pro Gln Thr Leu Lys Glu Thr
35 40 45

Ser Phe Asn Gln Ala Tyr Gly Arg Asp Leu Met Glu Ala Gln Glu Trp
50 55 60

Cys Arg Lys Tyr Met Lys Ser Gly Asn Val Lys Asp Leu Leu Gln Ala
65 70 75 80

Trp Asp Leu Tyr Tyr His Val Phe Arg Arg Ile Ser Lys Thr Ser
85 90 95

<210> 139
<211> 95
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

_SL

<400> 139
Ile Leu Trp His Glu Met Trp His Glu Gly Leu Leu Glu Ala Ser Arg
1 5 10 15

Leu Tyr Phe Gly Glu Arg Asn Val Lys Gly Met Phe Glu Val Leu Glu
20 25 30

Pro Leu His Ala Met Met Glu Arg Gly Pro Gln Thr Leu Lys Glu Thr
35 40 45

Ser Phe Asn Gln Ala Tyr Gly Arg Asp Leu Met Glu Ala Gln Glu Trp
50 55 60

Cys Arg Lys Tyr Met Lys Ser Gly Asn Val Lys Asp Leu Leu Gln Ala
65 70 75 80

Trp Asp Leu Tyr Tyr His Val Phe Arg Arg Ile Ser Lys Thr Ser
85 90 95

<210> 140
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 140
Arg Gly Asp Ser
1

<210> 141
<211> 813
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 141
atggccctgc ccgtcaccgc tctgctgctg ccccttgctc tgcttcttca tgcagcaagg 60

ccggacatcc agatgaccca aaccacctca tccctctctg cctctcttgg agacagggtg 120

accatttctt gtcgcgccag ccaggacatc agcaagtatc tgaactggta tcagcagaag 180

ccggacggaa ccgtgaagct cctgatctac catacctctc gcctgcatag cggcgtgccc 240

tcacgcttct ctggaagcgg atcaggaacc gattattctc tcactatttc aaatcttgag 300

caggaagata ttgccaccta tttctgccag cagggtaata ccctgcccta caccttcgga 360

ggagggacca agctcgaaat caccggtgga ggaggcagcg gcggtggagg gtctggtgga 420

ggtggttctg aggtgaagct gcaagaatca ggccctggac ttgtggcccc ttcacagtcc 480

ctgagcgtga cttgcaccgt gtccggagtc tccctgcccg actacggagt gtcatggatc 540

agacaacctc cacggaaagg actggaatgg ctcggtgtca tctggggtag cgaaactact 600

tactacaatt cagccctcaa aagcaggctg actattatca aggacaacag caagtcccaa 660

gtctttctta agatgaactc actccagact gacgacaccg caatctacta ttgtgctaag 720

cactactact acggaggatc ctacgctatg gattactggg gacaaggtac ttccgtcact 780

gtctcttcac accatcatca ccatcaccat cac 813

<210> 142
<211> 249
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 142
Asp Ile Val Leu Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Glu Arg Ala Thr Ile Asn Cys Arg Ala Ser Glu Ser Val Asp Asn Tyr
20 25 30

Gly Asn Thr Phe Met His Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Tyr Arg Ala Ser Asn Leu Glu Ser Gly Val Pro Asp
50 55 60

Arg Phe Ser Gly Ser Gly Ser Arg Thr Asp Phe Thr Leu Thr Ile Ser
65 70 75 80

Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln Ser Asn
85 90 95

Glu Asp Pro Pro Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Gly
100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
115 120 125

Gly Gly Ser Gln Ile Gln Leu Val Gln Ser Gly Ser Glu Leu Lys Lys
130 135 140

```
                                                _SL
Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe
145                 150                 155                 160

Thr Asn Tyr Gly Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu
                165                 170                 175

Glu Trp Met Gly Trp Ile Asn Thr Tyr Thr Gly Glu Ser Thr Tyr Ser
            180                 185                 190

Ala Asp Phe Lys Gly Arg Phe Val Phe Ser Leu Asp Thr Ser Val Ser
        195                 200                 205

Thr Ala Tyr Leu Gln Ile Asn Ala Leu Lys Ala Glu Asp Thr Ala Val
    210                 215                 220

Tyr Tyr Cys Ala Arg Ser Gly Gly Tyr Asp Pro Met Asp Tyr Trp Gly
225                 230                 235                 240

Gln Gly Thr Thr Val Thr Val Ser Ser
                245
```

<210> 143
<211> 747
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 143

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gacatcgtgc tgacccaatc cccggacagc ctcgcagtct cactcggaga acgcgccact       60

atcaattgta gggcgtcgga gtccgtggac aattacggaa acaccttcat gcactggtac      120

caacaaaaac ctggtcagcc acctaagctg ctgatctacc gcgcctcgaa tctggaatca      180

ggagtgccgg acagattctc ggggtccggc tcccggacgg atttcacttt gaccatctcg      240

tcacttcaag ctgaggacgt cgcggtgtac tactgccagc agagcaacga agatccaccc      300

acgttcggac aaggcaccaa gctggagatt aaaggaggcg gaggctccgg tggaggagga      360

tcgggaggag gcggctccgg cggaggtgga tcgcagattc agctggtgca gtcgggttca      420

gaattgaaga aaccaggagc ctcggtgaag gtcagctgca aggcatcagg gtacatcttc      480

actaactacg gcatgaactg ggtgcgccag gctccgggac aggggctgga gtggatggga      540

tggatcaaca cttacaccgg ggagtcaact tactcggctg actttaaggg ccggtttgtg      600

ttctccctcg acactagcgt gagcaccgcc tatcttcaaa tcaacgccct caaggcggaa      660

gataccgccg tctactactg cgcaagatcc ggtgggtacg atccgatgga ttattgggga      720
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cagggaacca ctgtcaccgt gagcagc 747

<210> 144
<211> 843
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 144
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgacatcg tgctgaccca atccccggac agcctcgcag tctcactcgg agaacgcgcc 120

actatcaatt gtagggcgtc ggagtccgtg gacaattacg gaaacacctt catgcactgg 180

taccaacaaa aacctggtca gccacctaag ctgctgatct accgcgcctc gaatctggaa 240

tcaggagtgc cggacagatt ctcggggtcc ggctcccgga cggatttcac tttgaccatc 300

tcgtcacttc aagctgagga cgtcgcggtg tactactgcc agcagagcaa cgaagatcca 360

cccacgttcg gacaaggcac caagctggag attaaaggag gcggaggctc cggtggagga 420

ggatcgggag gaggcggctc cggcggaggt ggatcgcaga ttcagctggt gcagtcgggt 480

tcagaattga agaaaccagg agcctcggtg aaggtcagct gcaaggcatc agggtacatc 540

ttcactaact acggcatgaa ctgggtgcgc caggctccgg gacaggggct ggagtggatg 600

ggatggatca acacttacac cggggagtca acttactcgg ctgactttaa gggccggttt 660

gtgttctccc tcgacactag cgtgagcacc gcctatcttc aaatcaacgc cctcaaggcg 720

gaagataccg ccgtctacta ctgcgcaaga tccggtgggt acgatccgat ggattattgg 780

ggacagggaa ccactgtcac cgtgagcagc ggctcgcacc accatcacca tcatcatcac 840

cac 843

<210> 145
<211> 281
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 145
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Asp Ile Val Leu Thr Gln Ser Pro Asp Ser Leu
20 25 30

```
Ala Val Ser Leu Gly Glu Arg Ala Thr Ile Asn Cys Arg Ala Ser Glu
        35                  40                  45

Ser Val Asp Asn Tyr Gly Asn Thr Phe Met His Trp Tyr Gln Gln Lys
    50                  55                  60

Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Arg Ala Ser Asn Leu Glu
65                  70                  75                  80

Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Arg Thr Asp Phe
                85                  90                  95

Thr Leu Thr Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr
            100                 105                 110

Cys Gln Gln Ser Asn Glu Asp Pro Pro Thr Phe Gly Gln Gly Thr Lys
        115                 120                 125

Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
    130                 135                 140

Gly Gly Ser Gly Gly Gly Gly Ser Gln Ile Gln Leu Val Gln Ser Gly
145                 150                 155                 160

Ser Glu Leu Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala
                165                 170                 175

Ser Gly Tyr Ile Phe Thr Asn Tyr Gly Met Asn Trp Val Arg Gln Ala
            180                 185                 190

Pro Gly Gln Gly Leu Glu Trp Met Gly Trp Ile Asn Thr Tyr Thr Gly
        195                 200                 205

Glu Ser Thr Tyr Ser Ala Asp Phe Lys Gly Arg Phe Val Phe Ser Leu
    210                 215                 220

Asp Thr Ser Val Ser Thr Ala Tyr Leu Gln Ile Asn Ala Leu Lys Ala
225                 230                 235                 240

Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Gly Gly Tyr Asp Pro
                245                 250                 255

Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Ser
            260                 265                 270

His His His His His His His His His
        275                 280
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<210> 146
<211> 1479
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 146
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgacatcg tgctgaccca atccccggac agcctcgcag tctcactcgg agaacgcgcc 120

actatcaatt gtagggcgtc ggagtccgtg gacaattacg gaaacacctt catgcactgg 180

taccaacaaa aacctggtca gccacctaag ctgctgatct accgcgcctc gaatctggaa 240

tcaggagtgc cggacagatt ctcggggtcc ggctcccgga cggatttcac tttgaccatc 300

tcgtcacttc aagctgagga cgtcgcggtg tactactgcc agcagagcaa cgaagatcca 360

cccacgttcg gacaaggcac caagctggag attaaaggag gcggaggctc cggtggagga 420

ggatcgggag gaggcggctc cggcggaggt ggatcgcaga ttcagctggt gcagtcgggt 480

tcagaattga agaaaccagg agcctcggtg aaggtcagct gcaaggcatc agggtacatc 540

ttcactaact acggcatgaa ctgggtgcgc caggctccgg gacaggggct ggagtggatg 600

ggatggatca acacttacac cggggagtca acttactcgg ctgactttaa gggccggttt 660

gtgttctccc tcgacactag cgtgagcacc gcctatcttc aaatcaacgc cctcaaggcg 720

gaagataccg ccgtctacta ctgcgcaaga tccggtgggt acgatccgat ggattattgg 780

ggacagggaa ccactgtcac cgtgagcagc accactaccc cagcaccgag gccacccacc 840

ccggctccta ccatcgcctc ccagcctctg tccctgcgtc cggaggcatg tagacccgca 900

gctggtgggg ccgtgcatac ccggggtctt gacttcgcct gcgatatcta catttgggcc 960

cctctggctg gtacttgcgg ggtcctgctg ctttcactcg tgatcactct ttactgtaag 1020

cgcggtcgga agaagctgct gtacatcttt aagcaaccct tcatgaggcc tgtgcagact 1080

actcaagagg aggacggctg ttcatgccgg ttcccagagg aggaggaagg cggctgcgaa 1140

ctgcgcgtga aattcagccg cagcgcagat gctccagcct acaagcaggg gcagaaccag 1200

ctctacaacg aactcaatct tggtcggaga gaggagtacg acgtgctgga caagcggaga 1260

ggacgggacc cagaaatggg cgggaagccg cgcagaaaga atccccaaga gggcctgtac 1320

aacgagctcc aaaaggataa gatggcagaa gcctatagcg agattggtat gaaaggggaa 1380

cgcagaagag gcaaaggcca cgacggactg taccagggac tcagcaccgc caccaaggac 1440

acctatgacg ctcttcacat gcaggccctg ccgcctcgg 1479

<210> 147
<211> 493
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 147
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Asp Ile Val Leu Thr Gln Ser Pro Asp Ser Leu
20 25 30

Ala Val Ser Leu Gly Glu Arg Ala Thr Ile Asn Cys Arg Ala Ser Glu
35 40 45

Ser Val Asp Asn Tyr Gly Asn Thr Phe Met His Trp Tyr Gln Gln Lys
50 55 60

Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Arg Ala Ser Asn Leu Glu
65 70 75 80

Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Arg Thr Asp Phe
85 90 95

Thr Leu Thr Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr
100 105 110

Cys Gln Gln Ser Asn Glu Asp Pro Pro Thr Phe Gly Gln Gly Thr Lys
115 120 125

Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
130 135 140

Gly Gly Ser Gly Gly Gly Gly Ser Gln Ile Gln Leu Val Gln Ser Gly
145 150 155 160

Ser Glu Leu Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala
165 170 175

Ser Gly Tyr Ile Phe Thr Asn Tyr Gly Met Asn Trp Val Arg Gln Ala
180 185 190

Pro Gly Gln Gly Leu Glu Trp Met Gly Trp Ile Asn Thr Tyr Thr Gly
195 200 205

```
Glu Ser Thr Tyr Ser Ala Asp Phe Lys Gly Arg Phe Val Phe Ser Leu
    210                 215                 220

Asp Thr Ser Val Ser Thr Ala Tyr Leu Gln Ile Asn Ala Leu Lys Ala
225                 230                 235                 240

Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Gly Gly Tyr Asp Pro
                245                 250                 255

Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Thr Thr
            260                 265                 270

Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln
        275                 280                 285

Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala
    290                 295                 300

Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala
305                 310                 315                 320

Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr
                325                 330                 335

Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln
            340                 345                 350

Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser
        355                 360                 365

Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys
    370                 375                 380

Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln
385                 390                 395                 400

Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu
                405                 410                 415

Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg
            420                 425                 430

Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met
        435                 440                 445

Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly
    450                 455                 460
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Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp
465 470 475 480

Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 148
<211> 249
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 148
Asp Ile Val Leu Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Glu Arg Ala Thr Ile Asn Cys Arg Ala Ser Glu Ser Val Asp Asn Tyr
20 25 30

Gly Asn Thr Phe Met His Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Tyr Arg Ala Ser Asn Leu Glu Ser Gly Val Pro Asp
50 55 60

Arg Phe Ser Gly Ser Gly Ser Arg Thr Asp Phe Thr Leu Thr Ile Ser
65 70 75 80

Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln Ser Asn
85 90 95

Glu Asp Pro Pro Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Gly
100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
115 120 125

Gly Gly Ser Gln Ile Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys
130 135 140

Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe
145 150 155 160

Thr Asn Tyr Gly Met Asn Trp Val Arg Gln Ala Pro Gly Gln Arg Leu
165 170 175

Glu Trp Met Gly Trp Ile Asn Thr Tyr Thr Gly Glu Ser Thr Tyr Ser
180 185 190

Ala Asp Phe Lys Gly Arg Val Thr Ile Thr Leu Asp Thr Ser Ala Ser
195 200 205

Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val
210 215 220

Tyr Tyr Cys Ala Arg Ser Gly Gly Tyr Asp Pro Met Asp Tyr Trp Gly
225 230 235 240

Gln Gly Thr Thr Val Thr Val Ser Ser
245

<210> 149
<211> 747
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 149
gatattgtcc tcactcaatc gccggactca ctggcggtgt ccctcggaga gagggcgacg 60

atcaattgcc gggcttccga atccgtcgat aactacggaa acacctttat gcactggtac 120

caacagaagc caggacagcc accaaagctg ttgatctacc gcgcttcaaa ccttgagtcg 180

ggtgtgccgg accgcttcag cggcagcggt tccagaaccg actttaccct caccatcagc 240

tcgctgcagg ccgaagatgt cgccgtctat tactgccaac agagcaacga agatccgcct 300

actttcggac aggggactaa actggaaatc aagggcggag gaggctcggg tggaggagga 360

tcgggaggag gcgggtccgg tggtggcgga tcgcaaatcc agctggtgca gtccggcgca 420

gaagtgaaga agccgggagc gtccgtgaaa gtgagctgca aggcctcagg gtacatcttc 480

accaattacg gcatgaattg ggtgcggcag gcacccggac agcgcctgga gtggatgggc 540

tggatcaaca cttacaccgg ggaaagcacg tactcggccg acttcaaagg acgggtgacc 600

attaccctgg atacctcggc ctcaaccgct tacatggagc tctcatcact tagatccgag 660

gacactgccg tctactactg tgcaaggagc ggaggctacg accctatgga ctattgggga 720

caaggcacta ctgtgactgt gtcgtcc 747

<210> 150
<211> 843
<212> DNA

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 150
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgatattg tcctcactca atcgccggac tcactggcgg tgtccctcgg agagagggcg 120

acgatcaatt gccgggcttc cgaatccgtc gataactacg gaaacacctt tatgcactgg 180

taccaacaga agccaggaca gccaccaaag ctgttgatct accgcgcttc aaaccttgag 240

tcgggtgtgc cggaccgctt cagcggcagc ggttccagaa ccgactttac cctcaccatc 300

agctcgctgc aggccgaaga tgtcgccgtc tattactgcc aacagagcaa cgaagatccg 360

cctactttcg gacaggggac taaactggaa atcaagggcg gaggaggctc gggtggagga 420

ggatcgggag gaggcgggtc cggtggtggc ggatcgcaaa tccagctggt gcagtccggc 480

gcagaagtga agaagccggg agcgtccgtg aaagtgagct gcaaggcctc agggtacatc 540

ttcaccaatt acggcatgaa ttgggtgcgg caggcacccg gacagcgcct ggagtggatg 600

ggctggatca acacttacac cggggaaagc acgtactcgg ccgacttcaa aggacgggtg 660

accattaccc tggatacctc ggcctcaacc gcttacatgg agctctcatc acttagatcc 720

gaggacactg ccgtctacta ctgtgcaagg agcggaggct acgaccctat ggactattgg 780

ggacaaggca ctactgtgac tgtgtcgtcc ggctcgcacc accatcacca tcatcatcac 840

cac 843

<210> 151
<211> 281
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 151
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Asp Ile Val Leu Thr Gln Ser Pro Asp Ser Leu
20 25 30

Ala Val Ser Leu Gly Glu Arg Ala Thr Ile Asn Cys Arg Ala Ser Glu
35 40 45

Ser Val Asp Asn Tyr Gly Asn Thr Phe Met His Trp Tyr Gln Gln Lys

_SL

50 55 60

Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Arg Ala Ser Asn Leu Glu
65 70 75 80

Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Arg Thr Asp Phe
85 90 95

Thr Leu Thr Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr
100 105 110

Cys Gln Gln Ser Asn Glu Asp Pro Pro Thr Phe Gly Gln Gly Thr Lys
115 120 125

Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
130 135 140

Gly Gly Ser Gly Gly Gly Gly Ser Gln Ile Gln Leu Val Gln Ser Gly
145 150 155 160

Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala
165 170 175

Ser Gly Tyr Ile Phe Thr Asn Tyr Gly Met Asn Trp Val Arg Gln Ala
180 185 190

Pro Gly Gln Arg Leu Glu Trp Met Gly Trp Ile Asn Thr Tyr Thr Gly
195 200 205

Glu Ser Thr Tyr Ser Ala Asp Phe Lys Gly Arg Val Thr Ile Thr Leu
210 215 220

Asp Thr Ser Ala Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser
225 230 235 240

Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Gly Gly Tyr Asp Pro
245 250 255

Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Ser
260 265 270

His His His His His His His His His
275 280

<210> 152
<211> 1479
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 152
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgatattg tcctcactca atcgccggac tcactggcgg tgtccctcgg agagagggcg 120

acgatcaatt gccgggcttc cgaatccgtc gataactacg gaaacacctt tatgcactgg 180

taccaacaga agccaggaca gccaccaaag ctgttgatct accgcgcttc aaaccttgag 240

tcgggtgtgc cggaccgctt cagcggcagc ggttccagaa ccgactttac cctcaccatc 300

agctcgctgc aggccgaaga tgtcgccgtc tattactgcc aacagagcaa cgaagatccg 360

cctactttcg gacaggggac taaactggaa atcaagggcg gaggaggctc gggtggagga 420

ggatcgggag gaggcgggtc cggtggtggc ggatcgcaaa tccagctggt gcagtccggc 480

gcagaagtga agaagccggg agcgtccgtg aaagtgagct gcaaggcctc agggtacatc 540

ttcaccaatt acggcatgaa ttgggtgcgg caggcacccg gacagcgcct ggagtggatg 600

ggctggatca acacttacac cggggaaagc acgtactcgg ccgacttcaa aggacgggtg 660

accattaccc tggatacctc ggcctcaacc gcttacatgg agctctcatc acttagatcc 720

gaggacactg ccgtctacta ctgtgcaagg agcggaggct acgaccctat ggactattgg 780

ggacaaggca ctactgtgac tgtgtcgtcc accactaccc agcaccgag gccacccacc 840

ccggctccta ccatcgcctc ccagcctctg tccctgcgtc cggaggcatg tagacccgca 900

gctggtgggg ccgtgcatac ccggggtctt gacttcgcct gcgatatcta catttgggcc 960

cctctggctg gtacttgcgg ggtcctgctg ctttcactcg tgatcactct ttactgtaag 1020

cgcggtcgga agaagctgct gtacatcttt aagcaaccct tcatgaggcc tgtgcagact 1080

actcaagagg aggacggctg ttcatgccgg ttcccagagg aggaggaagg cggctgcgaa 1140

ctgcgcgtga aattcagccg cagcgcagat gctccagcct acaagcaggg gcagaaccag 1200

ctctacaacg aactcaatct tggtcggaga gaggagtacg acgtgctgga caagcggaga 1260

ggacgggacc cagaaatggg cgggaagccg cgcagaaaga atccccaaga gggcctgtac 1320

aacgagctcc aaaaggataa gatggcagaa gcctatagcg agattggtat gaaaggggaa 1380

cgcagaagag gcaaaggcca cgacggactg taccagggac tcagcaccgc caccaaggac 1440

acctatgacg ctcttcacat gcaggccctg ccgcctcgg 1479

<210> 153
<211> 493
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 153

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15

His Ala Ala Arg Pro Asp Ile Val Leu Thr Gln Ser Pro Asp Ser Leu
            20                  25                  30

Ala Val Ser Leu Gly Glu Arg Ala Thr Ile Asn Cys Arg Ala Ser Glu
        35                  40                  45

Ser Val Asp Asn Tyr Gly Asn Thr Phe Met His Trp Tyr Gln Gln Lys
    50                  55                  60

Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Arg Ala Ser Asn Leu Glu
65                  70                  75                  80

Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Arg Thr Asp Phe
                85                  90                  95

Thr Leu Thr Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr
            100                 105                 110

Cys Gln Gln Ser Asn Glu Asp Pro Pro Thr Phe Gly Gln Gly Thr Lys
        115                 120                 125

Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
    130                 135                 140

Gly Gly Ser Gly Gly Gly Gly Ser Gln Ile Gln Leu Val Gln Ser Gly
145                 150                 155                 160

Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala
                165                 170                 175

Ser Gly Tyr Ile Phe Thr Asn Tyr Gly Met Asn Trp Val Arg Gln Ala
            180                 185                 190

Pro Gly Gln Arg Leu Glu Trp Met Gly Trp Ile Asn Thr Tyr Thr Gly
        195                 200                 205

Glu Ser Thr Tyr Ser Ala Asp Phe Lys Gly Arg Val Thr Ile Thr Leu
    210                 215                 220

Asp Thr Ser Ala Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser
```

_SL
225 230 235 240

Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Gly Gly Tyr Asp Pro
245 250 255

Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Thr Thr
260 265 270

Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln
275 280 285

Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala
290 295 300

Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala
305 310 315 320

Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr
325 330 335

Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln
340 345 350

Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser
355 360 365

Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys
370 375 380

Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln
385 390 395 400

Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu
405 410 415

Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg
420 425 430

Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met
435 440 445

Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly
450 455 460

Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp
465 470 475 480

_SL
Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 154
<211> 249
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 154
Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Glu Ser Val Asp Asn Tyr
20 25 30

Gly Asn Thr Phe Met His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro
35 40 45

Arg Leu Leu Ile Tyr Arg Ala Ser Asn Leu Glu Ser Gly Ile Pro Ala
50 55 60

Arg Phe Ser Gly Ser Gly Ser Arg Thr Asp Phe Thr Leu Thr Ile Ser
65 70 75 80

Ser Leu Glu Pro Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln Ser Asn
85 90 95

Glu Asp Pro Pro Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Gly
100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
115 120 125

Gly Gly Ser Gln Ile Gln Leu Val Gln Ser Gly Ser Glu Leu Lys Lys
130 135 140

Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe
145 150 155 160

Thr Asn Tyr Gly Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu
165 170 175

Glu Trp Met Gly Trp Ile Asn Thr Tyr Thr Gly Glu Ser Thr Tyr Ser
180 185 190

```
                                          _SL
Ala Asp Phe Lys Gly Arg Phe Val Phe Ser Leu Asp Thr Ser Val Ser
        195                 200                 205


Thr Ala Tyr Leu Gln Ile Asn Ala Leu Lys Ala Glu Asp Thr Ala Val
    210                 215                 220


Tyr Tyr Cys Ala Arg Ser Gly Gly Tyr Asp Pro Met Asp Tyr Trp Gly
225                 230                 235                 240


Gln Gly Thr Thr Val Thr Val Ser Ser
                245
```

<210> 155
<211> 747
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 155
gaaattgtgc tcacgcaatc acccgccact ctgtcgcttt ccccgggaga gcgggccacc 60

ctctcctgcc gcgcttcgga atcggtcgac aattacggaa atacttttat gcactggtac 120

caacagaagc cagggcaggc gccaaggctg ctgatctaca gagcctcgaa cctcgaaagc 180

ggcatccctg cgcggttcag cggtagcgga agccgcaccg atttcaccct gaccatctca 240

tcactggagc cggaggatgt ggcagtgtac tattgtcagc agtcgaacga ggacccgccg 300

actttcgggc agggaaccaa gctggaaatc aagggtggag gagggagcgg cggaggagga 360

tcgggaggag gaggcagcgg aggcggagga tcgcaaatcc aacttgtcca gtcgggctcc 420

gaactcaaaa agcctggcgc gtccgtgaag gtcagctgca aagcatcagg atacatcttc 480

actaactacg gtatgaattg ggtcagacag gctccgggtc agggtctgga gtggatggga 540

tggattaaca cctacactgg ggaatcgact tactccgcgg acttcaaagg gcggttcgtg 600

ttttcactgg acaccagcgt gtccaccgct tacttgcaaa tcaacgccct caaggccgag 660

gacaccgccg tgtactactg cgcacgctca ggcggatacg atccaatgga ctactgggga 720

cagggcacta cggtgactgt gtcctcc 747

<210> 156
<211> 843
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 156
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaaattg tgctcacgca atcacccgcc actctgtcgc tttccccggg agagcgggcc 120

accctctcct gccgcgcttc ggaatcggtc gacaattacg gaaatacttt tatgcactgg 180

taccaacaga agccagggca ggcgccaagg ctgctgatct acagagcctc gaacctcgaa 240

agcggcatcc ctgcgcggtt cagcggtagc ggaagccgca ccgatttcac cctgaccatc 300

tcatcactgg agccggagga tgtggcagtg tactattgtc agcagtcgaa cgaggacccg 360

ccgactttcg ggcagggaac caagctggaa atcaagggtg gaggagggag cggcggagga 420

ggatcgggag gaggaggcag cggaggcgga ggatcgcaaa tccaacttgt ccagtcgggc 480

tccgaactca aaaagcctgg cgcgtccgtg aaggtcagct gcaaagcatc aggatacatc 540

ttcactaact acggtatgaa ttgggtcaga caggctccgg gtcagggtct ggagtggatg 600

ggatggatta acacctacac tggggaatcg acttactccg cggacttcaa agggcggttc 660

gtgttttcac tggacaccag cgtgtccacc gcttacttgc aaatcaacgc cctcaaggcc 720

gaggacaccg ccgtgtacta ctgcgcacgc tcaggcggat acgatccaat ggactactgg 780

ggacagggca ctacggtgac tgtgtcctcc ggctcgcacc accatcacca tcatcatcac 840

cac 843

<210> 157
<211> 281
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 157
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu
20 25 30

Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Glu
35 40 45

Ser Val Asp Asn Tyr Gly Asn Thr Phe Met His Trp Tyr Gln Gln Lys
50 55 60

Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Arg Ala Ser Asn Leu Glu
65 70 75 80

```
Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Arg Thr Asp Phe
                85                  90                  95

Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp Val Ala Val Tyr Tyr
            100                 105                 110

Cys Gln Gln Ser Asn Glu Asp Pro Pro Thr Phe Gly Gln Gly Thr Lys
        115                 120                 125

Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
    130                 135                 140

Gly Gly Ser Gly Gly Gly Gly Ser Gln Ile Gln Leu Val Gln Ser Gly
145                 150                 155                 160

Ser Glu Leu Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala
                165                 170                 175

Ser Gly Tyr Ile Phe Thr Asn Tyr Gly Met Asn Trp Val Arg Gln Ala
            180                 185                 190

Pro Gly Gln Gly Leu Glu Trp Met Gly Trp Ile Asn Thr Tyr Thr Gly
        195                 200                 205

Glu Ser Thr Tyr Ser Ala Asp Phe Lys Gly Arg Phe Val Phe Ser Leu
    210                 215                 220

Asp Thr Ser Val Ser Thr Ala Tyr Leu Gln Ile Asn Ala Leu Lys Ala
225                 230                 235                 240

Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Gly Gly Tyr Asp Pro
                245                 250                 255

Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Ser
            260                 265                 270

His His His His His His His His His
        275                 280
```

<210> 158
<211> 1479
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 158
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaaattg tgctcacgca atcacccgcc actctgtcgc tttccccggg agagcgggcc 120

accctctcct gccgcgcttc ggaatcggtc gacaattacg gaaatacttt tatgcactgg 180

taccaacaga agccagggca ggcgccaagg ctgctgatct acagagcctc gaacctcgaa 240

agcggcatcc ctgcgcggtt cagcggtagc ggaagccgca ccgatttcac cctgaccatc 300

tcatcactgg agccggagga tgtggcagtg tactattgtc agcagtcgaa cgaggacccg 360

ccgactttcg ggcagggaac caagctggaa atcaagggtg gaggagggag cggcggagga 420

ggatcgggag gaggaggcag cggaggcgga ggatcgcaaa tccaacttgt ccagtcgggc 480

tccgaactca aaaagcctgg cgcgtccgtg aaggtcagct gcaaagcatc aggatacatc 540

ttcactaact acggtatgaa ttgggtcaga caggctccgg gtcagggtct ggagtggatg 600

ggatggatta acacctacac tggggaatcg acttactccg cggacttcaa agggcggttc 660

gtgttttcac tggacaccag cgtgtccacc gcttacttgc aaatcaacgc cctcaaggcc 720

gaggacaccg ccgtgtacta ctgcgcacgc tcaggcggat acgatccaat ggactactgg 780

ggacagggca ctacggtgac tgtgtcctcc accactaccc cagcaccgag gccacccacc 840

ccggctccta ccatcgcctc ccagcctctg tccctgcgtc cggaggcatg tagacccgca 900

gctggtgggg ccgtgcatac ccggggtctt gacttcgcct gcgatatcta catttgggcc 960

cctctggctg gtacttgcgg ggtcctgctg ctttcactcg tgatcactct ttactgtaag 1020

cgcggtcgga agaagctgct gtacatcttt aagcaaccct tcatgaggcc tgtgcagact 1080

actcaagagg aggacggctg ttcatgccgg ttcccagagg aggaggaagg cggctgcgaa 1140

ctgcgcgtga aattcagccg cagcgcagat gctccagcct acaagcaggg gcagaaccag 1200

ctctacaacg aactcaatct tggtcggaga gaggagtacg acgtgctgga caagcggaga 1260

ggacgggacc cagaaatggg cgggaagccg cgcagaaaga atccccaaga gggcctgtac 1320

aacgagctcc aaaaggataa gatggcagaa gcctatagcg agattggtat gaaaggggaa 1380

cgcagaagag gcaaaggcca cgacggactg taccagggac tcagcaccgc caccaaggac 1440

acctatgacg ctcttcacat gcaggccctg ccgcctcgg 1479

<210> 159
<211> 493
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 159

```
                                                    _SL
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15

His Ala Ala Arg Pro Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu
            20                  25                  30

Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Glu
        35                  40                  45

Ser Val Asp Asn Tyr Gly Asn Thr Phe Met His Trp Tyr Gln Gln Lys
    50                  55                  60

Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Arg Ala Ser Asn Leu Glu
65                  70                  75                  80

Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Arg Thr Asp Phe
                85                  90                  95

Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp Val Ala Val Tyr Tyr
            100                 105                 110

Cys Gln Gln Ser Asn Glu Asp Pro Pro Thr Phe Gly Gln Gly Thr Lys
        115                 120                 125

Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
    130                 135                 140

Gly Gly Ser Gly Gly Gly Gly Ser Gln Ile Gln Leu Val Gln Ser Gly
145                 150                 155                 160

Ser Glu Leu Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala
                165                 170                 175

Ser Gly Tyr Ile Phe Thr Asn Tyr Gly Met Asn Trp Val Arg Gln Ala
            180                 185                 190

Pro Gly Gln Gly Leu Glu Trp Met Gly Trp Ile Asn Thr Tyr Thr Gly
        195                 200                 205

Glu Ser Thr Tyr Ser Ala Asp Phe Lys Gly Arg Phe Val Phe Ser Leu
    210                 215                 220

Asp Thr Ser Val Ser Thr Ala Tyr Leu Gln Ile Asn Ala Leu Lys Ala
225                 230                 235                 240

Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Gly Gly Tyr Asp Pro
                245                 250                 255
```

```
Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Thr Thr
            260                 265                 270

Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln
        275                 280                 285

Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala
    290                 295                 300

Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala
305                 310                 315                 320

Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr
                325                 330                 335

Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln
            340                 345                 350

Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser
        355                 360                 365

Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys
    370                 375                 380

Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln
385                 390                 395                 400

Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu
                405                 410                 415

Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg
            420                 425                 430

Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met
        435                 440                 445

Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly
    450                 455                 460

Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp
465                 470                 475                 480

Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
                485                 490
```

<210> 160
<211> 249

<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 160

```
Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1               5                  10                  15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Glu Ser Val Asp Asn Tyr
            20                  25                  30

Gly Asn Thr Phe Met His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro
        35                  40                  45

Arg Leu Leu Ile Tyr Arg Ala Ser Asn Leu Glu Ser Gly Ile Pro Ala
    50                  55                  60

Arg Phe Ser Gly Ser Gly Ser Arg Thr Asp Phe Thr Leu Thr Ile Ser
65                  70                  75                  80

Ser Leu Glu Pro Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln Ser Asn
                85                  90                  95

Glu Asp Pro Pro Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Gly
            100                 105                 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
        115                 120                 125

Gly Gly Ser Gln Ile Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys
    130                 135                 140

Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe
145                 150                 155                 160

Thr Asn Tyr Gly Met Asn Trp Val Arg Gln Ala Pro Gly Gln Arg Leu
                165                 170                 175

Glu Trp Met Gly Trp Ile Asn Thr Tyr Thr Gly Glu Ser Thr Tyr Ser
            180                 185                 190

Ala Asp Phe Lys Gly Arg Val Thr Ile Thr Leu Asp Thr Ser Ala Ser
        195                 200                 205

Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val
    210                 215                 220
```

Tyr Tyr Cys Ala Arg Ser Gly Gly Tyr Asp Pro Met Asp Tyr Trp Gly
225 230 235 240

Gln Gly Thr Thr Val Thr Val Ser Ser
245

<210> 161
<211> 747
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 161
gagatcgtct tgacgcaatc gccagccacc ctgtccctga gcccaggcga gcgcgccacc 60

ctcagctgtc gggcgagcga aagcgtggac aattacggaa acacctttat gcactggtac 120

caacagaaac cggggcaggc tccgcgcctc ctcatctacc gcgcatccaa tctggaatca 180

ggaatccccg cgaggttctc cggtagcgga tcgcggactg actttactct gaccatctcg 240

tcccttgaac cggaggatgt ggctgtgtat tactgccagc agtcaaacga ggaccctcca 300

actttcgggc agggaaccaa gctcgaaatc aagggcggtg gcggaagcgg aggaggagga 360

tcaggcggag gcggctcagg cggtggaggt tcacaaattc aactggtgca gtcgggagcg 420

gaggtcaaga agccgggagc ctcagtgaaa gtgagctgca aggcttcggg ttacattttc 480

actaattacg gcatgaactg ggtgaggcag gcccctggcc aacggttgga atggatggga 540

tggatcaaca cctacaccgg ggagtcgact tactccgcgg acttcaaggg gagagtcacg 600

atcaccctgg atacgtccgc aagcactgcc tacatggaac tgtcctccct gcgctcggaa 660

gataccgcag tctactactg cgccagatcg ggcggatatg acccgatgga ctactgggga 720

cagggaacta ctgtcaccgt gtcctcg 747

<210> 162
<211> 843
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 162
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgagatcg tcttgacgca atcgccagcc accctgtccc tgagcccagg cgagcgcgcc 120

accctcagct gtcgggcgag cgaaagcgtg gacaattacg gaaacacctt tatgcactgg 180

taccaacaga aaccggggca ggctccgcgc ctcctcatct accgcgcatc caatctggaa 240

tcaggaatcc ccgcgaggtt ctccggtagc ggatcgcgga ctgactttac tctgaccatc 300

tcgtcccttg aaccggagga tgtggctgtg tattactgcc agcagtcaaa cgaggaccct 360

ccaactttcg ggcagggaac caagctcgaa atcaagggcg gtggcggaag cggaggagga 420

ggatcaggcg gaggcggctc aggcggtgga ggttcacaaa ttcaactggt gcagtcggga 480

gcggaggtca agaagccggg agcctcagtg aaagtgagct gcaaggcttc gggttacatt 540

ttcactaatt acggcatgaa ctgggtgagg caggcccctg gccaacggtt ggaatggatg 600

ggatggatca acacctacac cggggagtcg acttactccg cggacttcaa ggggagagtc 660

acgatcaccc tggatacgtc cgcaagcact gcctacatgg aactgtcctc cctgcgctcg 720

gaagataccg cagtctacta ctgcgccaga tcgggcggat atgacccgat ggactactgg 780

ggacagggaa ctactgtcac cgtgtcctcg ggctcgcacc accatcacca tcatcatcac 840

cac 843

<210> 163
<211> 281
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 163
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu
20 25 30

Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Glu
35 40 45

Ser Val Asp Asn Tyr Gly Asn Thr Phe Met His Trp Tyr Gln Gln Lys
50 55 60

Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Arg Ala Ser Asn Leu Glu
65 70 75 80

Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Arg Thr Asp Phe
85 90 95

Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp Val Ala Val Tyr Tyr

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100 105 110

Cys Gln Gln Ser Asn Glu Asp Pro Pro Thr Phe Gly Gln Gly Thr Lys
115 120 125

Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
130 135 140

Gly Gly Ser Gly Gly Gly Gly Ser Gln Ile Gln Leu Val Gln Ser Gly
145 150 155 160

Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala
165 170 175

Ser Gly Tyr Ile Phe Thr Asn Tyr Gly Met Asn Trp Val Arg Gln Ala
180 185 190

Pro Gly Gln Arg Leu Glu Trp Met Gly Trp Ile Asn Thr Tyr Thr Gly
195 200 205

Glu Ser Thr Tyr Ser Ala Asp Phe Lys Gly Arg Val Thr Ile Thr Leu
210 215 220

Asp Thr Ser Ala Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser
225 230 235 240

Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Gly Gly Tyr Asp Pro
245 250 255

Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Ser
260 265 270

His His His His His His His His His
275 280

<210> 164
<211> 1479
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 164
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgagatcg tcttgacgca atcgccagcc accctgtccc tgagcccagg cgagcgcgcc 120

accctcagct gtcgggcgag cgaaagcgtg gacaattacg gaaacacctt tatgcactgg 180

taccaacaga aaccggggca ggctccgcgc ctcctcatct accgcgcatc caatctggaa 240

tcaggaatcc ccgcgaggtt ctccggtagc ggatcgcgga ctgactttac tctgaccatc 300

tcgtcccttg aaccggagga tgtggctgtg tattactgcc agcagtcaaa cgaggaccct 360

ccaactttcg ggcagggaac caagctcgaa atcaagggcg gtggcggaag cggaggagga 420

ggatcaggcg gaggcggctc aggcggtgga ggttcacaaa ttcaactggt gcagtcggga 480

gcggaggtca agaagccggg agcctcagtg aaagtgagct gcaaggcttc gggttacatt 540

ttcactaatt acggcatgaa ctgggtgagg caggcccctg gccaacggtt ggaatggatg 600

ggatggatca acacctacac cggggagtcg acttactccg cggacttcaa ggggagagtc 660

acgatcaccc tggatacgtc cgcaagcact gcctacatgg aactgtcctc cctgcgctcg 720

gaagataccg cagtctacta ctgcgccaga tcgggcggat atgacccgat ggactactgg 780

ggacagggaa ctactgtcac cgtgtcctcg accactaccc cagcaccgag gccacccacc 840

ccggctccta ccatcgcctc ccagcctctg tccctgcgtc cggaggcatg tagacccgca 900

gctggtgggg ccgtgcatac ccggggtctt gacttcgcct gcgatatcta catttgggcc 960

cctctggctg gtacttgcgg ggtcctgctg ctttcactcg tgatcactct ttactgtaag 1020

cgcggtcgga agaagctgct gtacatcttt aagcaaccct tcatgaggcc tgtgcagact 1080

actcaagagg aggacggctg ttcatgccgg ttcccagagg aggaggaagg cggctgcgaa 1140

ctgcgcgtga aattcagccg cagcgcagat gctccagcct acaagcaggg gcagaaccag 1200

ctctacaacg aactcaatct tggtcggaga gaggagtacg acgtgctgga caagcggaga 1260

ggacgggacc cagaaatggg cgggaagccg cgcagaaaga atccccaaga gggcctgtac 1320

aacgagctcc aaaaggataa gatggcagaa gcctatagcg agattggtat gaaaggggaa 1380

cgcagaagag gcaaaggcca cgacggactg taccagggac tcagcaccgc caccaaggac 1440

acctatgacg ctcttcacat gcaggccctg ccgcctcgg 1479

<210> 165
<211> 493
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 165
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu
20 25 30

```
Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Glu
        35                  40                  45

Ser Val Asp Asn Tyr Gly Asn Thr Phe Met His Trp Tyr Gln Gln Lys
    50                  55                  60

Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Arg Ala Ser Asn Leu Glu
65                  70                  75                  80

Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Arg Thr Asp Phe
                85                  90                  95

Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp Val Ala Val Tyr Tyr
            100                 105                 110

Cys Gln Gln Ser Asn Glu Asp Pro Pro Thr Phe Gly Gln Gly Thr Lys
        115                 120                 125

Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
    130                 135                 140

Gly Gly Ser Gly Gly Gly Gly Ser Gln Ile Gln Leu Val Gln Ser Gly
145                 150                 155                 160

Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala
                165                 170                 175

Ser Gly Tyr Ile Phe Thr Asn Tyr Gly Met Asn Trp Val Arg Gln Ala
            180                 185                 190

Pro Gly Gln Arg Leu Glu Trp Met Gly Trp Ile Asn Thr Tyr Thr Gly
        195                 200                 205

Glu Ser Thr Tyr Ser Ala Asp Phe Lys Gly Arg Val Thr Ile Thr Leu
    210                 215                 220

Asp Thr Ser Ala Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser
225                 230                 235                 240

Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Gly Gly Tyr Asp Pro
                245                 250                 255

Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Thr Thr
            260                 265                 270

Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln
```

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275 280 285

Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala
290 295 300

Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala
305 310 315 320

Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr
325 330 335

Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln
340 345 350

Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser
355 360 365

Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys
370 375 380

Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln
385 390 395 400

Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu
405 410 415

Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg
420 425 430

Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met
435 440 445

Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly
450 455 460

Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp
465 470 475 480

Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 166
<211> 249
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

polypeptide"

<400> 166

```
Gln Ile Gln Leu Val Gln Ser Gly Ser Glu Leu Lys Lys Pro Gly Ala
1               5                   10                  15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Asn Tyr
            20                  25                  30

Gly Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Ser Thr Tyr Ser Ala Asp Phe
    50                  55                  60

Lys Gly Arg Phe Val Phe Ser Leu Asp Thr Ser Val Ser Thr Ala Tyr
65                  70                  75                  80

Leu Gln Ile Asn Ala Leu Lys Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ser Gly Gly Tyr Asp Pro Met Asp Tyr Trp Gly Gln Gly Thr
            100                 105                 110

Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Leu Thr Gln
    130                 135                 140

Ser Pro Asp Ser Leu Ala Val Ser Leu Gly Glu Arg Ala Thr Ile Asn
145                 150                 155                 160

Cys Arg Ala Ser Glu Ser Val Asp Asn Tyr Gly Asn Thr Phe Met His
                165                 170                 175

Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Arg
            180                 185                 190

Ala Ser Asn Leu Glu Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly
        195                 200                 205

Ser Arg Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala Glu Asp
    210                 215                 220

Val Ala Val Tyr Tyr Cys Gln Gln Ser Asn Glu Asp Pro Pro Thr Phe
225                 230                 235                 240
```

_SL

Gly Gln Gly Thr Lys Leu Glu Ile Lys
245

<210> 167
<211> 747
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 167
cagatccagt tggtccagtc aggctccgaa ctgaaaaagc cgggtgcatc cgtcaaggtg 60

tcgtgcaaag cctccggtta cattttcacc aactacggca tgaactgggt ccgccaggcc 120

cctgggcagg gactcgaatg gatggggtgg atcaacactt acaccggaga gtcgacttac 180

tcggccgatt tcaagggacg gttcgtgttt tccctggaca cttcagtctc gaccgcatat 240

ctccaaatca acgcgcttaa ggcggaagat actgctgtct actactgcgc cagatcagga 300

ggttacgatc caatggacta ctggggacag ggcaccactg tgacggtgtc gtcgggagga 360

ggaggatcgg gcggaggcgg gtccggcggt ggagggagcg gaggaggcgg aagcgacatc 420

gtgctgaccc agtcgccaga tagcctggcg gtgtccttgg gtgagagggc taccatcaat 480

tgtcgcgcgt cagagtccgt ggacaattac gggaatacct tcatgcactg gtaccaacaa 540

aagcccggac aaccgccgaa gctgctgatc tacagagcaa gcaacctcga atcaggagtg 600

ccggaccgct ttagcgggtc aggaagccgg actgacttca ccctgactat ctcctcgctc 660

caggccgagg acgtggccgt gtattactgc cagcagagca acgaagatcc tccaacgttc 720

ggccaaggaa ccaaactgga gattaag 747

<210> 168
<211> 843
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 168
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccagatcc agttggtcca gtcaggctcc gaactgaaaa agccgggtgc atccgtcaag 120

gtgtcgtgca aagcctccgg ttacattttc accaactacg gcatgaactg ggtccgccag 180

gcccctgggc agggactcga atggatgggg tggatcaaca cttacaccgg agagtcgact 240

tactcggccg atttcaaggg acggttcgtg ttttccctgg acacttcagt ctcgaccgca 300

_SL

tatctccaaa tcaacgcgct taaggcggaa gatactgctg tctactactg cgccagatca 360

ggaggttacg atccaatgga ctactgggga cagggcacca ctgtgacggt gtcgtcggga 420

ggaggaggat cgggcggagg cgggtccggc ggtggaggga gcggaggagg cggaagcgac 480

atcgtgctga cccagtcgcc agatagcctg gcggtgtcct tgggtgagag ggctaccatc 540

aattgtcgcg cgtcagagtc cgtggacaat tacgggaata ccttcatgca ctggtaccaa 600

caaaagcccg gacaaccgcc gaagctgctg atctacagag caagcaacct cgaatcagga 660

gtgccggacc gctttagcgg gtcaggaagc cggactgact tcaccctgac tatctcctcg 720

ctccaggccg aggacgtggc cgtgtattac tgccagcaga gcaacgaaga tcctccaacg 780

ttcggccaag gaaccaaact ggagattaag ggctcgcacc accatcacca tcatcatcac 840

cac 843

<210> 169
<211> 281
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 169

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Ile Gln Leu Val Gln Ser Gly Ser Glu Leu
20 25 30

Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
35 40 45

Ile Phe Thr Asn Tyr Gly Met Asn Trp Val Arg Gln Ala Pro Gly Gln
50 55 60

Gly Leu Glu Trp Met Gly Trp Ile Asn Thr Tyr Thr Gly Glu Ser Thr
65 70 75 80

Tyr Ser Ala Asp Phe Lys Gly Arg Phe Val Phe Ser Leu Asp Thr Ser
85 90 95

Val Ser Thr Ala Tyr Leu Gln Ile Asn Ala Leu Lys Ala Glu Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Ala Arg Ser Gly Gly Tyr Asp Pro Met Asp Tyr
115 120 125

```
Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
    130                 135                 140

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp
145                 150                 155                 160

Ile Val Leu Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly Glu
                165                 170                 175

Arg Ala Thr Ile Asn Cys Arg Ala Ser Glu Ser Val Asp Asn Tyr Gly
            180                 185                 190

Asn Thr Phe Met His Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys
        195                 200                 205

Leu Leu Ile Tyr Arg Ala Ser Asn Leu Glu Ser Gly Val Pro Asp Arg
    210                 215                 220

Phe Ser Gly Ser Gly Ser Arg Thr Asp Phe Thr Leu Thr Ile Ser Ser
225                 230                 235                 240

Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln Ser Asn Glu
                245                 250                 255

Asp Pro Pro Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Gly Ser
            260                 265                 270

His His His His His His His His His
        275                 280
```

<210> 170
<211> 1479
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 170
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccagatcc agttggtcca gtcaggctcc gaactgaaaa agccgggtgc atccgtcaag 120

gtgtcgtgca aagcctccgg ttacattttc accaactacg gcatgaactg ggtccgccag 180

gcccctgggc agggactcga atggatgggg tggatcaaca cttacaccgg agagtcgact 240

tactcggccg atttcaaggg acggttcgtg ttttccctgg acacttcagt ctcgaccgca 300

tatctccaaa tcaacgcgct taaggcggaa gatactgctg tctactactg cgccagatca 360

ggaggttacg atccaatgga ctactgggga cagggcacca ctgtgacggt gtcgtcggga 420

ggaggaggat cgggcggagg cgggtccggc ggtggaggga gcggaggagg cggaagcgac 480

atcgtgctga cccagtcgcc agatagcctg gcggtgtcct tgggtgagag ggctaccatc 540

aattgtcgcg cgtcagagtc cgtggacaat tacgggaata ccttcatgca ctggtaccaa 600

caaaagcccg gacaaccgcc gaagctgctg atctacagag caagcaacct cgaatcagga 660

gtgccggacc gctttagcgg gtcaggaagc cggactgact tcaccctgac tatctcctcg 720

ctccaggccg aggacgtggc cgtgtattac tgccagcaga gcaacgaaga tcctccaacg 780

ttcggccaag gaaccaaact ggagattaag accactaccc cagcaccgag gccacccacc 840

ccggctccta ccatcgcctc ccagcctctg tccctgcgtc cggaggcatg tagacccgca 900

gctggtgggg ccgtgcatac ccggggtctt gacttcgcct gcgatatcta catttgggcc 960

cctctggctg gtacttgcgg ggtcctgctg ctttcactcg tgatcactct ttactgtaag 1020

cgcggtcgga agaagctgct gtacatcttt aagcaaccct tcatgaggcc tgtgcagact 1080

actcaagagg aggacggctg ttcatgccgg ttcccagagg aggaggaagg cggctgcgaa 1140

ctgcgcgtga aattcagccg cagcgcagat gctccagcct acaagcaggg gcagaaccag 1200

ctctacaacg aactcaatct tggtcggaga gaggagtacg acgtgctgga caagcggaga 1260

ggacgggacc cagaaatggg cgggaagccg cgcagaaaga atccccaaga gggcctgtac 1320

aacgagctcc aaaaggataa gatggcagaa gcctatagcg agattggtat gaaaggggaa 1380

cgcagaagag gcaaaggcca cgacggactg taccagggac tcagcaccgc caccaaggac 1440

acctatgacg ctcttcacat gcaggccctg ccgcctcgg 1479

<210> 171
<211> 493
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 171
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Ile Gln Leu Val Gln Ser Gly Ser Glu Leu
20 25 30

Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
35 40 45

```
                                                _SL
Ile Phe Thr Asn Tyr Gly Met Asn Trp Val Arg Gln Ala Pro Gly Gln
    50                  55                  60

Gly Leu Glu Trp Met Gly Trp Ile Asn Thr Tyr Thr Gly Glu Ser Thr
65                  70                  75                  80

Tyr Ser Ala Asp Phe Lys Gly Arg Phe Val Phe Ser Leu Asp Thr Ser
                85                  90                  95

Val Ser Thr Ala Tyr Leu Gln Ile Asn Ala Leu Lys Ala Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Arg Ser Gly Gly Tyr Asp Pro Met Asp Tyr
        115                 120                 125

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
    130                 135                 140

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp
145                 150                 155                 160

Ile Val Leu Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly Glu
                165                 170                 175

Arg Ala Thr Ile Asn Cys Arg Ala Ser Glu Ser Val Asp Asn Tyr Gly
            180                 185                 190

Asn Thr Phe Met His Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys
        195                 200                 205

Leu Leu Ile Tyr Arg Ala Ser Asn Leu Glu Ser Gly Val Pro Asp Arg
    210                 215                 220

Phe Ser Gly Ser Gly Ser Arg Thr Asp Phe Thr Leu Thr Ile Ser Ser
225                 230                 235                 240

Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln Ser Asn Glu
                245                 250                 255

Asp Pro Pro Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Thr Thr
            260                 265                 270

Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln
        275                 280                 285

Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala
    290                 295                 300
```

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Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala
305                 310                 315                 320

Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr
                325                 330                 335

Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln
            340                 345                 350

Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser
        355                 360                 365

Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys
    370                 375                 380

Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln
385                 390                 395                 400

Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu
                405                 410                 415

Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg
            420                 425                 430

Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met
        435                 440                 445

Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly
    450                 455                 460

Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp
465                 470                 475                 480

Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
                485                 490


<210> 172
<211> 249
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 172
Gln Ile Gln Leu Val Gln Ser Gly Ser Glu Leu Lys Lys Pro Gly Ala
1               5                   10                  15
```

```
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Asn Tyr
            20                  25                  30

Gly Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Ser Thr Tyr Ser Ala Asp Phe
    50                  55                  60

Lys Gly Arg Phe Val Phe Ser Leu Asp Thr Ser Val Ser Thr Ala Tyr
65                  70                  75                  80

Leu Gln Ile Asn Ala Leu Lys Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ser Gly Gly Tyr Asp Pro Met Asp Tyr Trp Gly Gln Gly Thr
            100                 105                 110

Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln
    130                 135                 140

Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser
145                 150                 155                 160

Cys Arg Ala Ser Glu Ser Val Asp Asn Tyr Gly Asn Thr Phe Met His
                165                 170                 175

Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Arg
            180                 185                 190

Ala Ser Asn Leu Glu Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly
        195                 200                 205

Ser Arg Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp
    210                 215                 220

Val Ala Val Tyr Tyr Cys Gln Gln Ser Asn Glu Asp Pro Pro Thr Phe
225                 230                 235                 240

Gly Gln Gly Thr Lys Leu Glu Ile Lys
                245
```

<210> 173
<211> 747

<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 173
cagatccaac tggtgcaatc aggatcggag ctgaagaagc ctggggcttc agtgaaagtc 60

agctgcaaag cctccggtta catcttcacc aactacggca tgaactgggt gcgccaggcc 120

cctggacagg gactcgaatg gatggggtgg atcaacacct ataccgggga atccacgtac 180

tcagcagatt tcaagggacg cttcgtcttt tcgctggata cctccgtgtc cactgcgtac 240

ctccaaatca atgccctcaa agccgaagat actgcggtct actactgcgc acggagcgga 300

ggctacgacc cgatggacta ctggggacag ggaaccacgg tgaccgtgtc cagcggagga 360

ggcggatcgg gaggcggtgg ttcaggcggt ggaggcagcg gcggaggtgg aagcgaaatc 420

gtcttgactc agagcccagc gactttgtcc ctgtcgcccg gagagcgggc aactctgtca 480

tgccgcgctt cggaatcggt ggacaactat ggaaacacct ttatgcactg gtaccaacag 540

aagccgggac aagccccgag acttctgatc taccgggcct cgaatctcga aagcggcatc 600

ccggctagat tctcggggtc gggatcaagg accgacttca ctcttactat ttcctcactg 660

gagccagaag atgtggcggt gtactactgt cagcagtcca atgaggaccc gccaactttc 720

gggcagggca ccaagctgga gattaag 747

<210> 174
<211> 843
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 174
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccagatcc aactggtgca atcaggatcg gagctgaaga agcctggggc ttcagtgaaa 120

gtcagctgca aagcctccgg ttacatcttc accaactacg gcatgaactg ggtgcgccag 180

gcccctggac agggactcga atggatgggg tggatcaaca cctataccgg ggaatccacg 240

tactcagcag atttcaaggg acgcttcgtc ttttcgctgg atacctccgt gtccactgcg 300

tacctccaaa tcaatgccct caaagccgaa gatactgcgg tctactactg cgcacggagc 360

ggaggctacg acccgatgga ctactgggga cagggaacca cggtgaccgt gtccagcgga 420

ggaggcggat cgggaggcgg tggttcaggc ggtggaggca gcggcggagg tggaagcgaa 480

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atcgtcttga ctcagagccc agcgactttg tccctgtcgc ccggagagcg ggcaactctg 540

tcatgccgcg cttcggaatc ggtggacaac tatggaaaca cctttatgca ctggtaccaa 600

cagaagccgg gacaagcccc gagacttctg atctaccggg cctcgaatct cgaaagcggc 660

atcccggcta gattctcggg gtcgggatca aggaccgact tcactcttac tatttcctca 720

ctggagccag aagatgtggc ggtgtactac tgtcagcagt ccaatgagga cccgccaact 780

ttcgggcagg gcaccaagct ggagattaag ggctcgcacc accatcacca tcatcatcac 840

cac 843

<210> 175
<211> 281
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 175
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Ile Gln Leu Val Gln Ser Gly Ser Glu Leu
20 25 30

Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
35 40 45

Ile Phe Thr Asn Tyr Gly Met Asn Trp Val Arg Gln Ala Pro Gly Gln
50 55 60

Gly Leu Glu Trp Met Gly Trp Ile Asn Thr Tyr Thr Gly Glu Ser Thr
65 70 75 80

Tyr Ser Ala Asp Phe Lys Gly Arg Phe Val Phe Ser Leu Asp Thr Ser
85 90 95

Val Ser Thr Ala Tyr Leu Gln Ile Asn Ala Leu Lys Ala Glu Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Ala Arg Ser Gly Gly Tyr Asp Pro Met Asp Tyr
115 120 125

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
130 135 140

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu

_SL
145 150 155 160

Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu
165 170 175

Arg Ala Thr Leu Ser Cys Arg Ala Ser Glu Ser Val Asp Asn Tyr Gly
180 185 190

Asn Thr Phe Met His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg
195 200 205

Leu Leu Ile Tyr Arg Ala Ser Asn Leu Glu Ser Gly Ile Pro Ala Arg
210 215 220

Phe Ser Gly Ser Gly Ser Arg Thr Asp Phe Thr Leu Thr Ile Ser Ser
225 230 235 240

Leu Glu Pro Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln Ser Asn Glu
245 250 255

Asp Pro Pro Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Gly Ser
260 265 270

His His His His His His His His His
275 280

<210> 176
<211> 1479
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 176
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccagatcc aactggtgca atcaggatcg gagctgaaga agcctggggc ttcagtgaaa 120

gtcagctgca aagcctccgg ttacatcttc accaactacg gcatgaactg ggtgcgccag 180

gcccctggac agggactcga atggatgggg tggatcaaca cctataccgg ggaatccacg 240

tactcagcag atttcaaggg acgcttcgtc ttttcgctgg atacctccgt gtccactgcg 300

tacctccaaa tcaatgccct caaagccgaa gatactgcgg tctactactg cgcacggagc 360

ggaggctacg acccgatgga ctactgggga cagggaacca cggtgaccgt gtccagcgga 420

ggaggcggat cgggaggcgg tggttcaggc ggtggaggca gcggcggagg tggaagcgaa 480

atcgtcttga ctcagagccc agcgactttg tccctgtcgc ccggagagcg ggcaactctg 540

tcatgccgcg cttcggaatc ggtggacaac tatggaaaca cctttatgca ctggtaccaa 600

cagaagccgg gacaagcccc gagacttctg atctaccggg cctcgaatct cgaaagcggc 660

atcccggcta gattctcggg gtcgggatca aggaccgact tcactcttac tatttcctca 720

ctggagccag aagatgtggc ggtgtactac tgtcagcagt ccaatgagga cccgccaact 780

ttcgggcagg gcaccaagct ggagattaag accactaccc cagcaccgag gccacccacc 840

ccggctccta ccatcgcctc ccagcctctg tccctgcgtc cggaggcatg tagacccgca 900

gctggtgggg ccgtgcatac ccggggtctt gacttcgcct gcgatatcta catttgggcc 960

cctctggctg gtacttgcgg ggtcctgctg ctttcactcg tgatcactct ttactgtaag 1020

cgcggtcgga agaagctgct gtacatcttt aagcaaccct tcatgaggcc tgtgcagact 1080

actcaagagg aggacggctg ttcatgccgg ttcccagagg aggaggaagg cggctgcgaa 1140

ctgcgcgtga aattcagccg cagcgcagat gctccagcct acaagcaggg gcagaaccag 1200

ctctacaacg aactcaatct tggtcggaga gaggagtacg acgtgctgga caagcggaga 1260

ggacgggacc cagaaatggg cgggaagccg cgcagaaaga atccccaaga gggcctgtac 1320

aacgagctcc aaaaggataa gatggcagaa gcctatagcg agattggtat gaaaggggaa 1380

cgcagaagag gcaaaggcca cgacggactg taccagggac tcagcaccgc caccaaggac 1440

acctatgacg ctcttcacat gcaggccctg ccgcctcgg 1479

<210> 177
<211> 493
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 177
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Ile Gln Leu Val Gln Ser Gly Ser Glu Leu
20 25 30

Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
35 40 45

Ile Phe Thr Asn Tyr Gly Met Asn Trp Val Arg Gln Ala Pro Gly Gln
50 55 60

Gly Leu Glu Trp Met Gly Trp Ile Asn Thr Tyr Thr Gly Glu Ser Thr
65 70 75 80

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Tyr Ser Ala Asp Phe Lys Gly Arg Phe Val Phe Ser Leu Asp Thr Ser
                85                  90                  95

Val Ser Thr Ala Tyr Leu Gln Ile Asn Ala Leu Lys Ala Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Arg Ser Gly Gly Tyr Asp Pro Met Asp Tyr
        115                 120                 125

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
    130                 135                 140

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu
145                 150                 155                 160

Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu
                165                 170                 175

Arg Ala Thr Leu Ser Cys Arg Ala Ser Glu Ser Val Asp Asn Tyr Gly
            180                 185                 190

Asn Thr Phe Met His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg
        195                 200                 205

Leu Leu Ile Tyr Arg Ala Ser Asn Leu Glu Ser Gly Ile Pro Ala Arg
    210                 215                 220

Phe Ser Gly Ser Gly Ser Arg Thr Asp Phe Thr Leu Thr Ile Ser Ser
225                 230                 235                 240

Leu Glu Pro Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln Ser Asn Glu
                245                 250                 255

Asp Pro Pro Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Thr Thr
            260                 265                 270

Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln
        275                 280                 285

Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala
    290                 295                 300

Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala
305                 310                 315                 320

Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr
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325 330 335

Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln
340 345 350

Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser
355 360 365

Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys
370 375 380

Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln
385 390 395 400

Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu
405 410 415

Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg
420 425 430

Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met
435 440 445

Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly
450 455 460

Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp
465 470 475 480

Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 178
<211> 249
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 178
Gln Ile Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Asn Tyr
20 25 30

Gly Met Asn Trp Val Arg Gln Ala Pro Gly Gln Arg Leu Glu Trp Met

_SL
35 40 45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Ser Thr Tyr Ser Ala Asp Phe
50 55 60

Lys Gly Arg Val Thr Ile Thr Leu Asp Thr Ser Ala Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Gly Gly Tyr Asp Pro Met Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Leu Thr Gln
130 135 140

Ser Pro Asp Ser Leu Ala Val Ser Leu Gly Glu Arg Ala Thr Ile Asn
145 150 155 160

Cys Arg Ala Ser Glu Ser Val Asp Asn Tyr Gly Asn Thr Phe Met His
165 170 175

Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Arg
180 185 190

Ala Ser Asn Leu Glu Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly
195 200 205

Ser Arg Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala Glu Asp
210 215 220

Val Ala Val Tyr Tyr Cys Gln Gln Ser Asn Glu Asp Pro Pro Thr Phe
225 230 235 240

Gly Gln Gly Thr Lys Leu Glu Ile Lys
245

<210> 179
<211> 747
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

polynucleotide"

<400> 179
cagatccagc tggtgcagtc gggagctgaa gtgaaaaagc cgggagcatc ggtgaaggtg 60

tcatgcaaag ccagcggtta catcttcact aactacggta tgaactgggt gagacaagcg 120

cctggccaga gattggaatg gatgggatgg atcaatacct acaccgggga atcaacttac 180

agcgccgact tcaagggacg cgtgaccatc acgctggaca cctccgcgtc cactgcctac 240

atggagctct cgtcattgcg gagcgaggac accgccgtct actactgcgc acggtcagga 300

gggtacgatc cgatggacta ctggggacag ggcactaccg tcaccgtgag ctccggtgga 360

ggcggcagcg gcggtggcgg atcaggtgga ggaggatcag gaggaggagg gtccgatatc 420

gtgcttactc agtcacccga ttcgctggca gtctccctcg gagaacgcgc caccatcaat 480

tgtcgcgcgt ccgaatccgt cgacaactac ggcaacacct ttatgcactg gtaccaacag 540

aagcctggac aaccgccaaa actgctgatc taccgcgcta gcaacctcga atcgggcgtg 600

ccagataggt tctcgggctc ggggagccgg acggatttta ctctgactat ttcgtccctc 660

caagcagagg acgtcgccgt gtattactgc cagcaatcga atgaggaccc gccaactttc 720

ggacagggga ccaagctgga gattaag 747

<210> 180
<211> 843
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 180
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccagatcc agctggtgca gtcgggagct gaagtgaaaa agccgggagc atcggtgaag 120

gtgtcatgca aagccagcgg ttacatcttc actaactacg gtatgaactg ggtgagacaa 180

gcgcctggcc agagattgga atggatggga tggatcaata cctacaccgg ggaatcaact 240

tacagcgccg acttcaaggg acgcgtgacc atcacgctgg acacctccgc gtccactgcc 300

tacatggagc tctcgtcatt gcggagcgag gacaccgccg tctactactg cgcacggtca 360

ggagggtacg atccgatgga ctactgggga cagggcacta ccgtcaccgt gagctccggt 420

ggaggcggca gcggcggtgg cggatcaggt ggaggaggat caggaggagg agggtccgat 480

atcgtgctta ctcagtcacc cgattcgctg gcagtctccc tcggagaacg cgccaccatc 540

aattgtcgcg cgtccgaatc cgtcgacaac tacggcaaca cctttatgca ctggtaccaa 600

cagaagcctg gacaaccgcc aaaactgctg atctaccgcg ctagcaacct cgaatcgggc 660

gtgccagata ggttctcggg ctcggggagc cggacggatt ttactctgac tatttcgtcc 720

ctccaagcag aggacgtcgc cgtgtattac tgccagcaat cgaatgagga cccgccaact 780

ttcggacagg ggaccaagct ggagattaag ggctcgcacc accatcacca tcatcatcac 840

cac 843

<210> 181
<211> 281
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 181

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Ile Gln Leu Val Gln Ser Gly Ala Glu Val
20 25 30

Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
35 40 45

Ile Phe Thr Asn Tyr Gly Met Asn Trp Val Arg Gln Ala Pro Gly Gln
50 55 60

Arg Leu Glu Trp Met Gly Trp Ile Asn Thr Tyr Thr Gly Glu Ser Thr
65 70 75 80

Tyr Ser Ala Asp Phe Lys Gly Arg Val Thr Ile Thr Leu Asp Thr Ser
85 90 95

Ala Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Ala Arg Ser Gly Gly Tyr Asp Pro Met Asp Tyr
115 120 125

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
130 135 140

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp
145 150 155 160

Ile Val Leu Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly Glu
165 170 175

Arg Ala Thr Ile Asn Cys Arg Ala Ser Glu Ser Val Asp Asn Tyr Gly
180 185 190

Asn Thr Phe Met His Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys
195 200 205

Leu Leu Ile Tyr Arg Ala Ser Asn Leu Glu Ser Gly Val Pro Asp Arg
210 215 220

Phe Ser Gly Ser Gly Ser Arg Thr Asp Phe Thr Leu Thr Ile Ser Ser
225 230 235 240

Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln Ser Asn Glu
245 250 255

Asp Pro Pro Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Gly Ser
260 265 270

His His His His His His His His His
275 280

<210> 182
<211> 1479
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 182
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccagatcc agctggtgca gtcgggagct gaagtgaaaa agccgggagc atcggtgaag 120

gtgtcatgca aagccagcgg ttacatcttc actaactacg gtatgaactg ggtgagacaa 180

gcgcctggcc agagattgga atggatggga tggatcaata cctacaccgg ggaatcaact 240

tacagcgccg acttcaaggg acgcgtgacc atcacgctgg acacctccgc gtccactgcc 300

tacatggagc tctcgtcatt gcggagcgag gacaccgccg tctactactg cgcacggtca 360

ggagggtacg atccgatgga ctactgggga cagggcacta ccgtcaccgt gagctccggt 420

ggaggcggca gcggcggtgg cggatcaggt ggaggaggat caggaggagg agggtccgat 480

atcgtgctta ctcagtcacc cgattcgctg gcagtctccc tcggagaacg cgccaccatc 540

aattgtcgcg cgtccgaatc cgtcgacaac tacggcaaca cctttatgca ctggtaccaa 600

cagaagcctg gacaaccgcc aaaactgctg atctaccgcg ctagcaacct cgaatcgggc 660

gtgccagata ggttctcggg ctcggggagc cggacggatt ttactctgac tatttcgtcc 720

ctccaagcag aggacgtcgc cgtgtattac tgccagcaat cgaatgagga cccgccaact 780

ttcggacagg ggaccaagct ggagattaag accactaccc cagcaccgag gccacccacc 840

ccggctccta ccatcgcctc ccagcctctg tccctgcgtc cggaggcatg tagacccgca 900

gctggtgggg ccgtgcatac ccggggtctt gacttcgcct gcgatatcta catttgggcc 960

cctctggctg gtacttgcgg ggtcctgctg ctttcactcg tgatcactct ttactgtaag 1020

cgcggtcgga agaagctgct gtacatcttt aagcaaccct tcatgaggcc tgtgcagact 1080

actcaagagg aggacggctg ttcatgccgg ttcccagagg aggaggaagg cggctgcgaa 1140

ctgcgcgtga aattcagccg cagcgcagat gctccagcct acaagcaggg gcagaaccag 1200

ctctacaacg aactcaatct tggtcggaga gaggagtacg acgtgctgga caagcggaga 1260

ggacgggacc cagaaatggg cgggaagccg cgcagaaaga atccccaaga gggcctgtac 1320

aacgagctcc aaaaggataa gatggcagaa gcctatagcg agattggtat gaaaggggaa 1380

cgcagaagag gcaaaggcca cgacggactg taccagggac tcagcaccgc caccaaggac 1440

acctatgacg ctcttcacat gcaggccctg ccgcctcgg 1479

<210> 183
<211> 493
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 183
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Ile Gln Leu Val Gln Ser Gly Ala Glu Val
20 25 30

Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
35 40 45

Ile Phe Thr Asn Tyr Gly Met Asn Trp Val Arg Gln Ala Pro Gly Gln
50 55 60

Arg Leu Glu Trp Met Gly Trp Ile Asn Thr Tyr Thr Gly Glu Ser Thr
65 70 75 80

Tyr Ser Ala Asp Phe Lys Gly Arg Val Thr Ile Thr Leu Asp Thr Ser
85 90 95

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                                                    _SL
Ala Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Arg Ser Gly Gly Tyr Asp Pro Met Asp Tyr
        115                 120                 125

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
    130                 135                 140

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp
145                 150                 155                 160

Ile Val Leu Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly Glu
                165                 170                 175

Arg Ala Thr Ile Asn Cys Arg Ala Ser Glu Ser Val Asp Asn Tyr Gly
            180                 185                 190

Asn Thr Phe Met His Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys
        195                 200                 205

Leu Leu Ile Tyr Arg Ala Ser Asn Leu Glu Ser Gly Val Pro Asp Arg
    210                 215                 220

Phe Ser Gly Ser Gly Ser Arg Thr Asp Phe Thr Leu Thr Ile Ser Ser
225                 230                 235                 240

Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln Ser Asn Glu
                245                 250                 255

Asp Pro Pro Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Thr Thr
            260                 265                 270

Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln
        275                 280                 285

Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala
    290                 295                 300

Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala
305                 310                 315                 320

Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr
                325                 330                 335

Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln
            340                 345                 350
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Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser
355 360 365

Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys
370 375 380

Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln
385 390 395 400

Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu
405 410 415

Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg
420 425 430

Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met
435 440 445

Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly
450 455 460

Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp
465 470 475 480

Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 184
<211> 249
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 184
Gln Ile Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Asn Tyr
20 25 30

Gly Met Asn Trp Val Arg Gln Ala Pro Gly Gln Arg Leu Glu Trp Met
35 40 45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Ser Thr Tyr Ser Ala Asp Phe
50 55 60

Lys Gly Arg Val Thr Ile Thr Leu Asp Thr Ser Ala Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Gly Gly Tyr Asp Pro Met Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln
130 135 140

Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser
145 150 155 160

Cys Arg Ala Ser Glu Ser Val Asp Asn Tyr Gly Asn Thr Phe Met His
165 170 175

Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Arg
180 185 190

Ala Ser Asn Leu Glu Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly
195 200 205

Ser Arg Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp
210 215 220

Val Ala Val Tyr Tyr Cys Gln Gln Ser Asn Glu Asp Pro Pro Thr Phe
225 230 235 240

Gly Gln Gly Thr Lys Leu Glu Ile Lys
245

<210> 185
<211> 747
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 185
cagatccagc tggtgcaatc gggagctgaa gtgaagaagc ccggagcttc agtcaaagtc 60

agctgcaagg cgtcgggcta tatcttcacc aactacggga tgaactgggt gcggcaggcc 120

cctggacaaa gactggaatg gatgggatgg atcaacactt atactggcga gagcacgtac 180

tcagccgact ttaagggacg ggtgactatc accctcgata cctccgcctc cactgcgtac 240

atggaactct cgtccttgcg ctccgaggac actgccgtgt actactgcgc caggtcgggt 300

ggctacgatc cgatggatta ctggggtcaa ggaaccaccg tcactgtgtc gtccggcgga 360

ggcgggagcg gaggtggtgg ttcgggagga ggagggtcag gcggaggagg cagcgaaatc 420

gtgctgaccc aaagcccggc aactctgtca ctcagcccag gggagagggc aaccctgtca 480

tgtcgggcta gcgaatccgt ggacaattac ggaaacacgt ttatgcactg gtaccaacag 540

aaaccaggac aggcgcctag acttctcatc taccgcgcga gcaatttgga atccggcatc 600

ccagcccgct tctccgggtc ggggtcacgc accgatttca ctctgaccat ttcctccctg 660

gaacccgagg acgtggcagt ctactactgc cagcagtcga atgaggaccc gccgaccttc 720

ggacagggca ccaagctgga gattaag 747

<210> 186
<211> 843
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 186
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccagatcc agctggtgca atcgggagct gaagtgaaga agcccggagc ttcagtcaaa 120

gtcagctgca aggcgtcggg ctatatcttc accaactacg ggatgaactg ggtgcggcag 180

gcccctggac aaagactgga atggatggga tggatcaaca cttatactgg cgagagcacg 240

tactcagccg actttaaggg acgggtgact atcaccctcg atacctccgc ctccactgcg 300

tacatggaac tctcgtcctt gcgctccgag gacactgccg tgtactactg cgccaggtcg 360

ggtggctacg atccgatgga ttactggggt caaggaacca ccgtcactgt gtcgtccggc 420

ggaggcggga gcggaggtgg tggttcggga ggaggagggt caggcggagg aggcagcgaa 480

atcgtgctga cccaaagccc ggcaactctg tcactcagcc caggggagag ggcaaccctg 540

tcatgtcggg ctagcgaatc cgtggacaat tacggaaaca cgtttatgca ctggtaccaa 600

cagaaaccag gacaggcgcc tagacttctc atctaccgcg cgagcaattt ggaatccggc 660

atcccagccc gcttctccgg gtcggggtca cgcaccgatt tcactctgac catttcctcc 720

ctggaacccg aggacgtggc agtctactac tgccagcagt cgaatgagga cccgccgacc 780

ttcggacagg gcaccaagct ggagattaag ggctcgcacc accatcacca tcatcatcac 840

<210> 187
<211> 281
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 187
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Ile Gln Leu Val Gln Ser Gly Ala Glu Val
20 25 30

Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
35 40 45

Ile Phe Thr Asn Tyr Gly Met Asn Trp Val Arg Gln Ala Pro Gly Gln
50 55 60

Arg Leu Glu Trp Met Gly Trp Ile Asn Thr Tyr Thr Gly Glu Ser Thr
65 70 75 80

Tyr Ser Ala Asp Phe Lys Gly Arg Val Thr Ile Thr Leu Asp Thr Ser
85 90 95

Ala Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Ala Arg Ser Gly Gly Tyr Asp Pro Met Asp Tyr
115 120 125

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
130 135 140

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu
145 150 155 160

Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu
165 170 175

Arg Ala Thr Leu Ser Cys Arg Ala Ser Glu Ser Val Asp Asn Tyr Gly
180 185 190

Asn Thr Phe Met His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg

_SL

195 200 205

Leu Leu Ile Tyr Arg Ala Ser Asn Leu Glu Ser Gly Ile Pro Ala Arg
210 215 220

Phe Ser Gly Ser Gly Ser Arg Thr Asp Phe Thr Leu Thr Ile Ser Ser
225 230 235 240

Leu Glu Pro Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln Ser Asn Glu
245 250 255

Asp Pro Pro Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Gly Ser
260 265 270

His His His His His His His His His
275 280

<210> 188
<211> 1479
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 188
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccagatcc agctggtgca atcgggagct gaagtgaaga agcccggagc ttcagtcaaa 120

gtcagctgca aggcgtcggg ctatatcttc accaactacg ggatgaactg ggtgcggcag 180

gcccctggac aaagactgga atggatggga tggatcaaca cttatactgg cgagagcacg 240

tactcagccg actttaaggg acgggtgact atcaccctcg atacctccgc ctccactgcg 300

tacatggaac tctcgtcctt gcgctccgag gacactgccg tgtactactg cgccaggtcg 360

ggtggctacg atccgatgga ttactggggt caaggaacca ccgtcactgt gtcgtccggc 420

ggaggcggga gcggaggtgg tggttcggga ggaggagggt caggcggagg aggcagcgaa 480

atcgtgctga cccaaagccc ggcaactctg tcactcagcc caggggagag ggcaaccctg 540

tcatgtcggg ctagcgaatc cgtggacaat tacggaaaca cgtttatgca ctggtaccaa 600

cagaaaccag gacaggcgcc tagacttctc atctaccgcg cgagcaattt ggaatccggc 660

atcccagccc gcttctccgg gtcggggtca cgcaccgatt tcactctgac catttcctcc 720

ctggaacccg aggacgtggc agtctactac tgccagcagt cgaatgagga cccgccgacc 780

ttcggacagg gcaccaagct ggagattaag accactaccc cagcaccgag gccacccacc 840

ccggctccta ccatcgcctc ccagcctctg tccctgcgtc cggaggcatg tagacccgca 900

gctggtgggg ccgtgcatac ccggggtctt gacttcgcct gcgatatcta catttgggcc 960

cctctggctg gtacttgcgg ggtcctgctg ctttcactcg tgatcactct ttactgtaag 1020

cgcggtcgga agaagctgct gtacatcttt aagcaaccct tcatgaggcc tgtgcagact 1080

actcaagagg aggacggctg ttcatgccgg ttcccagagg aggaggaagg cggctgcgaa 1140

ctgcgcgtga aattcagccg cagcgcagat gctccagcct acaagcaggg gcagaaccag 1200

ctctacaacg aactcaatct tggtcggaga gaggagtacg acgtgctgga caagcggaga 1260

ggacgggacc cagaaatggg cgggaagccg cgcagaaaga atccccaaga gggcctgtac 1320

aacgagctcc aaaaggataa gatggcagaa gcctatagcg agattggtat gaaaggggaa 1380

cgcagaagag gcaaaggcca cgacggactg taccagggac tcagcaccgc caccaaggac 1440

acctatgacg ctcttcacat gcaggccctg ccgcctcgg 1479

<210> 189
<211> 493
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 189

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Ile Gln Leu Val Gln Ser Gly Ala Glu Val
20 25 30

Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
35 40 45

Ile Phe Thr Asn Tyr Gly Met Asn Trp Val Arg Gln Ala Pro Gly Gln
50 55 60

Arg Leu Glu Trp Met Gly Trp Ile Asn Thr Tyr Thr Gly Glu Ser Thr
65 70 75 80

Tyr Ser Ala Asp Phe Lys Gly Arg Val Thr Ile Thr Leu Asp Thr Ser
85 90 95

Ala Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Ala Arg Ser Gly Gly Tyr Asp Pro Met Asp Tyr
115 120 125

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Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
    130                 135                 140

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu
145                 150                 155                 160

Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu
                165                 170                 175

Arg Ala Thr Leu Ser Cys Arg Ala Ser Glu Ser Val Asp Asn Tyr Gly
            180                 185                 190

Asn Thr Phe Met His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg
        195                 200                 205

Leu Leu Ile Tyr Arg Ala Ser Asn Leu Glu Ser Gly Ile Pro Ala Arg
    210                 215                 220

Phe Ser Gly Ser Gly Ser Arg Thr Asp Phe Thr Leu Thr Ile Ser Ser
225                 230                 235                 240

Leu Glu Pro Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln Ser Asn Glu
                245                 250                 255

Asp Pro Pro Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Thr Thr
            260                 265                 270

Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln
        275                 280                 285

Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala
    290                 295                 300

Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala
305                 310                 315                 320

Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr
                325                 330                 335

Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln
            340                 345                 350

Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser
        355                 360                 365

Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys
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370 375 380

Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln
385 390 395 400

Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu
405 410 415

Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg
420 425 430

Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met
435 440 445

Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly
450 455 460

Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp
465 470 475 480

Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 190
<211> 2003
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 190
ggcagcggag agggcagagg aagtcttcta acatgcggtg acgtggagga gaatcccggc 60

cctagagcca ccatggccct gcctgtgaca gccctgctgc tgcctctggc tctgctgctg 120

catgccgcta gacccggatc cgacatcgtg ctgacacaga gccctgcttc cctggccgtg 180

tccctgggac agagagccac aatcagctgc agggccagcg agagcgtgga caactacggc 240

aacaccttca tgcactggta tcagcagaag cccggccagc cccccaagct gctgatctac 300

agagccagca acctggaaag cggcatcccc gccagatttt ccggcagcgg cagcagaacc 360

gacttcaccc tgaccatcaa ccccgtggaa gccgacgacg tggccaccta ctactgccag 420

cagagcaacg aggacccccc cacatttgga gccggcacca agctggaact gaagggcgga 480

ggcggatctg gcggcggagg atcttctggg ggaggctctc agattcagct ggtgcagagc 540

ggcccagagc tgaagaaacc cggcgagaca gtgaagatct cctgcaaggc ctccggctac 600

atcttcacca attacggcat gaactgggtc aagcaggccc ctggcaagag cttcaagtgg 660

atgggctgga tcaacaccta caccggcgag agcacctaca gcgccgactt caagggcaga 720

ttcgccttca gcctggaaac cagcgccagc accgcctacc tgcacatcaa cgacctgaag 780

aacgaggaca ccgccaccta tttctgcgcc agaagcggcg gctacgaccc catggattat 840

tggggccagg gcaccagcgt gaccgtgtcc tctgctagct ccggaaccac gacgccagcg 900

ccgcgaccac caacaccggc gcccaccatc gcgtcgcagc ccctgtccct gcgcccagag 960

gcgtgccggc cagcggcggg gggcgcagtg cacacgaggg ggctggactt cgcctgtgat 1020

atctacatct gggcgccctt ggccgggact tgtggggtcc ttctcctgtc actggttatc 1080

acccttact gcaaacgggg cagaaagaaa ctcctgtata tattcaaaca accatttatg 1140

agaccagtac aaactactca agaggaagat ggctgtagct gccgatttcc agaagaagaa 1200

gaaggaggat gtgaactgag agtgaagttc agcaggagcg cagacgcccc cgcgtacaag 1260

cagggccaga accagctcta taacgagctc aatctaggac gaagagagga gtacgatgtt 1320

ttggacaaga gacgtggccg ggaccctgag atgggggaa agccgagaag gaagaaccct 1380

caggaaggcc tgtacaatga actgcagaaa gataagatgg cggaggccta cagtgagatt 1440

gggatgaaag gcgagcgccg gaggggcaag gggcacgatg gcctttacca gggtctcagt 1500

acagccacca aggacaccta cgacgccctt cacatgcagg ccctgccccc tcgctaagtc 1560

gacagctcgc tttcttgctg tccaatttct attaaaggtt cctttgttcc ctaagtccaa 1620

ctactaaact gggggatatt atgaagggcc ttgagcatct ggattctgcc taataaaaaa 1680

catttatttt cattgctgcg tcgagagctc gctttcttgc tgtccaattt ctattaaagg 1740

ttcctttgtt ccctaagtcc aactactaaa ctgggggata ttatgaaggg ccttgagcat 1800

ctggattctg cctaataaaa aacatttatt ttcattgctg cctcgacgaa ttcaaaaaaa 1860

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1920

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1980

aaaaaaaaaa aaaaaaaaaa aaa 2003

<210> 191
<211> 494
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 191
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

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                                                    _SL
His Ala Ala Arg Pro Gly Ser Asp Ile Val Leu Thr Gln Ser Pro Ala
            20                  25                  30

Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys Arg Ala
        35                  40                  45

Ser Glu Ser Val Asp Asn Tyr Gly Asn Thr Phe Met His Trp Tyr Gln
    50                  55                  60

Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Arg Ala Ser Asn
65                  70                  75                  80

Leu Glu Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Arg Thr
                85                  90                  95

Asp Phe Thr Leu Thr Ile Asn Pro Val Glu Ala Asp Asp Val Ala Thr
            100                 105                 110

Tyr Tyr Cys Gln Gln Ser Asn Glu Asp Pro Pro Thr Phe Gly Ala Gly
        115                 120                 125

Thr Lys Leu Glu Leu Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
    130                 135                 140

Ser Gly Gly Gly Ser Gln Ile Gln Leu Val Gln Ser Gly Pro Glu Leu
145                 150                 155                 160

Lys Lys Pro Gly Glu Thr Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr
                165                 170                 175

Ile Phe Thr Asn Tyr Gly Met Asn Trp Val Lys Gln Ala Pro Gly Lys
            180                 185                 190

Ser Phe Lys Trp Met Gly Trp Ile Asn Thr Tyr Thr Gly Glu Ser Thr
        195                 200                 205

Tyr Ser Ala Asp Phe Lys Gly Arg Phe Ala Phe Ser Leu Glu Thr Ser
    210                 215                 220

Ala Ser Thr Ala Tyr Leu His Ile Asn Asp Leu Lys Asn Glu Asp Thr
225                 230                 235                 240

Ala Thr Tyr Phe Cys Ala Arg Ser Gly Gly Tyr Asp Pro Met Asp Tyr
                245                 250                 255

Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser Ala Ser Ser Gly Thr
            260                 265                 270
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Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser
        275                 280                 285

Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly
    290                 295                 300

Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp
305                 310                 315                 320

Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile
                325                 330                 335

Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys
            340                 345                 350

Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys
        355                 360                 365

Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val
    370                 375                 380

Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn
385                 390                 395                 400

Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val
                405                 410                 415

Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg
            420                 425                 430

Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys
        435                 440                 445

Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg
    450                 455                 460

Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys
465                 470                 475                 480

Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
                485                 490
```

<210> 192
<211> 2019
<212> DNA
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 192
atggccctgc ctgtgacagc cctgctgctg cctctggctc tgctgctgca cgccgctaga 60

cctggatccc aggtgcagct gcagcagcct ggcgctgaac tcgtgcggcc aggcgcttct 120

gtgaagctga gctgtaaagc cagcggctac accttcacca gctactggat gaactgggtc 180

aagcagcggc ccgaccaggg cctggagtgg atcggcagaa tcgaccccta cgacagcgag 240

acacactaca accagaagtt caaggacaag gccatcctga ccgtggacaa gagcagcagc 300

accgcctaca tgcagctgtc cagcctgacc agcgaggaca gcgccgtgta ctactgcgcc 360

aggggcaact gggacgacta ttggggccag ggcaccaccc tgacagtgtc tagcggaggc 420

ggaggatctg gcggcggagg aagttctggc ggaggctccg acgtgcagat cacccagagc 480

cctagctacc tggccgcctc tcctggcgag acaatcacca tcaactgccg ggccagcaag 540

agcatctcca aggacctggc ctggtatcag gaaaagcccg gcaagaccaa caagctgctg 600

atctacagcg gcagcaccct gcagagcggc atccccagca gattttccgg cagcggctcc 660

ggcaccgact tcaccctgac catcagctcc ctggaacccg aggactttgc catgtactat 720

tgccagcagc acaacaagta cccttacacc ttcggcggag gcaccaagct ggaaatcaag 780

gccagctccg gagagagcaa gtacggccct ccctgccccc cttgccctgc ccccgagttc 840

ctgggcggac ccagcgtgtt cctgttcccc cccaagccca aggacaccct gatgatcagc 900

cggacccccg aggtgacctg tgtggtggtg gacgtgtccc aggaggaccc cgaggtccag 960

ttcaactggt acgtggacgg cgtggaggtg cacaacgcca agaccaagcc ccgggaggag 1020

cagttcaata gcacctaccg ggtggtgtcc gtgctgaccg tgctgcacca ggactggctg 1080

aacggcaagg aatacaagtg taaggtgtcc aacaagggcc tgcccagcag catcgagaaa 1140

accatcagca aggccaaggg ccagcctcgg gagccccagg tgtacaccct gccccctagc 1200

caagaggaga tgaccaagaa ccaggtgtcc ctgacctgcc tggtgaaggg cttctacccc 1260

agcgacatcg ccgtggagtg ggagagcaac ggccagcccg agaacaacta caagaccacc 1320

ccccctgtgc tggacagcga cggcagcttc ttcctgtaca gccggctgac cgtggacaag 1380

agccggtggc aggagggcaa cgtctttagc tgctccgtga tgcacgaggc cctgcacaac 1440

cactacaccc agaagagcct gagcctgtcc ctgggcaaga tggatatcta catctgggcg 1500

cccttggccg ggacttgtgg ggtccttctc ctgtcactgg ttatcaccct ttactgcaaa 1560

cggggcagaa agaaactcct gtatatattc aaacaaccat ttatgagacc agtacaaact 1620

actcaagagg aagatggctg tagctgccga tttccagaag aagaagaagg aggatgtgaa 1680

ctgagagtga agttcagcag gagcgcagac gcccccgcgt acaagcaggg ccagaaccag 1740

ctctataacg agctcaatct aggacgaaga gaggagtacg atgttttgga caagagacgt 1800

ggccgggacc ctgagatggg gggaaagccg agaaggaaga accctcagga aggcctgtac 1860

aatgaactgc agaaagataa gatggcggag gcctacagtg agattgggat gaaaggcgag 1920

cgccggaggg gcaaggggca cgatggcctt taccagggtc tcagtacagc caccaaggac 1980

acctacgacg cccttcacat gcaggccctg ccccctcgc 2019

<210> 193
<211> 673
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 193

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gly Ser Gln Val Gln Leu Gln Gln Pro Gly Ala
20 25 30

Glu Leu Val Arg Pro Gly Ala Ser Val Lys Leu Ser Cys Lys Ala Ser
35 40 45

Gly Tyr Thr Phe Thr Ser Tyr Trp Met Asn Trp Val Lys Gln Arg Pro
50 55 60

Asp Gln Gly Leu Glu Trp Ile Gly Arg Ile Asp Pro Tyr Asp Ser Glu
65 70 75 80

Thr His Tyr Asn Gln Lys Phe Lys Asp Lys Ala Ile Leu Thr Val Asp
85 90 95

Lys Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Thr Ser Glu
100 105 110

Asp Ser Ala Val Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp
115 120 125

Gly Gln Gly Thr Thr Leu Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
130 135 140

Gly Gly Gly Ser Ser Gly Gly Gly Ser Asp Val Gln Ile Thr Gln Ser
145 150 155 160

Pro Ser Tyr Leu Ala Ala Ser Pro Gly Glu Thr Ile Thr Ile Asn Cys

_SL

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                165                 170                 175

Arg Ala Ser Lys Ser Ile Ser Lys Asp Leu Ala Trp Tyr Gln Glu Lys
            180                 185                 190

Pro Gly Lys Thr Asn Lys Leu Leu Ile Tyr Ser Gly Ser Thr Leu Gln
        195                 200                 205

Ser Gly Ile Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
    210                 215                 220

Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp Phe Ala Met Tyr Tyr
225                 230                 235                 240

Cys Gln Gln His Asn Lys Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys
                245                 250                 255

Leu Glu Ile Lys Ala Ser Ser Gly Glu Ser Lys Tyr Gly Pro Pro Cys
            260                 265                 270

Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser Val Phe Leu
        275                 280                 285

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
    290                 295                 300

Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu Val Gln
305                 310                 315                 320

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
                325                 330                 335

Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu
            340                 345                 350

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
        355                 360                 365

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
    370                 375                 380

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
385                 390                 395                 400

Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
                405                 410                 415
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                                                _SL
Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
            420                 425                 430

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
        435                 440                 445

Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg Trp Gln
    450                 455                 460

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
465                 470                 475                 480

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys Met Asp Ile
                485                 490                 495

Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser
            500                 505                 510

Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr
        515                 520                 525

Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu
    530                 535                 540

Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu
545                 550                 555                 560

Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln
                565                 570                 575

Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu
            580                 585                 590

Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly
        595                 600                 605

Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln
    610                 615                 620

Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu
625                 630                 635                 640

Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr
                645                 650                 655

Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro
            660                 665                 670
```

Arg

<210> 194
<211> 1461
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 194
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtgc aactcgtcca aagcggagcg gaagtcaaga aacccggagc gagcgtgaaa 120

gtgtcctgca aagcctccgg ctacaccttt acgggctact acatgcactg ggtgcgccag 180

gcaccaggac agggtcttga atggatggga tggatcaacc ctaattcggg cggaactaac 240

tacgcacaga agttccaggg gagagtgact ctgactcggg atacctccat ctcaactgtc 300

tacatggaac tctcccgctt gcggtcagat gatacggcag tgtactactg cgcccgcgac 360

atgaatatcc tggctaccgt gccgttcgac atctggggac aggggactat ggttactgtc 420

tcatcgggcg gtggaggttc aggaggaggc ggctcgggag gcggaggttc ggacattcag 480

atgacccagt ccccatcctc tctgtcggcc agcgtcggag atagggtgac cattacctgt 540

cgggcctcgc aaagcatctc ctcgtacctc aactggtatc agcaaaagcc gggaaaggcg 600

cctaagctgc tgatctacgc cgcttcgagc ttgcaaagcg gggtgccatc cagattctcg 660

ggatcaggct caggaaccga cttcaccctg accgtgaaca gcctccagcc ggaggacttt 720

gccacttact actgccagca gggagactcc gtgccgctta ctttcggggg gggtacccgc 780

ctggagatca agaccactac cccagcaccg aggccaccca ccccggctcc taccatcgcc 840

tcccagcctc tgtccctgcg tccggaggca tgtagacccg cagctggtgg ggccgtgcat 900

acccggggtc ttgacttcgc ctgcgatatc tacatttggg cccctctggc tggtacttgc 960

ggggtcctgc tgctttcact cgtgatcact ctttactgta agcgcggtcg gaagaagctg 1020

ctgtacatct ttaagcaacc cttcatgagg cctgtgcaga ctactcaaga ggaggacggc 1080

tgttcatgcc ggttcccaga ggaggaggaa ggcggctgcg aactgcgcgt gaaattcagc 1140

cgcagcgcag atgctccagc ctacaagcag gggcagaacc agctctacaa cgaactcaat 1200

cttggtcgga gagaggagta cgacgtgctg gacaagcgga gaggacggga cccagaaatg 1260

ggcgggaagc cgcgcagaaa gaatccccaa gagggcctgt acaacgagct ccaaaaggat 1320

aagatggcag aagcctatag cgagattggt atgaaagggg aacgcagaag aggcaaaggc 1380

cacgacggac tgtaccaggg actcagcacc gccaccaagg acacctatga cgctcttcac 1440

atgcaggccc tgccgcctcg g 1461

<210> 195
<211> 487
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 195
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
20 25 30

Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
35 40 45

Thr Phe Thr Gly Tyr Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln
50 55 60

Gly Leu Glu Trp Met Gly Trp Ile Asn Pro Asn Ser Gly Gly Thr Asn
65 70 75 80

Tyr Ala Gln Lys Phe Gln Gly Arg Val Thr Leu Thr Arg Asp Thr Ser
85 90 95

Ile Ser Thr Val Tyr Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Ala Arg Asp Met Asn Ile Leu Ala Thr Val Pro
115 120 125

Phe Asp Ile Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Gly Gly
130 135 140

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln
145 150 155 160

Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
165 170 175

Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp
180 185 190

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                                                    _SL
Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala
        195                 200                 205

Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser
    210                 215                 220

Gly Thr Asp Phe Thr Leu Thr Val Asn Ser Leu Gln Pro Glu Asp Phe
225                 230                 235                 240

Ala Thr Tyr Tyr Cys Gln Gln Gly Asp Ser Val Pro Leu Thr Phe Gly
                245                 250                 255

Gly Gly Thr Arg Leu Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro
            260                 265                 270

Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro
        275                 280                 285

Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu
    290                 295                 300

Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys
305                 310                 315                 320

Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly
                325                 330                 335

Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val
            340                 345                 350

Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu
        355                 360                 365

Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp
    370                 375                 380

Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn
385                 390                 395                 400

Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg
                405                 410                 415

Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly
            420                 425                 430

Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu
        435                 440                 445
```

Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu
450 455 460

Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His
465 470 475 480

Met Gln Ala Leu Pro Pro Arg
485

<210> 196
<211> 264
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 196
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
20 25 30

Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
35 40 45

Thr Phe Thr Gly Tyr Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln
50 55 60

Gly Leu Glu Trp Met Gly Trp Ile Asn Pro Asn Ser Gly Gly Thr Asn
65 70 75 80

Tyr Ala Gln Lys Phe Gln Gly Arg Val Thr Leu Thr Arg Asp Thr Ser
85 90 95

Ile Ser Thr Val Tyr Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Ala Arg Asp Met Asn Ile Leu Ala Thr Val Pro
115 120 125

Phe Asp Ile Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Gly Gly
130 135 140

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln
145 150 155 160

```
Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
                165                 170                 175

Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp
            180                 185                 190

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala
        195                 200                 205

Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser
    210                 215                 220

Gly Thr Asp Phe Thr Leu Thr Val Asn Ser Leu Gln Pro Glu Asp Phe
225                 230                 235                 240

Ala Thr Tyr Tyr Cys Gln Gln Gly Asp Ser Val Pro Leu Thr Phe Gly
                245                 250                 255

Gly Gly Thr Arg Leu Glu Ile Lys
            260
```

<210> 197
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 197

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr
            20                  25                  30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

Gly Trp Ile Asn Pro Asn Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe
    50                  55                  60

Gln Gly Arg Val Thr Leu Thr Arg Asp Thr Ser Ile Ser Thr Val Tyr
65                  70                  75                  80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
```

Ala Arg Asp Met Asn Ile Leu Ala Thr Val Pro Phe Asp Ile Trp Gly
100 105 110

Gln Gly Thr Met Val Thr Val Ser Ser
115 120

<210> 198
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 198
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Val Asn Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Gly Asp Ser Val Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Arg Leu Glu Ile Lys
100 105

<210> 199
<211> 1461
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 199
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtcc aactcgttca atccggcgca gaagtcaaga agccaggagc atcagtgaaa 120

gtgtcctgca aagcctcagg ctacatcttc acgggatact acatccactg ggtgcgccag 180

gctccgggcc agggccttga gtggatgggc tggatcaacc ctaactctgg gggaaccaac 240

tacgctcaga agttccaggg gagggtcact atgactcgcg atacctccat ctccactgcg 300

tacatggaac tctcgggact gagatccgac gatcctgccg tgtactactg cgcccgggac 360

atgaacatct tggcgaccgt gccgtttgac atttggggac agggcaccct cgtcactgtg 420

tcgagcggtg gaggaggctc ggggggtggc ggatcaggag ggggaggaag cgacatccag 480

ctgactcaga gcccatcgtc gttgtccgcg tcggtggggg atagagtgac cattacttgc 540

cgcgccagcc agagcatctc atcatatctg aattggtacc agcagaagcc cggaaaggcc 600

ccaaaactgc tgatctacgc tgcaagcagc ctccaatcgg gagtgccgtc acggttctcc 660

gggtccggtt cgggaactga ctttaccctg accgtgaatt cgctgcaacc ggaggatttc 720

gccacgtact actgtcagca aggagactcc gtgccgctga ccttcggtgg aggcaccaag 780

gtcgaaatca agaccactac cccagcaccg aggccaccca ccccggctcc taccatcgcc 840

tcccagcctc tgtccctgcg tccggaggca tgtagacccg cagctggtgg ggccgtgcat 900

acccggggtc ttgacttcgc ctgcgatatc tacatttggg cccctctggc tggtacttgc 960

ggggtcctgc tgctttcact cgtgatcact ctttactgta agcgcggtcg gaagaagctg 1020

ctgtacatct ttaagcaacc cttcatgagg cctgtgcaga ctactcaaga ggaggacggc 1080

tgttcatgcc ggttcccaga ggaggaggaa ggcggctgcg aactgcgcgt gaaattcagc 1140

cgcagcgcag atgctccagc ctacaagcag gggcagaacc agctctacaa cgaactcaat 1200

cttggtcgga gagaggagta cgacgtgctg gacaagcgga gaggacggga cccagaaatg 1260

ggcgggaagc cgcgcagaaa gaatccccaa gagggcctgt acaacgagct ccaaaaggat 1320

aagatggcag aagcctatag cgagattggt atgaaagggg aacgcagaag aggcaaaggc 1380

cacgacggac tgtaccaggg actcagcacc gccaccaagg acacctatga cgctcttcac 1440

atgcaggccc tgccgcctcg g 1461

<210> 200
<211> 487
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 200
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val

_SL

```
            20                  25                  30

Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
        35                  40                  45

Ile Phe Thr Gly Tyr Tyr Ile His Trp Val Arg Gln Ala Pro Gly Gln
    50                  55                  60

Gly Leu Glu Trp Met Gly Trp Ile Asn Pro Asn Ser Gly Gly Thr Asn
65                  70                  75                  80

Tyr Ala Gln Lys Phe Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser
                85                  90                  95

Ile Ser Thr Ala Tyr Met Glu Leu Ser Gly Leu Arg Ser Asp Asp Pro
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Arg Asp Met Asn Ile Leu Ala Thr Val Pro
        115                 120                 125

Phe Asp Ile Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly
    130                 135                 140

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln
145                 150                 155                 160

Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
                165                 170                 175

Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp
            180                 185                 190

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala
        195                 200                 205

Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser
    210                 215                 220

Gly Thr Asp Phe Thr Leu Thr Val Asn Ser Leu Gln Pro Glu Asp Phe
225                 230                 235                 240

Ala Thr Tyr Tyr Cys Gln Gln Gly Asp Ser Val Pro Leu Thr Phe Gly
                245                 250                 255

Gly Gly Thr Lys Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro
            260                 265                 270
```

_SL
Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro
275 280 285

Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu
290 295 300

Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys
305 310 315 320

Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly
325 330 335

Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val
340 345 350

Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu
355 360 365

Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp
370 375 380

Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn
385 390 395 400

Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg
405 410 415

Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly
420 425 430

Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu
435 440 445

Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu
450 455 460

Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His
465 470 475 480

Met Gln Ala Leu Pro Pro Arg
485

<210> 201
<211> 264
<212> PRT
<213> Artificial Sequence

<220>
<221> source

_SL

<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 201

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
            20                  25                  30

Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
        35                  40                  45

Ile Phe Thr Gly Tyr Tyr Ile His Trp Val Arg Gln Ala Pro Gly Gln
    50                  55                  60

Gly Leu Glu Trp Met Gly Trp Ile Asn Pro Asn Ser Gly Gly Thr Asn
65                  70                  75                  80

Tyr Ala Gln Lys Phe Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser
                85                  90                  95

Ile Ser Thr Ala Tyr Met Glu Leu Ser Gly Leu Arg Ser Asp Asp Pro
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Arg Asp Met Asn Ile Leu Ala Thr Val Pro
        115                 120                 125

Phe Asp Ile Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly
    130                 135                 140

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln
145                 150                 155                 160

Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
                165                 170                 175

Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp
            180                 185                 190

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala
        195                 200                 205

Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser
    210                 215                 220

Gly Thr Asp Phe Thr Leu Thr Val Asn Ser Leu Gln Pro Glu Asp Phe
225                 230                 235                 240
```

Ala Thr Tyr Tyr Cys Gln Gln Gly Asp Ser Val Pro Leu Thr Phe Gly
245 250 255

Gly Gly Thr Lys Val Glu Ile Lys
260

<210> 202
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 202
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Tyr Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Asn Pro Asn Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Gly Leu Arg Ser Asp Asp Pro Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Met Asn Ile Leu Ala Thr Val Pro Phe Asp Ile Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 203
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 203

```
                                          _SL
Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15


Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr
            20                  25                  30


Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45


Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60


Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Val Asn Ser Leu Gln Pro
65                  70                  75                  80


Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Gly Asp Ser Val Pro Leu
                85                  90                  95


Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            100                 105


<210> 204
<211> 1467
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 204
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg       60

ccccaagtcc aactccaaca gtcaggcgca gaagtgaaaa agagcggtgc atcggtgaaa      120

gtgtcatgca aagcctcggg ctacaccttc actgactact atatgcactg gctgcggcag      180

gcaccgggac agggacttga gtggatggga tggatcaacc cgaattcagg ggacactaac      240

tacgcgcaga agttccaggg gagagtgacc ctgacgaggg acacctcaat ttcgaccgtc      300

tacatggaat tgtcgcgcct gagatcggac gatactgctg tgtactactg tgcccgcgac      360

atgaacatcc tcgcgactgt gccttttgat atctggggac aggggactat ggtcaccgtt      420

tcctccgctt ccggtggcgg aggctcggga ggccgggcct ccggtggagg aggcagcgac      480

atccagatga ctcagagccc ttcctcgctg agcgcctcag tgggagatcg cgtgaccatc      540

acttgccggg ccagccagtc catttcgtcc tacctcaatt ggtaccagca gaagccggga      600

aaggcgccca agctcttgat ctacgctgcg agctccctgc aaagcggggt gccgagccga      660

ttctcgggtt ccggctcggg aaccgacttc actctgacca tctcatccct gcaaccagag      720
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gactttgcca cctactactg ccaacaagga gattctgtcc cactgacgtt cggcggagga 780

accaaggtcg aaatcaagac cactacccca gcaccgaggc cacccacccc ggctcctacc 840

atcgcctccc agcctctgtc cctgcgtccg gaggcatgta gacccgcagc tggtggggcc 900

gtgcataccc ggggtcttga cttcgcctgc gatatctaca tttgggcccc tctggctggt 960

acttgcgggg tcctgctgct ttcactcgtg atcactcttt actgtaagcg cggtcggaag 1020

aagctgctgt acatctttaa gcaacccttc atgaggcctg tgcagactac tcaagaggag 1080

gacggctgtt catgccggtt cccagaggag gaggaaggcg gctgcgaact gcgcgtgaaa 1140

ttcagccgca gcgcagatgc tccagcctac aagcaggggc agaaccagct ctacaacgaa 1200

ctcaatcttg gtcggagaga ggagtacgac gtgctggaca agcggagagg acgggaccca 1260

gaaatgggcg ggaagccgcg cagaaagaat ccccaagagg gcctgtacaa cgagctccaa 1320

aaggataaga tggcagaagc ctatagcgag attggtatga aaggggaacg cagaagaggc 1380

aaaggccacg acggactgta ccagggactc agcaccgcca ccaaggacac ctatgacgct 1440

cttcacatgc aggccctgcc gcctcgg 1467

<210> 205
<211> 336
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 205
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Val
20 25 30

Lys Lys Ser Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
35 40 45

Thr Phe Thr Asp Tyr Tyr Met His Trp Leu Arg Gln Ala Pro Gly Gln
50 55 60

Gly Leu Glu Trp Met Gly Trp Ile Asn Pro Asn Ser Gly Asp Thr Asn
65 70 75 80

Tyr Ala Gln Lys Phe Gln Gly Arg Val Thr Leu Thr Arg Asp Thr Ser
85 90 95

Ile Ser Thr Val Tyr Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr

_SL

100 105 110

Ala Val Tyr Tyr Cys Ala Arg Asp Met Asn Ile Leu Ala Thr Val Pro
115 120 125

Phe Asp Ile Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Ala Ser
130 135 140

Gly Gly Gly Gly Ser Gly Gly Arg Ala Ser Gly Gly Gly Gly Ser Asp
145 150 155 160

Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp
165 170 175

Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu
180 185 190

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
195 200 205

Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
210 215 220

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
225 230 235 240

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Gly Asp Ser Val Pro Leu Thr
245 250 255

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Thr Thr Thr Pro Ala Pro
260 265 270

Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu
275 280 285

Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg
290 295 300

Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly
305 310 315 320

Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys
325 330 335

<210> 206
<211> 266
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 206

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15

His Ala Ala Arg Pro Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Val
            20                  25                  30

Lys Lys Ser Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
        35                  40                  45

Thr Phe Thr Asp Tyr Tyr Met His Trp Leu Arg Gln Ala Pro Gly Gln
    50                  55                  60

Gly Leu Glu Trp Met Gly Trp Ile Asn Pro Asn Ser Gly Asp Thr Asn
65                  70                  75                  80

Tyr Ala Gln Lys Phe Gln Gly Arg Val Thr Leu Thr Arg Asp Thr Ser
                85                  90                  95

Ile Ser Thr Val Tyr Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Arg Asp Met Asn Ile Leu Ala Thr Val Pro
        115                 120                 125

Phe Asp Ile Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Ala Ser
    130                 135                 140

Gly Gly Gly Gly Ser Gly Gly Arg Ala Ser Gly Gly Gly Gly Ser Asp
145                 150                 155                 160

Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp
                165                 170                 175

Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu
            180                 185                 190

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
        195                 200                 205

Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
    210                 215                 220
```

_SL
Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
225 230 235 240

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Gly Asp Ser Val Pro Leu Thr
245 250 255

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
260 265

<210> 207
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 207
Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Val Lys Lys Ser Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Tyr Met His Trp Leu Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Asn Pro Asn Ser Gly Asp Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Leu Thr Arg Asp Thr Ser Ile Ser Thr Val Tyr
65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Met Asn Ile Leu Ala Thr Val Pro Phe Asp Ile Trp Gly
100 105 110

Gln Gly Thr Met Val Thr Val Ser Ser
115 120

<210> 208
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

polypeptide"

<400> 208
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Gly Asp Ser Val Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 209
<211> 1461
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 209
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtcc aactcgtcca gtcaggagcg gaagtcaaga agcccggagc gtcagtcaaa 120

gtgtcatgca aagcctcggg ctacactttc actgggtact acatgcactg ggtgcgccag 180

gctccaggac agggactgga atggatggga tggatcaacc cgaactccgg tggcaccaat 240

tacgcccaga agttccaggg gagggtgacc atgactcgcg acacgtcgat cagcaccgca 300

tacatggagc tgtcaagact ccggtccgac gatactgccg tgtactactg cgcacgggac 360

atgaacattc tggccaccgt gccttttgac atctggggtc agggaactat ggttaccgtg 420

tcctctggtg gaggcggctc cggcgggggg ggaagcggag gcggtggaag cgacattcag 480

atgacccagt cgccttcatc cctttcggcg agcgtgggag atcgcgtcac tatcacttgt 540

cgggcctcgc agtccatctc cacctacctc aattggtacc agcagaagcc aggaaaagca 600

ccgaatctgc tgatctacgc cgcgttttcc ttgcaatcgg gagtgccaag cagattcagc 660

ggatcgggat caggcactga tttcaccctc accatcaact cgctgcaacc ggaggatttc 720

gctacgtact attgccaaca aggagacagc gtgccgctca ccttcggcgg agggactaag 780

ctggaaatca agaccactac cccagcaccg aggccaccca ccccggctcc taccatcgcc 840

tcccagcctc tgtccctgcg tccggaggca tgtagacccg cagctggtgg ggccgtgcat 900

acccggggtc ttgacttcgc ctgcgatatc tacatttggg cccctctggc tggtacttgc 960

ggggtcctgc tgctttcact cgtgatcact ctttactgta agcgcggtcg gaagaagctg 1020

ctgtacatct ttaagcaacc cttcatgagg cctgtgcaga ctactcaaga ggaggacggc 1080

tgttcatgcc ggttcccaga ggaggaggaa ggcggctgcg aactgcgcgt gaaattcagc 1140

cgcagcgcag atgctccagc ctacaagcag gggcagaacc agctctacaa cgaactcaat 1200

cttggtcgga gagaggagta cgacgtgctg gacaagcgga gaggacggga cccagaaatg 1260

ggcgggaagc cgcgcagaaa gaatccccaa gagggcctgt acaacgagct ccaaaaggat 1320

aagatggcag aagcctatag cgagattggt atgaaagggg aacgcagaag aggcaaaggc 1380

cacgacggac tgtaccaggg actcagcacc gccaccaagg acacctatga cgctcttcac 1440

atgcaggccc tgccgcctcg g 1461

<210> 210
<211> 487
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 210
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
20 25 30

Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
35 40 45

Thr Phe Thr Gly Tyr Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln
50 55 60

Gly Leu Glu Trp Met Gly Trp Ile Asn Pro Asn Ser Gly Gly Thr Asn
65 70 75 80

Tyr Ala Gln Lys Phe Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser
85 90 95

```
Ile Ser Thr Ala Tyr Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Arg Asp Met Asn Ile Leu Ala Thr Val Pro
        115                 120                 125

Phe Asp Ile Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Gly Gly
    130                 135                 140

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln
145                 150                 155                 160

Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
                165                 170                 175

Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Thr Tyr Leu Asn Trp
            180                 185                 190

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Asn Leu Leu Ile Tyr Ala Ala
        195                 200                 205

Phe Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser
    210                 215                 220

Gly Thr Asp Phe Thr Leu Thr Ile Asn Ser Leu Gln Pro Glu Asp Phe
225                 230                 235                 240

Ala Thr Tyr Tyr Cys Gln Gln Gly Asp Ser Val Pro Leu Thr Phe Gly
                245                 250                 255

Gly Gly Thr Lys Leu Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro
            260                 265                 270

Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro
        275                 280                 285

Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu
    290                 295                 300

Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys
305                 310                 315                 320

Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly
                325                 330                 335

Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val
```

_SL
340 345 350

Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu
355 360 365

Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp
370 375 380

Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn
385 390 395 400

Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg
405 410 415

Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly
420 425 430

Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu
435 440 445

Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu
450 455 460

Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His
465 470 475 480

Met Gln Ala Leu Pro Pro Arg
485

<210> 211
<211> 264
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 211
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
20 25 30

Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
35 40 45

Thr Phe Thr Gly Tyr Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln

_SL

50 55 60

Gly Leu Glu Trp Met Gly Trp Ile Asn Pro Asn Ser Gly Gly Thr Asn
65 70 75 80

Tyr Ala Gln Lys Phe Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser
85 90 95

Ile Ser Thr Ala Tyr Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Ala Arg Asp Met Asn Ile Leu Ala Thr Val Pro
115 120 125

Phe Asp Ile Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Gly Gly
130 135 140

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln
145 150 155 160

Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
165 170 175

Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Thr Tyr Leu Asn Trp
180 185 190

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Asn Leu Leu Ile Tyr Ala Ala
195 200 205

Phe Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser
210 215 220

Gly Thr Asp Phe Thr Leu Thr Ile Asn Ser Leu Gln Pro Glu Asp Phe
225 230 235 240

Ala Thr Tyr Tyr Cys Gln Gln Gly Asp Ser Val Pro Leu Thr Phe Gly
245 250 255

Gly Gly Thr Lys Leu Glu Ile Lys
260

<210> 212
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

polypeptide"

<400> 212
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Asn Pro Asn Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Met Asn Ile Leu Ala Thr Val Pro Phe Asp Ile Trp Gly
100 105 110

Gln Gly Thr Met Val Thr Val Ser Ser
115 120

<210> 213
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 213
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Thr Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Asn Leu Leu Ile
35 40 45

Tyr Ala Ala Phe Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asn Ser Leu Gln Pro

_SL
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Gly Asp Ser Val Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 214
<211> 1458
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 214
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtgc agctggtcca gtcgggagcc gaagtcaaga agcccggcgc tagcgtgaaa 120

gtgtcctgca aagcctccgg gtacacattc acctcctact ggatgaattg ggtcagacag 180

gcgcccggcc agggactcga gtggatggga aggattgatc cttacgactc cgaaacccat 240

tacaaccaga agttcaagga ccgcgtgacc atgactgtgg ataagtccac ttccaccgct 300

tacatggagc tgtccagcct gcgctccgag gataccgcag tgtactactg cgcccgggga 360

aactgggacg actattgggg acagggaact accgtgaccg tgtcaagcgg gggtggcggt 420

agcggaggag ggggctccgg cggcggcggc tcaggggcg gaggaagcga cgtgcagctc 480

acccagtcgc cctcatttct gtcggcctca gtgggagaca gagtgaccat tacttgtcgg 540

gcctccaaga gcatctccaa ggacctggcc tggtatcagc agaagccagg aaaggcgcct 600

aagttgctca tctactcggg gtcgaccctg caatctggcg tgccgtcccg gttctccggt 660

tcgggaagcg gtaccgaatt cacccttact atctcctccc tgcaaccgga ggacttcgcc 720

acctactact gccaacagca caacaagtac ccgtacactt tcgggggtgg cacgaaggtc 780

gaaatcaaga ccactacccc agcaccgagg ccacccaccc cggctcctac catcgcctcc 840

cagcctctgt ccctgcgtcc ggaggcatgt agacccgcag ctggtggggc cgtgcatacc 900

cggggtcttg acttcgcctg cgatatctac atttgggccc ctctggctgg tacttgcggg 960

gtcctgctgc tttcactcgt gatcactctt tactgtaagc gcggtcggaa gaagctgctg 1020

tacatcttta agcaaccctt catgaggcct gtgcagacta ctcaagagga ggacggctgt 1080

tcatgccggt tcccagagga ggaggaaggc ggctgcgaac tgcgcgtgaa attcagccgc 1140

agcgcagatg ctccagccta caagcagggg cagaaccagc tctacaacga actcaatctt 1200

ggtcggagag aggagtacga cgtgctggac aagcggagag gacgggaccc agaaatgggc 1260

gggaagccgc gcagaaagaa tccccaagag ggcctgtaca acgagctcca aaaggataag 1320

atggcagaag cctatagcga gattggtatg aaaggggaac gcagaagagg caaaggccac 1380

gacggactgt accagggact cagcaccgcc accaaggaca cctatgacgc tcttcacatg 1440

caggccctgc cgcctcgg 1458

<210> 215
<211> 486
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 215
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
20 25 30

Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
35 40 45

Thr Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Ala Pro Gly Gln
50 55 60

Gly Leu Glu Trp Met Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His
65 70 75 80

Tyr Asn Gln Lys Phe Lys Asp Arg Val Thr Met Thr Val Asp Lys Ser
85 90 95

Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln
115 120 125

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
130 135 140

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Gln Leu
145 150 155 160

Thr Gln Ser Pro Ser Phe Leu Ser Ala Ser Val Gly Asp Arg Val Thr
165 170 175

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Ile Thr Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp Leu Ala Trp Tyr
            180                 185                 190

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Gly Ser
        195                 200                 205

Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
    210                 215                 220

Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
225                 230                 235                 240

Thr Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr Thr Phe Gly Gly
                245                 250                 255

Gly Thr Lys Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro
            260                 265                 270

Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu
        275                 280                 285

Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
    290                 295                 300

Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly
305                 310                 315                 320

Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg
                325                 330                 335

Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln
            340                 345                 350

Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu
        355                 360                 365

Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
    370                 375                 380

Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
385                 390                 395                 400

Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
                405                 410                 415

Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
```

_SL
420 425 430

Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
435 440 445

Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
450 455 460

Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
465 470 475 480

Gln Ala Leu Pro Pro Arg
485

<210> 216
<211> 263
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 216
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
20 25 30

Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
35 40 45

Thr Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Ala Pro Gly Gln
50 55 60

Gly Leu Glu Trp Met Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His
65 70 75 80

Tyr Asn Gln Lys Phe Lys Asp Arg Val Thr Met Thr Val Asp Lys Ser
85 90 95

Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln
115 120 125

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly

_SL
130 135 140

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Gln Leu
145 150 155 160

Thr Gln Ser Pro Ser Phe Leu Ser Ala Ser Val Gly Asp Arg Val Thr
165 170 175

Ile Thr Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp Leu Ala Trp Tyr
180 185 190

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Gly Ser
195 200 205

Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
210 215 220

Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
225 230 235 240

Thr Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr Thr Phe Gly Gly
245 250 255

Gly Thr Lys Val Glu Ile Lys
260

<210> 217
<211> 115
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 217
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Trp Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Val Thr Met Thr Val Asp Lys Ser Thr Ser Thr Ala Tyr

_SL
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser
115

<210> 218
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 218
Asp Val Gln Leu Thr Gln Ser Pro Ser Phe Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 219
<211> 1458
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 219
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtgc agctggtcca gtcgggagcc gaagtcaaga agcccggcgc tagcgtgaaa 120

gtgtcctgca aagcctccgg gtacacattc acctcctact ggatgaattg ggtcagacag 180

gcgcccggcc agggactcga gtggatggga aggattgatc cttacgactc cgaaacccat 240

tacaaccaga agttcaagga ccgcgtgacc atgactgtgg ataagtccac ttccaccgct 300

tacatggagc tgtccagcct gcgctccgag gataccgcag tgtactactg cgcccgggga 360

aactgggacg actattgggg acagggaact accgtgaccg tgtcaagcgg gggtggcggt 420

agcggaggag ggggctccgg cggcggcggc tcaggggcg gaggaagcga agtggtgctg 480

acccagtcgc ccgcaaccct ctctctgtcg ccgggagaac gcgccactct ttcctgtcgg 540

gcgtccaaga gcatctcaaa ggacctcgcc tggtaccagc agaagcctgg tcaagccccg 600

cggctgctga tctactccgg ctccacgctg caatcaggaa tcccagccag attttccggt 660

tcggggtcgg ggactgactt caccttgacc attagctcgc tggaacctga ggacttcgcc 720

gtgtattact gccagcagca caacaagtac ccgtacacct tcggaggcgg tactaaggtc 780

gagatcaaga ccactacccc agcaccgagg ccacccaccc cggctcctac catcgcctcc 840

cagcctctgt ccctgcgtcc ggaggcatgt agacccgcag ctggtggggc cgtgcatacc 900

cggggtcttg acttcgcctg cgatatctac atttgggccc ctctggctgg tacttgcggg 960

gtcctgctgc tttcactcgt gatcactctt tactgtaagc gcggtcggaa gaagctgctg 1020

tacatcttta agcaaccctt catgaggcct gtgcagacta ctcaagagga ggacggctgt 1080

tcatgccggt tcccagagga ggaggaaggc ggctgcgaac tgcgcgtgaa attcagccgc 1140

agcgcagatg ctccagccta caagcagggg cagaaccagc tctacaacga actcaatctt 1200

ggtcggagag aggagtacga cgtgctggac aagcggagag gacgggaccc agaaatgggc 1260

gggaagccgc gcagaaagaa tccccaagag ggcctgtaca acgagctcca aaaggataag 1320

atggcagaag cctatagcga gattggtatg aaaggggaac gcagaagagg caaaggccac 1380

gacggactgt accagggact cagcaccgcc accaaggaca cctatgacgc tcttcacatg 1440

caggccctgc cgcctcgg 1458

<210> 220
<211> 486
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 220

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
20 25 30

Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
35 40 45

Thr Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Ala Pro Gly Gln
50 55 60

Gly Leu Glu Trp Met Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His
65 70 75 80

Tyr Asn Gln Lys Phe Lys Asp Arg Val Thr Met Thr Val Asp Lys Ser
85 90 95

Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln
115 120 125

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
130 135 140

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Val Leu
145 150 155 160

Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr
165 170 175

Leu Ser Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp Leu Ala Trp Tyr
180 185 190

Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Ser Gly Ser
195 200 205

Thr Leu Gln Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly
210 215 220

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp Phe Ala
225 230 235 240

Val Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr Thr Phe Gly Gly
245 250 255

```
Gly Thr Lys Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro
            260                 265                 270

Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu
        275                 280                 285

Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
    290                 295                 300

Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly
305                 310                 315                 320

Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg
                325                 330                 335

Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln
            340                 345                 350

Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu
        355                 360                 365

Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
    370                 375                 380

Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
385                 390                 395                 400

Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
                405                 410                 415

Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
            420                 425                 430

Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
        435                 440                 445

Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
    450                 455                 460

Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
465                 470                 475                 480

Gln Ala Leu Pro Pro Arg
                485
```

<210> 221

<211> 263
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 221

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
            20                  25                  30

Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
        35                  40                  45

Thr Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Ala Pro Gly Gln
    50                  55                  60

Gly Leu Glu Trp Met Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His
65                  70                  75                  80

Tyr Asn Gln Lys Phe Lys Asp Arg Val Thr Met Thr Val Asp Lys Ser
                85                  90                  95

Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln
        115                 120                 125

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
    130                 135                 140

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Val Leu
145                 150                 155                 160

Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr
                165                 170                 175

Leu Ser Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp Leu Ala Trp Tyr
            180                 185                 190

Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Ser Gly Ser
        195                 200                 205

Thr Leu Gln Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly
```

_SL
210 215 220

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp Phe Ala
225 230 235 240

Val Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr Thr Phe Gly Gly
245 250 255

Gly Thr Lys Val Glu Ile Lys
260

<210> 222
<211> 115
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 222
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Trp Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Val Thr Met Thr Val Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser
115

<210> 223
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 223
Glu Val Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45

Tyr Ser Gly Ser Thr Leu Gln Ser Gly Ile Pro Ala Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
65 70 75 80

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 224
<211> 1458
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 224
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtgc agctggtcca gtcgggagcc gaagtcaaga agcccggcgc tagcgtgaaa 120

gtgtcctgca aagcctccgg gtacacattc acctcctact ggatgaattg ggtcagacag 180

gcgcccggcc agggactcga gtggatggga aggattgatc cttacgactc cgaaacccat 240

tacaaccaga agttcaagga ccgcgtgacc atgactgtgg ataagtccac ttccaccgct 300

tacatggagc tgtccagcct gcgctccgag gataccgcag tgtactactg cgcccgggga 360

aactgggacg actattgggg acagggaact accgtgaccg tgtcaagcgg gggtggcggt 420

agcggaggag ggggctccgg cggcggcggc tcaggggggcg gaggaagcga cgtcgtgatg 480

acccagtcac cggcattcct gtccgtgact cccggagaaa aggtcacgat tacttgccgg 540

gcgtccaaga gcatctccaa ggacctcgcc tggtaccaac agaagccgga ccaggcccct 600

aagctgttga tctactcggg gtccaccctt caatcgggag tgccatcgcg gtttagcggt 660

tcgggttctg ggaccgactt cactttcacc atctcctcac tggaagccga ggatgccgcc 720

acttactact gtcagcagca caacaagtat ccgtacacct tcggaggcgg taccaaagtg 780

gagatcaaga ccactacccc agcaccgagg ccacccaccc cggctcctac catcgcctcc 840

cagcctctgt ccctgcgtcc ggaggcatgt agacccgcag ctggtggggc cgtgcatacc 900

cggggtcttg acttcgcctg cgatatctac atttgggccc ctctggctgg tacttgcggg 960

gtcctgctgc tttcactcgt gatcactctt tactgtaagc gcggtcggaa gaagctgctg 1020

tacatcttta agcaaccctt catgaggcct gtgcagacta ctcaagagga ggacggctgt 1080

tcatgccggt tcccagagga ggaggaaggc ggctgcgaac tgcgcgtgaa attcagccgc 1140

agcgcagatg ctccagccta caagcagggg cagaaccagc tctacaacga actcaatctt 1200

ggtcggagag aggagtacga cgtgctggac aagcggagag gacgggaccc agaaatgggc 1260

gggaagccgc gcagaaagaa tccccaagag ggcctgtaca acgagctcca aaaggataag 1320

atggcagaag cctatagcga gattggtatg aaaggggaac gcagaagagg caaaggccac 1380

gacggactgt accagggact cagcaccgcc accaaggaca cctatgacgc tcttcacatg 1440

caggccctgc cgcctcgg 1458

<210> 225
<211> 486
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 225
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
20 25 30

Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
35 40 45

Thr Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Ala Pro Gly Gln
50 55 60

Gly Leu Glu Trp Met Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His
65 70 75 80

```
Tyr Asn Gln Lys Phe Lys Asp Arg Val Thr Met Thr Val Asp Lys Ser
                85                  90                  95

Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln
        115                 120                 125

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
    130                 135                 140

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met
145                 150                 155                 160

Thr Gln Ser Pro Ala Phe Leu Ser Val Thr Pro Gly Glu Lys Val Thr
                165                 170                 175

Ile Thr Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp Leu Ala Trp Tyr
            180                 185                 190

Gln Gln Lys Pro Asp Gln Ala Pro Lys Leu Leu Ile Tyr Ser Gly Ser
        195                 200                 205

Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
    210                 215                 220

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Glu Ala Glu Asp Ala Ala
225                 230                 235                 240

Thr Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr Thr Phe Gly Gly
                245                 250                 255

Gly Thr Lys Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro
            260                 265                 270

Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu
        275                 280                 285

Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
    290                 295                 300

Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly
305                 310                 315                 320

Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg
                325                 330                 335
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Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln
            340                 345                 350

Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu
        355                 360                 365

Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
    370                 375                 380

Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
385                 390                 395                 400

Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
                405                 410                 415

Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
            420                 425                 430

Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
        435                 440                 445

Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
    450                 455                 460

Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
465                 470                 475                 480

Gln Ala Leu Pro Pro Arg
                485


<210> 226
<211> 263
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 226
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
            20                  25                  30

Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
        35                  40                  45
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Thr Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Ala Pro Gly Gln
    50                  55                  60

Gly Leu Glu Trp Met Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His
65                  70                  75                  80

Tyr Asn Gln Lys Phe Lys Asp Arg Val Thr Met Thr Val Asp Lys Ser
                85                  90                  95

Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln
        115                 120                 125

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
    130                 135                 140

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met
145                 150                 155                 160

Thr Gln Ser Pro Ala Phe Leu Ser Val Thr Pro Gly Glu Lys Val Thr
                165                 170                 175

Ile Thr Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp Leu Ala Trp Tyr
            180                 185                 190

Gln Gln Lys Pro Asp Gln Ala Pro Lys Leu Leu Ile Tyr Ser Gly Ser
        195                 200                 205

Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
    210                 215                 220

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Glu Ala Glu Asp Ala Ala
225                 230                 235                 240

Thr Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr Thr Phe Gly Gly
                245                 250                 255

Gly Thr Lys Val Glu Ile Lys
            260
```

<210> 227
<211> 115
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 227
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Trp Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Val Thr Met Thr Val Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser
115

<210> 228
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 228
Asp Val Val Met Thr Gln Ser Pro Ala Phe Leu Ser Val Thr Pro Gly
1 5 10 15

Glu Lys Val Thr Ile Thr Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Asp Gln Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Glu Ala
65 70 75 80

Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 229
<211> 1458
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 229
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtgc agctggtcca gtcgggagcc gaagtcaaga agcccggcgc tagcgtgaaa 120

gtgtcctgca aagcctccgg gtacacattc acctcctact ggatgaattg ggtcagacag 180

gcgcccggcc agggactcga gtggatggga aggattgatc cttacgactc cgaaacccat 240

tacaaccaga agttcaagga ccgcgtgacc atgactgtgg ataagtccac ttccaccgct 300

tacatggagc tgtccagcct gcgctccgag gataccgcag tgtactactg cgcccgggga 360

aactgggacg actattgggg acagggaact accgtgaccg tgtcaagcgg gggtggcggt 420

agcggaggag ggggctccgg cggcggcggc tcaggggcg gaggaagcga cgtggtcatg 480

actcagtccc cggactcact cgcggtgtcg cttggagaga gagcgaccat caactgtcgg 540

gcctcaaaga gcatcagcaa ggacctggcc tggtaccagc agaagccggg acagccgcca 600

aagctgctga tctactccgg gtccaccttg caatctggtg tccctgaccg gttctccggt 660

tccgggtcgg gtaccgactt cacgctcact atttcgtcgc tgcaagccga agatgtggcc 720

gtgtactatt gccaacagca caacaagtac ccctacactt ttggcggagg caccaaggtg 780

gaaatcaaga ccactacccc agcaccgagg ccacccaccc cggctcctac catcgcctcc 840

cagcctctgt ccctgcgtcc ggaggcatgt agacccgcag ctggtggggc cgtgcatacc 900

cggggtcttg acttcgcctg cgatatctac atttgggccc ctctggctgg tacttgcggg 960

gtcctgctgc tttcactcgt gatcactctt tactgtaagc gcggtcggaa gaagctgctg 1020

tacatcttta agcaaccctt catgaggcct gtgcagacta ctcaagagga ggacggctgt 1080

tcatgccggt tcccagagga ggaggaaggc ggctgcgaac tgcgcgtgaa attcagccgc 1140

_SL

agcgcagatg ctccagccta caagcagggg cagaaccagc tctacaacga actcaatctt 1200

ggtcggagag aggagtacga cgtgctggac aagcggagag gacgggaccc agaaatgggc 1260

gggaagccgc gcagaaagaa tccccaagag ggcctgtaca acgagctcca aaaggataag 1320

atggcagaag cctatagcga gattggtatg aaaggggaac gcagaagagg caaaggccac 1380

gacggactgt accagggact cagcaccgcc accaaggaca cctatgacgc tcttcacatg 1440

caggccctgc cgcctcgg 1458

<210> 230
<211> 486
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 230

Met	Ala	Leu	Pro	Val	Thr	Ala	Leu	Leu	Leu	Pro	Leu	Ala	Leu	Leu	Leu
1				5				10					15		
His	Ala	Ala	Arg	Pro	Gln	Val	Gln	Leu	Val	Gln	Ser	Gly	Ala	Glu	Val
			20					25					30		
Lys	Lys	Pro	Gly	Ala	Ser	Val	Lys	Val	Ser	Cys	Lys	Ala	Ser	Gly	Tyr
		35					40					45			
Thr	Phe	Thr	Ser	Tyr	Trp	Met	Asn	Trp	Val	Arg	Gln	Ala	Pro	Gly	Gln
	50					55					60				
Gly	Leu	Glu	Trp	Met	Gly	Arg	Ile	Asp	Pro	Tyr	Asp	Ser	Glu	Thr	His
65					70					75					80
Tyr	Asn	Gln	Lys	Phe	Lys	Asp	Arg	Val	Thr	Met	Thr	Val	Asp	Lys	Ser
				85					90					95	
Thr	Ser	Thr	Ala	Tyr	Met	Glu	Leu	Ser	Ser	Leu	Arg	Ser	Glu	Asp	Thr
			100					105					110		
Ala	Val	Tyr	Tyr	Cys	Ala	Arg	Gly	Asn	Trp	Asp	Asp	Tyr	Trp	Gly	Gln
		115					120					125			
Gly	Thr	Thr	Val	Thr	Val	Ser	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly
	130					135					140				
Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Asp	Val	Val	Met
145					150					155					160

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Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly Glu Arg Ala Thr
                165                 170                 175

Ile Asn Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp Leu Ala Trp Tyr
            180                 185                 190

Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Ser Gly Ser
        195                 200                 205

Thr Leu Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly
    210                 215                 220

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala Glu Asp Val Ala
225                 230                 235                 240

Val Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr Thr Phe Gly Gly
                245                 250                 255

Gly Thr Lys Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro
            260                 265                 270

Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu
        275                 280                 285

Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
    290                 295                 300

Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly
305                 310                 315                 320

Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg
                325                 330                 335

Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln
            340                 345                 350

Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu
        355                 360                 365

Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
    370                 375                 380

Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
385                 390                 395                 400

Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
                405                 410                 415
```

```
Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
            420                 425                 430

Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
        435                 440                 445

Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
    450                 455                 460

Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
465                 470                 475                 480

Gln Ala Leu Pro Pro Arg
                485
```

<210> 231
<211> 263
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 231

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
            20                  25                  30

Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
        35                  40                  45

Thr Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Ala Pro Gly Gln
    50                  55                  60

Gly Leu Glu Trp Met Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His
65                  70                  75                  80

Tyr Asn Gln Lys Phe Lys Asp Arg Val Thr Met Thr Val Asp Lys Ser
                85                  90                  95

Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln
        115                 120                 125
```

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
130 135 140

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met
145 150 155 160

Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly Glu Arg Ala Thr
165 170 175

Ile Asn Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp Leu Ala Trp Tyr
180 185 190

Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Ser Gly Ser
195 200 205

Thr Leu Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly
210 215 220

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala Glu Asp Val Ala
225 230 235 240

Val Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr Thr Phe Gly Gly
245 250 255

Gly Thr Lys Val Glu Ile Lys
260

<210> 232
<211> 115
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 232
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Trp Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Val Thr Met Thr Val Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser
115

<210> 233
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 233
Asp Val Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Glu Arg Ala Thr Ile Asn Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile
35 40 45

Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro Asp Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala
65 70 75 80

Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 234
<211> 1458
<212> DNA
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 234
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgacgtgc agctcaccca gtcgccctca tttctgtcgg cctcagtggg agacagagtg 120

accattactt gtcgggcctc caagagcatc tccaaggacc tggcctggta tcagcagaag 180

ccaggaaagg cgcctaagtt gctcatctac tcggggtcga ccctgcaatc tggcgtgccg 240

tcccggttct ccggttcggg aagcggtacc gaattcaccc ttactatctc ctccctgcaa 300

ccggaggact tcgccaccta ctactgccaa cagcacaaca agtacccgta cactttcggg 360

ggtggcacga aggtcgaaat caaggggggt ggcggtagcg gaggaggggg ctccggcggc 420

ggcggctcag ggggcggagg aagccaagtg cagctggtcc agtcgggagc cgaagtcaag 480

aagcccggcg ctagcgtgaa agtgtcctgc aaagcctccg ggtacacatt cacctcctac 540

tggatgaatt gggtcagaca ggcgcccggc cagggactcg agtggatggg aaggattgat 600

ccttacgact ccgaaaccca ttacaaccag aagttcaagg accgcgtgac catgactgtg 660

gataagtcca cttccaccgc ttacatggag ctgtccagcc tgcgctccga ggataccgca 720

gtgtactact gcgcccgggg aaactgggac gactattggg gacagggaac taccgtgacc 780

gtgtcaagca ccactacccc agcaccgagg ccacccaccc cggctcctac catcgcctcc 840

cagcctctgt ccctgcgtcc ggaggcatgt agacccgcag ctggtggggc cgtgcatacc 900

cggggtcttg acttcgcctg cgatatctac atttgggccc ctctggctgg tacttgcggg 960

gtcctgctgc tttcactcgt gatcactctt tactgtaagc gcggtcggaa gaagctgctg 1020

tacatcttta agcaaccctt catgaggcct gtgcagacta ctcaagagga ggacggctgt 1080

tcatgccggt tcccagagga ggaggaaggc ggctgcgaac tgcgcgtgaa attcagccgc 1140

agcgcagatg ctccagccta caagcagggg cagaaccagc tctacaacga actcaatctt 1200

ggtcggagag aggagtacga cgtgctggac aagcggagag gacgggaccc agaaatgggc 1260

gggaagccgc gcagaaagaa tccccaagag ggcctgtaca acgagctcca aaaggataag 1320

atggcagaag cctatagcga gattggtatg aaaggggaac gcagaagagg caaaggccac 1380

gacggactgt accagggact cagcaccgcc accaaggaca cctatgacgc tcttcacatg 1440

caggccctgc cgcctcgg 1458

<210> 235
<211> 486
<212> PRT
<213> Artificial Sequence

<220>
<221> source

_SL
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 235

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15

His Ala Ala Arg Pro Asp Val Gln Leu Thr Gln Ser Pro Ser Phe Leu
            20                  25                  30

Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Lys
        35                  40                  45

Ser Ile Ser Lys Asp Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala
    50                  55                  60

Pro Lys Leu Leu Ile Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro
65                  70                  75                  80

Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile
                85                  90                  95

Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln His
            100                 105                 110

Asn Lys Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys
145                 150                 155                 160

Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr
                165                 170                 175

Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly
            180                 185                 190

Leu Glu Trp Met Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr
        195                 200                 205

Asn Gln Lys Phe Lys Asp Arg Val Thr Met Thr Val Asp Lys Ser Thr
    210                 215                 220

Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala
225                 230                 235                 240
```

```
Val Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly
                245                 250                 255

Thr Thr Val Thr Val Ser Ser Thr Thr Thr Pro Ala Pro Arg Pro Pro
            260                 265                 270

Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu
        275                 280                 285

Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
    290                 295                 300

Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly
305                 310                 315                 320

Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg
                325                 330                 335

Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln
            340                 345                 350

Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu
        355                 360                 365

Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
    370                 375                 380

Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
385                 390                 395                 400

Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
                405                 410                 415

Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
            420                 425                 430

Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
        435                 440                 445

Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
    450                 455                 460

Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
465                 470                 475                 480

Gln Ala Leu Pro Pro Arg
                485
```

<210> 236
<211> 263
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 236
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Asp Val Gln Leu Thr Gln Ser Pro Ser Phe Leu
20 25 30

Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Lys
35 40 45

Ser Ile Ser Lys Asp Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala
50 55 60

Pro Lys Leu Leu Ile Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro
65 70 75 80

Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile
85 90 95

Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln His
100 105 110

Asn Lys Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
130 135 140

Gly Gly Gly Ser Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys
145 150 155 160

Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr
165 170 175

Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly
180 185 190

Leu Glu Trp Met Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr
195 200 205

```
Asn Gln Lys Phe Lys Asp Arg Val Thr Met Thr Val Asp Lys Ser Thr
    210                 215                 220

Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala
225                 230                 235                 240

Val Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly
                245                 250                 255

Thr Thr Val Thr Val Ser Ser
            260
```

<210> 237
<211> 115
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 237

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30

Trp Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe
    50                  55                  60

Lys Asp Arg Val Thr Met Thr Val Asp Lys Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
            100                 105                 110

Val Ser Ser
        115
```

<210> 238
<211> 107

<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 238
Asp Val Gln Leu Thr Gln Ser Pro Ser Phe Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 239
<211> 1458
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 239
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaagtgg tgctgaccca gtcgcccgca accctctctc tgtcgccggg agaacgcgcc 120

actctttcct gtcgggcgtc caagagcatc tcaaaggacc tcgcctggta ccagcagaag 180

cctggtcaag ccccgcggct gctgatctac tccggctcca cgctgcaatc aggaatccca 240

gccagatttt ccggttcggg gtcggggact gacttcacct tgaccattag ctcgctggaa 300

cctgaggact tcgccgtgta ttactgccag cagcacaaca agtacccgta caccttcgga 360

ggcggtacta aggtcgagat caaggggggt ggcggtagcg gaggaggggg ctccggcggc 420

ggcggctcag ggggcggagg aagccaagtg cagctggtcc agtcgggagc cgaagtcaag 480

aagcccggcg ctagcgtgaa agtgtcctgc aaagcctccg ggtacacatt cacctcctac 540

tggatgaatt gggtcagaca ggcgcccggc cagggactcg agtggatggg aaggattgat 600

ccttacgact ccgaaaccca ttacaaccag aagttcaagg accgcgtgac catgactgtg 660

gataagtcca cttccaccgc ttacatggag ctgtccagcc tgcgctccga ggataccgca 720

gtgtactact gcgcccgggg aaactgggac gactattggg gacagggaac taccgtgacc 780

gtgtcaagca ccactacccc agcaccgagg ccacccaccc cggctcctac catcgcctcc 840

cagcctctgt ccctgcgtcc ggaggcatgt agacccgcag ctggtggggc cgtgcatacc 900

cggggtcttg acttcgcctg cgatatctac atttgggccc ctctggctgg tacttgcggg 960

gtcctgctgc tttcactcgt gatcactctt tactgtaagc gcggtcggaa gaagctgctg 1020

tacatcttta agcaaccctt catgaggcct gtgcagacta ctcaagagga ggacggctgt 1080

tcatgccggt tcccagagga ggaggaaggc ggctgcgaac tgcgcgtgaa attcagccgc 1140

agcgcagatg ctccagccta caagcagggg cagaaccagc tctacaacga actcaatctt 1200

ggtcggagag aggagtacga cgtgctggac aagcggagag gacgggaccc agaaatgggc 1260

gggaagccgc gcagaaagaa tccccaagag ggcctgtaca acgagctcca aaaggataag 1320

atggcagaag cctatagcga gattggtatg aaaggggaac gcagaagagg caaaggccac 1380

gacggactgt accagggact cagcaccgcc accaaggaca cctatgacgc tcttcacatg 1440

caggccctgc cgcctcgg 1458

<210> 240
<211> 486
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 240
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Val Val Leu Thr Gln Ser Pro Ala Thr Leu
20 25 30

Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Lys
35 40 45

Ser Ile Ser Lys Asp Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala
50 55 60

```
                                                    _SL
Pro Arg Leu Leu Ile Tyr Ser Gly Ser Thr Leu Gln Ser Gly Ile Pro
65                  70                  75                  80

Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile
                85                  90                  95

Ser Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln His
            100                 105                 110

Asn Lys Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys
145                 150                 155                 160

Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr
                165                 170                 175

Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly
            180                 185                 190

Leu Glu Trp Met Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr
        195                 200                 205

Asn Gln Lys Phe Lys Asp Arg Val Thr Met Thr Val Asp Lys Ser Thr
    210                 215                 220

Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala
225                 230                 235                 240

Val Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly
                245                 250                 255

Thr Thr Val Thr Val Ser Ser Thr Thr Thr Pro Ala Pro Arg Pro Pro
            260                 265                 270

Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu
        275                 280                 285

Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
    290                 295                 300

Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly
305                 310                 315                 320
```

Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg
325 330 335

Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln
340 345 350

Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu
355 360 365

Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
370 375 380

Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
385 390 395 400

Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
405 410 415

Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
420 425 430

Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
435 440 445

Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
450 455 460

Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
465 470 475 480

Gln Ala Leu Pro Pro Arg
485

<210> 241
<211> 263
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 241
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Val Val Leu Thr Gln Ser Pro Ala Thr Leu
20 25 30

```
Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Lys
        35                  40                  45

Ser Ile Ser Lys Asp Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala
    50                  55                  60

Pro Arg Leu Leu Ile Tyr Ser Gly Ser Thr Leu Gln Ser Gly Ile Pro
65                  70                  75                  80

Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile
                85                  90                  95

Ser Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln His
            100                 105                 110

Asn Lys Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys
145                 150                 155                 160

Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr
                165                 170                 175

Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly
            180                 185                 190

Leu Glu Trp Met Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr
        195                 200                 205

Asn Gln Lys Phe Lys Asp Arg Val Thr Met Thr Val Asp Lys Ser Thr
    210                 215                 220

Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala
225                 230                 235                 240

Val Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly
                245                 250                 255

Thr Thr Val Thr Val Ser Ser
            260
```

<210> 242
<211> 115

<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 242
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Trp Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Val Thr Met Thr Val Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser
115

<210> 243
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 243
Glu Val Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45

Tyr Ser Gly Ser Thr Leu Gln Ser Gly Ile Pro Ala Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
65 70 75 80

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 244
<211> 1458
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 244
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgacgtcg tgatgaccca gtcaccggca ttcctgtccg tgactcccgg agaaaaggtc 120

acgattactt gccgggcgtc caagagcatc tccaaggacc tcgcctggta ccaacagaag 180

ccggaccagg cccctaagct gttgatctac tcggggtcca cccttcaatc gggagtgcca 240

tcgcggttta gcggttcggg ttctgggacc gacttcactt tcaccatctc ctcactggaa 300

gccgaggatg ccgccactta ctactgtcag cagcacaaca agtatccgta caccttcgga 360

ggcggtacca aagtggagat caaggggggt ggcggtagcg gaggaggggg ctccggcggc 420

ggcggctcag ggggcggagg aagccaagtg cagctggtcc agtcgggagc cgaagtcaag 480

aagcccggcg ctagcgtgaa agtgtcctgc aaagcctccg ggtacacatt cacctcctac 540

tggatgaatt gggtcagaca ggcgcccggc cagggactcg agtggatggg aaggattgat 600

ccttacgact ccgaaaccca ttacaaccag aagttcaagg accgcgtgac catgactgtg 660

gataagtcca cttccaccgc ttacatggag ctgtccagcc tgcgctccga ggataccgca 720

gtgtactact gcgcccgggg aaactgggac gactattggg gacagggaac taccgtgacc 780

gtgtcaagca ccactacccc agcaccgagg ccacccaccc cggctcctac catcgcctcc 840

cagcctctgt ccctgcgtcc ggaggcatgt agacccgcag ctggtggggc cgtgcatacc 900

cggggtcttg acttcgcctg cgatatctac atttgggccc ctctggctgg tacttgcggg 960

gtcctgctgc tttcactcgt gatcactctt tactgtaagc gcggtcggaa gaagctgctg 1020

tacatcttta agcaaccctt catgaggcct gtgcagacta ctcaagagga ggacggctgt 1080

tcatgccggt tcccagagga ggaggaaggc ggctgcgaac tgcgcgtgaa attcagccgc 1140

agcgcagatg ctccagccta caagcagggg cagaaccagc tctacaacga actcaatctt 1200

ggtcggagag aggagtacga cgtgctggac aagcggagag gacgggaccc agaaatgggc 1260

gggaagccgc gcagaaagaa tccccaagag ggcctgtaca acgagctcca aaaggataag 1320

atggcagaag cctatagcga gattggtatg aaaggggaac gcagaagagg caaaggccac 1380

gacggactgt accagggact cagcaccgcc accaaggaca cctatgacgc tcttcacatg 1440

caggccctgc cgcctcgg 1458

<210> 245
<211> 486
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 245
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Asp Val Val Met Thr Gln Ser Pro Ala Phe Leu
20 25 30

Ser Val Thr Pro Gly Glu Lys Val Thr Ile Thr Cys Arg Ala Ser Lys
35 40 45

Ser Ile Ser Lys Asp Leu Ala Trp Tyr Gln Gln Lys Pro Asp Gln Ala
50 55 60

Pro Lys Leu Leu Ile Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro
65 70 75 80

Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile
85 90 95

Ser Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln His
100 105 110

Asn Lys Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
130 135 140

```
                                                _SL
Gly Gly Gly Ser Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys
145                 150                 155                 160

Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr
                165                 170                 175

Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly
            180                 185                 190

Leu Glu Trp Met Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr
        195                 200                 205

Asn Gln Lys Phe Lys Asp Arg Val Thr Met Thr Val Asp Lys Ser Thr
    210                 215                 220

Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala
225                 230                 235                 240

Val Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly
                245                 250                 255

Thr Thr Val Thr Val Ser Ser Thr Thr Thr Pro Ala Pro Arg Pro Pro
            260                 265                 270

Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu
        275                 280                 285

Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
    290                 295                 300

Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly
305                 310                 315                 320

Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg
                325                 330                 335

Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln
            340                 345                 350

Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu
        355                 360                 365

Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
    370                 375                 380

Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
385                 390                 395                 400
```

Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
405 410 415

Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
420 425 430

Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
435 440 445

Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
450 455 460

Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
465 470 475 480

Gln Ala Leu Pro Pro Arg
485

<210> 246
<211> 263
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 246
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Asp Val Val Met Thr Gln Ser Pro Ala Phe Leu
20 25 30

Ser Val Thr Pro Gly Glu Lys Val Thr Ile Thr Cys Arg Ala Ser Lys
35 40 45

Ser Ile Ser Lys Asp Leu Ala Trp Tyr Gln Gln Lys Pro Asp Gln Ala
50 55 60

Pro Lys Leu Leu Ile Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro
65 70 75 80

Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile
85 90 95

Ser Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln His
100 105 110

```
Asn Lys Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys
145                 150                 155                 160

Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr
                165                 170                 175

Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly
            180                 185                 190

Leu Glu Trp Met Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr
        195                 200                 205

Asn Gln Lys Phe Lys Asp Arg Val Thr Met Thr Val Asp Lys Ser Thr
    210                 215                 220

Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala
225                 230                 235                 240

Val Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly
                245                 250                 255

Thr Thr Val Thr Val Ser Ser
            260
```

<210> 247
<211> 115
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 247

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30

Trp Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45
```

```
Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe
    50                  55                  60

Lys Asp Arg Val Thr Met Thr Val Asp Lys Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
            100                 105                 110

Val Ser Ser
        115
```

<210> 248
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 248

```
Asp Val Val Met Thr Gln Ser Pro Ala Phe Leu Ser Val Thr Pro Gly
1               5                   10                  15

Glu Lys Val Thr Ile Thr Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp
            20                  25                  30

Leu Ala Trp Tyr Gln Gln Lys Pro Asp Gln Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Glu Ala
65                  70                  75                  80

Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr
                85                  90                  95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            100                 105
```

<210> 249
<211> 1458
<212> DNA

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 249
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgacgtgg tcatgactca gtccccggac tcactcgcgg tgtcgcttgg agagagagcg 120

accatcaact gtcgggcctc aaagagcatc agcaaggacc tggcctggta ccagcagaag 180

ccgggacagc cgccaaagct gctgatctac tccgggtcca ccttgcaatc tggtgtccct 240

gaccggttct ccggttccgg gtcgggtacc gacttcacgc tcactatttc gtcgctgcaa 300

gccgaagatg tggccgtgta ctattgccaa cagcacaaca agtaccccta cacttttggc 360

ggaggcacca aggtggaaat caaggggggt ggcggtagcg gaggaggggg ctccggcggc 420

ggcggctcag ggggcggagg aagccaagtg cagctggtcc agtcgggagc cgaagtcaag 480

aagcccggcg ctagcgtgaa agtgtcctgc aaagcctccg ggtacacatt cacctcctac 540

tggatgaatt gggtcagaca ggcgcccggc cagggactcg agtggatggg aaggattgat 600

ccttacgact ccgaaaccca ttacaaccag aagttcaagg accgcgtgac catgactgtg 660

gataagtcca cttccaccgc ttacatggag ctgtccagcc tgcgctccga ggataccgca 720

gtgtactact gcgcccgggg aaactgggac gactattggg gacagggaac taccgtgacc 780

gtgtcaagca ccactacccc agcaccgagg ccacccaccc cggctcctac catcgcctcc 840

cagcctctgt ccctgcgtcc ggaggcatgt agacccgcag ctggtggggc cgtgcatacc 900

cggggtcttg acttcgcctg cgatatctac atttgggccc ctctggctgg tacttgcggg 960

gtcctgctgc tttcactcgt gatcactctt tactgtaagc gcggtcggaa gaagctgctg 1020

tacatcttta agcaaccctt catgaggcct gtgcagacta ctcaagagga ggacggctgt 1080

tcatgccggt tcccagagga ggaggaaggc ggctgcgaac tgcgcgtgaa attcagccgc 1140

agcgcagatg ctccagccta caagcagggg cagaaccagc tctacaacga actcaatctt 1200

ggtcggagag aggagtacga cgtgctggac aagcggagag gacgggaccc agaaatgggc 1260

gggaagccgc gcagaaagaa tccccaagag ggcctgtaca acgagctcca aaaggataag 1320

atggcagaag cctatagcga gattggtatg aaaggggaac gcagaagagg caaaggccac 1380

gacggactgt accagggact cagcaccgcc accaaggaca cctatgacgc tcttcacatg 1440

caggccctgc cgcctcgg 1458

<210> 250
<211> 486
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 250
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Asp Val Val Met Thr Gln Ser Pro Asp Ser Leu
20 25 30

Ala Val Ser Leu Gly Glu Arg Ala Thr Ile Asn Cys Arg Ala Ser Lys
35 40 45

Ser Ile Ser Lys Asp Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro
50 55 60

Pro Lys Leu Leu Ile Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro
65 70 75 80

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile
85 90 95

Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln His
100 105 110

Asn Lys Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
130 135 140

Gly Gly Gly Ser Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys
145 150 155 160

Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr
165 170 175

Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly
180 185 190

Leu Glu Trp Met Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr
195 200 205

Asn Gln Lys Phe Lys Asp Arg Val Thr Met Thr Val Asp Lys Ser Thr
210 215 220

```
                                                _SL
Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala
225                 230                 235                 240

Val Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly
                245                 250                 255

Thr Thr Val Thr Val Ser Ser Thr Thr Thr Pro Ala Pro Arg Pro Pro
            260                 265                 270

Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu
        275                 280                 285

Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
    290                 295                 300

Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly
305                 310                 315                 320

Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg
                325                 330                 335

Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln
            340                 345                 350

Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu
        355                 360                 365

Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
    370                 375                 380

Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
385                 390                 395                 400

Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
                405                 410                 415

Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
            420                 425                 430

Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
        435                 440                 445

Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
    450                 455                 460

Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
465                 470                 475                 480
```

Gln Ala Leu Pro Pro Arg
485

<210> 251
<211> 263
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 251
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Asp Val Val Met Thr Gln Ser Pro Asp Ser Leu
20 25 30

Ala Val Ser Leu Gly Glu Arg Ala Thr Ile Asn Cys Arg Ala Ser Lys
35 40 45

Ser Ile Ser Lys Asp Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro
50 55 60

Pro Lys Leu Leu Ile Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro
65 70 75 80

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile
85 90 95

Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln His
100 105 110

Asn Lys Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
130 135 140

Gly Gly Gly Ser Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys
145 150 155 160

Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr
165 170 175

Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly
180 185 190

```
Leu Glu Trp Met Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr
        195                 200                 205

Asn Gln Lys Phe Lys Asp Arg Val Thr Met Thr Val Asp Lys Ser Thr
    210                 215                 220

Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala
225                 230                 235                 240

Val Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly
                245                 250                 255

Thr Thr Val Thr Val Ser Ser
            260
```

<210> 252
<211> 115
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 252

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30

Trp Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe
    50                  55                  60

Lys Asp Arg Val Thr Met Thr Val Asp Lys Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
            100                 105                 110

Val Ser Ser
        115
```

<210> 253
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 253
Asp Val Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Glu Arg Ala Thr Ile Asn Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile
35 40 45

Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro Asp Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala
65 70 75 80

Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 254
<211> 1458
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 254
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtgc agctggtgca gtcaggcagc gaactgaaga agcccggagc ctccgtcaaa 120

gtgtcctgca aagcctcggg atacaccttc acctcctact ggatgaactg ggtccgccag 180

gcacctggac aggggctgga gtggatggga aggatcgatc cctacgattc cgaaacccat 240

tacaatcaga agttcaagga ccggtttgtg ttctccgtgg acaagtccgt gtccaccgcc 300

tacctccaaa ttagcagcct gaaggcggag gatacagctg tctactactg cgctcgcgga 360

aactgggatg actattgggg ccagggaact accgtgactg tgtcctccgg gggtggcggt 420

agcggaggag ggggctccgg cggcggcggc tcaggggggcg gaggaagcga cgtgcagctc 480

acccagtcgc cctcatttct gtcggcctca gtgggagaca gagtgaccat tacttgtcgg 540

gcctccaaga gcatctccaa ggacctggcc tggtatcagc agaagccagg aaaggcgcct 600

aagttgctca tctactcggg gtcgaccctg caatctggcg tgccgtcccg gttctccggt 660

tcgggaagcg gtaccgaatt cacccttact atctcctccc tgcaaccgga ggacttcgcc 720

acctactact gccaacagca caacaagtac ccgtacactt tcgggggtgg cacgaaggtc 780

gaaatcaaga ccactacccc agcaccgagg ccacccaccc cggctcctac catcgcctcc 840

cagcctctgt ccctgcgtcc ggaggcatgt agacccgcag ctggtggggc cgtgcatacc 900

cggggtcttg acttcgcctg cgatatctac atttgggccc ctctggctgg tacttgcggg 960

gtcctgctgc tttcactcgt gatcactctt tactgtaagc gcggtcggaa gaagctgctg 1020

tacatcttta agcaaccctt catgaggcct gtgcagacta ctcaagagga ggacggctgt 1080

tcatgccggt tcccagagga ggaggaaggc ggctgcgaac tgcgcgtgaa attcagccgc 1140

agcgcagatg ctccagccta caagcagggg cagaaccagc tctacaacga actcaatctt 1200

ggtcggagag aggagtacga cgtgctggac aagcggagag gacgggaccc agaaatgggc 1260

gggaagccgc gcagaaagaa tccccaagag ggcctgtaca acgagctcca aaaggataag 1320

atggcagaag cctatagcga gattggtatg aaaggggaac gcagaagagg caaaggccac 1380

gacggactgt accagggact cagcaccgcc accaaggaca cctatgacgc tcttcacatg 1440

caggccctgc cgcctcgg 1458

<210> 255
<211> 486
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 255
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ser Glu Leu
20 25 30

Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
35 40 45

Thr Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Ala Pro Gly Gln

_SL

50 55 60

Gly Leu Glu Trp Met Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His
65 70 75 80

Tyr Asn Gln Lys Phe Lys Asp Arg Phe Val Phe Ser Val Asp Lys Ser
85 90 95

Val Ser Thr Ala Tyr Leu Gln Ile Ser Ser Leu Lys Ala Glu Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln
115 120 125

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
130 135 140

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Gln Leu
145 150 155 160

Thr Gln Ser Pro Ser Phe Leu Ser Ala Ser Val Gly Asp Arg Val Thr
165 170 175

Ile Thr Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp Leu Ala Trp Tyr
180 185 190

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Gly Ser
195 200 205

Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
210 215 220

Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
225 230 235 240

Thr Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr Thr Phe Gly Gly
245 250 255

Gly Thr Lys Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro
260 265 270

Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu
275 280 285

Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
290 295 300

_SL
Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly
305 310 315 320

Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg
325 330 335

Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln
340 345 350

Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu
355 360 365

Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
370 375 380

Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
385 390 395 400

Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
405 410 415

Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
420 425 430

Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
435 440 445

Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
450 455 460

Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
465 470 475 480

Gln Ala Leu Pro Pro Arg
485

<210> 256
<211> 263
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 256
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

```
                                                _SL
His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ser Glu Leu
            20                  25                  30

Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
        35                  40                  45

Thr Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Ala Pro Gly Gln
    50                  55                  60

Gly Leu Glu Trp Met Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His
65                  70                  75                  80

Tyr Asn Gln Lys Phe Lys Asp Arg Phe Val Phe Ser Val Asp Lys Ser
                85                  90                  95

Val Ser Thr Ala Tyr Leu Gln Ile Ser Ser Leu Lys Ala Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln
        115                 120                 125

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
    130                 135                 140

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Gln Leu
145                 150                 155                 160

Thr Gln Ser Pro Ser Phe Leu Ser Ala Ser Val Gly Asp Arg Val Thr
                165                 170                 175

Ile Thr Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp Leu Ala Trp Tyr
            180                 185                 190

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Gly Ser
        195                 200                 205

Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
    210                 215                 220

Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
225                 230                 235                 240

Thr Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr Thr Phe Gly Gly
                245                 250                 255

Gly Thr Lys Val Glu Ile Lys
            260
```

<210> 257
<211> 115
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 257
Gln Val Gln Leu Val Gln Ser Gly Ser Glu Leu Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Trp Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Phe Val Phe Ser Val Asp Lys Ser Val Ser Thr Ala Tyr
65 70 75 80

Leu Gln Ile Ser Ser Leu Lys Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser
115

<210> 258
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 258
Asp Val Gln Leu Thr Gln Ser Pro Ser Phe Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp
20 25 30

```
                                        _SL
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr
                85                  90                  95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            100                 105
```

<210> 259
<211> 1458
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 259
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtgc agctggtgca gtcaggcagc gaactgaaga agcccggagc ctccgtcaaa 120

gtgtcctgca aagcctcggg atacaccttc acctcctact ggatgaactg ggtccgccag 180

gcacctggac aggggctgga gtggatggga aggatcgatc cctacgattc cgaaacccat 240

tacaatcaga agttcaagga ccggtttgtg ttctccgtgg acaagtccgt gtccaccgcc 300

tacctccaaa ttagcagcct gaaggcggag gatacagctg tctactactg cgctcgcgga 360

aactgggatg actattgggg ccagggaact accgtgactg tgtcctccgg gggtggcggt 420

agcggaggag ggggctccgg cggcggcggc tcagggggcg gaggaagcga agtggtgctg 480

acccagtcgc ccgcaaccct ctctctgtcg ccgggagaac gcgccactct ttcctgtcgg 540

gcgtccaaga gcatctcaaa ggacctcgcc tggtaccagc agaagcctgg tcaagccccg 600

cggctgctga tctactccgg ctccacgctg caatcaggaa tcccagccag attttccggt 660

tcggggtcgg ggactgactt caccttgacc attagctcgc tggaacctga ggacttcgcc 720

gtgtattact gccagcagca caacaagtac ccgtacacct tcggaggcgg tactaaggtc 780

gagatcaaga ccactacccc agcaccgagg ccacccaccc cggctcctac catcgcctcc 840

cagcctctgt ccctgcgtcc ggaggcatgt agacccgcag ctggtggggc cgtgcatacc 900

cggggtcttg acttcgcctg cgatatctac atttgggccc ctctggctgg tacttgcggg 960

gtcctgctgc tttcactcgt gatcactctt tactgtaagc gcggtcggaa gaagctgctg 1020

tacatcttta agcaaccctt catgaggcct gtgcagacta ctcaagagga ggacggctgt 1080

tcatgccggt tcccagagga ggaggaaggc ggctgcgaac tgcgcgtgaa attcagccgc 1140

agcgcagatg ctccagccta caagcagggg cagaaccagc tctacaacga actcaatctt 1200

ggtcggagag aggagtacga cgtgctggac aagcggagag gacgggaccc agaaatgggc 1260

gggaagccgc gcagaaagaa tccccaagag ggcctgtaca acgagctcca aaaggataag 1320

atggcagaag cctatagcga gattggtatg aaaggggaac gcagaagagg caaaggccac 1380

gacggactgt accagggact cagcaccgcc accaaggaca cctatgacgc tcttcacatg 1440

caggccctgc cgcctcgg 1458

<210> 260
<211> 486
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 260
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ser Glu Leu
20 25 30

Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
35 40 45

Thr Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Ala Pro Gly Gln
50 55 60

Gly Leu Glu Trp Met Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His
65 70 75 80

Tyr Asn Gln Lys Phe Lys Asp Arg Phe Val Phe Ser Val Asp Lys Ser
85 90 95

Val Ser Thr Ala Tyr Leu Gln Ile Ser Ser Leu Lys Ala Glu Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln
115 120 125

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly

_SL

130 135 140

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Val Leu
145 150 155 160

Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr
165 170 175

Leu Ser Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp Leu Ala Trp Tyr
180 185 190

Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Ser Gly Ser
195 200 205

Thr Leu Gln Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly
210 215 220

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp Phe Ala
225 230 235 240

Val Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr Thr Phe Gly Gly
245 250 255

Gly Thr Lys Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro
260 265 270

Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu
275 280 285

Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
290 295 300

Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly
305 310 315 320

Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg
325 330 335

Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln
340 345 350

Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu
355 360 365

Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
370 375 380

```
                                                _SL
Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
385                 390                 395                 400


Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
                405                 410                 415


Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
            420                 425                 430


Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
        435                 440                 445


Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
    450                 455                 460


Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
465                 470                 475                 480


Gln Ala Leu Pro Pro Arg
                485


<210> 261
<211> 263
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 261
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15


His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ser Glu Leu
            20                  25                  30


Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
        35                  40                  45


Thr Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Ala Pro Gly Gln
    50                  55                  60


Gly Leu Glu Trp Met Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His
65                  70                  75                  80


Tyr Asn Gln Lys Phe Lys Asp Arg Phe Val Phe Ser Val Asp Lys Ser
                85                  90                  95
```

```
                                                _SL
Val Ser Thr Ala Tyr Leu Gln Ile Ser Ser Leu Lys Ala Glu Asp Thr
            100                 105                 110


Ala Val Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln
        115                 120                 125


Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
    130                 135                 140


Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Val Leu
145                 150                 155                 160


Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr
                165                 170                 175


Leu Ser Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp Leu Ala Trp Tyr
            180                 185                 190


Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Ser Gly Ser
        195                 200                 205


Thr Leu Gln Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly
    210                 215                 220


Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp Phe Ala
225                 230                 235                 240


Val Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr Thr Phe Gly Gly
                245                 250                 255


Gly Thr Lys Val Glu Ile Lys
            260


<210> 262
<211> 115
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 262
Gln Val Gln Leu Val Gln Ser Gly Ser Glu Leu Lys Lys Pro Gly Ala
1               5                   10                  15


Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30
```

_SL
Trp Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35   40   45

Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe
    50   55   60

Lys Asp Arg Phe Val Phe Ser Val Asp Lys Ser Val Ser Thr Ala Tyr
65   70   75   80

Leu Gln Ile Ser Ser Leu Lys Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
            100   105   110

Val Ser Ser
        115

<210> 263
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 263
Glu Val Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1   5   10   15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp
            20   25   30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
        35   40   45

Tyr Ser Gly Ser Thr Leu Gln Ser Gly Ile Pro Ala Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
65   70   75   80

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr
                85   90   95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            100   105

<210> 264
<211> 1458
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 264
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtgc agctggtgca gtcaggcagc gaactgaaga agcccggagc ctccgtcaaa 120

gtgtcctgca aagcctcggg atacaccttc acctcctact ggatgaactg ggtccgccag 180

gcacctggac aggggctgga gtggatggga aggatcgatc cctacgattc cgaaacccat 240

tacaatcaga agttcaagga ccggtttgtg ttctccgtgg acaagtccgt gtccaccgcc 300

tacctccaaa ttagcagcct gaaggcggag gatacagctg tctactactg cgctcgcgga 360

aactgggatg actattgggg ccagggaact accgtgactg tgtcctccgg gggtggcggt 420

agcggaggag ggggctccgg cggcggcggc tcagggggcg gaggaagcga cgtcgtgatg 480

acccagtcac cggcattcct gtccgtgact cccggagaaa aggtcacgat tacttgccgg 540

gcgtccaaga gcatctccaa ggacctcgcc tggtaccaac agaagccgga ccaggcccct 600

aagctgttga tctactcggg gtccaccctt caatcgggag tgccatcgcg gtttagcggt 660

tcgggttctg ggaccgactt cactttcacc atctcctcac tggaagccga ggatgccgcc 720

acttactact gtcagcagca caacaagtat ccgtacacct tcggaggcgg taccaaagtg 780

gagatcaaga ccactacccc agcaccgagg ccacccaccc cggctcctac catcgcctcc 840

cagcctctgt ccctgcgtcc ggaggcatgt agacccgcag ctggtggggc cgtgcatacc 900

cggggtcttg acttcgcctg cgatatctac atttgggccc ctctggctgg tacttgcggg 960

gtcctgctgc tttcactcgt gatcactctt tactgtaagc gcggtcggaa gaagctgctg 1020

tacatcttta agcaaccctt catgaggcct gtgcagacta ctcaagagga ggacggctgt 1080

tcatgccggt tcccagagga ggaggaaggc ggctgcgaac tgcgcgtgaa attcagccgc 1140

agcgcagatg ctccagccta caagcagggg cagaaccagc tctacaacga actcaatctt 1200

ggtcggagag aggagtacga cgtgctggac aagcggagag gacgggaccc agaaatgggc 1260

gggaagccgc gcagaaagaa tccccaagag ggcctgtaca acgagctcca aaaggataag 1320

atggcagaag cctatagcga gattggtatg aaaggggaac gcagaagagg caaaggccac 1380

gacggactgt accagggact cagcaccgcc accaaggaca cctatgacgc tcttcacatg 1440

caggccctgc cgcctcgg 1458

<210> 265

<211> 486
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 265

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ser Glu Leu
            20                  25                  30

Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
        35                  40                  45

Thr Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Ala Pro Gly Gln
    50                  55                  60

Gly Leu Glu Trp Met Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His
65                  70                  75                  80

Tyr Asn Gln Lys Phe Lys Asp Arg Phe Val Phe Ser Val Asp Lys Ser
                85                  90                  95

Val Ser Thr Ala Tyr Leu Gln Ile Ser Ser Leu Lys Ala Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln
        115                 120                 125

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
    130                 135                 140

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met
145                 150                 155                 160

Thr Gln Ser Pro Ala Phe Leu Ser Val Thr Pro Gly Glu Lys Val Thr
                165                 170                 175

Ile Thr Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp Leu Ala Trp Tyr
            180                 185                 190

Gln Gln Lys Pro Asp Gln Ala Pro Lys Leu Leu Ile Tyr Ser Gly Ser
        195                 200                 205

Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
```

_SL

210 215 220

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Glu Ala Glu Asp Ala Ala
225 230 235 240

Thr Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr Thr Phe Gly Gly
245 250 255

Gly Thr Lys Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro
260 265 270

Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu
275 280 285

Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
290 295 300

Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly
305 310 315 320

Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg
325 330 335

Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln
340 345 350

Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu
355 360 365

Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
370 375 380

Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
385 390 395 400

Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
405 410 415

Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
420 425 430

Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
435 440 445

Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
450 455 460

```
                                                _SL
Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
465                 470                 475                 480


Gln Ala Leu Pro Pro Arg
                485


<210> 266
<211> 263
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 266
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15


His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ser Glu Leu
            20                  25                  30


Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
        35                  40                  45


Thr Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Ala Pro Gly Gln
    50                  55                  60


Gly Leu Glu Trp Met Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His
65                  70                  75                  80


Tyr Asn Gln Lys Phe Lys Asp Arg Phe Val Phe Ser Val Asp Lys Ser
                85                  90                  95


Val Ser Thr Ala Tyr Leu Gln Ile Ser Ser Leu Lys Ala Glu Asp Thr
            100                 105                 110


Ala Val Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln
        115                 120                 125


Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
    130                 135                 140


Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met
145                 150                 155                 160


Thr Gln Ser Pro Ala Phe Leu Ser Val Thr Pro Gly Glu Lys Val Thr
                165                 170                 175
```

_SL
Ile Thr Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp Leu Ala Trp Tyr
            180   185   190

Gln Gln Lys Pro Asp Gln Ala Pro Lys Leu Leu Ile Tyr Ser Gly Ser
        195   200   205

Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
    210   215   220

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Glu Ala Glu Asp Ala Ala
225   230   235   240

Thr Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr Thr Phe Gly Gly
                245   250   255

Gly Thr Lys Val Glu Ile Lys
            260

<210> 267
<211> 115
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 267
Gln Val Gln Leu Val Gln Ser Gly Ser Glu Leu Lys Lys Pro Gly Ala
1   5   10   15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20   25   30

Trp Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35   40   45

Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe
    50   55   60

Lys Asp Arg Phe Val Phe Ser Val Asp Lys Ser Val Ser Thr Ala Tyr
65   70   75   80

Leu Gln Ile Ser Ser Leu Lys Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
            100   105   110

Val Ser Ser
        115

<210> 268
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 268
Asp Val Val Met Thr Gln Ser Pro Ala Phe Leu Ser Val Thr Pro Gly
1   5   10   15

Glu Lys Val Thr Ile Thr Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp
            20   25   30

Leu Ala Trp Tyr Gln Gln Lys Pro Asp Gln Ala Pro Lys Leu Leu Ile
        35   40   45

Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Glu Ala
65   70   75   80

Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr
                85   90   95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            100   105

<210> 269
<211> 1458
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 269
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtgc agctggtgca gtcaggcagc gaactgaaga agcccggagc ctccgtcaaa 120

gtgtcctgca aagcctcggg atacaccttc acctcctact ggatgaactg ggtccgccag 180

gcacctggac aggggctgga gtggatggga aggatcgatc cctacgattc cgaaacccat 240

tacaatcaga agttcaagga ccggtttgtg ttctccgtgg acaagtccgt gtccaccgcc 300

tacctccaaa ttagcagcct gaaggcggag gatacagctg tctactactg cgctcgcgga 360

aactgggatg actattgggg ccagggaact accgtgactg tgtcctccgg gggtggcggt 420

agcggaggag ggggctccgg cggcggcggc tcagggggcg gaggaagcga cgtggtcatg 480

actcagtccc cggactcact cgcggtgtcg cttggagaga gagcgaccat caactgtcgg 540

gcctcaaaga gcatcagcaa ggacctggcc tggtaccagc agaagccggg acagccgcca 600

aagctgctga tctactccgg gtccaccttg caatctggtg tccctgaccg gttctccggt 660

tccgggtcgg gtaccgactt cacgctcact atttcgtcgc tgcaagccga agatgtggcc 720

gtgtactatt gccaacagca caacaagtac ccctacactt ttggcggagg caccaaggtg 780

gaaatcaaga ccactacccc agcaccgagg ccacccaccc cggctcctac catcgcctcc 840

cagcctctgt ccctgcgtcc ggaggcatgt agacccgcag ctggtggggc cgtgcatacc 900

cggggtcttg acttcgcctg cgatatctac atttgggccc ctctggctgg tacttgcggg 960

gtcctgctgc tttcactcgt gatcactctt tactgtaagc gcggtcggaa gaagctgctg 1020

tacatcttta agcaaccctt catgaggcct gtgcagacta ctcaagagga ggacggctgt 1080

tcatgccggt tcccagagga ggaggaaggc ggctgcgaac tgcgcgtgaa attcagccgc 1140

agcgcagatg ctccagccta caagcagggg cagaaccagc tctacaacga actcaatctt 1200

ggtcggagag aggagtacga cgtgctggac aagcggagag gacgggaccc agaaatgggc 1260

gggaagccgc gcagaaagaa tccccaagag ggcctgtaca acgagctcca aaaggataag 1320

atggcagaag cctatagcga gattggtatg aaaggggaac gcagaagagg caaaggccac 1380

gacggactgt accagggact cagcaccgcc accaaggaca cctatgacgc tcttcacatg 1440

caggccctgc cgcctcgg 1458

<210> 270
<211> 486
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 270
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ser Glu Leu
20 25 30

Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
35 40 45

```
Thr Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Ala Pro Gly Gln
    50                  55                  60

Gly Leu Glu Trp Met Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His
65                  70                  75                  80

Tyr Asn Gln Lys Phe Lys Asp Arg Phe Val Phe Ser Val Asp Lys Ser
                85                  90                  95

Val Ser Thr Ala Tyr Leu Gln Ile Ser Ser Leu Lys Ala Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln
        115                 120                 125

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
    130                 135                 140

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met
145                 150                 155                 160

Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly Glu Arg Ala Thr
                165                 170                 175

Ile Asn Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp Leu Ala Trp Tyr
            180                 185                 190

Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Ser Gly Ser
        195                 200                 205

Thr Leu Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly
    210                 215                 220

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala Glu Asp Val Ala
225                 230                 235                 240

Val Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr Thr Phe Gly Gly
                245                 250                 255

Gly Thr Lys Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro
            260                 265                 270

Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu
        275                 280                 285

Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
```

_SL
290 295 300

Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly
305 310 315 320

Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg
325 330 335

Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln
340 345 350

Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu
355 360 365

Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
370 375 380

Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
385 390 395 400

Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
405 410 415

Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
420 425 430

Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
435 440 445

Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
450 455 460

Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
465 470 475 480

Gln Ala Leu Pro Pro Arg
485

<210> 271
<211> 263
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 271
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu

```
                                                _SL
1               5                   10                  15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ser Glu Leu
            20                  25                  30

Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
        35                  40                  45

Thr Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Ala Pro Gly Gln
    50                  55                  60

Gly Leu Glu Trp Met Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His
65                  70                  75                  80

Tyr Asn Gln Lys Phe Lys Asp Arg Phe Val Phe Ser Val Asp Lys Ser
                85                  90                  95

Val Ser Thr Ala Tyr Leu Gln Ile Ser Ser Leu Lys Ala Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln
        115                 120                 125

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
    130                 135                 140

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met
145                 150                 155                 160

Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly Glu Arg Ala Thr
                165                 170                 175

Ile Asn Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp Leu Ala Trp Tyr
            180                 185                 190

Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Ser Gly Ser
        195                 200                 205

Thr Leu Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly
    210                 215                 220

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala Glu Asp Val Ala
225                 230                 235                 240

Val Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr Thr Phe Gly Gly
                245                 250                 255
```

Gly Thr Lys Val Glu Ile Lys
260

<210> 272
<211> 115
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 272
Gln Val Gln Leu Val Gln Ser Gly Ser Glu Leu Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Trp Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Phe Val Phe Ser Val Asp Lys Ser Val Ser Thr Ala Tyr
65 70 75 80

Leu Gln Ile Ser Ser Leu Lys Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser
115

<210> 273
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 273
Asp Val Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Glu Arg Ala Thr Ile Asn Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp

_SL

20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile
35 40 45

Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro Asp Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala
65 70 75 80

Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 274
<211> 1458
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 274
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgacgtgc agctcaccca gtcgccctca tttctgtcgg cctcagtggg agacagagtg 120

accattactt gtcgggcctc caagagcatc tccaaggacc tggcctggta tcagcagaag 180

ccaggaaagg cgcctaagtt gctcatctac tcggggtcga ccctgcaatc tggcgtgccg 240

tcccggttct ccggttcggg aagcggtacc gaattcaccc ttactatctc ctccctgcaa 300

ccggaggact tcgccaccta ctactgccaa cagcacaaca agtacccgta cactttcggg 360

ggtggcacga aggtcgaaat caaggggggt ggcggtagcg gaggaggggg ctccggcggc 420

ggcggctcag ggggcggagg aagccaagtg cagctggtgc agtcaggcag cgaactgaag 480

aagcccggag cctccgtcaa agtgtcctgc aaagcctcgg gatacacctt cacctcctac 540

tggatgaact gggtccgcca ggcacctgga caggggctgg agtggatggg aaggatcgat 600

ccctacgatt ccgaaaccca ttacaatcag aagttcaagg accggtttgt gttctccgtg 660

gacaagtccg tgtccaccgc ctacctccaa attagcagcc tgaaggcgga ggatacagct 720

gtctactact gcgctcgcgg aaactgggat gactattggg gccagggaac taccgtgact 780

gtgtcctcca ccactacccc agcaccgagg ccacccaccc cggctcctac catcgcctcc 840

cagcctctgt ccctgcgtcc ggaggcatgt agacccgcag ctggtggggc cgtgcatacc 900

cggggtcttg acttcgcctg cgatatctac atttgggccc ctctggctgg tacttgcggg 960

gtcctgctgc tttcactcgt gatcactctt tactgtaagc gcggtcggaa gaagctgctg 1020

tacatcttta agcaaccctt catgaggcct gtgcagacta ctcaagagga ggacggctgt 1080

tcatgccggt tcccagagga ggaggaaggc ggctgcgaac tgcgcgtgaa attcagccgc 1140

agcgcagatg ctccagccta caagcagggg cagaaccagc tctacaacga actcaatctt 1200

ggtcggagag aggagtacga cgtgctggac aagcggagag gacgggaccc agaaatgggc 1260

gggaagccgc gcagaaagaa tccccaagag ggcctgtaca acgagctcca aaaggataag 1320

atggcagaag cctatagcga gattggtatg aaaggggaac gcagaagagg caaaggccac 1380

gacggactgt accagggact cagcaccgcc accaaggaca cctatgacgc tcttcacatg 1440

caggccctgc cgcctcgg 1458

<210> 275
<211> 486
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 275

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Asp Val Gln Leu Thr Gln Ser Pro Ser Phe Leu
20 25 30

Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Lys
35 40 45

Ser Ile Ser Lys Asp Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala
50 55 60

Pro Lys Leu Leu Ile Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro
65 70 75 80

Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile
85 90 95

Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln His
100 105 110

Asn Lys Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
115 120 125

```
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gln Val Gln Leu Val Gln Ser Gly Ser Glu Leu Lys
145                 150                 155                 160

Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr
                165                 170                 175

Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly
            180                 185                 190

Leu Glu Trp Met Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr
        195                 200                 205

Asn Gln Lys Phe Lys Asp Arg Phe Val Phe Ser Val Asp Lys Ser Val
    210                 215                 220

Ser Thr Ala Tyr Leu Gln Ile Ser Ser Leu Lys Ala Glu Asp Thr Ala
225                 230                 235                 240

Val Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly
                245                 250                 255

Thr Thr Val Thr Val Ser Ser Thr Thr Thr Pro Ala Pro Arg Pro Pro
            260                 265                 270

Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu
        275                 280                 285

Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
    290                 295                 300

Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly
305                 310                 315                 320

Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg
                325                 330                 335

Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln
            340                 345                 350

Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu
        355                 360                 365

Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
```

_SL
370 375 380

Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
385 390 395 400

Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
405 410 415

Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
420 425 430

Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
435 440 445

Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
450 455 460

Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
465 470 475 480

Gln Ala Leu Pro Pro Arg
485

<210> 276
<211> 263
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 276
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Asp Val Gln Leu Thr Gln Ser Pro Ser Phe Leu
20 25 30

Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Lys
35 40 45

Ser Ile Ser Lys Asp Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala
50 55 60

Pro Lys Leu Leu Ile Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro
65 70 75 80

Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile

_SL
85 90 95

Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln His
100 105 110

Asn Lys Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
130 135 140

Gly Gly Gly Ser Gln Val Gln Leu Val Gln Ser Gly Ser Glu Leu Lys
145 150 155 160

Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr
165 170 175

Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly
180 185 190

Leu Glu Trp Met Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr
195 200 205

Asn Gln Lys Phe Lys Asp Arg Phe Val Phe Ser Val Asp Lys Ser Val
210 215 220

Ser Thr Ala Tyr Leu Gln Ile Ser Ser Leu Lys Ala Glu Asp Thr Ala
225 230 235 240

Val Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly
245 250 255

Thr Thr Val Thr Val Ser Ser
260

<210> 277
<211> 115
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 277
Gln Val Gln Leu Val Gln Ser Gly Ser Glu Leu Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr

_SL

20 25 30

Trp Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Phe Val Phe Ser Val Asp Lys Ser Val Ser Thr Ala Tyr
65 70 75 80

Leu Gln Ile Ser Ser Leu Lys Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser
115

<210> 278
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 278
Asp Val Gln Leu Thr Gln Ser Pro Ser Phe Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys

_SL
100 105

<210> 279
<211> 1458
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 279
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaagtgg tgctgaccca gtcgcccgca accctctctc tgtcgccggg agaacgcgcc 120

actctttcct gtcgggcgtc caagagcatc tcaaaggacc tcgcctggta ccagcagaag 180

cctggtcaag ccccgcggct gctgatctac tccggctcca cgctgcaatc aggaatccca 240

gccagatttt ccggttcggg gtcggggact gacttcacct tgaccattag ctcgctggaa 300

cctgaggact tcgccgtgta ttactgccag cagcacaaca agtacccgta caccttcgga 360

ggcggtacta aggtcgagat caaggggggt ggcggtagcg gaggaggggg ctccggcggc 420

ggcggctcag ggggcggagg aagccaagtg cagctggtgc agtcaggcag cgaactgaag 480

aagcccggag cctccgtcaa agtgtcctgc aaagcctcgg gatacacctt cacctcctac 540

tggatgaact gggtccgcca ggcacctgga caggggctgg agtggatggg aaggatcgat 600

ccctacgatt ccgaaaccca ttacaatcag aagttcaagg accggtttgt gttctccgtg 660

gacaagtccg tgtccaccgc ctacctccaa attagcagcc tgaaggcgga ggatacagct 720

gtctactact gcgctcgcgg aaactgggat gactattggg gccagggaac taccgtgact 780

gtgtcctcca ccactacccc agcaccgagg ccacccaccc cggctcctac catcgcctcc 840

cagcctctgt ccctgcgtcc ggaggcatgt agacccgcag ctggtggggc cgtgcatacc 900

cggggtcttg acttcgcctg cgatatctac atttgggccc ctctggctgg tacttgcggg 960

gtcctgctgc tttcactcgt gatcactctt tactgtaagc gcggtcggaa gaagctgctg 1020

tacatcttta agcaaccctt catgaggcct gtgcagacta ctcaagagga ggacggctgt 1080

tcatgccggt tcccagagga ggaggaaggc ggctgcgaac tgcgcgtgaa attcagccgc 1140

agcgcagatg ctccagccta caagcagggg cagaaccagc tctacaacga actcaatctt 1200

ggtcggagag aggagtacga cgtgctggac aagcggagag gacgggaccc agaaatgggc 1260

gggaagccgc gcagaaagaa tccccaagag ggcctgtaca acgagctcca aaaggataag 1320

atggcagaag cctatagcga gattggtatg aaaggggaac gcagaagagg caaaggccac 1380

gacggactgt accagggact cagcaccgcc accaaggaca cctatgacgc tcttcacatg 1440

caggccctgc cgcctcgg 1458

<210> 280
<211> 486
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 280
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Val Val Leu Thr Gln Ser Pro Ala Thr Leu
20 25 30

Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Lys
35 40 45

Ser Ile Ser Lys Asp Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala
50 55 60

Pro Arg Leu Leu Ile Tyr Ser Gly Ser Thr Leu Gln Ser Gly Ile Pro
65 70 75 80

Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile
85 90 95

Ser Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln His
100 105 110

Asn Lys Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
130 135 140

Gly Gly Gly Ser Gln Val Gln Leu Val Gln Ser Gly Ser Glu Leu Lys
145 150 155 160

Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr
165 170 175

Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly
180 185 190

Leu Glu Trp Met Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr
195 200 205

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Asn Gln Lys Phe Lys Asp Arg Phe Val Phe Ser Val Asp Lys Ser Val
    210                 215                 220

Ser Thr Ala Tyr Leu Gln Ile Ser Ser Leu Lys Ala Glu Asp Thr Ala
225                 230                 235                 240

Val Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly
                245                 250                 255

Thr Thr Val Thr Val Ser Ser Thr Thr Thr Pro Ala Pro Arg Pro Pro
            260                 265                 270

Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu
        275                 280                 285

Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
    290                 295                 300

Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly
305                 310                 315                 320

Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg
                325                 330                 335

Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln
            340                 345                 350

Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu
        355                 360                 365

Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
    370                 375                 380

Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
385                 390                 395                 400

Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
                405                 410                 415

Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
            420                 425                 430

Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
        435                 440                 445

Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
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_SL
450 455 460

Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
465 470 475 480

Gln Ala Leu Pro Pro Arg
485

<210> 281
<211> 263
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 281
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Val Val Leu Thr Gln Ser Pro Ala Thr Leu
20 25 30

Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Lys
35 40 45

Ser Ile Ser Lys Asp Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala
50 55 60

Pro Arg Leu Leu Ile Tyr Ser Gly Ser Thr Leu Gln Ser Gly Ile Pro
65 70 75 80

Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile
85 90 95

Ser Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln His
100 105 110

Asn Lys Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
130 135 140

Gly Gly Gly Ser Gln Val Gln Leu Val Gln Ser Gly Ser Glu Leu Lys
145 150 155 160

Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr

_SL
165 170 175

Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly
180 185 190

Leu Glu Trp Met Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr
195 200 205

Asn Gln Lys Phe Lys Asp Arg Phe Val Phe Ser Val Asp Lys Ser Val
210 215 220

Ser Thr Ala Tyr Leu Gln Ile Ser Ser Leu Lys Ala Glu Asp Thr Ala
225 230 235 240

Val Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly
245 250 255

Thr Thr Val Thr Val Ser Ser
260

<210> 282
<211> 115
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 282
Gln Val Gln Leu Val Gln Ser Gly Ser Glu Leu Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Trp Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Phe Val Phe Ser Val Asp Lys Ser Val Ser Thr Ala Tyr
65 70 75 80

Leu Gln Ile Ser Ser Leu Lys Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr

_SL
100 105 110

Val Ser Ser
115

<210> 283
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 283
Glu Val Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45

Tyr Ser Gly Ser Thr Leu Gln Ser Gly Ile Pro Ala Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
65 70 75 80

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 284
<211> 1458
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 284
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgacgtcg tgatgaccca gtcaccggca ttcctgtccg tgactcccgg agaaaaggtc 120

acgattactt gccgggcgtc caagagcatc tccaaggacc tcgcctggta ccaacagaag 180

ccggaccagg cccctaagct gttgatctac tcggggtcca cccttcaatc gggagtgcca 240

tcgcggttta gcggttcggg ttctgggacc gacttcactt tcaccatctc ctcactggaa 300

gccgaggatg ccgccactta ctactgtcag cagcacaaca agtatccgta caccttcgga 360

ggcggtacca aagtggagat caaggggggt ggcggtagcg gaggaggggg ctccggcggc 420

ggcggctcag ggggcggagg aagccaagtg cagctggtgc agtcaggcag cgaactgaag 480

aagcccggag cctccgtcaa agtgtcctgc aaagcctcgg gatacacctt cacctcctac 540

tggatgaact gggtccgcca ggcacctgga caggggctgg agtggatggg aaggatcgat 600

ccctacgatt ccgaaaccca ttacaatcag aagttcaagg accggtttgt gttctccgtg 660

gacaagtccg tgtccaccgc ctacctccaa attagcagcc tgaaggcgga ggatacagct 720

gtctactact gcgctcgcgg aaactgggat gactattggg gccagggaac taccgtgact 780

gtgtcctcca ccactacccc agcaccgagg ccacccaccc cggctcctac catcgcctcc 840

cagcctctgt ccctgcgtcc ggaggcatgt agacccgcag ctggtggggc cgtgcatacc 900

cggggtcttg acttcgcctg cgatatctac atttgggccc ctctggctgg tacttgcggg 960

gtcctgctgc tttcactcgt gatcactctt tactgtaagc gcggtcggaa gaagctgctg 1020

tacatcttta agcaaccctt catgaggcct gtgcagacta ctcaagagga ggacggctgt 1080

tcatgccggt tcccagagga ggaggaaggc ggctgcgaac tgcgcgtgaa attcagccgc 1140

agcgcagatg ctccagccta caagcagggg cagaaccagc tctacaacga actcaatctt 1200

ggtcggagag aggagtacga cgtgctggac aagcggagag gacgggaccc agaaatgggc 1260

gggaagccgc gcagaaagaa tccccaagag ggcctgtaca acgagctcca aaaggataag 1320

atggcagaag cctatagcga gattggtatg aaaggggaac gcagaagagg caaaggccac 1380

gacggactgt accagggact cagcaccgcc accaaggaca cctatgacgc tcttcacatg 1440

caggccctgc cgcctcgg 1458

<210> 285
<211> 486
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 285
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Asp Val Val Met Thr Gln Ser Pro Ala Phe Leu
20 25 30

```
Ser Val Thr Pro Gly Glu Lys Val Thr Ile Thr Cys Arg Ala Ser Lys
        35                  40                  45

Ser Ile Ser Lys Asp Leu Ala Trp Tyr Gln Gln Lys Pro Asp Gln Ala
    50                  55                  60

Pro Lys Leu Leu Ile Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro
65                  70                  75                  80

Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile
                85                  90                  95

Ser Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln His
            100                 105                 110

Asn Lys Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gln Val Gln Leu Val Gln Ser Gly Ser Glu Leu Lys
145                 150                 155                 160

Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr
                165                 170                 175

Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly
            180                 185                 190

Leu Glu Trp Met Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr
        195                 200                 205

Asn Gln Lys Phe Lys Asp Arg Phe Val Phe Ser Val Asp Lys Ser Val
    210                 215                 220

Ser Thr Ala Tyr Leu Gln Ile Ser Ser Leu Lys Ala Glu Asp Thr Ala
225                 230                 235                 240

Val Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly
                245                 250                 255

Thr Thr Val Thr Val Ser Ser Thr Thr Thr Pro Ala Pro Arg Pro Pro
            260                 265                 270

Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu
        275                 280                 285
```

```
Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
    290                 295                 300

Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly
305                 310                 315                 320

Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg
                325                 330                 335

Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln
            340                 345                 350

Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu
        355                 360                 365

Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
    370                 375                 380

Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
385                 390                 395                 400

Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
                405                 410                 415

Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
            420                 425                 430

Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
        435                 440                 445

Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
    450                 455                 460

Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
465                 470                 475                 480

Gln Ala Leu Pro Pro Arg
                485
```

<210> 286
<211> 263
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 286
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Asp Val Val Met Thr Gln Ser Pro Ala Phe Leu
20 25 30

Ser Val Thr Pro Gly Glu Lys Val Thr Ile Thr Cys Arg Ala Ser Lys
35 40 45

Ser Ile Ser Lys Asp Leu Ala Trp Tyr Gln Gln Lys Pro Asp Gln Ala
50 55 60

Pro Lys Leu Leu Ile Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro
65 70 75 80

Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile
85 90 95

Ser Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln His
100 105 110

Asn Lys Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
130 135 140

Gly Gly Gly Ser Gln Val Gln Leu Val Gln Ser Gly Ser Glu Leu Lys
145 150 155 160

Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr
165 170 175

Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly
180 185 190

Leu Glu Trp Met Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr
195 200 205

Asn Gln Lys Phe Lys Asp Arg Phe Val Phe Ser Val Asp Lys Ser Val
210 215 220

Ser Thr Ala Tyr Leu Gln Ile Ser Ser Leu Lys Ala Glu Asp Thr Ala
225 230 235 240

Val Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly

_SL
245 250 255

Thr Thr Val Thr Val Ser Ser
260

<210> 287
<211> 115
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 287
Gln Val Gln Leu Val Gln Ser Gly Ser Glu Leu Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Trp Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Phe Val Phe Ser Val Asp Lys Ser Val Ser Thr Ala Tyr
65 70 75 80

Leu Gln Ile Ser Ser Leu Lys Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser
115

<210> 288
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 288
Asp Val Val Met Thr Gln Ser Pro Ala Phe Leu Ser Val Thr Pro Gly
1 5 10 15

```
Glu Lys Val Thr Ile Thr Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp
            20                  25                  30

Leu Ala Trp Tyr Gln Gln Lys Pro Asp Gln Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Glu Ala
65                  70                  75                  80

Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr
                85                  90                  95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            100                 105
```

<210> 289
<211> 1458
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 289
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgacgtgg tcatgactca gtccccggac tcactcgcgg tgtcgcttgg agagagagcg 120

accatcaact gtcgggcctc aaagagcatc agcaaggacc tggcctggta ccagcagaag 180

ccgggacagc cgccaaagct gctgatctac tccgggtcca ccttgcaatc tggtgtccct 240

gaccggttct ccggttccgg gtcgggtacc gacttcacgc tcactatttc gtcgctgcaa 300

gccgaagatg tggccgtgta ctattgccaa cagcacaaca agtaccccta cacttttggc 360

ggaggcacca aggtggaaat caaggggggt ggcggtagcg gaggaggggg ctccggcggc 420

ggcggctcag ggggcggagg aagccaagtg cagctggtgc agtcaggcag cgaactgaag 480

aagcccggag cctccgtcaa agtgtcctgc aaagcctcgg gatacacctt cacctcctac 540

tggatgaact gggtccgcca ggcacctgga caggggctgg agtggatggg aaggatcgat 600

ccctacgatt ccgaaaccca ttacaatcag aagttcaagg accggtttgt gttctccgtg 660

gacaagtccg tgtccaccgc ctacctccaa attagcagcc tgaaggcgga ggatacagct 720

gtctactact gcgctcgcgg aaactgggat gactattggg gccagggaac taccgtgact 780

_SL

gtgtcctcca ccactacccc agcaccgagg ccacccaccc cggctcctac catcgcctcc 840

cagcctctgt ccctgcgtcc ggaggcatgt agacccgcag ctggtggggc cgtgcatacc 900

cggggtcttg acttcgcctg cgatatctac atttgggccc ctctggctgg tacttgcggg 960

gtcctgctgc tttcactcgt gatcactctt tactgtaagc gcggtcggaa gaagctgctg 1020

tacatcttta agcaaccctt catgaggcct gtgcagacta ctcaagagga ggacggctgt 1080

tcatgccggt tcccagagga ggaggaaggc ggctgcgaac tgcgcgtgaa attcagccgc 1140

agcgcagatg ctccagccta caagcagggg cagaaccagc tctacaacga actcaatctt 1200

ggtcggagag aggagtacga cgtgctggac aagcggagag gacgggaccc agaaatgggc 1260

gggaagccgc gcagaaagaa tccccaagag ggcctgtaca acgagctcca aaaggataag 1320

atggcagaag cctatagcga gattggtatg aaaggggaac gcagaagagg caaaggccac 1380

gacggactgt accagggact cagcaccgcc accaaggaca cctatgacgc tcttcacatg 1440

caggccctgc cgcctcgg 1458

<210> 290
<211> 486
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 290
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Asp Val Val Met Thr Gln Ser Pro Asp Ser Leu
20 25 30

Ala Val Ser Leu Gly Glu Arg Ala Thr Ile Asn Cys Arg Ala Ser Lys
35 40 45

Ser Ile Ser Lys Asp Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro
50 55 60

Pro Lys Leu Leu Ile Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro
65 70 75 80

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile
85 90 95

Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln His
100 105 110

```
Asn Lys Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gln Val Gln Leu Val Gln Ser Gly Ser Glu Leu Lys
145                 150                 155                 160

Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr
                165                 170                 175

Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly
            180                 185                 190

Leu Glu Trp Met Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr
        195                 200                 205

Asn Gln Lys Phe Lys Asp Arg Phe Val Phe Ser Val Asp Lys Ser Val
    210                 215                 220

Ser Thr Ala Tyr Leu Gln Ile Ser Ser Leu Lys Ala Glu Asp Thr Ala
225                 230                 235                 240

Val Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly
                245                 250                 255

Thr Thr Val Thr Val Ser Ser Thr Thr Thr Pro Ala Pro Arg Pro Pro
            260                 265                 270

Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu
        275                 280                 285

Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
    290                 295                 300

Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly
305                 310                 315                 320

Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg
                325                 330                 335

Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln
            340                 345                 350

Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu
        355                 360                 365
```

Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
370 375 380

Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
385 390 395 400

Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
405 410 415

Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
420 425 430

Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
435 440 445

Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
450 455 460

Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
465 470 475 480

Gln Ala Leu Pro Pro Arg
485

<210> 291
<211> 263
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 291
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Asp Val Val Met Thr Gln Ser Pro Asp Ser Leu
20 25 30

Ala Val Ser Leu Gly Glu Arg Ala Thr Ile Asn Cys Arg Ala Ser Lys
35 40 45

Ser Ile Ser Lys Asp Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro
50 55 60

Pro Lys Leu Leu Ile Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro
65 70 75 80

```
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile
                85                  90                  95

Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln His
            100                 105                 110

Asn Lys Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gln Val Gln Leu Val Gln Ser Gly Ser Glu Leu Lys
145                 150                 155                 160

Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr
                165                 170                 175

Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly
            180                 185                 190

Leu Glu Trp Met Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr
        195                 200                 205

Asn Gln Lys Phe Lys Asp Arg Phe Val Phe Ser Val Asp Lys Ser Val
    210                 215                 220

Ser Thr Ala Tyr Leu Gln Ile Ser Ser Leu Lys Ala Glu Asp Thr Ala
225                 230                 235                 240

Val Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly
                245                 250                 255

Thr Thr Val Thr Val Ser Ser
            260
```

<210> 292
<211> 115
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 292

```
Gln Val Gln Leu Val Gln Ser Gly Ser Glu Leu Lys Lys Pro Gly Ala
1               5                   10                  15
```

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Trp Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Phe Val Phe Ser Val Asp Lys Ser Val Ser Thr Ala Tyr
65 70 75 80

Leu Gln Ile Ser Ser Leu Lys Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser
115

<210> 293
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 293
Asp Val Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Glu Arg Ala Thr Ile Asn Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile
35 40 45

Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro Asp Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala
65 70 75 80

Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 294
<211> 1458
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 294
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaggtgc agctggtgca gagcggagcc gaggtcaaga agcctggaga atccctgagg 120

atcagctgca aaggcagcgg gtataccttc acctcctact ggatgaattg ggtccgccag 180

atgcccggaa aaggcctgga gtggatggga cggattgacc cctacgactc ggaaacccat 240

tacaaccaga agttcaagga tcacgtgacc atctccgtgg acaagtccat ttccactgcg 300

tacctccagt ggtcaagcct gaaggcctcc gacactgcta tgtactactg cgcacgcgga 360

aactgggatg attactgggg acagggaaca accgtgactg tgtcctccgg gggtggcggt 420

agcggaggag ggggctccgg cggcggcggc tcaggggcg gaggaagcga cgtgcagctc 480

acccagtcgc cctcatttct gtcggcctca gtgggagaca gagtgaccat tacttgtcgg 540

gcctccaaga gcatctccaa ggacctggcc tggtatcagc agaagccagg aaaggcgcct 600

aagttgctca tctactcggg gtcgaccctg caatctggcg tgccgtcccg gttctccggt 660

tcgggaagcg gtaccgaatt cacccttact atctcctccc tgcaaccgga ggacttcgcc 720

acctactact gccaacagca caacaagtac ccgtacactt tcgggggtgg cacgaaggtc 780

gaaatcaaga ccactacccc agcaccgagg ccacccaccc cggctcctac catcgcctcc 840

cagcctctgt ccctgcgtcc ggaggcatgt agacccgcag ctggtggggc cgtgcatacc 900

cggggtcttg acttcgcctg cgatatctac atttgggccc ctctggctgg tacttgcggg 960

gtcctgctgc tttcactcgt gatcactctt tactgtaagc gcggtcggaa gaagctgctg 1020

tacatcttta agcaaccctt catgaggcct gtgcagacta ctcaagagga ggacggctgt 1080

tcatgccggt tcccagagga ggaggaaggc ggctgcgaac tgcgcgtgaa attcagccgc 1140

agcgcagatg ctccagccta caagcagggg cagaaccagc tctacaacga actcaatctt 1200

ggtcggagag aggagtacga cgtgctggac aagcggagag gacgggaccc agaaatgggc 1260

gggaagccgc gcagaaagaa tccccaagag ggcctgtaca acgagctcca aaaggataag 1320

atggcagaag cctatagcga gattggtatg aaaggggaac gcagaagagg caaaggccac 1380

gacggactgt accagggact cagcaccgcc accaaggaca cctatgacgc tcttcacatg 1440

caggccctgc cgcctcgg 1458

<210> 295
<211> 486
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 295
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val
20 25 30

Lys Lys Pro Gly Glu Ser Leu Arg Ile Ser Cys Lys Gly Ser Gly Tyr
35 40 45

Thr Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Met Pro Gly Lys
50 55 60

Gly Leu Glu Trp Met Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His
65 70 75 80

Tyr Asn Gln Lys Phe Lys Asp His Val Thr Ile Ser Val Asp Lys Ser
85 90 95

Ile Ser Thr Ala Tyr Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr
100 105 110

Ala Met Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln
115 120 125

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
130 135 140

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Gln Leu
145 150 155 160

Thr Gln Ser Pro Ser Phe Leu Ser Ala Ser Val Gly Asp Arg Val Thr
165 170 175

Ile Thr Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp Leu Ala Trp Tyr
180 185 190

```
Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Gly Ser
        195                 200                 205

Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
    210                 215                 220

Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
225                 230                 235                 240

Thr Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr Thr Phe Gly Gly
                245                 250                 255

Gly Thr Lys Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro
            260                 265                 270

Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu
        275                 280                 285

Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
    290                 295                 300

Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly
305                 310                 315                 320

Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg
                325                 330                 335

Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln
            340                 345                 350

Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu
        355                 360                 365

Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
    370                 375                 380

Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
385                 390                 395                 400

Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
                405                 410                 415

Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
            420                 425                 430

Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
        435                 440                 445
```

Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
450 455 460

Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
465 470 475 480

Gln Ala Leu Pro Pro Arg
485

<210> 296
<211> 263
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 296
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val
20 25 30

Lys Lys Pro Gly Glu Ser Leu Arg Ile Ser Cys Lys Gly Ser Gly Tyr
35 40 45

Thr Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Met Pro Gly Lys
50 55 60

Gly Leu Glu Trp Met Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His
65 70 75 80

Tyr Asn Gln Lys Phe Lys Asp His Val Thr Ile Ser Val Asp Lys Ser
85 90 95

Ile Ser Thr Ala Tyr Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr
100 105 110

Ala Met Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln
115 120 125

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
130 135 140

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Gln Leu
145 150 155 160

```
Thr Gln Ser Pro Ser Phe Leu Ser Ala Ser Val Gly Asp Arg Val Thr
                165                 170                 175

Ile Thr Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp Leu Ala Trp Tyr
            180                 185                 190

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Gly Ser
        195                 200                 205

Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
    210                 215                 220

Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
225                 230                 235                 240

Thr Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr Thr Phe Gly Gly
                245                 250                 255

Gly Thr Lys Val Glu Ile Lys
            260
```

<210> 297
<211> 115
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 297

```
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1               5                   10                  15

Ser Leu Arg Ile Ser Cys Lys Gly Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30

Trp Met Asn Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
        35                  40                  45

Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe
    50                  55                  60

Lys Asp His Val Thr Ile Ser Val Asp Lys Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80

Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
                85                  90                  95
```

```
Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
            100                 105                 110


Val Ser Ser
        115


<210> 298
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 298
Asp Val Gln Leu Thr Gln Ser Pro Ser Phe Leu Ser Ala Ser Val Gly
1               5                   10                  15


Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp
            20                  25                  30


Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45


Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60


Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80


Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr
                85                  90                  95


Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            100                 105


<210> 299
<211> 1458
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 299
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg       60

cccgaggtgc agctggtgca gagcggagcc gaggtcaaga agcctggaga atccctgagg      120
```

atcagctgca aaggcagcgg gtataccttc acctcctact ggatgaattg ggtccgccag 180

atgcccggaa aaggcctgga gtggatggga cggattgacc cctacgactc ggaaacccat 240

tacaaccaga agttcaagga tcacgtgacc atctccgtgg acaagtccat ttccactgcg 300

tacctccagt ggtcaagcct gaaggcctcc gacactgcta tgtactactg cgcacgcgga 360

aactgggatg attactgggg acagggaaca accgtgactg tgtcctccgg gggtggcggt 420

agcggaggag ggggctccgg cggcggcggc tcagggggcg gaggaagcga agtggtgctg 480

acccagtcgc ccgcaaccct ctctctgtcg ccgggagaac gcgccactct ttcctgtcgg 540

gcgtccaaga gcatctcaaa ggacctcgcc tggtaccagc agaagcctgg tcaagccccg 600

cggctgctga tctactccgg ctccacgctg caatcaggaa tcccagccag attttccggt 660

tcggggtcgg ggactgactt caccttgacc attagctcgc tggaacctga ggacttcgcc 720

gtgtattact gccagcagca caacaagtac ccgtacacct tcggaggcgg tactaaggtc 780

gagatcaaga ccactacccc agcaccgagg ccacccaccc cggctcctac catcgcctcc 840

cagcctctgt ccctgcgtcc ggaggcatgt agacccgcag ctggtggggc cgtgcatacc 900

cggggtcttg acttcgcctg cgatatctac atttgggccc ctctggctgg tacttgcggg 960

gtcctgctgc tttcactcgt gatcactctt tactgtaagc gcggtcggaa gaagctgctg 1020

tacatcttta agcaaccctt catgaggcct gtgcagacta ctcaagagga ggacggctgt 1080

tcatgccggt tcccagagga ggaggaaggc ggctgcgaac tgcgcgtgaa attcagccgc 1140

agcgcagatg ctccagccta caagcagggg cagaaccagc tctacaacga actcaatctt 1200

ggtcggagag aggagtacga cgtgctggac aagcggagag gacgggaccc agaaatgggc 1260

gggaagccgc gcagaaagaa tccccaagag ggcctgtaca acgagctcca aaaggataag 1320

atggcagaag cctatagcga gattggtatg aaaggggaac gcagaagagg caaaggccac 1380

gacggactgt accagggact cagcaccgcc accaaggaca cctatgacgc tcttcacatg 1440

caggccctgc cgcctcgg 1458

<210> 300
<211> 486
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 300
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

```
                                                _SL
His Ala Ala Arg Pro Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val
            20                  25                  30

Lys Lys Pro Gly Glu Ser Leu Arg Ile Ser Cys Lys Gly Ser Gly Tyr
        35                  40                  45

Thr Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Met Pro Gly Lys
    50                  55                  60

Gly Leu Glu Trp Met Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His
65                  70                  75                  80

Tyr Asn Gln Lys Phe Lys Asp His Val Thr Ile Ser Val Asp Lys Ser
                85                  90                  95

Ile Ser Thr Ala Tyr Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr
            100                 105                 110

Ala Met Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln
        115                 120                 125

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
    130                 135                 140

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Val Leu
145                 150                 155                 160

Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr
                165                 170                 175

Leu Ser Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp Leu Ala Trp Tyr
            180                 185                 190

Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Ser Gly Ser
        195                 200                 205

Thr Leu Gln Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly
    210                 215                 220

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp Phe Ala
225                 230                 235                 240

Val Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr Thr Phe Gly Gly
                245                 250                 255

Gly Thr Lys Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro
            260                 265                 270
```

Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu
275 280 285

Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
290 295 300

Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly
305 310 315 320

Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg
325 330 335

Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln
340 345 350

Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu
355 360 365

Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
370 375 380

Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
385 390 395 400

Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
405 410 415

Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
420 425 430

Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
435 440 445

Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
450 455 460

Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
465 470 475 480

Gln Ala Leu Pro Pro Arg
485

<210> 301
<211> 263
<212> PRT
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 301
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val
20 25 30

Lys Lys Pro Gly Glu Ser Leu Arg Ile Ser Cys Lys Gly Ser Gly Tyr
35 40 45

Thr Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Met Pro Gly Lys
50 55 60

Gly Leu Glu Trp Met Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His
65 70 75 80

Tyr Asn Gln Lys Phe Lys Asp His Val Thr Ile Ser Val Asp Lys Ser
85 90 95

Ile Ser Thr Ala Tyr Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr
100 105 110

Ala Met Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln
115 120 125

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
130 135 140

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Val Leu
145 150 155 160

Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr
165 170 175

Leu Ser Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp Leu Ala Trp Tyr
180 185 190

Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Ser Gly Ser
195 200 205

Thr Leu Gln Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly
210 215 220

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp Phe Ala
225 230 235 240

Val Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr Thr Phe Gly Gly
245 250 255

Gly Thr Lys Val Glu Ile Lys
260

<210> 302
<211> 115
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 302
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15

Ser Leu Arg Ile Ser Cys Lys Gly Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Trp Met Asn Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
35 40 45

Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe
50 55 60

Lys Asp His Val Thr Ile Ser Val Asp Lys Ser Ile Ser Thr Ala Tyr
65 70 75 80

Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
85 90 95

Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser
115

<210> 303
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 303
Glu Val Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45

Tyr Ser Gly Ser Thr Leu Gln Ser Gly Ile Pro Ala Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
65 70 75 80

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 304
<211> 1458
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 304
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaggtgc agctggtgca gagcggagcc gaggtcaaga agcctggaga atccctgagg 120

atcagctgca aaggcagcgg gtataccttc acctcctact ggatgaattg ggtccgccag 180

atgcccggaa aaggcctgga gtggatggga cggattgacc cctacgactc ggaaacccat 240

tacaaccaga agttcaagga tcacgtgacc atctccgtgg acaagtccat ttccactgcg 300

tacctccagt ggtcaagcct gaaggcctcc gacactgcta tgtactactg cgcacgcgga 360

aactgggatg attactgggg acagggaaca accgtgactg tgtcctccgg gggtggcggt 420

agcggaggag ggggctccgg cggcggcggc tcaggggcg gaggaagcga cgtcgtgatg 480

acccagtcac cggcattcct gtccgtgact cccggagaaa aggtcacgat tacttgccgg 540

gcgtccaaga gcatctccaa ggacctcgcc tggtaccaac agaagccgga ccaggcccct 600

aagctgttga tctactcggg gtccaccctt caatcgggag tgccatcgcg gtttagcggt 660

tcgggttctg ggaccgactt cactttcacc atctcctcac tggaagccga ggatgccgcc 720

acttactact gtcagcagca caacaagtat ccgtacacct tcggaggcgg taccaaagtg 780

gagatcaaga ccactacccc agcaccgagg ccacccaccc cggctcctac catcgcctcc 840

cagcctctgt ccctgcgtcc ggaggcatgt agacccgcag ctggtggggc cgtgcatacc 900

cggggtcttg acttcgcctg cgatatctac atttgggccc ctctggctgg tacttgcggg 960

gtcctgctgc tttcactcgt gatcactctt tactgtaagc gcggtcggaa gaagctgctg 1020

tacatcttta agcaaccctt catgaggcct gtgcagacta ctcaagagga ggacggctgt 1080

tcatgccggt tcccagagga ggaggaaggc ggctgcgaac tgcgcgtgaa attcagccgc 1140

agcgcagatg ctccagccta caagcagggg cagaaccagc tctacaacga actcaatctt 1200

ggtcggagag aggagtacga cgtgctggac aagcggagag gacgggaccc agaaatgggc 1260

gggaagccgc gcagaaagaa tccccaagag ggcctgtaca acgagctcca aaaggataag 1320

atggcagaag cctatagcga gattggtatg aaaggggaac gcagaagagg caaaggccac 1380

gacggactgt accagggact cagcaccgcc accaaggaca cctatgacgc tcttcacatg 1440

caggccctgc cgcctcgg 1458

<210> 305
<211> 486
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 305
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val
20 25 30

Lys Lys Pro Gly Glu Ser Leu Arg Ile Ser Cys Lys Gly Ser Gly Tyr
35 40 45

Thr Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Met Pro Gly Lys
50 55 60

Gly Leu Glu Trp Met Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His
65 70 75 80

Tyr Asn Gln Lys Phe Lys Asp His Val Thr Ile Ser Val Asp Lys Ser
85 90 95

```
                                                    _SL
Ile Ser Thr Ala Tyr Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr
            100                 105                 110

Ala Met Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln
        115                 120                 125

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
    130                 135                 140

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met
145                 150                 155                 160

Thr Gln Ser Pro Ala Phe Leu Ser Val Thr Pro Gly Glu Lys Val Thr
                165                 170                 175

Ile Thr Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp Leu Ala Trp Tyr
            180                 185                 190

Gln Gln Lys Pro Asp Gln Ala Pro Lys Leu Leu Ile Tyr Ser Gly Ser
        195                 200                 205

Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
    210                 215                 220

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Glu Ala Glu Asp Ala Ala
225                 230                 235                 240

Thr Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr Thr Phe Gly Gly
                245                 250                 255

Gly Thr Lys Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro
            260                 265                 270

Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu
        275                 280                 285

Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
    290                 295                 300

Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly
305                 310                 315                 320

Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg
                325                 330                 335

Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln
            340                 345                 350
```

Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu
355 360 365

Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
370 375 380

Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
385 390 395 400

Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
405 410 415

Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
420 425 430

Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
435 440 445

Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
450 455 460

Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
465 470 475 480

Gln Ala Leu Pro Pro Arg
485

<210> 306
<211> 263
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 306
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val
20 25 30

Lys Lys Pro Gly Glu Ser Leu Arg Ile Ser Cys Lys Gly Ser Gly Tyr
35 40 45

Thr Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Met Pro Gly Lys
50 55 60

```
Gly Leu Glu Trp Met Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His
65                  70                  75                  80

Tyr Asn Gln Lys Phe Lys Asp His Val Thr Ile Ser Val Asp Lys Ser
                85                  90                  95

Ile Ser Thr Ala Tyr Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr
            100                 105                 110

Ala Met Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln
        115                 120                 125

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
    130                 135                 140

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met
145                 150                 155                 160

Thr Gln Ser Pro Ala Phe Leu Ser Val Thr Pro Gly Glu Lys Val Thr
                165                 170                 175

Ile Thr Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp Leu Ala Trp Tyr
            180                 185                 190

Gln Gln Lys Pro Asp Gln Ala Pro Lys Leu Leu Ile Tyr Ser Gly Ser
        195                 200                 205

Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
    210                 215                 220

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Glu Ala Glu Asp Ala Ala
225                 230                 235                 240

Thr Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr Thr Phe Gly Gly
                245                 250                 255

Gly Thr Lys Val Glu Ile Lys
            260
```

<210> 307
<211> 115
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 307
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15

Ser Leu Arg Ile Ser Cys Lys Gly Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Trp Met Asn Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
35 40 45

Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe
50 55 60

Lys Asp His Val Thr Ile Ser Val Asp Lys Ser Ile Ser Thr Ala Tyr
65 70 75 80

Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
85 90 95

Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser
115

<210> 308
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 308
Asp Val Val Met Thr Gln Ser Pro Ala Phe Leu Ser Val Thr Pro Gly
1 5 10 15

Glu Lys Val Thr Ile Thr Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Asp Gln Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Glu Ala
65 70 75 80

Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 309
<211> 1458
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 309
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaggtgc agctggtgca gagcggagcc gaggtcaaga agcctggaga atccctgagg 120

atcagctgca aaggcagcgg gtataccttc acctcctact ggatgaattg ggtccgccag 180

atgcccggaa aaggcctgga gtggatggga cggattgacc cctacgactc ggaaacccat 240

tacaaccaga agttcaagga tcacgtgacc atctccgtgg acaagtccat ttccactgcg 300

tacctccagt ggtcaagcct gaaggcctcc gacactgcta tgtactactg cgcacgcgga 360

aactgggatg attactgggg acagggaaca accgtgactg tgtcctccgg gggtggcggt 420

agcggaggag ggggctccgg cggcggcggc tcaggggcg gaggaagcga cgtggtcatg 480

actcagtccc cggactcact cgcggtgtcg cttggagaga gagcgaccat caactgtcgg 540

gcctcaaaga gcatcagcaa ggacctggcc tggtaccagc agaagccggg acagccgcca 600

aagctgctga tctactccgg gtccaccttg caatctggtg tccctgaccg gttctccggt 660

tccgggtcgg gtaccgactt cacgctcact atttcgtcgc tgcaagccga agatgtggcc 720

gtgtactatt gccaacagca caacaagtac ccctacactt ttggcggagg caccaaggtg 780

gaaatcaaga ccactacccc agcaccgagg ccacccaccc cggctcctac catcgcctcc 840

cagcctctgt ccctgcgtcc ggaggcatgt agacccgcag ctggtggggc cgtgcatacc 900

cggggtcttg acttcgcctg cgatatctac atttgggccc ctctggctgg tacttgcggg 960

gtcctgctgc tttcactcgt gatcactctt tactgtaagc gcggtcggaa gaagctgctg 1020

tacatcttta agcaaccctt catgaggcct gtgcagacta ctcaagagga ggacggctgt 1080

tcatgccggt tcccagagga ggaggaaggc ggctgcgaac tgcgcgtgaa attcagccgc 1140

agcgcagatg ctccagccta caagcagggg cagaaccagc tctacaacga actcaatctt 1200

ggtcggagag aggagtacga cgtgctggac aagcggagag gacgggaccc agaaatgggc 1260

gggaagccgc gcagaaagaa tccccaagag ggcctgtaca acgagctcca aaaggataag 1320

atggcagaag cctatagcga gattggtatg aaaggggaac gcagaagagg caaaggccac 1380

gacggactgt accagggact cagcaccgcc accaaggaca cctatgacgc tcttcacatg 1440

caggccctgc cgcctcgg 1458

<210> 310
<211> 486
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 310

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15

His Ala Ala Arg Pro Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val
            20                  25                  30

Lys Lys Pro Gly Glu Ser Leu Arg Ile Ser Cys Lys Gly Ser Gly Tyr
        35                  40                  45

Thr Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Met Pro Gly Lys
    50                  55                  60

Gly Leu Glu Trp Met Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His
65                  70                  75                  80

Tyr Asn Gln Lys Phe Lys Asp His Val Thr Ile Ser Val Asp Lys Ser
                85                  90                  95

Ile Ser Thr Ala Tyr Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr
            100                 105                 110

Ala Met Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln
        115                 120                 125

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
    130                 135                 140

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met
145                 150                 155                 160

Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly Glu Arg Ala Thr
                165                 170                 175
```

_SL
Ile Asn Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp Leu Ala Trp Tyr
            180   185   190

Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Ser Gly Ser
        195   200   205

Thr Leu Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly
    210   215   220

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala Glu Asp Val Ala
225   230   235   240

Val Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr Thr Phe Gly Gly
                245   250   255

Gly Thr Lys Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro
            260   265   270

Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu
        275   280   285

Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
    290   295   300

Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly
305   310   315   320

Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg
                325   330   335

Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln
            340   345   350

Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu
        355   360   365

Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
    370   375   380

Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
385   390   395   400

Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
                405   410   415

Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
            420   425   430

Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
435 440 445

Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
450 455 460

Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
465 470 475 480

Gln Ala Leu Pro Pro Arg
485

<210> 311
<211> 263
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 311
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val
20 25 30

Lys Lys Pro Gly Glu Ser Leu Arg Ile Ser Cys Lys Gly Ser Gly Tyr
35 40 45

Thr Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Met Pro Gly Lys
50 55 60

Gly Leu Glu Trp Met Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His
65 70 75 80

Tyr Asn Gln Lys Phe Lys Asp His Val Thr Ile Ser Val Asp Lys Ser
85 90 95

Ile Ser Thr Ala Tyr Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr
100 105 110

Ala Met Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln
115 120 125

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
130 135 140

```
Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met
145                 150                 155                 160

Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly Glu Arg Ala Thr
                165                 170                 175

Ile Asn Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp Leu Ala Trp Tyr
            180                 185                 190

Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Ser Gly Ser
        195                 200                 205

Thr Leu Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly
    210                 215                 220

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala Glu Asp Val Ala
225                 230                 235                 240

Val Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr Thr Phe Gly Gly
                245                 250                 255

Gly Thr Lys Val Glu Ile Lys
            260
```

<210> 312
<211> 115
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 312

```
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1               5                   10                  15

Ser Leu Arg Ile Ser Cys Lys Gly Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30

Trp Met Asn Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
        35                  40                  45

Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe
    50                  55                  60

Lys Asp His Val Thr Ile Ser Val Asp Lys Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80
```

```
Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
                85                  90                  95


Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
            100                 105                 110


Val Ser Ser
        115


<210> 313
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 313
Asp Val Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
1               5                   10                  15


Glu Arg Ala Thr Ile Asn Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp
            20                  25                  30


Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile
        35                  40                  45


Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro Asp Arg Phe Ser Gly
    50                  55                  60


Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala
65                  70                  75                  80


Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr
                85                  90                  95


Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            100                 105


<210> 314
<211> 1458
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 314
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atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgacgtgc agctcaccca gtcgccctca tttctgtcgg cctcagtggg agacagagtg 120

accattactt gtcgggcctc caagagcatc tccaaggacc tggcctggta tcagcagaag 180

ccaggaaagg cgcctaagtt gctcatctac tcggggtcga ccctgcaatc tggcgtgccg 240

tcccggttct ccggttcggg aagcggtacc gaattcaccc ttactatctc ctccctgcaa 300

ccggaggact tcgccaccta ctactgccaa cagcacaaca agtacccgta cactttcggg 360

ggtggcacga aggtcgaaat caaggggggt ggcggtagcg gaggaggggg ctccggcggc 420

ggcggctcag ggggcggagg aagcgaggtg cagctggtgc agagcggagc cgaggtcaag 480

aagcctggag aatccctgag gatcagctgc aaaggcagcg ggtatacctt cacctcctac 540

tggatgaatt gggtccgcca gatgcccgga aaaggcctgg agtggatggg acggattgac 600

ccctacgact cggaaaccca ttacaaccag aagttcaagg atcacgtgac catctccgtg 660

gacaagtcca tttccactgc gtacctccag tggtcaagcc tgaaggcctc cgacactgct 720

atgtactact gcgcacgcgg aaactgggat gattactggg gacagggaac aaccgtgact 780

gtgtcctcca ccactacccc agcaccgagg ccacccaccc cggctcctac catcgcctcc 840

cagcctctgt ccctgcgtcc ggaggcatgt agacccgcag ctggtggggc cgtgcatacc 900

cggggtcttg acttcgcctg cgatatctac atttgggccc ctctggctgg tacttgcggg 960

gtcctgctgc tttcactcgt gatcactctt tactgtaagc gcggtcggaa gaagctgctg 1020

tacatcttta agcaaccctt catgaggcct gtgcagacta ctcaagagga ggacggctgt 1080

tcatgccggt tcccagagga ggaggaaggc ggctgcgaac tgcgcgtgaa attcagccgc 1140

agcgcagatg ctccagccta caagcagggg cagaaccagc tctacaacga actcaatctt 1200

ggtcggagag aggagtacga cgtgctggac aagcggagag gacgggaccc agaaatgggc 1260

gggaagccgc gcagaaagaa tccccaagag ggcctgtaca acgagctcca aaaggataag 1320

atggcagaag cctatagcga gattggtatg aaaggggaac gcagaagagg caaaggccac 1380

gacggactgt accagggact cagcaccgcc accaaggaca cctatgacgc tcttcacatg 1440

caggccctgc cgcctcgg 1458

<210> 315
<211> 486
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 315
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu

_SL

1 5 10 15

His Ala Ala Arg Pro Asp Val Gln Leu Thr Gln Ser Pro Ser Phe Leu
20 25 30

Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Lys
35 40 45

Ser Ile Ser Lys Asp Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala
50 55 60

Pro Lys Leu Leu Ile Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro
65 70 75 80

Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile
85 90 95

Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln His
100 105 110

Asn Lys Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
130 135 140

Gly Gly Gly Ser Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys
145 150 155 160

Lys Pro Gly Glu Ser Leu Arg Ile Ser Cys Lys Gly Ser Gly Tyr Thr
165 170 175

Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Met Pro Gly Lys Gly
180 185 190

Leu Glu Trp Met Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr
195 200 205

Asn Gln Lys Phe Lys Asp His Val Thr Ile Ser Val Asp Lys Ser Ile
210 215 220

Ser Thr Ala Tyr Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala
225 230 235 240

Met Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly
245 250 255

_SL
Thr Thr Val Thr Val Ser Ser Thr Thr Thr Pro Ala Pro Arg Pro Pro
260 265 270

Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu
275 280 285

Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
290 295 300

Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly
305 310 315 320

Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg
325 330 335

Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln
340 345 350

Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu
355 360 365

Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
370 375 380

Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
385 390 395 400

Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
405 410 415

Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
420 425 430

Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
435 440 445

Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
450 455 460

Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
465 470 475 480

Gln Ala Leu Pro Pro Arg
485

<210> 316
<211> 263
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 316

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15

His Ala Ala Arg Pro Asp Val Gln Leu Thr Gln Ser Pro Ser Phe Leu
            20                  25                  30

Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Lys
        35                  40                  45

Ser Ile Ser Lys Asp Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala
    50                  55                  60

Pro Lys Leu Leu Ile Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro
65                  70                  75                  80

Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile
                85                  90                  95

Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln His
            100                 105                 110

Asn Lys Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
    130                 135                 140

Gly Gly Gly Ser Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys
145                 150                 155                 160

Lys Pro Gly Glu Ser Leu Arg Ile Ser Cys Lys Gly Ser Gly Tyr Thr
                165                 170                 175

Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Met Pro Gly Lys Gly
            180                 185                 190

Leu Glu Trp Met Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr
        195                 200                 205

Asn Gln Lys Phe Lys Asp His Val Thr Ile Ser Val Asp Lys Ser Ile
    210                 215                 220
```

Ser Thr Ala Tyr Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala
225 230 235 240

Met Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly
245 250 255

Thr Thr Val Thr Val Ser Ser
260

<210> 317
<211> 115
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 317
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15

Ser Leu Arg Ile Ser Cys Lys Gly Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Trp Met Asn Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
35 40 45

Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe
50 55 60

Lys Asp His Val Thr Ile Ser Val Asp Lys Ser Ile Ser Thr Ala Tyr
65 70 75 80

Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
85 90 95

Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser
115

<210> 318
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source

_SL
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 318
Asp Val Gln Leu Thr Gln Ser Pro Ser Phe Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 319
<211> 1458
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 319
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaagtgg tgctgaccca gtcgcccgca accctctctc tgtcgccggg agaacgcgcc 120

actctttcct gtcgggcgtc caagagcatc tcaaaggacc tcgcctggta ccagcagaag 180

cctggtcaag ccccgcggct gctgatctac tccggctcca cgctgcaatc aggaatccca 240

gccagatttt ccggttcggg gtcggggact gacttcacct tgaccattag ctcgctggaa 300

cctgaggact tcgccgtgta ttactgccag cagcacaaca agtacccgta caccttcgga 360

ggcggtacta aggtcgagat caaggggggt ggcggtagcg gaggaggggg ctccggcggc 420

ggcggctcag ggggcggagg aagcgaggtg cagctggtgc agagcggagc cgaggtcaag 480

aagcctggag aatccctgag gatcagctgc aaaggcagcg ggtatacctt cacctcctac 540

tggatgaatt gggtccgcca gatgcccgga aaaggcctgg agtggatggg acggattgac 600

ccctacgact cggaaaccca ttacaaccag aagttcaagg atcacgtgac catctccgtg 660

gacaagtcca tttccactgc gtacctccag tggtcaagcc tgaaggcctc cgacactgct 720

atgtactact gcgcacgcgg aaactgggat gattactggg gacagggaac aaccgtgact 780

gtgtcctcca ccactacccc agcaccgagg ccacccaccc cggctcctac catcgcctcc 840

cagcctctgt ccctgcgtcc ggaggcatgt agacccgcag ctggtggggc cgtgcatacc 900

cggggtcttg acttcgcctg cgatatctac atttgggccc ctctggctgg tacttgcggg 960

gtcctgctgc tttcactcgt gatcactctt tactgtaagc gcggtcggaa gaagctgctg 1020

tacatcttta agcaaccctt catgaggcct gtgcagacta ctcaagagga ggacggctgt 1080

tcatgccggt tcccagagga ggaggaaggc ggctgcgaac tgcgcgtgaa attcagccgc 1140

agcgcagatg ctccagccta caagcagggg cagaaccagc tctacaacga actcaatctt 1200

ggtcggagag aggagtacga cgtgctggac aagcggagag gacgggaccc agaaatgggc 1260

gggaagccgc gcagaaagaa tccccaagag ggcctgtaca acgagctcca aaaggataag 1320

atggcagaag cctatagcga gattggtatg aaaggggaac gcagaagagg caaaggccac 1380

gacggactgt accagggact cagcaccgcc accaaggaca cctatgacgc tcttcacatg 1440

caggccctgc cgcctcgg 1458

<210> 320
<211> 486
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 320
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Val Val Leu Thr Gln Ser Pro Ala Thr Leu
20 25 30

Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Lys
35 40 45

Ser Ile Ser Lys Asp Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala
50 55 60

Pro Arg Leu Leu Ile Tyr Ser Gly Ser Thr Leu Gln Ser Gly Ile Pro
65 70 75 80

Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile

_SL

85 90 95

Ser Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln His
100 105 110

Asn Lys Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
130 135 140

Gly Gly Gly Ser Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys
145 150 155 160

Lys Pro Gly Glu Ser Leu Arg Ile Ser Cys Lys Gly Ser Gly Tyr Thr
165 170 175

Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Met Pro Gly Lys Gly
180 185 190

Leu Glu Trp Met Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr
195 200 205

Asn Gln Lys Phe Lys Asp His Val Thr Ile Ser Val Asp Lys Ser Ile
210 215 220

Ser Thr Ala Tyr Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala
225 230 235 240

Met Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly
245 250 255

Thr Thr Val Thr Val Ser Ser Thr Thr Thr Pro Ala Pro Arg Pro Pro
260 265 270

Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu
275 280 285

Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
290 295 300

Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly
305 310 315 320

Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg
325 330 335

_SL
Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln
            340   345   350

Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu
        355   360   365

Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
    370   375   380

Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
385   390   395   400

Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
                405   410   415

Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
            420   425   430

Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
        435   440   445

Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
    450   455   460

Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
465   470   475   480

Gln Ala Leu Pro Pro Arg
                485

<210> 321
<211> 263
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 321
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1   5   10   15

His Ala Ala Arg Pro Glu Val Val Leu Thr Gln Ser Pro Ala Thr Leu
            20   25   30

Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Lys
        35   40   45

_SL
Ser Ile Ser Lys Asp Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala
50 55 60

Pro Arg Leu Leu Ile Tyr Ser Gly Ser Thr Leu Gln Ser Gly Ile Pro
65 70 75 80

Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile
85 90 95

Ser Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln His
100 105 110

Asn Lys Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
130 135 140

Gly Gly Gly Ser Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys
145 150 155 160

Lys Pro Gly Glu Ser Leu Arg Ile Ser Cys Lys Gly Ser Gly Tyr Thr
165 170 175

Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Met Pro Gly Lys Gly
180 185 190

Leu Glu Trp Met Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr
195 200 205

Asn Gln Lys Phe Lys Asp His Val Thr Ile Ser Val Asp Lys Ser Ile
210 215 220

Ser Thr Ala Tyr Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala
225 230 235 240

Met Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly
245 250 255

Thr Thr Val Thr Val Ser Ser
260

<210> 322
<211> 115
<212> PRT
<213> Artificial Sequence

<220>
<221> source

_SL
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 322
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15

Ser Leu Arg Ile Ser Cys Lys Gly Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Trp Met Asn Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
35 40 45

Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe
50 55 60

Lys Asp His Val Thr Ile Ser Val Asp Lys Ser Ile Ser Thr Ala Tyr
65 70 75 80

Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
85 90 95

Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser
115

<210> 323
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 323
Glu Val Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45

Tyr Ser Gly Ser Thr Leu Gln Ser Gly Ile Pro Ala Arg Phe Ser Gly
50 55 60

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                                            _SL
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
65                  70                  75                  80


Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr
                85                  90                  95


Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            100                 105


<210> 324
<211> 1458
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 324
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg       60

cccgacgtcg tgatgaccca gtcaccggca ttcctgtccg tgactcccgg agaaaaggtc      120

acgattactt gccgggcgtc caagagcatc tccaaggacc tcgcctggta ccaacagaag      180

ccggaccagg cccctaagct gttgatctac tcggggtcca cccttcaatc gggagtgcca      240

tcgcggttta gcggttcggg ttctgggacc gacttcactt tcaccatctc ctcactggaa      300

gccgaggatg ccgccactta ctactgtcag cagcacaaca agtatccgta caccttcgga      360

ggcggtacca aagtggagat caaggggggt ggcggtagcg gaggaggggg ctccggcggc      420

ggcggctcag ggggcggagg aagcgaggtg cagctggtgc agagcggagc cgaggtcaag      480

aagcctggag aatccctgag gatcagctgc aaaggcagcg ggtatacctt cacctcctac      540

tggatgaatt gggtccgcca gatgcccgga aaaggcctgg agtggatggg acggattgac      600

ccctacgact cggaaaccca ttacaaccag aagttcaagg atcacgtgac catctccgtg      660

gacaagtcca tttccactgc gtacctccag tggtcaagcc tgaaggcctc cgacactgct      720

atgtactact gcgcacgcgg aaactgggat gattactggg gacagggaac aaccgtgact      780

gtgtcctcca ccactacccc agcaccgagg ccacccaccc cggctcctac catcgcctcc      840

cagcctctgt ccctgcgtcc ggaggcatgt agacccgcag ctggtggggc cgtgcatacc      900

cggggtcttg acttcgcctg cgatatctac atttgggccc ctctggctgg tacttgcggg      960

gtcctgctgc tttcactcgt gatcactctt tactgtaagc gcggtcggaa gaagctgctg     1020

tacatcttta agcaaccctt catgaggcct gtgcagacta ctcaagagga ggacggctgt     1080

tcatgccggt tcccagagga ggaggaaggc ggctgcgaac tgcgcgtgaa attcagccgc     1140

agcgcagatg ctccagccta caagcagggg cagaaccagc tctacaacga actcaatctt     1200
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ggtcggagag aggagtacga cgtgctggac aagcggagag gacgggaccc agaaatgggc 1260

gggaagccgc gcagaaagaa tccccaagag ggcctgtaca acgagctcca aaaggataag 1320

atggcagaag cctatagcga gattggtatg aaaggggaac gcagaagagg caaaggccac 1380

gacggactgt accagggact cagcaccgcc accaaggaca cctatgacgc tcttcacatg 1440

caggccctgc cgcctcgg 1458

<210> 325
<211> 486
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 325
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Asp Val Val Met Thr Gln Ser Pro Ala Phe Leu
20 25 30

Ser Val Thr Pro Gly Glu Lys Val Thr Ile Thr Cys Arg Ala Ser Lys
35 40 45

Ser Ile Ser Lys Asp Leu Ala Trp Tyr Gln Gln Lys Pro Asp Gln Ala
50 55 60

Pro Lys Leu Leu Ile Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro
65 70 75 80

Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile
85 90 95

Ser Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln His
100 105 110

Asn Lys Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
130 135 140

Gly Gly Gly Ser Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys
145 150 155 160

Lys Pro Gly Glu Ser Leu Arg Ile Ser Cys Lys Gly Ser Gly Tyr Thr

_SL

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                165                 170                 175

Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Met Pro Gly Lys Gly
            180                 185                 190

Leu Glu Trp Met Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr
        195                 200                 205

Asn Gln Lys Phe Lys Asp His Val Thr Ile Ser Val Asp Lys Ser Ile
    210                 215                 220

Ser Thr Ala Tyr Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala
225                 230                 235                 240

Met Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly
                245                 250                 255

Thr Thr Val Thr Val Ser Ser Thr Thr Thr Pro Ala Pro Arg Pro Pro
            260                 265                 270

Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu
        275                 280                 285

Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
    290                 295                 300

Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly
305                 310                 315                 320

Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg
                325                 330                 335

Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln
            340                 345                 350

Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu
        355                 360                 365

Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
    370                 375                 380

Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
385                 390                 395                 400

Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
                405                 410                 415
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_SL
Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
420 425 430

Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
435 440 445

Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
450 455 460

Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
465 470 475 480

Gln Ala Leu Pro Pro Arg
485

<210> 326
<211> 263
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 326
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Asp Val Val Met Thr Gln Ser Pro Ala Phe Leu
20 25 30

Ser Val Thr Pro Gly Glu Lys Val Thr Ile Thr Cys Arg Ala Ser Lys
35 40 45

Ser Ile Ser Lys Asp Leu Ala Trp Tyr Gln Gln Lys Pro Asp Gln Ala
50 55 60

Pro Lys Leu Leu Ile Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro
65 70 75 80

Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile
85 90 95

Ser Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln His
100 105 110

Asn Lys Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
115 120 125

_SL
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
130 135 140

Gly Gly Gly Ser Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys
145 150 155 160

Lys Pro Gly Glu Ser Leu Arg Ile Ser Cys Lys Gly Ser Gly Tyr Thr
165 170 175

Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Met Pro Gly Lys Gly
180 185 190

Leu Glu Trp Met Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr
195 200 205

Asn Gln Lys Phe Lys Asp His Val Thr Ile Ser Val Asp Lys Ser Ile
210 215 220

Ser Thr Ala Tyr Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala
225 230 235 240

Met Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly
245 250 255

Thr Thr Val Thr Val Ser Ser
260

<210> 327
<211> 115
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 327
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15

Ser Leu Arg Ile Ser Cys Lys Gly Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Trp Met Asn Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
35 40 45

Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe
50 55 60

_SL
Lys Asp His Val Thr Ile Ser Val Asp Lys Ser Ile Ser Thr Ala Tyr
65 70 75 80

Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
85 90 95

Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser
115

<210> 328
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 328
Asp Val Val Met Thr Gln Ser Pro Ala Phe Leu Ser Val Thr Pro Gly
1 5 10 15

Glu Lys Val Thr Ile Thr Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Asp Gln Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Glu Ala
65 70 75 80

Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 329
<211> 1458
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

polynucleotide"

<400> 329
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgacgtgg tcatgactca gtccccggac tcactcgcgg tgtcgcttgg agagagagcg 120

accatcaact gtcgggcctc aaagagcatc agcaaggacc tggcctggta ccagcagaag 180

ccgggacagc cgccaaagct gctgatctac tccgggtcca ccttgcaatc tggtgtccct 240

gaccggttct ccggttccgg gtcgggtacc gacttcacgc tcactatttc gtcgctgcaa 300

gccgaagatg tggccgtgta ctattgccaa cagcacaaca agtaccccta cacttttggc 360

ggaggcacca aggtggaaat caaggggggt ggcggtagcg gaggaggggg ctccggcggc 420

ggcggctcag ggggcggagg aagcgaggtg cagctggtgc agagcggagc cgaggtcaag 480

aagcctggag aatccctgag gatcagctgc aaaggcagcg ggtatacctt cacctcctac 540

tggatgaatt gggtccgcca gatgcccgga aaaggcctgg agtggatggg acggattgac 600

ccctacgact cggaaaccca ttacaaccag aagttcaagg atcacgtgac catctccgtg 660

gacaagtcca tttccactgc gtacctccag tggtcaagcc tgaaggcctc cgacactgct 720

atgtactact gcgcacgcgg aaactgggat gattactggg gacagggaac aaccgtgact 780

gtgtcctcca ccactacccc agcaccgagg ccacccaccc cggctcctac catcgcctcc 840

cagcctctgt ccctgcgtcc ggaggcatgt agacccgcag ctggtggggc cgtgcatacc 900

cggggtcttg acttcgcctg cgatatctac atttgggccc ctctggctgg tacttgcggg 960

gtcctgctgc tttcactcgt gatcactctt tactgtaagc gcggtcggaa gaagctgctg 1020

tacatcttta agcaaccctt catgaggcct gtgcagacta ctcaagagga ggacggctgt 1080

tcatgccggt tcccagagga ggaggaaggc ggctgcgaac tgcgcgtgaa attcagccgc 1140

agcgcagatg ctccagccta caagcagggg cagaaccagc tctacaacga actcaatctt 1200

ggtcggagag aggagtacga cgtgctggac aagcggagag gacgggaccc agaaatgggc 1260

gggaagccgc gcagaaagaa tccccaagag ggcctgtaca acgagctcca aaaggataag 1320

atggcagaag cctatagcga gattggtatg aaaggggaac gcagaagagg caaaggccac 1380

gacggactgt accagggact cagcaccgcc accaaggaca cctatgacgc tcttcacatg 1440

caggccctgc cgcctcgg 1458

<210> 330
<211> 486
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 330
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Asp Val Val Met Thr Gln Ser Pro Asp Ser Leu
20 25 30

Ala Val Ser Leu Gly Glu Arg Ala Thr Ile Asn Cys Arg Ala Ser Lys
35 40 45

Ser Ile Ser Lys Asp Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro
50 55 60

Pro Lys Leu Leu Ile Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro
65 70 75 80

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile
85 90 95

Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln His
100 105 110

Asn Lys Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
130 135 140

Gly Gly Gly Ser Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys
145 150 155 160

Lys Pro Gly Glu Ser Leu Arg Ile Ser Cys Lys Gly Ser Gly Tyr Thr
165 170 175

Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Met Pro Gly Lys Gly
180 185 190

Leu Glu Trp Met Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr
195 200 205

Asn Gln Lys Phe Lys Asp His Val Thr Ile Ser Val Asp Lys Ser Ile
210 215 220

Ser Thr Ala Tyr Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala
225 230 235 240

Met Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly

_SL

245 250 255

Thr Thr Val Thr Val Ser Ser Thr Thr Thr Pro Ala Pro Arg Pro Pro
260 265 270

Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu
275 280 285

Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
290 295 300

Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly
305 310 315 320

Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg
325 330 335

Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln
340 345 350

Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu
355 360 365

Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
370 375 380

Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
385 390 395 400

Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
405 410 415

Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
420 425 430

Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
435 440 445

Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
450 455 460

Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
465 470 475 480

Gln Ala Leu Pro Pro Arg
485

<210> 331
<211> 263
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 331

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15

His Ala Ala Arg Pro Asp Val Val Met Thr Gln Ser Pro Asp Ser Leu
            20                  25                  30

Ala Val Ser Leu Gly Glu Arg Ala Thr Ile Asn Cys Arg Ala Ser Lys
        35                  40                  45

Ser Ile Ser Lys Asp Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro
    50                  55                  60

Pro Lys Leu Leu Ile Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro
65                  70                  75                  80

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile
                85                  90                  95

Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln His
            100                 105                 110

Asn Lys Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
    130                 135                 140

Gly Gly Gly Ser Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys
145                 150                 155                 160

Lys Pro Gly Glu Ser Leu Arg Ile Ser Cys Lys Gly Ser Gly Tyr Thr
                165                 170                 175

Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Met Pro Gly Lys Gly
            180                 185                 190

Leu Glu Trp Met Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr
        195                 200                 205
```

_SL
Asn Gln Lys Phe Lys Asp His Val Thr Ile Ser Val Asp Lys Ser Ile
    210   215   220

Ser Thr Ala Tyr Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala
225   230   235   240

Met Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly
                245   250   255

Thr Thr Val Thr Val Ser Ser
            260

<210> 332
<211> 115
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 332
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1   5   10   15

Ser Leu Arg Ile Ser Cys Lys Gly Ser Gly Tyr Thr Phe Thr Ser Tyr
            20   25   30

Trp Met Asn Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
        35   40   45

Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe
    50   55   60

Lys Asp His Val Thr Ile Ser Val Asp Lys Ser Ile Ser Thr Ala Tyr
65   70   75   80

Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
                85   90   95

Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
            100   105   110

Val Ser Ser
        115

<210> 333
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 333
Asp Val Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Glu Arg Ala Thr Ile Asn Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile
35 40 45

Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro Asp Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala
65 70 75 80

Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 334
<211> 1458
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 334
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaagtgc agctcgtcga gagcggaggg ggactggtgc agcccggagg aagcctgagg 120

ctgtcctgcg ctgcctccgg ctacaccttc acctcctact ggatgaactg ggtcagacag 180

gcacctggaa agggactggt ctgggtgtcg cgcattgacc cctacgactc cgaaacccat 240

tacaatcaga aattcaagga ccgcttcacc atctccgtgg acaaagccaa gagcaccgcg 300

tacctccaaa tgaactccct gcgcgctgag gatacagcag tgtactattg cgcccgggga 360

aactgggatg attactgggg ccagggaact actgtgactg tgtcatccgg gggtggcggt 420

agcggaggag ggggctccgg cggcggcggc tcagggggcg gaggaagcga cgtgcagctc 480

acccagtcgc cctcatttct gtcggcctca gtgggagaca gagtgaccat tacttgtcgg 540

gcctccaaga gcatctccaa ggacctggcc tggtatcagc agaagccagg aaaggcgcct 600

aagttgctca tctactcggg gtcgaccctg caatctggcg tgccgtcccg gttctccggt 660

tcgggaagcg gtaccgaatt cacccttact atctcctccc tgcaaccgga ggacttcgcc 720

acctactact gccaacagca caacaagtac ccgtacactt tcgggggtgg cacgaaggtc 780

gaaatcaaga ccactacccc agcaccgagg ccacccaccc cggctcctac catcgcctcc 840

cagcctctgt ccctgcgtcc ggaggcatgt agacccgcag ctggtggggc cgtgcatacc 900

cggggtcttg acttcgcctg cgatatctac atttgggccc ctctggctgg tacttgcggg 960

gtcctgctgc tttcactcgt gatcactctt tactgtaagc gcggtcggaa gaagctgctg 1020

tacatcttta agcaaccctt catgaggcct gtgcagacta ctcaagagga ggacggctgt 1080

tcatgccggt tcccagagga ggaggaaggc ggctgcgaac tgcgcgtgaa attcagccgc 1140

agcgcagatg ctccagccta caagcagggg cagaaccagc tctacaacga actcaatctt 1200

ggtcggagag aggagtacga cgtgctggac aagcggagag gacgggaccc agaaatgggc 1260

gggaagccgc gcagaaagaa tccccaagag ggcctgtaca acgagctcca aaaggataag 1320

atggcagaag cctatagcga gattggtatg aaaggggaac gcagaagagg caaaggccac 1380

gacggactgt accagggact cagcaccgcc accaaggaca cctatgacgc tcttcacatg 1440

caggccctgc cgcctcgg 1458

<210> 335
<211> 486
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 335
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
20 25 30

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr
35 40 45

Thr Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys
50 55 60

Gly Leu Val Trp Val Ser Arg Ile Asp Pro Tyr Asp Ser Glu Thr His
65 70 75 80

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Tyr Asn Gln Lys Phe Lys Asp Arg Phe Thr Ile Ser Val Asp Lys Ala
                85                  90                  95

Lys Ser Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln
        115                 120                 125

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
    130                 135                 140

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Gln Leu
145                 150                 155                 160

Thr Gln Ser Pro Ser Phe Leu Ser Ala Ser Val Gly Asp Arg Val Thr
                165                 170                 175

Ile Thr Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp Leu Ala Trp Tyr
            180                 185                 190

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Gly Ser
        195                 200                 205

Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
    210                 215                 220

Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
225                 230                 235                 240

Thr Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr Thr Phe Gly Gly
                245                 250                 255

Gly Thr Lys Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro
            260                 265                 270

Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu
        275                 280                 285

Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
    290                 295                 300

Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly
305                 310                 315                 320

Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg
```

_SL
325 330 335

Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln
340 345 350

Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu
355 360 365

Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
370 375 380

Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
385 390 395 400

Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
405 410 415

Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
420 425 430

Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
435 440 445

Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
450 455 460

Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
465 470 475 480

Gln Ala Leu Pro Pro Arg
485

<210> 336
<211> 263
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 336
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
20 25 30

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr

_SL

35 40 45

Thr Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys
50 55 60

Gly Leu Val Trp Val Ser Arg Ile Asp Pro Tyr Asp Ser Glu Thr His
65 70 75 80

Tyr Asn Gln Lys Phe Lys Asp Arg Phe Thr Ile Ser Val Asp Lys Ala
85 90 95

Lys Ser Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln
115 120 125

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
130 135 140

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Gln Leu
145 150 155 160

Thr Gln Ser Pro Ser Phe Leu Ser Ala Ser Val Gly Asp Arg Val Thr
165 170 175

Ile Thr Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp Leu Ala Trp Tyr
180 185 190

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Gly Ser
195 200 205

Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
210 215 220

Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
225 230 235 240

Thr Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr Thr Phe Gly Gly
245 250 255

Gly Thr Lys Val Glu Ile Lys
260

<210> 337
<211> 115
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 337
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Val Trp Val
35 40 45

Ser Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Phe Thr Ile Ser Val Asp Lys Ala Lys Ser Thr Ala Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser
115

<210> 338
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 338
Asp Val Gln Leu Thr Gln Ser Pro Ser Phe Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly

_SL
50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 339
<211> 1458
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 339
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaagtgc agctcgtcga gagcggaggg ggactggtgc agcccggagg aagcctgagg 120

ctgtcctgcg ctgcctccgg ctacaccttc acctcctact ggatgaactg ggtcagacag 180

gcacctggaa agggactggt ctgggtgtcg cgcattgacc cctacgactc cgaaacccat 240

tacaatcaga aattcaagga ccgcttcacc atctccgtgg acaaagccaa gagcaccgcg 300

tacctccaaa tgaactccct gcgcgctgag gatacagcag tgtactattg cgcccgggga 360

aactgggatg attactgggg ccagggaact actgtgactg tgtcatccgg gggtggcggt 420

agcggaggag ggggctccgg cggcggcggc tcaggggcg gaggaagcga agtggtgctg 480

acccagtcgc ccgcaaccct ctctctgtcg ccgggagaac gcgccactct ttcctgtcgg 540

gcgtccaaga gcatctcaaa ggacctcgcc tggtaccagc agaagcctgg tcaagccccg 600

cggctgctga tctactccgg ctccacgctg caatcaggaa tcccagccag attttccggt 660

tcggggtcgg ggactgactt caccttgacc attagctcgc tggaacctga ggacttcgcc 720

gtgtattact gccagcagca caacaagtac ccgtacacct tcggaggcgg tactaaggtc 780

gagatcaaga ccactacccc agcaccgagg ccacccaccc cggctcctac catcgcctcc 840

cagcctctgt ccctgcgtcc ggaggcatgt agacccgcag ctggtggggc cgtgcatacc 900

cggggtcttg acttcgcctg cgatatctac atttgggccc ctctggctgg tacttgcggg 960

gtcctgctgc tttcactcgt gatcactctt tactgtaagc gcggtcggaa gaagctgctg 1020

tacatcttta agcaaccctt catgaggcct gtgcagacta ctcaagagga ggacggctgt 1080

tcatgccggt tcccagagga ggaggaaggc ggctgcgaac tgcgcgtgaa attcagccgc 1140

agcgcagatg ctccagccta caagcagggg cagaaccagc tctacaacga actcaatctt 1200

ggtcggagag aggagtacga cgtgctggac aagcggagag gacgggaccc agaaatgggc 1260

gggaagccgc gcagaaagaa tccccaagag ggcctgtaca acgagctcca aaaggataag 1320

atggcagaag cctatagcga gattggtatg aaaggggaac gcagaagagg caaaggccac 1380

gacggactgt accagggact cagcaccgcc accaaggaca cctatgacgc tcttcacatg 1440

caggccctgc cgcctcgg 1458

<210> 340
<211> 486
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 340
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
20 25 30

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr
35 40 45

Thr Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys
50 55 60

Gly Leu Val Trp Val Ser Arg Ile Asp Pro Tyr Asp Ser Glu Thr His
65 70 75 80

Tyr Asn Gln Lys Phe Lys Asp Arg Phe Thr Ile Ser Val Asp Lys Ala
85 90 95

Lys Ser Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln
115 120 125

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
130 135 140

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Val Leu
145 150 155 160

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Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr
                165                 170                 175

Leu Ser Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp Leu Ala Trp Tyr
            180                 185                 190

Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Ser Gly Ser
        195                 200                 205

Thr Leu Gln Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly
    210                 215                 220

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp Phe Ala
225                 230                 235                 240

Val Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr Thr Phe Gly Gly
                245                 250                 255

Gly Thr Lys Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro
            260                 265                 270

Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu
        275                 280                 285

Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
    290                 295                 300

Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly
305                 310                 315                 320

Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg
                325                 330                 335

Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln
            340                 345                 350

Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu
        355                 360                 365

Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
    370                 375                 380

Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
385                 390                 395                 400

Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
```

_SL
405 410 415

Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
420 425 430

Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
435 440 445

Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
450 455 460

Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
465 470 475 480

Gln Ala Leu Pro Pro Arg
485

<210> 341
<211> 263
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 341
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
20 25 30

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr
35 40 45

Thr Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys
50 55 60

Gly Leu Val Trp Val Ser Arg Ile Asp Pro Tyr Asp Ser Glu Thr His
65 70 75 80

Tyr Asn Gln Lys Phe Lys Asp Arg Phe Thr Ile Ser Val Asp Lys Ala
85 90 95

Lys Ser Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln

_SL
115 120 125

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
130 135 140

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Val Leu
145 150 155 160

Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr
165 170 175

Leu Ser Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp Leu Ala Trp Tyr
180 185 190

Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Ser Gly Ser
195 200 205

Thr Leu Gln Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly
210 215 220

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp Phe Ala
225 230 235 240

Val Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr Thr Phe Gly Gly
245 250 255

Gly Thr Lys Val Glu Ile Lys
260

<210> 342
<211> 115
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 342
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Val Trp Val
35 40 45

Ser Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe

_SL
50 55 60

Lys Asp Arg Phe Thr Ile Ser Val Asp Lys Ala Lys Ser Thr Ala Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser
115

<210> 343
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 343
Glu Val Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45

Tyr Ser Gly Ser Thr Leu Gln Ser Gly Ile Pro Ala Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
65 70 75 80

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 344
<211> 1458
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 344
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaagtgc agctcgtcga gagcggaggg ggactggtgc agcccggagg aagcctgagg 120

ctgtcctgcg ctgcctccgg ctacaccttc acctcctact ggatgaactg ggtcagacag 180

gcacctggaa agggactggt ctgggtgtcg cgcattgacc cctacgactc cgaaacccat 240

tacaatcaga aattcaagga ccgcttcacc atctccgtgg acaaagccaa gagcaccgcg 300

tacctccaaa tgaactccct gcgcgctgag gatacagcag tgtactattg cgcccgggga 360

aactgggatg attactgggg ccagggaact actgtgactg tgtcatccgg gggtggcggt 420

agcggaggag ggggctccgg cggcggcggc tcaggggcg gaggaagcga cgtcgtgatg 480

acccagtcac cggcattcct gtccgtgact cccggagaaa aggtcacgat tacttgccgg 540

gcgtccaaga gcatctccaa ggacctcgcc tggtaccaac agaagccgga ccaggcccct 600

aagctgttga tctactcggg gtccaccctt caatcgggag tgccatcgcg gtttagcggt 660

tcgggttctg ggaccgactt cactttcacc atctcctcac tggaagccga ggatgccgcc 720

acttactact gtcagcagca caacaagtat ccgtacacct tcggaggcgg taccaaagtg 780

gagatcaaga ccactacccc agcaccgagg ccacccaccc cggctcctac catcgcctcc 840

cagcctctgt ccctgcgtcc ggaggcatgt agacccgcag ctggtggggc cgtgcatacc 900

cggggtcttg acttcgcctg cgatatctac atttgggccc ctctggctgg tacttgcggg 960

gtcctgctgc tttcactcgt gatcactctt tactgtaagc gcggtcggaa gaagctgctg 1020

tacatcttta agcaaccctt catgaggcct gtgcagacta ctcaagagga ggacggctgt 1080

tcatgccggt tcccagagga ggaggaaggc ggctgcgaac tgcgcgtgaa attcagccgc 1140

agcgcagatg ctccagccta caagcagggg cagaaccagc tctacaacga actcaatctt 1200

ggtcggagag aggagtacga cgtgctggac aagcggagag gacgggaccc agaaatgggc 1260

gggaagccgc gcagaaagaa tccccaagag ggcctgtaca acgagctcca aaaggataag 1320

atggcagaag cctatagcga gattggtatg aaaggggaac gcagaagagg caaaggccac 1380

gacggactgt accagggact cagcaccgcc accaaggaca cctatgacgc tcttcacatg 1440

caggccctgc cgcctcgg 1458

<210> 345
<211> 486
<212> PRT
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 345
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
20 25 30

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr
35 40 45

Thr Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys
50 55 60

Gly Leu Val Trp Val Ser Arg Ile Asp Pro Tyr Asp Ser Glu Thr His
65 70 75 80

Tyr Asn Gln Lys Phe Lys Asp Arg Phe Thr Ile Ser Val Asp Lys Ala
85 90 95

Lys Ser Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln
115 120 125

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
130 135 140

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met
145 150 155 160

Thr Gln Ser Pro Ala Phe Leu Ser Val Thr Pro Gly Glu Lys Val Thr
165 170 175

Ile Thr Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp Leu Ala Trp Tyr
180 185 190

Gln Gln Lys Pro Asp Gln Ala Pro Lys Leu Leu Ile Tyr Ser Gly Ser
195 200 205

Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
210 215 220

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Glu Ala Glu Asp Ala Ala
225 230 235 240

```
Thr Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr Thr Phe Gly Gly
                245                 250                 255

Gly Thr Lys Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro
            260                 265                 270

Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu
        275                 280                 285

Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
    290                 295                 300

Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly
305                 310                 315                 320

Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg
                325                 330                 335

Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln
            340                 345                 350

Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu
        355                 360                 365

Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
    370                 375                 380

Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
385                 390                 395                 400

Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
                405                 410                 415

Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
            420                 425                 430

Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
        435                 440                 445

Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
    450                 455                 460

Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
465                 470                 475                 480

Gln Ala Leu Pro Pro Arg
```

<210> 346
<211> 263
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 346
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
20 25 30

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr
35 40 45

Thr Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys
50 55 60

Gly Leu Val Trp Val Ser Arg Ile Asp Pro Tyr Asp Ser Glu Thr His
65 70 75 80

Tyr Asn Gln Lys Phe Lys Asp Arg Phe Thr Ile Ser Val Asp Lys Ala
85 90 95

Lys Ser Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln
115 120 125

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
130 135 140

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met
145 150 155 160

Thr Gln Ser Pro Ala Phe Leu Ser Val Thr Pro Gly Glu Lys Val Thr
165 170 175

Ile Thr Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp Leu Ala Trp Tyr
180 185 190

Gln Gln Lys Pro Asp Gln Ala Pro Lys Leu Leu Ile Tyr Ser Gly Ser

_SL
195 200 205

Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
210 215 220

Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Glu Ala Glu Asp Ala Ala
225 230 235 240

Thr Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr Thr Phe Gly Gly
245 250 255

Gly Thr Lys Val Glu Ile Lys
260

<210> 347
<211> 115
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 347
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Val Trp Val
35 40 45

Ser Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Phe Thr Ile Ser Val Asp Lys Ala Lys Ser Thr Ala Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser
115

<210> 348

<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 348
Asp Val Val Met Thr Gln Ser Pro Ala Phe Leu Ser Val Thr Pro Gly
1 5 10 15

Glu Lys Val Thr Ile Thr Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Asp Gln Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Glu Ala
65 70 75 80

Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 349
<211> 1458
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 349
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaagtgc agctcgtcga gagcggaggg ggactggtgc agcccggagg aagcctgagg 120

ctgtcctgcg ctgcctccgg ctacaccttc acctcctact ggatgaactg ggtcagacag 180

gcacctggaa agggactggt ctgggtgtcg cgcattgacc cctacgactc cgaaacccat 240

tacaatcaga aattcaagga ccgcttcacc atctccgtgg acaaagccaa gagcaccgcg 300

tacctccaaa tgaactccct gcgcgctgag gatacagcag tgtactattg cgcccgggga 360

aactgggatg attactgggg ccagggaact actgtgactg tgtcatccgg gggtggcggt 420

agcggaggag ggggctccgg cggcggcggc tcaggggggcg gaggaagcga cgtggtcatg 480

actcagtccc cggactcact cgcggtgtcg cttggagaga gagcgaccat caactgtcgg 540

gcctcaaaga gcatcagcaa ggacctggcc tggtaccagc agaagccggg acagccgcca 600

aagctgctga tctactccgg gtccaccttg caatctggtg tccctgaccg gttctccggt 660

tccgggtcgg gtaccgactt cacgctcact atttcgtcgc tgcaagccga agatgtggcc 720

gtgtactatt gccaacagca caacaagtac ccctacactt ttggcggagg caccaaggtg 780

gaaatcaaga ccactacccc agcaccgagg ccacccaccc cggctcctac catcgcctcc 840

cagcctctgt ccctgcgtcc ggaggcatgt agacccgcag ctggtggggc cgtgcatacc 900

cggggtcttg acttcgcctg cgatatctac atttgggccc ctctggctgg tacttgcggg 960

gtcctgctgc tttcactcgt gatcactctt tactgtaagc gcggtcggaa gaagctgctg 1020

tacatcttta agcaaccctt catgaggcct gtgcagacta ctcaagagga ggacggctgt 1080

tcatgccggt tcccagagga ggaggaaggc ggctgcgaac tgcgcgtgaa attcagccgc 1140

agcgcagatg ctccagccta caagcagggg cagaaccagc tctacaacga actcaatctt 1200

ggtcggagag aggagtacga cgtgctggac aagcggagag gacgggaccc agaaatgggc 1260

gggaagccgc gcagaaagaa tccccaagag ggcctgtaca acgagctcca aaaggataag 1320

atggcagaag cctatagcga gattggtatg aaaggggaac gcagaagagg caaaggccac 1380

gacggactgt accagggact cagcaccgcc accaaggaca cctatgacgc tcttcacatg 1440

caggccctgc cgcctcgg 1458

<210> 350
<211> 486
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 350
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
20 25 30

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr
35 40 45

Thr Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys
50 55 60

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Gly Leu Val Trp Val Ser Arg Ile Asp Pro Tyr Asp Ser Glu Thr His
65                  70                  75                  80

Tyr Asn Gln Lys Phe Lys Asp Arg Phe Thr Ile Ser Val Asp Lys Ala
                85                  90                  95

Lys Ser Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln
        115                 120                 125

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
    130                 135                 140

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met
145                 150                 155                 160

Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly Glu Arg Ala Thr
                165                 170                 175

Ile Asn Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp Leu Ala Trp Tyr
            180                 185                 190

Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Ser Gly Ser
        195                 200                 205

Thr Leu Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly
    210                 215                 220

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala Glu Asp Val Ala
225                 230                 235                 240

Val Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr Thr Phe Gly Gly
                245                 250                 255

Gly Thr Lys Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro
            260                 265                 270

Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu
        275                 280                 285

Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
    290                 295                 300

Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly
305                 310                 315                 320
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Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg
                325                 330                 335

Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln
            340                 345                 350

Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu
        355                 360                 365

Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
    370                 375                 380

Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
385                 390                 395                 400

Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
                405                 410                 415

Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
            420                 425                 430

Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
        435                 440                 445

Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
    450                 455                 460

Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
465                 470                 475                 480

Gln Ala Leu Pro Pro Arg
                485
```

<210> 351
<211> 263
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 351

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15

His Ala Ala Arg Pro Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
            20                  25                  30
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```
Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr
        35                  40                  45

Thr Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys
    50                  55                  60

Gly Leu Val Trp Val Ser Arg Ile Asp Pro Tyr Asp Ser Glu Thr His
65                  70                  75                  80

Tyr Asn Gln Lys Phe Lys Asp Arg Phe Thr Ile Ser Val Asp Lys Ala
                85                  90                  95

Lys Ser Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln
        115                 120                 125

Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
    130                 135                 140

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met
145                 150                 155                 160

Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly Glu Arg Ala Thr
                165                 170                 175

Ile Asn Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp Leu Ala Trp Tyr
            180                 185                 190

Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Ser Gly Ser
        195                 200                 205

Thr Leu Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly
    210                 215                 220

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala Glu Asp Val Ala
225                 230                 235                 240

Val Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr Thr Phe Gly Gly
                245                 250                 255

Gly Thr Lys Val Glu Ile Lys
            260
```

<210> 352

<211> 115
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 352
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Val Trp Val
35 40 45

Ser Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Phe Thr Ile Ser Val Asp Lys Ala Lys Ser Thr Ala Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser
115

<210> 353
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 353
Asp Val Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Glu Arg Ala Thr Ile Asn Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile
35 40 45

Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro Asp Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala
65 70 75 80

Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 354
<211> 1458
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 354
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgacgtgc agctcaccca gtcgccctca tttctgtcgg cctcagtggg agacagagtg 120

accattactt gtcgggcctc caagagcatc tccaaggacc tggcctggta tcagcagaag 180

ccaggaaagg cgcctaagtt gctcatctac tcggggtcga ccctgcaatc tggcgtgccg 240

tcccggttct ccggttcggg aagcggtacc gaattcaccc ttactatctc ctccctgcaa 300

ccggaggact tcgccaccta ctactgccaa cagcacaaca agtacccgta cactttcggg 360

ggtggcacga aggtcgaaat caaggggggt ggcggtagcg gaggaggggg ctccggcggc 420

ggcggctcag ggggcggagg aagcgaagtg cagctcgtcg agagcggagg gggactggtg 480

cagcccggag gaagcctgag gctgtcctgc gctgcctccg gctacacctt cacctcctac 540

tggatgaact gggtcagaca ggcacctgga aagggactgg tctgggtgtc gcgcattgac 600

ccctacgact ccgaaaccca ttacaatcag aaattcaagg accgcttcac catctccgtg 660

gacaaagcca agagcaccgc gtacctccaa atgaactccc tgcgcgctga ggatacagca 720

gtgtactatt gcgcccgggg aaactgggat gattactggg gccagggaac tactgtgact 780

gtgtcatcca ccactacccc agcaccgagg ccacccaccc cggctcctac catcgcctcc 840

cagcctctgt ccctgcgtcc ggaggcatgt agacccgcag ctggtggggc cgtgcatacc 900

cggggtcttg acttcgcctg cgatatctac atttgggccc ctctggctgg tacttgcggg 960

gtcctgctgc tttcactcgt gatcactctt tactgtaagc gcggtcggaa gaagctgctg 1020

tacatcttta agcaaccctt catgaggcct gtgcagacta ctcaagagga ggacggctgt 1080

tcatgccggt tcccagagga ggaggaaggc ggctgcgaac tgcgcgtgaa attcagccgc 1140

agcgcagatg ctccagccta caagcagggg cagaaccagc tctacaacga actcaatctt 1200

ggtcggagag aggagtacga cgtgctggac aagcggagag gacgggaccc agaaatgggc 1260

gggaagccgc gcagaaagaa tccccaagag ggcctgtaca acgagctcca aaaggataag 1320

atggcagaag cctatagcga gattggtatg aaaggggaac gcagaagagg caaaggccac 1380

gacggactgt accagggact cagcaccgcc accaaggaca cctatgacgc tcttcacatg 1440

caggccctgc cgcctcgg 1458

<210> 355
<211> 486
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 355
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Asp Val Gln Leu Thr Gln Ser Pro Ser Phe Leu
20 25 30

Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Lys
35 40 45

Ser Ile Ser Lys Asp Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala
50 55 60

Pro Lys Leu Leu Ile Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro
65 70 75 80

Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile
85 90 95

Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln His
100 105 110

Asn Lys Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
130 135 140

```
Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val
145                 150                 155                 160

Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Thr
                165                 170                 175

Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly
            180                 185                 190

Leu Val Trp Val Ser Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr
        195                 200                 205

Asn Gln Lys Phe Lys Asp Arg Phe Thr Ile Ser Val Asp Lys Ala Lys
    210                 215                 220

Ser Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala
225                 230                 235                 240

Val Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly
                245                 250                 255

Thr Thr Val Thr Val Ser Ser Thr Thr Thr Pro Ala Pro Arg Pro Pro
            260                 265                 270

Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu
        275                 280                 285

Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
    290                 295                 300

Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly
305                 310                 315                 320

Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg
                325                 330                 335

Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln
            340                 345                 350

Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu
        355                 360                 365

Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
    370                 375                 380

Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
385                 390                 395                 400
```

Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
405 410 415

Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
420 425 430

Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
435 440 445

Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
450 455 460

Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
465 470 475 480

Gln Ala Leu Pro Pro Arg
485

<210> 356
<211> 263
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 356
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Asp Val Gln Leu Thr Gln Ser Pro Ser Phe Leu
20 25 30

Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Lys
35 40 45

Ser Ile Ser Lys Asp Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala
50 55 60

Pro Lys Leu Leu Ile Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro
65 70 75 80

Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile
85 90 95

Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln His
100 105 110

```
Asn Lys Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
    130                 135                 140

Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val
145                 150                 155                 160

Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Thr
                165                 170                 175

Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly
            180                 185                 190

Leu Val Trp Val Ser Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr
        195                 200                 205

Asn Gln Lys Phe Lys Asp Arg Phe Thr Ile Ser Val Asp Lys Ala Lys
    210                 215                 220

Ser Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala
225                 230                 235                 240

Val Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly
                245                 250                 255

Thr Thr Val Thr Val Ser Ser
            260
```

<210> 357
<211> 115
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 357

```
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30

Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Val Trp Val
        35                  40                  45
```

Ser Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Phe Thr Ile Ser Val Asp Lys Ala Lys Ser Thr Ala Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser
115

<210> 358
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 358
Asp Val Gln Leu Thr Gln Ser Pro Ser Phe Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 359
<211> 1458

<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 359
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaagtgg tgctgaccca gtcgcccgca accctctctc tgtcgccggg agaacgcgcc 120

actctttcct gtcgggcgtc caagagcatc tcaaaggacc tcgcctggta ccagcagaag 180

cctggtcaag ccccgcggct gctgatctac tccggctcca cgctgcaatc aggaatccca 240

gccagatttt ccggttcggg gtcggggact gacttcacct tgaccattag ctcgctggaa 300

cctgaggact tcgccgtgta ttactgccag cagcacaaca agtacccgta caccttcgga 360

ggcggtacta aggtcgagat caaggggggt ggcggtagcg gaggaggggg ctccggcggc 420

ggcggctcag ggggcggagg aagcgaagtg cagctcgtcg agagcggagg gggactggtg 480

cagcccggag gaagcctgag gctgtcctgc gctgcctccg gctacacctt cacctcctac 540

tggatgaact gggtcagaca ggcacctgga aagggactgg tctgggtgtc gcgcattgac 600

ccctacgact ccgaaaccca ttacaatcag aaattcaagg accgcttcac catctccgtg 660

gacaaagcca agagcaccgc gtacctccaa atgaactccc tgcgcgctga ggatacagca 720

gtgtactatt gcgcccgggg aaactgggat gattactggg gccagggaac tactgtgact 780

gtgtcatcca ccactacccc agcaccgagg ccacccaccc cggctcctac catcgcctcc 840

cagcctctgt ccctgcgtcc ggaggcatgt agacccgcag ctggtggggc cgtgcatacc 900

cggggtcttg acttcgcctg cgatatctac atttgggccc ctctggctgg tacttgcggg 960

gtcctgctgc tttcactcgt gatcactctt tactgtaagc gcggtcggaa gaagctgctg 1020

tacatcttta agcaaccctt catgaggcct gtgcagacta ctcaagagga ggacggctgt 1080

tcatgccggt tcccagagga ggaggaaggc ggctgcgaac tgcgcgtgaa attcagccgc 1140

agcgcagatg ctccagccta caagcagggg cagaaccagc tctacaacga actcaatctt 1200

ggtcggagag aggagtacga cgtgctggac aagcggagag gacgggaccc agaaatgggc 1260

gggaagccgc gcagaaagaa tccccaagag ggcctgtaca acgagctcca aaaggataag 1320

atggcagaag cctatagcga gattggtatg aaaggggaac gcagaagagg caaaggccac 1380

gacggactgt accagggact cagcaccgcc accaaggaca cctatgacgc tcttcacatg 1440

caggccctgc cgcctcgg 1458

<210> 360
<211> 486
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 360

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15

His Ala Ala Arg Pro Glu Val Val Leu Thr Gln Ser Pro Ala Thr Leu
            20                  25                  30

Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Lys
        35                  40                  45

Ser Ile Ser Lys Asp Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala
    50                  55                  60

Pro Arg Leu Leu Ile Tyr Ser Gly Ser Thr Leu Gln Ser Gly Ile Pro
65                  70                  75                  80

Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile
                85                  90                  95

Ser Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln His
            100                 105                 110

Asn Lys Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
    130                 135                 140

Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val
145                 150                 155                 160

Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Thr
                165                 170                 175

Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly
            180                 185                 190

Leu Val Trp Val Ser Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr
        195                 200                 205

Asn Gln Lys Phe Lys Asp Arg Phe Thr Ile Ser Val Asp Lys Ala Lys
    210                 215                 220
```

```
Ser Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala
225                 230                 235                 240

Val Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly
                245                 250                 255

Thr Thr Val Thr Val Ser Ser Thr Thr Thr Pro Ala Pro Arg Pro Pro
            260                 265                 270

Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu
        275                 280                 285

Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
    290                 295                 300

Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly
305                 310                 315                 320

Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg
                325                 330                 335

Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln
            340                 345                 350

Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu
        355                 360                 365

Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
    370                 375                 380

Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
385                 390                 395                 400

Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
                405                 410                 415

Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
            420                 425                 430

Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
        435                 440                 445

Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
    450                 455                 460

Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
465                 470                 475                 480
```

Gln Ala Leu Pro Pro Arg
485

<210> 361
<211> 263
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 361
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Val Val Leu Thr Gln Ser Pro Ala Thr Leu
20 25 30

Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Lys
35 40 45

Ser Ile Ser Lys Asp Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala
50 55 60

Pro Arg Leu Leu Ile Tyr Ser Gly Ser Thr Leu Gln Ser Gly Ile Pro
65 70 75 80

Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile
85 90 95

Ser Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln His
100 105 110

Asn Lys Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
130 135 140

Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val
145 150 155 160

Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Thr
165 170 175

Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly
180 185 190

Leu Val Trp Val Ser Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr
195 200 205

Asn Gln Lys Phe Lys Asp Arg Phe Thr Ile Ser Val Asp Lys Ala Lys
210 215 220

Ser Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala
225 230 235 240

Val Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly
245 250 255

Thr Thr Val Thr Val Ser Ser
260

<210> 362
<211> 115
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 362
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Val Trp Val
35 40 45

Ser Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Phe Thr Ile Ser Val Asp Lys Ala Lys Ser Thr Ala Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser
115

<210> 363
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 363
Glu Val Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45

Tyr Ser Gly Ser Thr Leu Gln Ser Gly Ile Pro Ala Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
65 70 75 80

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 364
<211> 1458
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 364
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgacgtcg tgatgaccca gtcaccggca ttcctgtccg tgactcccgg agaaaaggtc 120

acgattactt gccgggcgtc caagagcatc tccaaggacc tcgcctggta ccaacagaag 180

ccggaccagg cccctaagct gttgatctac tcggggtcca cccttcaatc gggagtgcca 240

tcgcggttta gcggttcggg ttctgggacc gacttcactt tcaccatctc ctcactggaa 300

gccgaggatg ccgccactta ctactgtcag cagcacaaca agtatccgta caccttcgga 360

ggcggtacca aagtggagat caaggggggt ggcggtagcg gaggaggggg ctccggcggc 420

ggcggctcag ggggcggagg aagcgaagtg cagctcgtcg agagcggagg gggactggtg 480

cagcccggag gaagcctgag gctgtcctgc gctgcctccg gctacacctt cacctcctac 540

tggatgaact gggtcagaca ggcacctgga aagggactgg tctgggtgtc gcgcattgac 600

ccctacgact ccgaaaccca ttacaatcag aaattcaagg accgcttcac catctccgtg 660

gacaaagcca agagcaccgc gtacctccaa atgaactccc tgcgcgctga ggatacagca 720

gtgtactatt gcgcccgggg aaactgggat gattactggg gccagggaac tactgtgact 780

gtgtcatcca ccactacccc agcaccgagg ccacccaccc cggctcctac catcgcctcc 840

cagcctctgt ccctgcgtcc ggaggcatgt agacccgcag ctggtggggc cgtgcatacc 900

cggggtcttg acttcgcctg cgatatctac atttgggccc ctctggctgg tacttgcggg 960

gtcctgctgc tttcactcgt gatcactctt tactgtaagc gcggtcggaa gaagctgctg 1020

tacatcttta agcaaccctt catgaggcct gtgcagacta ctcaagagga ggacggctgt 1080

tcatgccggt tcccagagga ggaggaaggc ggctgcgaac tgcgcgtgaa attcagccgc 1140

agcgcagatg ctccagccta caagcagggg cagaaccagc tctacaacga actcaatctt 1200

ggtcggagag aggagtacga cgtgctggac aagcggagag gacgggaccc agaaatgggc 1260

gggaagccgc gcagaaagaa tccccaagag ggcctgtaca acgagctcca aaaggataag 1320

atggcagaag cctatagcga gattggtatg aaaggggaac gcagaagagg caaaggccac 1380

gacggactgt accagggact cagcaccgcc accaaggaca cctatgacgc tcttcacatg 1440

caggccctgc cgcctcgg 1458

<210> 365
<211> 486
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 365
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Asp Val Val Met Thr Gln Ser Pro Ala Phe Leu
20 25 30

Ser Val Thr Pro Gly Glu Lys Val Thr Ile Thr Cys Arg Ala Ser Lys
35 40 45

```
                                                _SL
Ser Ile Ser Lys Asp Leu Ala Trp Tyr Gln Gln Lys Pro Asp Gln Ala
    50                  55                  60

Pro Lys Leu Leu Ile Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro
65                  70                  75                  80

Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile
                85                  90                  95

Ser Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln His
            100                 105                 110

Asn Lys Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
    130                 135                 140

Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val
145                 150                 155                 160

Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Thr
                165                 170                 175

Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly
            180                 185                 190

Leu Val Trp Val Ser Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr
        195                 200                 205

Asn Gln Lys Phe Lys Asp Arg Phe Thr Ile Ser Val Asp Lys Ala Lys
    210                 215                 220

Ser Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala
225                 230                 235                 240

Val Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly
                245                 250                 255

Thr Thr Val Thr Val Ser Ser Thr Thr Thr Pro Ala Pro Arg Pro Pro
            260                 265                 270

Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu
        275                 280                 285

Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
    290                 295                 300
```

```
Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly
305                 310                 315                 320

Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg
                325                 330                 335

Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln
            340                 345                 350

Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu
        355                 360                 365

Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
    370                 375                 380

Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
385                 390                 395                 400

Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
                405                 410                 415

Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
            420                 425                 430

Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
        435                 440                 445

Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
    450                 455                 460

Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
465                 470                 475                 480

Gln Ala Leu Pro Pro Arg
                485
```

<210> 366
<211> 263
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 366

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15
```

```
His Ala Ala Arg Pro Asp Val Val Met Thr Gln Ser Pro Ala Phe Leu
            20                  25                  30

Ser Val Thr Pro Gly Glu Lys Val Thr Ile Thr Cys Arg Ala Ser Lys
        35                  40                  45

Ser Ile Ser Lys Asp Leu Ala Trp Tyr Gln Gln Lys Pro Asp Gln Ala
    50                  55                  60

Pro Lys Leu Leu Ile Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro
65                  70                  75                  80

Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile
                85                  90                  95

Ser Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln His
            100                 105                 110

Asn Lys Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
    130                 135                 140

Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val
145                 150                 155                 160

Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Thr
                165                 170                 175

Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly
            180                 185                 190

Leu Val Trp Val Ser Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr
        195                 200                 205

Asn Gln Lys Phe Lys Asp Arg Phe Thr Ile Ser Val Asp Lys Ala Lys
    210                 215                 220

Ser Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala
225                 230                 235                 240

Val Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly
                245                 250                 255

Thr Thr Val Thr Val Ser Ser
            260
```

<210> 367
<211> 115
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 367
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Val Trp Val
35 40 45

Ser Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Phe Thr Ile Ser Val Asp Lys Ala Lys Ser Thr Ala Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser
115

<210> 368
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 368
Asp Val Val Met Thr Gln Ser Pro Ala Phe Leu Ser Val Thr Pro Gly
1 5 10 15

Glu Lys Val Thr Ile Thr Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp
20 25 30

_SL

Leu Ala Trp Tyr Gln Gln Lys Pro Asp Gln Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Glu Ala
65 70 75 80

Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 369
<211> 1458
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 369
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgacgtgg tcatgactca gtccccggac tcactcgcgg tgtcgcttgg agagagagcg 120

accatcaact gtcgggcctc aaagagcatc agcaaggacc tggcctggta ccagcagaag 180

ccgggacagc cgccaaagct gctgatctac tccgggtcca ccttgcaatc tggtgtccct 240

gaccggttct ccggttccgg gtcgggtacc gacttcacgc tcactatttc gtcgctgcaa 300

gccgaagatg tggccgtgta ctattgccaa cagcacaaca agtaccccta cacttttggc 360

ggaggcacca aggtggaaat caaggggggt ggcggtagcg gaggaggggg ctccggcggc 420

ggcggctcag ggggcggagg aagcgaagtg cagctcgtcg agagcggagg gggactggtg 480

cagcccggag gaagcctgag gctgtcctgc gctgcctccg gctacacctt cacctcctac 540

tggatgaact gggtcagaca ggcacctgga aagggactgg tctgggtgtc gcgcattgac 600

ccctacgact ccgaaaccca ttacaatcag aaattcaagg accgcttcac catctccgtg 660

gacaaagcca agagcaccgc gtacctccaa atgaactccc tgcgcgctga ggatacagca 720

gtgtactatt gcgcccgggg aaactgggat gattactggg gccagggaac tactgtgact 780

gtgtcatcca ccactacccc agcaccgagg ccacccaccc cggctcctac catcgcctcc 840

cagcctctgt ccctgcgtcc ggaggcatgt agacccgcag ctggtggggc cgtgcatacc 900

cggggtcttg acttcgcctg cgatatctac atttgggccc ctctggctgg tacttgcggg 960

gtcctgctgc tttcactcgt gatcactctt tactgtaagc gcggtcggaa gaagctgctg 1020

tacatcttta agcaaccctt catgaggcct gtgcagacta ctcaagagga ggacggctgt 1080

tcatgccggt tcccagagga ggaggaaggc ggctgcgaac tgcgcgtgaa attcagccgc 1140

agcgcagatg ctccagccta caagcagggg cagaaccagc tctacaacga actcaatctt 1200

ggtcggagag aggagtacga cgtgctggac aagcggagag gacgggaccc agaaatgggc 1260

gggaagccgc gcagaaagaa tccccaagag ggcctgtaca acgagctcca aaaggataag 1320

atggcagaag cctatagcga gattggtatg aaaggggaac gcagaagagg caaaggccac 1380

gacggactgt accagggact cagcaccgcc accaaggaca cctatgacgc tcttcacatg 1440

caggccctgc cgcctcgg 1458

<210> 370
<211> 486
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 370
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Asp Val Val Met Thr Gln Ser Pro Asp Ser Leu
20 25 30

Ala Val Ser Leu Gly Glu Arg Ala Thr Ile Asn Cys Arg Ala Ser Lys
35 40 45

Ser Ile Ser Lys Asp Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro
50 55 60

Pro Lys Leu Leu Ile Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro
65 70 75 80

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile
85 90 95

Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln His
100 105 110

Asn Lys Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
115 120 125

```
                                                    _SL
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
    130                 135                 140

Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val
145                 150                 155                 160

Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Thr
                165                 170                 175

Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly
            180                 185                 190

Leu Val Trp Val Ser Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr
        195                 200                 205

Asn Gln Lys Phe Lys Asp Arg Phe Thr Ile Ser Val Asp Lys Ala Lys
    210                 215                 220

Ser Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala
225                 230                 235                 240

Val Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly
                245                 250                 255

Thr Thr Val Thr Val Ser Ser Thr Thr Thr Pro Ala Pro Arg Pro Pro
            260                 265                 270

Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu
        275                 280                 285

Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
    290                 295                 300

Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly
305                 310                 315                 320

Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg
                325                 330                 335

Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln
            340                 345                 350

Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu
        355                 360                 365

Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
    370                 375                 380
```

Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
385 390 395 400

Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
405 410 415

Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
420 425 430

Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
435 440 445

Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
450 455 460

Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
465 470 475 480

Gln Ala Leu Pro Pro Arg
485

<210> 371
<211> 263
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 371
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Asp Val Val Met Thr Gln Ser Pro Asp Ser Leu
20 25 30

Ala Val Ser Leu Gly Glu Arg Ala Thr Ile Asn Cys Arg Ala Ser Lys
35 40 45

Ser Ile Ser Lys Asp Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro
50 55 60

Pro Lys Leu Leu Ile Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro
65 70 75 80

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile
85 90 95

Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln His
100 105 110

Asn Lys Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
130 135 140

Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val
145 150 155 160

Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Thr
165 170 175

Phe Thr Ser Tyr Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly
180 185 190

Leu Val Trp Val Ser Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr
195 200 205

Asn Gln Lys Phe Lys Asp Arg Phe Thr Ile Ser Val Asp Lys Ala Lys
210 215 220

Ser Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala
225 230 235 240

Val Tyr Tyr Cys Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly
245 250 255

Thr Thr Val Thr Val Ser Ser
260

<210> 372
<211> 115
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 372
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

```
Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Val Trp Val
        35                  40                  45

Ser Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe
    50                  55                  60

Lys Asp Arg Phe Thr Ile Ser Val Asp Lys Ala Lys Ser Thr Ala Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
            100                 105                 110

Val Ser Ser
        115


<210> 373
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 373
Asp Val Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
1               5                   10                  15

Glu Arg Ala Thr Ile Asn Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp
            20                  25                  30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro Asp Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala
65                  70                  75                  80

Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr
                85                  90                  95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            100                 105
```

<210> 374
<211> 729
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 374
caagtgcaac tcgtccaaag cggagcggaa gtcaagaaac ccggagcgag cgtgaaagtg 60

tcctgcaaag cctccggcta cacctttacg ggctactaca tgcactgggt gcgccaggca 120

ccaggacagg gtcttgaatg gatgggatgg atcaacccta attcgggcgg aactaactac 180

gcacagaagt tccaggggag agtgactctg actcgggata cctccatctc aactgtctac 240

atggaactct cccgcttgcg gtcagatgat acggcagtgt actactgcgc ccgcgacatg 300

aatatcctgg ctaccgtgcc gttcgacatc tggggacagg ggactatggt tactgtctca 360

tcgggcggtg gaggttcagg aggaggcggc tcgggaggcg gaggttcgga cattcagatg 420

acccagtccc catcctctct gtcggccagc gtcggagata gggtgaccat tacctgtcgg 480

gcctcgcaaa gcatctcctc gtacctcaac tggtatcagc aaaagccggg aaaggcgcct 540

aagctgctga tctacgccgc ttcgagcttg caaagcgggg tgccatccag attctcggga 600

tcaggctcag gaaccgactt caccctgacc gtgaacagcc tccagccgga ggactttgcc 660

acttactact gccagcaggg agactccgtg ccgcttactt tcgggggggg tacccgcctg 720

gagatcaag 729

<210> 375
<211> 243
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 375
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Asn Pro Asn Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe

_SL
50 55 60

Gln Gly Arg Val Thr Leu Thr Arg Asp Thr Ser Ile Ser Thr Val Tyr
65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Met Asn Ile Leu Ala Thr Val Pro Phe Asp Ile Trp Gly
100 105 110

Gln Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
115 120 125

Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro
130 135 140

Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
145 150 155 160

Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser
180 185 190

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
195 200 205

Leu Thr Val Asn Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Gly Asp Ser Val Pro Leu Thr Phe Gly Gly Gly Thr Arg Leu
225 230 235 240

Glu Ile Lys

<210> 376
<211> 1760
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 376
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtgc aactcgtcca aagcggagcg gaagtcaaga aacccggagc gagcgtgaaa 120

gtgtcctgca aagcctccgg ctacaccttt acgggctact acatgcactg ggtgcgccag 180

gcaccaggac agggtcttga atggatggga tggatcaacc ctaattcggg cggaactaac 240

tacgcacaga agttccaggg gagagtgact ctgactcggg atacctccat ctcaactgtc 300

tacatggaac tctcccgctt gcggtcagat gatacggcag tgtactactg cgcccgcgac 360

atgaatatcc tggctaccgt gccgttcgac atctggggac aggggactat ggttactgtc 420

tcatcgggcg gtggaggttc aggaggaggc ggctcgggag gcggaggttc ggacattcag 480

atgacccagt ccccatcctc tctgtcggcc agcgtcggag atagggtgac cattacctgt 540

cgggcctcgc aaagcatctc ctcgtacctc aactggtatc agcaaaagcc gggaaaggcg 600

cctaagctgc tgatctacgc cgcttcgagc ttgcaaagcg gggtgccatc cagattctcg 660

ggatcaggct caggaaccga cttcaccctg accgtgaaca gcctccagcc ggaggacttt 720

gccacttact actgccagca gggagactcc gtgccgctta ctttcggggg gggtacccgc 780

ctggagatca agaccactac cccagcaccg aggccaccca ccccggctcc taccatcgcc 840

tcccagcctc tgtccctgcg tccggaggca tgtagacccg cagctggtgg ggccgtgcat 900

acccggggtc ttgacttcgc ctgcgatatc tacatttggg cccctctggc tggtacttgc 960

ggggtcctgc tgctttcact cgtgatcact ctttactgta agcgcggtcg gaagaagctg 1020

ctgtacatct ttaagcaacc cttcatgagg cctgtgcaga ctactcaaga ggaggacggc 1080

tgttcttgcc ggttcccaga ggaggaggaa ggcggctgcg aactgcgcgt gaaattcagc 1140

cgcagcgcag acgctccagc ctacaagcag gggcagaacc agctctacaa cgaactcaat 1200

cttggtcgga gagaggagta cgacgtgctg gacaagcgga gaggacggga cccagaaatg 1260

ggcgggaagc cgcgcagaaa gaatccccaa gagggcctgt acaacgagct ccaaaaggat 1320

aagatggcag aagcctatag cgagattggt atgaaagggg aacgcagaag aggcaaaggc 1380

cacgacggac tgtaccaggg actcagcacc gccaccaagg acacctatga cgctcttcac 1440

atgcaggccc tgccgcctcg gtaagtcgac agctcgcttt cttgctgtcc aatttctatt 1500

aaaggttcct ttgttcccta agtccaacta ctaaactggg ggatattatg aagggccttg 1560

agcatctgga ttctgcctaa taaaaaacat ttattttcat tgctgcgtcg agagctcgct 1620

ttcttgctgt ccaatttcta ttaaaggttc ctttgttccc taagtccaac tactaaactg 1680

ggggatatta tgaagggcct tgagcatctg gattctgcct aataaaaaac atttattttc 1740

attgctgcct cgacgaattc 1760

<210> 377
<211> 729
<212> DNA

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 377
caagtccaac tcgttcaatc cggcgcagaa gtcaagaagc caggagcatc agtgaaagtg 60

tcctgcaaag cctcaggcta catcttcacg ggatactaca tccactgggt gcgccaggct 120

ccgggccagg gccttgagtg gatgggctgg atcaacccta actctggggg aaccaactac 180

gctcagaagt tccaggggag ggtcactatg actcgcgata cctccatctc cactgcgtac 240

atggaactct cgggactgag atccgacgat cctgccgtgt actactgcgc ccgggacatg 300

aacatcttgg cgaccgtgcc gtttgacatt tggggacagg gcaccctcgt cactgtgtcg 360

agcggtggag gaggctcggg gggtggcgga tcaggagggg gaggaagcga catccagctg 420

actcagagcc catcgtcgtt gtccgcgtcg gtgggggata gagtgaccat tacttgccgc 480

gccagccaga gcatctcatc atatctgaat tggtaccagc agaagcccgg aaaggcccca 540

aaactgctga tctacgctgc aagcagcctc caatcgggag tgccgtcacg gttctccggg 600

tccggttcgg gaactgactt taccctgacc gtgaattcgc tgcaaccgga ggatttcgcc 660

acgtactact gtcagcaagg agactccgtg ccgctgacct tcggtggagg caccaaggtc 720

gaaatcaag 729

<210> 378
<211> 243
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 378
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Tyr Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Asn Pro Asn Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr

_SL
65 70 75 80

Met Glu Leu Ser Gly Leu Arg Ser Asp Asp Pro Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Met Asn Ile Leu Ala Thr Val Pro Phe Asp Ile Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
115 120 125

Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro
130 135 140

Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
145 150 155 160

Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser
180 185 190

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
195 200 205

Leu Thr Val Asn Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Gly Asp Ser Val Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys

<210> 379
<211> 735
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 379
caagtccaac tccaacagtc aggcgcagaa gtgaaaaaga gcggtgcatc ggtgaaagtg 60

tcatgcaaag cctcgggcta caccttcact gactactata tgcactggct gcggcaggca 120

ccgggacagg gacttgagtg gatgggatgg atcaacccga attcagggga cactaactac 180

gcgcagaagt tccaggggag agtgaccctg acgagggaca cctcaatttc gaccgtctac 240

atggaattgt cgcgcctgag atcggacgat actgctgtgt actactgtgc ccgcgacatg 300

aacatcctcg cgactgtgcc ttttgatatc tggggacagg ggactatggt caccgtttcc 360

tccgcttccg gtggcggagg ctcgggaggc cgggcctccg gtggaggagg cagcgacatc 420

cagatgactc agagcccttc ctcgctgagc gcctcagtgg gagatcgcgt gaccatcact 480

tgccgggcca gccagtccat ttcgtcctac ctcaattggt accagcagaa gccgggaaag 540

gcgcccaagc tcttgatcta cgctgcgagc tccctgcaaa gcggggtgcc gagccgattc 600

tcgggttccg gctcgggaac cgacttcact ctgaccatct catccctgca accagaggac 660

tttgccacct actactgcca acaaggagat tctgtcccac tgacgttcgg cggaggaacc 720

aaggtcgaaa tcaag 735

<210> 380
<211> 245
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 380

Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Val Lys Lys Ser Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Tyr Met His Trp Leu Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Asn Pro Asn Ser Gly Asp Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Leu Thr Arg Asp Thr Ser Ile Ser Thr Val Tyr
65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Met Asn Ile Leu Ala Thr Val Pro Phe Asp Ile Trp Gly
100 105 110

Gln Gly Thr Met Val Thr Val Ser Ser Ala Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Arg Ala Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln
130 135 140

Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr
145 150 155 160

Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln
165 170 175

Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu
180 185 190

Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
195 200 205

Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr
210 215 220

Tyr Cys Gln Gln Gly Asp Ser Val Pro Leu Thr Phe Gly Gly Gly Thr
225 230 235 240

Lys Val Glu Ile Lys
245

<210> 381
<211> 243
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 381
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Asn Pro Asn Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

```
Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Asp Met Asn Ile Leu Ala Thr Val Pro Phe Asp Ile Trp Gly
            100                 105                 110

Gln Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
        115                 120                 125

Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro
    130                 135                 140

Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
145                 150                 155                 160

Ala Ser Gln Ser Ile Ser Thr Tyr Leu Asn Trp Tyr Gln Gln Lys Pro
                165                 170                 175

Gly Lys Ala Pro Asn Leu Leu Ile Tyr Ala Ala Phe Ser Leu Gln Ser
            180                 185                 190

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
        195                 200                 205

Leu Thr Ile Asn Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
    210                 215                 220

Gln Gln Gly Asp Ser Val Pro Leu Thr Phe Gly Gly Gly Thr Lys Leu
225                 230                 235                 240

Glu Ile Lys
```

<210> 382
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 382

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30
```

```
Trp Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe
    50                  55                  60

Lys Asp Arg Val Thr Met Thr Val Asp Lys Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
            100                 105                 110

Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115                 120                 125

Gly Ser Gly Gly Gly Gly Ser Asp Val Gln Leu Thr Gln Ser Pro Ser
    130                 135                 140

Phe Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala
145                 150                 155                 160

Ser Lys Ser Ile Ser Lys Asp Leu Ala Trp Tyr Gln Gln Lys Pro Gly
                165                 170                 175

Lys Ala Pro Lys Leu Leu Ile Tyr Ser Gly Ser Thr Leu Gln Ser Gly
            180                 185                 190

Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu
        195                 200                 205

Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln
    210                 215                 220

Gln His Asn Lys Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu
225                 230                 235                 240

Ile Lys
```

<210> 383
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 383

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                  10                  15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30

Trp Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe
    50                  55                  60

Lys Asp Arg Val Thr Met Thr Val Asp Lys Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
            100                 105                 110

Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115                 120                 125

Gly Ser Gly Gly Gly Gly Ser Glu Val Val Leu Thr Gln Ser Pro Ala
    130                 135                 140

Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala
145                 150                 155                 160

Ser Lys Ser Ile Ser Lys Asp Leu Ala Trp Tyr Gln Gln Lys Pro Gly
                165                 170                 175

Gln Ala Pro Arg Leu Leu Ile Tyr Ser Gly Ser Thr Leu Gln Ser Gly
            180                 185                 190

Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
        195                 200                 205

Thr Ile Ser Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln
    210                 215                 220

Gln His Asn Lys Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu
```

_SL
225 230 235 240

Ile Lys

<210> 384
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 384
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Trp Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Val Thr Met Thr Val Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln Ser Pro Ala
130 135 140

Phe Leu Ser Val Thr Pro Gly Glu Lys Val Thr Ile Thr Cys Arg Ala
145 150 155 160

Ser Lys Ser Ile Ser Lys Asp Leu Ala Trp Tyr Gln Gln Lys Pro Asp
165 170 175

Gln Ala Pro Lys Leu Leu Ile Tyr Ser Gly Ser Thr Leu Gln Ser Gly

_SL
180 185 190

Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Phe
195 200 205

Thr Ile Ser Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln
210 215 220

Gln His Asn Lys Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu
225 230 235 240

Ile Lys

<210> 385
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 385
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Trp Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Val Thr Met Thr Val Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln Ser Pro Asp

_SL
130 135 140

Ser Leu Ala Val Ser Leu Gly Glu Arg Ala Thr Ile Asn Cys Arg Ala
145 150 155 160

Ser Lys Ser Ile Ser Lys Asp Leu Ala Trp Tyr Gln Gln Lys Pro Gly
165 170 175

Gln Pro Pro Lys Leu Leu Ile Tyr Ser Gly Ser Thr Leu Gln Ser Gly
180 185 190

Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
195 200 205

Thr Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln
210 215 220

Gln His Asn Lys Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu
225 230 235 240

Ile Lys

<210> 386
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 386
Asp Val Gln Leu Thr Gln Ser Pro Ser Phe Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr

_SL
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser
100 105 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln
115 120 125

Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser
130 135 140

Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr Trp
145 150 155 160

Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met Gly
165 170 175

Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe Lys
180 185 190

Asp Arg Val Thr Met Thr Val Asp Lys Ser Thr Ser Thr Ala Tyr Met
195 200 205

Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala
210 215 220

Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val
225 230 235 240

Ser Ser

<210> 387
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 387
Glu Val Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile

_SL

35 40 45

Tyr Ser Gly Ser Thr Leu Gln Ser Gly Ile Pro Ala Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
65 70 75 80

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser
100 105 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln
115 120 125

Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser
130 135 140

Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr Trp
145 150 155 160

Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met Gly
165 170 175

Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe Lys
180 185 190

Asp Arg Val Thr Met Thr Val Asp Lys Ser Thr Ser Thr Ala Tyr Met
195 200 205

Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala
210 215 220

Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val
225 230 235 240

Ser Ser

<210> 388
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

_SL

polypeptide"

<400> 388

```
Asp Val Val Met Thr Gln Ser Pro Ala Phe Leu Ser Val Thr Pro Gly
1               5                  10                  15

Glu Lys Val Thr Ile Thr Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp
            20                  25                  30

Leu Ala Trp Tyr Gln Gln Lys Pro Asp Gln Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Glu Ala
65                  70                  75                  80

Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr
                85                  90                  95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser
            100                 105                 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln
        115                 120                 125

Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser
    130                 135                 140

Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr Trp
145                 150                 155                 160

Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met Gly
                165                 170                 175

Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe Lys
            180                 185                 190

Asp Arg Val Thr Met Thr Val Asp Lys Ser Thr Ser Thr Ala Tyr Met
        195                 200                 205

Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala
    210                 215                 220

Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val
225                 230                 235                 240
```

Ser Ser

<210> 389
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 389

```
Asp Val Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
1               5                  10                  15

Glu Arg Ala Thr Ile Asn Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp
            20                  25                  30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro Asp Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala
65                  70                  75                  80

Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr
                85                  90                  95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser
            100                 105                 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln
        115                 120                 125

Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser
    130                 135                 140

Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr Trp
145                 150                 155                 160

Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met Gly
                165                 170                 175

Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe Lys
            180                 185                 190
```

```
                                                _SL
Asp Arg Val Thr Met Thr Val Asp Lys Ser Thr Ser Thr Ala Tyr Met
        195                 200                 205


Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala
    210                 215                 220


Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val
225                 230                 235                 240


Ser Ser



<210> 390
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 390
Gln Val Gln Leu Val Gln Ser Gly Ser Glu Leu Lys Lys Pro Gly Ala
1               5                   10                  15


Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30


Trp Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45


Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe
    50                  55                  60


Lys Asp Arg Phe Val Phe Ser Val Asp Lys Ser Val Ser Thr Ala Tyr
65                  70                  75                  80


Leu Gln Ile Ser Ser Leu Lys Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
            100                 105                 110


Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115                 120                 125


Gly Ser Gly Gly Gly Gly Ser Asp Val Gln Leu Thr Gln Ser Pro Ser
    130                 135                 140
```

_SL
Phe Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala
145 150 155 160

Ser Lys Ser Ile Ser Lys Asp Leu Ala Trp Tyr Gln Gln Lys Pro Gly
165 170 175

Lys Ala Pro Lys Leu Leu Ile Tyr Ser Gly Ser Thr Leu Gln Ser Gly
180 185 190

Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu
195 200 205

Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln
210 215 220

Gln His Asn Lys Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu
225 230 235 240

Ile Lys

<210> 391
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 391
Gln Val Gln Leu Val Gln Ser Gly Ser Glu Leu Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Trp Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Phe Val Phe Ser Val Asp Lys Ser Val Ser Thr Ala Tyr
65 70 75 80

Leu Gln Ile Ser Ser Leu Lys Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

```
                                                _SL
Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
            100                 105                 110

Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115                 120                 125

Gly Ser Gly Gly Gly Gly Ser Glu Val Val Leu Thr Gln Ser Pro Ala
    130                 135                 140

Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala
145                 150                 155                 160

Ser Lys Ser Ile Ser Lys Asp Leu Ala Trp Tyr Gln Gln Lys Pro Gly
                165                 170                 175

Gln Ala Pro Arg Leu Leu Ile Tyr Ser Gly Ser Thr Leu Gln Ser Gly
            180                 185                 190

Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
        195                 200                 205

Thr Ile Ser Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln
    210                 215                 220

Gln His Asn Lys Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu
225                 230                 235                 240

Ile Lys
```

<210> 392
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 392

```
Gln Val Gln Leu Val Gln Ser Gly Ser Glu Leu Lys Lys Pro Gly Ala
1               5                   10                  15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30

Trp Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45
```

```
                                                _SL
Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe
    50                  55                  60

Lys Asp Arg Phe Val Phe Ser Val Asp Lys Ser Val Ser Thr Ala Tyr
65                  70                  75                  80

Leu Gln Ile Ser Ser Leu Lys Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
            100                 105                 110

Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115                 120                 125

Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln Ser Pro Ala
    130                 135                 140

Phe Leu Ser Val Thr Pro Gly Glu Lys Val Thr Ile Thr Cys Arg Ala
145                 150                 155                 160

Ser Lys Ser Ile Ser Lys Asp Leu Ala Trp Tyr Gln Gln Lys Pro Asp
                165                 170                 175

Gln Ala Pro Lys Leu Leu Ile Tyr Ser Gly Ser Thr Leu Gln Ser Gly
            180                 185                 190

Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Phe
        195                 200                 205

Thr Ile Ser Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln
    210                 215                 220

Gln His Asn Lys Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu
225                 230                 235                 240

Ile Lys
```

<210> 393
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 393

```
                                                  _SL
Gln Val Gln Leu Val Gln Ser Gly Ser Glu Leu Lys Lys Pro Gly Ala
1               5                   10                  15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30

Trp Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe
    50                  55                  60

Lys Asp Arg Phe Val Phe Ser Val Asp Lys Ser Val Ser Thr Ala Tyr
65                  70                  75                  80

Leu Gln Ile Ser Ser Leu Lys Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
            100                 105                 110

Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115                 120                 125

Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln Ser Pro Asp
    130                 135                 140

Ser Leu Ala Val Ser Leu Gly Glu Arg Ala Thr Ile Asn Cys Arg Ala
145                 150                 155                 160

Ser Lys Ser Ile Ser Lys Asp Leu Ala Trp Tyr Gln Gln Lys Pro Gly
                165                 170                 175

Gln Pro Pro Lys Leu Leu Ile Tyr Ser Gly Ser Thr Leu Gln Ser Gly
            180                 185                 190

Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
        195                 200                 205

Thr Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln
    210                 215                 220

Gln His Asn Lys Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu
225                 230                 235                 240

Ile Lys
```

<210> 394
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 394
Asp Val Gln Leu Thr Gln Ser Pro Ser Phe Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser
100 105 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln
115 120 125

Val Gln Leu Val Gln Ser Gly Ser Glu Leu Lys Lys Pro Gly Ala Ser
130 135 140

Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr Trp
145 150 155 160

Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met Gly
165 170 175

Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe Lys
180 185 190

Asp Arg Phe Val Phe Ser Val Asp Lys Ser Val Ser Thr Ala Tyr Leu
195 200 205

```
Gln Ile Ser Ser Leu Lys Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
    210                 215                 220

Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val
225                 230                 235                 240

Ser Ser
```

<210> 395
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 395

```
Glu Val Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1               5                   10                  15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp
            20                  25                  30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
        35                  40                  45

Tyr Ser Gly Ser Thr Leu Gln Ser Gly Ile Pro Ala Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
65                  70                  75                  80

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr
                85                  90                  95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser
            100                 105                 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln
        115                 120                 125

Val Gln Leu Val Gln Ser Gly Ser Glu Leu Lys Lys Pro Gly Ala Ser
    130                 135                 140

Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr Trp
145                 150                 155                 160
```

```
Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met Gly
                165                 170                 175

Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe Lys
            180                 185                 190

Asp Arg Phe Val Phe Ser Val Asp Lys Ser Val Ser Thr Ala Tyr Leu
        195                 200                 205

Gln Ile Ser Ser Leu Lys Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
    210                 215                 220

Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val
225                 230                 235                 240

Ser Ser
```

<210> 396
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 396

```
Asp Val Val Met Thr Gln Ser Pro Ala Phe Leu Ser Val Thr Pro Gly
1               5                   10                  15

Glu Lys Val Thr Ile Thr Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp
            20                  25                  30

Leu Ala Trp Tyr Gln Gln Lys Pro Asp Gln Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Glu Ala
65                  70                  75                  80

Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr
                85                  90                  95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser
            100                 105                 110
```

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln
115 120 125

Val Gln Leu Val Gln Ser Gly Ser Glu Leu Lys Lys Pro Gly Ala Ser
130 135 140

Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr Trp
145 150 155 160

Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met Gly
165 170 175

Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe Lys
180 185 190

Asp Arg Phe Val Phe Ser Val Asp Lys Ser Val Ser Thr Ala Tyr Leu
195 200 205

Gln Ile Ser Ser Leu Lys Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
210 215 220

Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val
225 230 235 240

Ser Ser

<210> 397
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 397
Asp Val Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Glu Arg Ala Thr Ile Asn Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile
35 40 45

Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro Asp Arg Phe Ser Gly
50 55 60

```
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala
65                  70                  75                  80

Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr
                85                  90                  95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser
            100                 105                 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln
        115                 120                 125

Val Gln Leu Val Gln Ser Gly Ser Glu Leu Lys Lys Pro Gly Ala Ser
    130                 135                 140

Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr Trp
145                 150                 155                 160

Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met Gly
                165                 170                 175

Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe Lys
            180                 185                 190

Asp Arg Phe Val Phe Ser Val Asp Lys Ser Val Ser Thr Ala Tyr Leu
        195                 200                 205

Gln Ile Ser Ser Leu Lys Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
    210                 215                 220

Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val
225                 230                 235                 240

Ser Ser
```

<210> 398
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 398

```
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1               5                   10                  15
```

```
Ser Leu Arg Ile Ser Cys Lys Gly Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30

Trp Met Asn Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
        35                  40                  45

Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe
    50                  55                  60

Lys Asp His Val Thr Ile Ser Val Asp Lys Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80

Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
                85                  90                  95

Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
            100                 105                 110

Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115                 120                 125

Gly Ser Gly Gly Gly Gly Ser Asp Val Gln Leu Thr Gln Ser Pro Ser
    130                 135                 140

Phe Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala
145                 150                 155                 160

Ser Lys Ser Ile Ser Lys Asp Leu Ala Trp Tyr Gln Gln Lys Pro Gly
                165                 170                 175

Lys Ala Pro Lys Leu Leu Ile Tyr Ser Gly Ser Thr Leu Gln Ser Gly
            180                 185                 190

Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu
        195                 200                 205

Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln
    210                 215                 220

Gln His Asn Lys Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu
225                 230                 235                 240

Ile Lys
```

<210> 399
<211> 242

<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 399

```
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1               5                   10                  15

Ser Leu Arg Ile Ser Cys Lys Gly Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30

Trp Met Asn Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
        35                  40                  45

Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe
    50                  55                  60

Lys Asp His Val Thr Ile Ser Val Asp Lys Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80

Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
                85                  90                  95

Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
            100                 105                 110

Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115                 120                 125

Gly Ser Gly Gly Gly Gly Ser Glu Val Val Leu Thr Gln Ser Pro Ala
    130                 135                 140

Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala
145                 150                 155                 160

Ser Lys Ser Ile Ser Lys Asp Leu Ala Trp Tyr Gln Gln Lys Pro Gly
                165                 170                 175

Gln Ala Pro Arg Leu Leu Ile Tyr Ser Gly Ser Thr Leu Gln Ser Gly
            180                 185                 190

Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
        195                 200                 205

Thr Ile Ser Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln
    210                 215                 220
```

Gln His Asn Lys Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu
225 230 235 240

Ile Lys

<210> 400
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 400
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15

Ser Leu Arg Ile Ser Cys Lys Gly Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Trp Met Asn Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
35 40 45

Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe
50 55 60

Lys Asp His Val Thr Ile Ser Val Asp Lys Ser Ile Ser Thr Ala Tyr
65 70 75 80

Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
85 90 95

Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln Ser Pro Ala
130 135 140

Phe Leu Ser Val Thr Pro Gly Glu Lys Val Thr Ile Thr Cys Arg Ala
145 150 155 160

Ser Lys Ser Ile Ser Lys Asp Leu Ala Trp Tyr Gln Gln Lys Pro Asp
165 170 175

```
Gln Ala Pro Lys Leu Leu Ile Tyr Ser Gly Ser Thr Leu Gln Ser Gly
            180                 185                 190

Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Phe
        195                 200                 205

Thr Ile Ser Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln
    210                 215                 220

Gln His Asn Lys Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu
225                 230                 235                 240

Ile Lys
```

<210> 401
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 401

```
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1               5                   10                  15

Ser Leu Arg Ile Ser Cys Lys Gly Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30

Trp Met Asn Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
        35                  40                  45

Gly Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe
    50                  55                  60

Lys Asp His Val Thr Ile Ser Val Asp Lys Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80

Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
                85                  90                  95

Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
            100                 105                 110

Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115                 120                 125
```

Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln Ser Pro Asp
130 135 140

Ser Leu Ala Val Ser Leu Gly Glu Arg Ala Thr Ile Asn Cys Arg Ala
145 150 155 160

Ser Lys Ser Ile Ser Lys Asp Leu Ala Trp Tyr Gln Gln Lys Pro Gly
165 170 175

Gln Pro Pro Lys Leu Leu Ile Tyr Ser Gly Ser Thr Leu Gln Ser Gly
180 185 190

Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
195 200 205

Thr Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln
210 215 220

Gln His Asn Lys Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu
225 230 235 240

Ile Lys

<210> 402
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 402
Asp Val Gln Leu Thr Gln Ser Pro Ser Phe Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

```
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr
                85                  90                  95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser
            100                 105                 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu
        115                 120                 125

Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu Ser
    130                 135                 140

Leu Arg Ile Ser Cys Lys Gly Ser Gly Tyr Thr Phe Thr Ser Tyr Trp
145                 150                 155                 160

Met Asn Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met Gly
                165                 170                 175

Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe Lys
            180                 185                 190

Asp His Val Thr Ile Ser Val Asp Lys Ser Ile Ser Thr Ala Tyr Leu
        195                 200                 205

Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys Ala
    210                 215                 220

Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val
225                 230                 235                 240

Ser Ser
```

<210> 403
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 403

```
Glu Val Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1               5                   10                  15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp
            20                  25                  30
```

```
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
        35                  40                  45

Tyr Ser Gly Ser Thr Leu Gln Ser Gly Ile Pro Ala Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
65                  70                  75                  80

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr
                85                  90                  95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser
            100                 105                 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu
        115                 120                 125

Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu Ser
    130                 135                 140

Leu Arg Ile Ser Cys Lys Gly Ser Gly Tyr Thr Phe Thr Ser Tyr Trp
145                 150                 155                 160

Met Asn Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met Gly
                165                 170                 175

Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe Lys
            180                 185                 190

Asp His Val Thr Ile Ser Val Asp Lys Ser Ile Ser Thr Ala Tyr Leu
        195                 200                 205

Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys Ala
    210                 215                 220

Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val
225                 230                 235                 240

Ser Ser
```

<210> 404
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 404

```
Asp Val Val Met Thr Gln Ser Pro Ala Phe Leu Ser Val Thr Pro Gly
1               5                  10                  15

Glu Lys Val Thr Ile Thr Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp
            20                  25                  30

Leu Ala Trp Tyr Gln Gln Lys Pro Asp Gln Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Glu Ala
65                  70                  75                  80

Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr
                85                  90                  95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser
            100                 105                 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu
        115                 120                 125

Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu Ser
    130                 135                 140

Leu Arg Ile Ser Cys Lys Gly Ser Gly Tyr Thr Phe Thr Ser Tyr Trp
145                 150                 155                 160

Met Asn Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met Gly
                165                 170                 175

Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe Lys
            180                 185                 190

Asp His Val Thr Ile Ser Val Asp Lys Ser Ile Ser Thr Ala Tyr Leu
        195                 200                 205

Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys Ala
    210                 215                 220

Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val
```

_SL
225 230 235 240

Ser Ser

<210> 405
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 405
Asp Val Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Glu Arg Ala Thr Ile Asn Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile
35 40 45

Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro Asp Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala
65 70 75 80

Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser
100 105 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu
115 120 125

Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu Ser
130 135 140

Leu Arg Ile Ser Cys Lys Gly Ser Gly Tyr Thr Phe Thr Ser Tyr Trp
145 150 155 160

Met Asn Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met Gly
165 170 175

Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe Lys

_SL
180 185 190

Asp His Val Thr Ile Ser Val Asp Lys Ser Ile Ser Thr Ala Tyr Leu
195 200 205

Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys Ala
210 215 220

Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val
225 230 235 240

Ser Ser

<210> 406
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 406
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Val Trp Val
35 40 45

Ser Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Phe Thr Ile Ser Val Asp Lys Ala Lys Ser Thr Ala Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Asp Val Gln Leu Thr Gln Ser Pro Ser

_SL
130 135 140

Phe Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala
145 150 155 160

Ser Lys Ser Ile Ser Lys Asp Leu Ala Trp Tyr Gln Gln Lys Pro Gly
165 170 175

Lys Ala Pro Lys Leu Leu Ile Tyr Ser Gly Ser Thr Leu Gln Ser Gly
180 185 190

Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu
195 200 205

Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln
210 215 220

Gln His Asn Lys Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu
225 230 235 240

Ile Lys

<210> 407
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 407
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Val Trp Val
35 40 45

Ser Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Phe Thr Ile Ser Val Asp Lys Ala Lys Ser Thr Ala Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys

_SL
85 90 95

Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Glu Val Val Leu Thr Gln Ser Pro Ala
130 135 140

Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala
145 150 155 160

Ser Lys Ser Ile Ser Lys Asp Leu Ala Trp Tyr Gln Gln Lys Pro Gly
165 170 175

Gln Ala Pro Arg Leu Leu Ile Tyr Ser Gly Ser Thr Leu Gln Ser Gly
180 185 190

Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
195 200 205

Thr Ile Ser Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln
210 215 220

Gln His Asn Lys Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu
225 230 235 240

Ile Lys

<210> 408
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 408
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Val Trp Val

_SL
35 40 45

Ser Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Phe Thr Ile Ser Val Asp Lys Ala Lys Ser Thr Ala Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln Ser Pro Ala
130 135 140

Phe Leu Ser Val Thr Pro Gly Glu Lys Val Thr Ile Thr Cys Arg Ala
145 150 155 160

Ser Lys Ser Ile Ser Lys Asp Leu Ala Trp Tyr Gln Gln Lys Pro Asp
165 170 175

Gln Ala Pro Lys Leu Leu Ile Tyr Ser Gly Ser Thr Leu Gln Ser Gly
180 185 190

Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Phe
195 200 205

Thr Ile Ser Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln
210 215 220

Gln His Asn Lys Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu
225 230 235 240

Ile Lys

<210> 409
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

polypeptide"

<400> 409

```
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                  10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30

Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Val Trp Val
        35                  40                  45

Ser Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe
    50                  55                  60

Lys Asp Arg Phe Thr Ile Ser Val Asp Lys Ala Lys Ser Thr Ala Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr
            100                 105                 110

Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115                 120                 125

Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln Ser Pro Asp
    130                 135                 140

Ser Leu Ala Val Ser Leu Gly Glu Arg Ala Thr Ile Asn Cys Arg Ala
145                 150                 155                 160

Ser Lys Ser Ile Ser Lys Asp Leu Ala Trp Tyr Gln Gln Lys Pro Gly
                165                 170                 175

Gln Pro Pro Lys Leu Leu Ile Tyr Ser Gly Ser Thr Leu Gln Ser Gly
            180                 185                 190

Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
        195                 200                 205

Thr Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln
    210                 215                 220

Gln His Asn Lys Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu
225                 230                 235                 240
```

Ile Lys

<210> 410
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 410

```
Asp Val Gln Leu Thr Gln Ser Pro Ser Phe Leu Ser Ala Ser Val Gly
1               5                  10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp
            20                  25                  30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr
                85                  90                  95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser
            100                 105                 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu
        115                 120                 125

Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
    130                 135                 140

Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Thr Phe Thr Ser Tyr Trp
145                 150                 155                 160

Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Val Trp Val Ser
                165                 170                 175

Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe Lys
            180                 185                 190
```

_SL
Asp Arg Phe Thr Ile Ser Val Asp Lys Ala Lys Ser Thr Ala Tyr Leu
        195   200   205

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
    210   215   220

Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val
225   230   235   240

Ser Ser

<210> 411
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 411
Glu Val Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1   5   10   15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp
            20   25   30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
        35   40   45

Tyr Ser Gly Ser Thr Leu Gln Ser Gly Ile Pro Ala Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
65   70   75   80

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr
                85   90   95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser
            100   105   110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu
        115   120   125

Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
    130   135   140

_SL
Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Thr Phe Thr Ser Tyr Trp
145 150 155 160

Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Val Trp Val Ser
165 170 175

Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe Lys
180 185 190

Asp Arg Phe Thr Ile Ser Val Asp Lys Ala Lys Ser Thr Ala Tyr Leu
195 200 205

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
210 215 220

Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val
225 230 235 240

Ser Ser

<210> 412
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 412
Asp Val Val Met Thr Gln Ser Pro Ala Phe Leu Ser Val Thr Pro Gly
1 5 10 15

Glu Lys Val Thr Ile Thr Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Asp Gln Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Glu Ala
65 70 75 80

Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr
85 90 95

```
                                                _SL
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser
            100                 105                 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu
        115                 120                 125

Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
    130                 135                 140

Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Thr Phe Thr Ser Tyr Trp
145                 150                 155                 160

Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Val Trp Val Ser
                165                 170                 175

Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe Lys
            180                 185                 190

Asp Arg Phe Thr Ile Ser Val Asp Lys Ala Lys Ser Thr Ala Tyr Leu
        195                 200                 205

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
    210                 215                 220

Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val
225                 230                 235                 240

Ser Ser
```

<210> 413
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 413

```
Asp Val Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
1               5                   10                  15

Glu Arg Ala Thr Ile Asn Cys Arg Ala Ser Lys Ser Ile Ser Lys Asp
            20                  25                  30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile
        35                  40                  45
```

```
                                                _SL
Tyr Ser Gly Ser Thr Leu Gln Ser Gly Val Pro Asp Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala
65                  70                  75                  80

Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln His Asn Lys Tyr Pro Tyr
                85                  90                  95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Gly Ser
            100                 105                 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu
        115                 120                 125

Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser
    130                 135                 140

Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Thr Phe Thr Ser Tyr Trp
145                 150                 155                 160

Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Val Trp Val Ser
                165                 170                 175

Arg Ile Asp Pro Tyr Asp Ser Glu Thr His Tyr Asn Gln Lys Phe Lys
            180                 185                 190

Asp Arg Phe Thr Ile Ser Val Asp Lys Ala Lys Ser Thr Ala Tyr Leu
        195                 200                 205

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
    210                 215                 220

Arg Gly Asn Trp Asp Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val
225                 230                 235                 240

Ser Ser
```

<210> 414
<211> 491
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 414

```
                                                    _SL
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15

His Ala Ala Arg Pro Gly Ser Glu Ile Gln Leu Gln Gln Ser Gly Ala
            20                  25                  30

Glu Leu Val Lys Pro Gly Ala Ser Val Lys Leu Ser Cys Thr Gly Ser
        35                  40                  45

Gly Phe Asn Ile Glu Asp Tyr Tyr Ile His Trp Val Lys Gln Arg Thr
    50                  55                  60

Glu Gln Gly Leu Glu Trp Ile Gly Arg Ile Asp Pro Glu Asn Asp Glu
65                  70                  75                  80

Thr Lys Tyr Gly Pro Ile Phe Gln Gly Arg Ala Thr Ile Thr Ala Asp
                85                  90                  95

Thr Ser Ser Asn Thr Val Tyr Leu Gln Leu Ser Ser Leu Thr Ser Glu
            100                 105                 110

Asp Thr Ala Val Tyr Tyr Cys Ala Phe Arg Gly Gly Val Tyr Trp Gly
        115                 120                 125

Pro Gly Thr Thr Leu Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
    130                 135                 140

Gly Gly Ser Gly Gly Gly Gly Ser His Met Asp Val Val Met Thr Gln
145                 150                 155                 160

Ser Pro Leu Thr Leu Ser Val Ala Ile Gly Gln Ser Ala Ser Ile Ser
                165                 170                 175

Cys Lys Ser Ser Gln Ser Leu Leu Asp Ser Asp Gly Lys Thr Tyr Leu
            180                 185                 190

Asn Trp Leu Leu Gln Arg Pro Gly Gln Ser Pro Lys Arg Leu Ile Ser
        195                 200                 205

Leu Val Ser Lys Leu Asp Ser Gly Val Pro Asp Arg Phe Thr Gly Ser
    210                 215                 220

Gly Ser Gly Thr Asp Phe Thr Leu Arg Ile Ser Arg Val Glu Ala Glu
225                 230                 235                 240

Asp Leu Gly Ile Tyr Tyr Cys Trp Gln Gly Thr His Phe Pro Gly Thr
                245                 250                 255
```

```
Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Ala Ser Thr Thr Thr Pro
            260                 265                 270

Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu
        275                 280                 285

Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His
    290                 295                 300

Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu
305                 310                 315                 320

Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr
                325                 330                 335

Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe
            340                 345                 350

Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg
        355                 360                 365

Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser
    370                 375                 380

Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr
385                 390                 395                 400

Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys
                405                 410                 415

Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn
            420                 425                 430

Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu
        435                 440                 445

Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly
    450                 455                 460

His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr
465                 470                 475                 480

Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
                485                 490
```

<210> 415
<211> 246

<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 415

```
Glu Ile Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                  10                  15

Thr Val Lys Ile Ser Cys Lys Gly Ser Gly Phe Asn Ile Glu Asp Tyr
            20                  25                  30

Tyr Ile His Trp Val Gln Gln Ala Pro Gly Lys Gly Leu Glu Trp Met
        35                  40                  45

Gly Arg Ile Asp Pro Glu Asn Asp Glu Thr Lys Tyr Gly Pro Ile Phe
    50                  55                  60

Gln Gly Arg Val Thr Ile Thr Ala Asp Thr Ser Thr Asn Thr Val Tyr
65                  70                  75                  80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Phe Arg Gly Gly Val Tyr Trp Gly Gln Gly Thr Thr Val Thr Val
            100                 105                 110

Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
        115                 120                 125

Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln Ser Pro Asp Ser
    130                 135                 140

Leu Ala Val Ser Leu Gly Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser
145                 150                 155                 160

Gln Ser Leu Leu Asp Ser Asp Gly Lys Thr Tyr Leu Asn Trp Leu Gln
                165                 170                 175

Gln Lys Pro Gly Gln Pro Pro Lys Arg Leu Ile Ser Leu Val Ser Lys
            180                 185                 190

Leu Asp Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr
        195                 200                 205

Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val
    210                 215                 220
```

Tyr Tyr Cys Trp Gln Gly Thr His Phe Pro Gly Thr Phe Gly Gly Gly
225 230 235 240

Thr Lys Val Glu Ile Lys
245

<210> 416
<211> 738
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 416
gaaatccagc tggtccaatc gggagctgag gtcaagaagc cgggagccac cgtcaagatc 60

tcatgcaagg ggtcgggatt caacatcgag gactactaca ttcactgggt gcagcaagct 120

ccgggaaaag gcctggaatg gatgggcaga atcgacccag aaaacgacga aactaagtac 180

ggaccgattt tccaaggaag agtgactatc accgccgata cttcaaccaa taccgtctac 240

atggaactga gctcgctccg gtccgaagat actgcagtgt attactgtgc ctttcgcgga 300

ggggtgtact ggggccaagg aactactgtc actgtctcgt caggaggcgg agggtcggga 360

ggaggcggga gcggaggcgg tggctcgggt ggcggaggaa gcgacgtggt gatgacccag 420

tccccggact ccctcgccgt gagcctcgga gagagggcga ctatcaattg caagtcgtcc 480

cagtcacttc tggattccga tggtaaaacg tacctcaact ggctgcagca aaagccaggg 540

cagccaccca aacggttgat ctcccttgtg tccaaactgg atagcggagt gcctgaccgc 600

ttctcgggtt ccggtagcgg gaccgacttc accctgacga tcagctcact gcaggcggag 660

gacgtggcag tgtactactg ctggcaggga acccacttcc ctggcacctt tggaggtggc 720

accaaggtgg agatcaag 738

<210> 417
<211> 831
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 417
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaaatcc agctggtcca atcgggagct gaggtcaaga agccgggagc caccgtcaag 120

_SL

atctcatgca aggggtcggg attcaacatc gaggactact acattcactg ggtgcagcaa 180

gctccgggaa aaggcctgga atggatgggc agaatcgacc cagaaaacga cgaaactaag 240

tacggaccga ttttccaagg aagagtgact atcaccgccg atacttcaac caataccgtc 300

tacatggaac tgagctcgct ccggtccgaa gatactgcag tgtattactg tgcctttcgc 360

ggaggggtgt actggggcca aggaactact gtcactgtct cgtcaggagg cggagggtcg 420

ggaggaggcg ggagcggagg cggtggctcg ggtggcggag gaagcgacgt ggtgatgacc 480

cagtccccgg actccctcgc cgtgagcctc ggagagaggg cgactatcaa ttgcaagtcg 540

tcccagtcac ttctggattc cgatggtaaa acgtacctca actggctgca gcaaaagcca 600

gggcagccac ccaaacggtt gatctccctt gtgtccaaac tggatagcgg agtgcctgac 660

cgcttctcgg gttccggtag cgggaccgac ttcaccctga cgatcagctc actgcaggcg 720

gaggacgtgg cagtgtacta ctgctggcag ggaacccact tccctggcac ctttggaggt 780

ggcaccaagg tggagatcaa gggatcgcac caccatcacc atcatcatca c 831

<210> 418
<211> 277
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 418
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Ile Gln Leu Val Gln Ser Gly Ala Glu Val
20 25 30

Lys Lys Pro Gly Ala Thr Val Lys Ile Ser Cys Lys Gly Ser Gly Phe
35 40 45

Asn Ile Glu Asp Tyr Tyr Ile His Trp Val Gln Gln Ala Pro Gly Lys
50 55 60

Gly Leu Glu Trp Met Gly Arg Ile Asp Pro Glu Asn Asp Glu Thr Lys
65 70 75 80

Tyr Gly Pro Ile Phe Gln Gly Arg Val Thr Ile Thr Ala Asp Thr Ser
85 90 95

Thr Asn Thr Val Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
100 105 110

```
Ala Val Tyr Tyr Cys Ala Phe Arg Gly Gly Val Tyr Trp Gly Gln Gly
        115                 120                 125

Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
    130                 135                 140

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr
145                 150                 155                 160

Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly Glu Arg Ala Thr Ile
                165                 170                 175

Asn Cys Lys Ser Ser Gln Ser Leu Leu Asp Ser Asp Gly Lys Thr Tyr
            180                 185                 190

Leu Asn Trp Leu Gln Gln Lys Pro Gly Gln Pro Pro Lys Arg Leu Ile
        195                 200                 205

Ser Leu Val Ser Lys Leu Asp Ser Gly Val Pro Asp Arg Phe Ser Gly
    210                 215                 220

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala
225                 230                 235                 240

Glu Asp Val Ala Val Tyr Tyr Cys Trp Gln Gly Thr His Phe Pro Gly
                245                 250                 255

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Ser His His His
            260                 265                 270

His His His His His
        275
```

<210> 419
<211> 1470
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 419

```
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg       60

cccgagatcc agctggtgca gtcgggagct gaagtcaaaa agcctggcgc aaccgtcaag      120

atctcgtgca aaggatcagg gttcaacatc gaggactact acatccattg ggtgcaacag      180

gcacccggaa aaggcctgga gtggatgggg aggattgacc cagaaaatga cgaaaccaag      240
```

tacggaccga tcttccaagg acgggtgacc atcacggctg acacttccac taacaccgtc 300

tacatggaac tctcgagcct tcgctcggaa gataccgcgg tgtactactg cgcctttaga 360

ggtggagtct actggggaca agggactacc gtcaccgtgt cgtcaggtgg cggaggatca 420

ggcggaggcg gctccggtgg aggaggaagc ggaggaggtg gctccgacgt ggtgatgacg 480

cagtcaccgg actccttggc ggtgagcctg ggtgaacgcg ccactatcaa ctgcaagagc 540

tcccagagct tgctggactc cgatggaaag acttatctca attggctgca acagaagcct 600

ggccagccgc caaagagact catctcactg gtgagcaagc tggatagcgg agtgccagat 660

cggttttcgg gatcgggctc aggcaccgac ttcaccctga ctatttcctc cctccaagcc 720

gaggatgtgg ccgtctacta ctgttggcag gggactcact tcccggggac cttcggtgga 780

ggcactaagg tggagatcaa aaccactacc ccagcaccga ggccacccac cccggctcct 840

accatcgcct cccagcctct gtccctgcgt ccggaggcat gtagacccgc agctggtggg 900

gccgtgcata cccggggtct tgacttcgcc tgcgatatct acatttgggc ccctctggct 960

ggtacttgcg gggtcctgct gctttcactc gtgatcactc tttactgtaa gcgcggtcgg 1020

aagaagctgc tgtacatctt taagcaaccc ttcatgaggc ctgtgcagac tactcaagag 1080

gaggacggct gttcatgccg gttcccagag gaggaggaag gcggctgcga actgcgcgtg 1140

aaattcagcc gcagcgcaga tgctccagcc tacaagcagg ggcagaacca gctctacaac 1200

gaactcaatc ttggtcggag agaggagtac gacgtgctgg acaagcggag aggacgggac 1260

ccagaaatgg gcgggaagcc gcgcagaaag aatccccaag agggcctgta caacgagctc 1320

caaaaggata agatggcaga agcctatagc gagattggta tgaaagggga acgcagaaga 1380

ggcaaaggcc acgacggact gtaccaggga ctcagcaccg ccaccaagga cacctatgac 1440

gctcttcaca tgcaggccct gccgcctcgg 1470

<210> 420
<211> 490
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 420
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Ile Gln Leu Val Gln Ser Gly Ala Glu Val
20 25 30

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                                                    _SL
Lys Lys Pro Gly Ala Thr Val Lys Ile Ser Cys Lys Gly Ser Gly Phe
        35                  40                  45

Asn Ile Glu Asp Tyr Tyr Ile His Trp Val Gln Gln Ala Pro Gly Lys
    50                  55                  60

Gly Leu Glu Trp Met Gly Arg Ile Asp Pro Glu Asn Asp Glu Thr Lys
65                  70                  75                  80

Tyr Gly Pro Ile Phe Gln Gly Arg Val Thr Ile Thr Ala Asp Thr Ser
                85                  90                  95

Thr Asn Thr Val Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Phe Arg Gly Gly Val Tyr Trp Gly Gln Gly
        115                 120                 125

Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
    130                 135                 140

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr
145                 150                 155                 160

Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly Glu Arg Ala Thr Ile
                165                 170                 175

Asn Cys Lys Ser Ser Gln Ser Leu Leu Asp Ser Asp Gly Lys Thr Tyr
            180                 185                 190

Leu Asn Trp Leu Gln Gln Lys Pro Gly Gln Pro Pro Lys Arg Leu Ile
        195                 200                 205

Ser Leu Val Ser Lys Leu Asp Ser Gly Val Pro Asp Arg Phe Ser Gly
    210                 215                 220

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala
225                 230                 235                 240

Glu Asp Val Ala Val Tyr Tyr Cys Trp Gln Gly Thr His Phe Pro Gly
                245                 250                 255

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Thr Thr Thr Pro Ala
            260                 265                 270

Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser
        275                 280                 285
```

```
Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr
    290                 295                 300

Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala
305                 310                 315                 320

Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys
                325                 330                 335

Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met
            340                 345                 350

Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe
        355                 360                 365

Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg
    370                 375                 380

Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn
385                 390                 395                 400

Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg
                405                 410                 415

Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro
            420                 425                 430

Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala
        435                 440                 445

Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His
    450                 455                 460

Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp
465                 470                 475                 480

Ala Leu His Met Gln Ala Leu Pro Pro Arg
                485                 490
```

<210> 421
<211> 246
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 421

```
Asp Val Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
1               5                  10                  15

Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser Gln Ser Leu Leu Asp Ser
            20                  25                  30

Asp Gly Lys Thr Tyr Leu Asn Trp Leu Gln Gln Lys Pro Gly Gln Pro
        35                  40                  45

Pro Lys Arg Leu Ile Ser Leu Val Ser Lys Leu Asp Ser Gly Val Pro
    50                  55                  60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile
65                  70                  75                  80

Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Trp Gln Gly
                85                  90                  95

Thr His Phe Pro Gly Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            100                 105                 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Glu Ile Gln Leu Val Gln Ser Gly Ala Glu Val Lys
    130                 135                 140

Lys Pro Gly Ala Thr Val Lys Ile Ser Cys Lys Gly Ser Gly Phe Asn
145                 150                 155                 160

Ile Glu Asp Tyr Tyr Ile His Trp Val Gln Gln Ala Pro Gly Lys Gly
                165                 170                 175

Leu Glu Trp Met Gly Arg Ile Asp Pro Glu Asn Asp Glu Thr Lys Tyr
            180                 185                 190

Gly Pro Ile Phe Gln Gly Arg Val Thr Ile Thr Ala Asp Thr Ser Thr
        195                 200                 205

Asn Thr Val Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala
    210                 215                 220

Val Tyr Tyr Cys Ala Phe Arg Gly Gly Val Tyr Trp Gly Gln Gly Thr
225                 230                 235                 240

Thr Val Thr Val Ser Ser
                245
```

<210> 422
<211> 738
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 422
gatgtcgtga tgacccagtc cccagactcc ctcgcagtgt ccttgggaga acgggccacc 60

atcaactgca aatcgagcca gtcactgctg gactcagacg gaaagaccta cctcaactgg 120

ctgcagcaga agcctggcca gccaccgaag cgcctgatct ccctggtgtc caagctggac 180

tcgggcgtcc cggacaggtt tagcggtagc ggctcgggaa ccgacttcac tctgaccatt 240

agctcgctcc aagctgaaga tgtggcggtc tactactgct ggcaggggac ccacttcccc 300

gggacctttg gcggaggaac taaagtcgaa atcaaaggag gaggcggatc aggtggagga 360

ggcagcggag gaggagggag cggcggtggc ggctccgaaa ttcaacttgt gcaatccggt 420

gccgaggtga agaaacctgg tgccactgtc aagatctcgt gtaagggatc gggattcaat 480

atcgaggact actacatcca ctgggtgcaa caggcgccag gaaagggatt ggagtggatg 540

ggtcgcatcg acccggaaaa cgatgagact aagtacggac cgatcttcca aggccgggtc 600

acgatcactg cggatacctc cactaatacc gtgtatatgg agctctcgtc actgagaagc 660

gaagatacgg ccgtgtacta ctgcgcattc agaggaggtg tgtactgggg ccagggaact 720

actgtgaccg tgtcgtcg 738

<210> 423
<211> 831
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 423
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgatgtcg tgatgaccca gtccccagac tccctcgcag tgtccttggg agaacgggcc 120

accatcaact gcaaatcgag ccagtcactg ctggactcag acggaaagac ctacctcaac 180

tggctgcagc agaagcctgg ccagccaccg aagcgcctga tctccctggt gtccaagctg 240

gactcgggcg tcccggacag gtttagcggt agcggctcgg gaaccgactt cactctgacc 300

attagctcgc tccaagctga agatgtggcg gtctactact gctggcaggg gacccacttc 360

_SL

cccgggacct ttggcggagg aactaaagtc gaaatcaaag gaggaggcgg atcaggtgga 420

ggaggcagcg gaggaggagg gagcggcggt ggcggctccg aaattcaact tgtgcaatcc 480

ggtgccgagg tgaagaaacc tggtgccact gtcaagatct cgtgtaaggg atcgggattc 540

aatatcgagg actactacat ccactgggtg caacaggcgc caggaaaggg attggagtgg 600

atgggtcgca tcgacccgga aaacgatgag actaagtacg gaccgatctt ccaaggccgg 660

gtcacgatca ctgcggatac ctccactaat accgtgtata tggagctctc gtcactgaga 720

agcgaagata cggccgtgta ctactgcgca ttcagaggag gtgtgtactg gggccaggga 780

actactgtga ccgtgtcgtc ggggtcacat caccaccatc atcatcacca c 831

<210> 424
<211> 277
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 424
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Asp Val Val Met Thr Gln Ser Pro Asp Ser Leu
20 25 30

Ala Val Ser Leu Gly Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser Gln
35 40 45

Ser Leu Leu Asp Ser Asp Gly Lys Thr Tyr Leu Asn Trp Leu Gln Gln
50 55 60

Lys Pro Gly Gln Pro Pro Lys Arg Leu Ile Ser Leu Val Ser Lys Leu
65 70 75 80

Asp Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
85 90 95

Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr
100 105 110

Tyr Cys Trp Gln Gly Thr His Phe Pro Gly Thr Phe Gly Gly Gly Thr
115 120 125

Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
130 135 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Gln Leu Val Gln Ser
145 150 155 160

Gly Ala Glu Val Lys Lys Pro Gly Ala Thr Val Lys Ile Ser Cys Lys
165 170 175

Gly Ser Gly Phe Asn Ile Glu Asp Tyr Tyr Ile His Trp Val Gln Gln
180 185 190

Ala Pro Gly Lys Gly Leu Glu Trp Met Gly Arg Ile Asp Pro Glu Asn
195 200 205

Asp Glu Thr Lys Tyr Gly Pro Ile Phe Gln Gly Arg Val Thr Ile Thr
210 215 220

Ala Asp Thr Ser Thr Asn Thr Val Tyr Met Glu Leu Ser Ser Leu Arg
225 230 235 240

Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Phe Arg Gly Gly Val Tyr
245 250 255

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Ser His His His
260 265 270

His His His His His
275

<210> 425
<211> 1470
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 425
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgacgtgg tcatgactca aagcccagat tccttggctg tctcccttgg agaaagagca 120

acgatcaatt gcaaaagctc gcagtccctg ttggactccg atggaaaaac ctacctcaac 180

tggctgcagc agaagccggg acaaccacca aagcggctga tttccctcgt gtccaagctg 240

gacagcggcg tgccggatcg cttctcgggc agcggctcgg gaaccgattt tactctcact 300

atttcgtcac tgcaagcgga ggacgtggcg gtgtattact gctggcaggg cactcacttc 360

ccgggtactt ttggtggagg taccaaagtc gaaatcaagg gtggaggcgg gagcggagga 420

ggcgggtcgg gaggaggagg atcgggtggc ggaggctcag aaatccagct ggtgcagtca 480

ggtgccgaag tgaagaagcc tggggccacg gtgaagatct cgtgcaaggg gagcggattc 540

aacatcgagg attactacat ccattgggtg caacaggccc ctggcaaagg gctggaatgg 600

atgggaagga tcgaccccga gaatgacgag actaagtacg gcccgatctt ccaaggacgg 660

gtgaccatca ctgcagacac ttcaaccaac accgtctaca tggaactctc ctcgctgcgc 720

tccgaggaca ccgccgtgta ctactgtgct ttcagaggag gagtctactg gggacaggga 780

acgaccgtga ccgtcagctc aaccactacc ccagcaccga ggccacccac cccggctcct 840

accatcgcct cccagcctct gtccctgcgt ccggaggcat gtagacccgc agctggtggg 900

gccgtgcata cccggggtct tgacttcgcc tgcgatatct acatttgggc ccctctggct 960

ggtacttgcg gggtcctgct gctttcactc gtgatcactc tttactgtaa gcgcggtcgg 1020

aagaagctgc tgtacatctt taagcaaccc ttcatgaggc ctgtgcagac tactcaagag 1080

gaggacggct gttcatgccg gttcccagag gaggaggaag gcggctgcga actgcgcgtg 1140

aaattcagcc gcagcgcaga tgctccagcc tacaagcagg ggcagaacca gctctacaac 1200

gaactcaatc ttggtcggag agaggagtac gacgtgctgg acaagcggag aggacgggac 1260

ccagaaatgg gcgggaagcc gcgcagaaag aatccccaag agggcctgta caacgagctc 1320

caaaaggata agatggcaga agcctatagc gagattggta tgaaaggggа acgcagaaga 1380

ggcaaaggcc acgacggact gtaccaggga ctcagcaccg ccaccaagga cacctatgac 1440

gctcttcaca tgcaggccct gccgcctcgg 1470

<210> 426
<211> 490
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 426
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Asp Val Val Met Thr Gln Ser Pro Asp Ser Leu
20 25 30

Ala Val Ser Leu Gly Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser Gln
35 40 45

Ser Leu Leu Asp Ser Asp Gly Lys Thr Tyr Leu Asn Trp Leu Gln Gln
50 55 60

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                                                _SL
Lys Pro Gly Gln Pro Pro Lys Arg Leu Ile Ser Leu Val Ser Lys Leu
65                  70                  75                  80

Asp Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
                85                  90                  95

Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr
            100                 105                 110

Tyr Cys Trp Gln Gly Thr His Phe Pro Gly Thr Phe Gly Gly Gly Thr
        115                 120                 125

Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Gln Leu Val Gln Ser
145                 150                 155                 160

Gly Ala Glu Val Lys Lys Pro Gly Ala Thr Val Lys Ile Ser Cys Lys
                165                 170                 175

Gly Ser Gly Phe Asn Ile Glu Asp Tyr Tyr Ile His Trp Val Gln Gln
            180                 185                 190

Ala Pro Gly Lys Gly Leu Glu Trp Met Gly Arg Ile Asp Pro Glu Asn
        195                 200                 205

Asp Glu Thr Lys Tyr Gly Pro Ile Phe Gln Gly Arg Val Thr Ile Thr
    210                 215                 220

Ala Asp Thr Ser Thr Asn Thr Val Tyr Met Glu Leu Ser Ser Leu Arg
225                 230                 235                 240

Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Phe Arg Gly Gly Val Tyr
                245                 250                 255

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Thr Thr Thr Pro Ala
            260                 265                 270

Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser
        275                 280                 285

Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr
    290                 295                 300

Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala
305                 310                 315                 320
```

```
Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys
                325                 330                 335

Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met
            340                 345                 350

Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe
        355                 360                 365

Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg
    370                 375                 380

Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn
385                 390                 395                 400

Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg
                405                 410                 415

Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro
            420                 425                 430

Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala
        435                 440                 445

Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His
    450                 455                 460

Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp
465                 470                 475                 480

Ala Leu His Met Gln Ala Leu Pro Pro Arg
                485                 490


<210> 427
<211> 246
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 427
Glu Ile Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1               5                   10                  15

Ser Leu Arg Ile Ser Cys Lys Gly Ser Gly Phe Asn Ile Glu Asp Tyr
            20                  25                  30
```

```
Tyr Ile His Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
        35                  40                  45

Gly Arg Ile Asp Pro Glu Asn Asp Glu Thr Lys Tyr Gly Pro Ile Phe
    50                  55                  60

Gln Gly His Val Thr Ile Ser Ala Asp Thr Ser Ile Asn Thr Val Tyr
65                  70                  75                  80

Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
                85                  90                  95

Ala Phe Arg Gly Gly Val Tyr Trp Gly Gln Gly Thr Thr Val Thr Val
            100                 105                 110

Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
        115                 120                 125

Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln Ser Pro Leu Ser
    130                 135                 140

Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser
145                 150                 155                 160

Gln Ser Leu Leu Asp Ser Asp Gly Lys Thr Tyr Leu Asn Trp Leu Gln
                165                 170                 175

Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Ser Leu Val Ser Lys
            180                 185                 190

Leu Asp Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr
        195                 200                 205

Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Val Gly Val
    210                 215                 220

Tyr Tyr Cys Trp Gln Gly Thr His Phe Pro Gly Thr Phe Gly Gly Gly
225                 230                 235                 240

Thr Lys Val Glu Ile Lys
                245
```

<210> 428
<211> 738
<212> DNA
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 428
gagattcagc tggtccaaag cggcgcagaa gtgaaaaagc caggggaatc gttgcgcatc 60

agctgtaaag gttccggctt caacatcgag gactattaca tccattgggt gcggcagatg 120

ccaggaaagg ggctggaatg gatgggacgg attgacccgg agaacgacga aaccaagtac 180

ggaccgatct ttcaaggaca cgtgactatc tccgccgaca ccagcatcaa tacggtgtac 240

ctccaatggt cctcactcaa ggcctcggat accgcgatgt actactgcgc gttcagagga 300

ggcgtctact ggggacaagg gactactgtg actgtctcat caggaggtgg aggaagcgga 360

ggaggtggct cgggcggagg tggatcggga ggaggagggt ccgatgtggt gatgacccag 420

tccccactgt cgctcccggt gaccctcgga cagcctgcta gcatctcgtg caaatcctcg 480

caatccctgc tggactcgga cggaaaaacg tacctcaatt ggctgcagca gcgccctggc 540

cagagcccga gaaggcttat ctcgctggtg tcaaagctgg atagcggtgt gcccgaccgg 600

ttcagcggct cagggtcagg aaccgatttc accttgaaga tctcccgcgt ggaagccgaa 660

gatgtcggag tctactactg ctggcagggt actcacttcc cggggacctt tggtggcggc 720

actaaggtcg agattaag 738

<210> 429
<211> 831
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 429
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgagattc agctggtcca aagcggcgca gaagtgaaaa agccagggga atcgttgcgc 120

atcagctgta aaggttccgg cttcaacatc gaggactatt acatccattg ggtgcggcag 180

atgccaggaa aggggctgga atggatggga cggattgacc cggagaacga cgaaaccaag 240

tacggaccga tctttcaagg acacgtgact atctccgccg acaccagcat caatacggtg 300

tacctccaat ggtcctcact caaggcctcg gataccgcga tgtactactg cgcgttcaga 360

ggaggcgtct actggggaca agggactact gtgactgtct catcaggagg tggaggaagc 420

ggaggaggtg gctcgggcgg aggtggatcg ggaggaggag ggtccgatgt ggtgatgacc 480

cagtccccac tgtcgctccc ggtgaccctc ggacagcctg ctagcatctc gtgcaaatcc 540

tcgcaatccc tgctggactc ggacggaaaa acgtacctca attggctgca gcagcgccct 600

ggccagagcc cgagaaggct tatctcgctg gtgtcaaagc tggatagcgg tgtgcccgac 660

cggttcagcg gctcagggtc aggaaccgat ttcaccttga agatctcccg cgtggaagcc 720

gaagatgtcg gagtctacta ctgctggcag ggtactcact tcccggggac ctttggtggc 780

ggcactaagg tcgagattaa gggctcacac catcatcacc atcaccacca c 831

<210> 430
<211> 277
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 430
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Ile Gln Leu Val Gln Ser Gly Ala Glu Val
20 25 30

Lys Lys Pro Gly Glu Ser Leu Arg Ile Ser Cys Lys Gly Ser Gly Phe
35 40 45

Asn Ile Glu Asp Tyr Tyr Ile His Trp Val Arg Gln Met Pro Gly Lys
50 55 60

Gly Leu Glu Trp Met Gly Arg Ile Asp Pro Glu Asn Asp Glu Thr Lys
65 70 75 80

Tyr Gly Pro Ile Phe Gln Gly His Val Thr Ile Ser Ala Asp Thr Ser
85 90 95

Ile Asn Thr Val Tyr Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr
100 105 110

Ala Met Tyr Tyr Cys Ala Phe Arg Gly Gly Val Tyr Trp Gly Gln Gly
115 120 125

Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
130 135 140

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr
145 150 155 160

Gln Ser Pro Leu Ser Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile
165 170 175

```
Ser Cys Lys Ser Ser Gln Ser Leu Leu Asp Ser Asp Gly Lys Thr Tyr
            180                 185                 190

Leu Asn Trp Leu Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile
        195                 200                 205

Ser Leu Val Ser Lys Leu Asp Ser Gly Val Pro Asp Arg Phe Ser Gly
    210                 215                 220

Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala
225                 230                 235                 240

Glu Asp Val Gly Val Tyr Tyr Cys Trp Gln Gly Thr His Phe Pro Gly
                245                 250                 255

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Ser His His His
            260                 265                 270

His His His His His
        275
```

<210> 431
<211> 1470
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 431

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atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg       60

cccgaaatcc agctggtgca aagcggagcc gaggtgaaga agcccggaga atccctgcgc      120

atctcgtgta agggttccgg ctttaacatc gaggattact acatccactg ggtgagacag      180

atgccgggca aaggtctgga atggatgggc cgcatcgacc cggagaacga cgaaaccaaa      240

tacggaccaa tcttccaagg acatgtgact atttccgcgg atacctccat caacactgtc      300

tacttgcagt ggagctcgct caaggcgtcg gataccgcca tgtactactg cgcattcaga      360

ggaggtgtgt actggggcca gggcactacg gtcaccgtgt cctcgggagg tggagggtca      420

ggaggcggag gctcgggcgg tggaggatca ggcggaggag gaagcgatgt ggtcatgact      480

caatccccac tgtcactgcc tgtcactctg gggcaaccgg cttccatctc atgcaagtca      540

agccaatcgc tgctcgactc cgacggaaaa acctacctca attggcttca gcagcgccca      600

ggccagtcgc ctcggaggct gatctcactc gtgtcgaagc ttgactccgg ggtgccggat      660

cggtttagcg gaagcggatc ggggaccgac ttcacgttga agattagccg ggtggaagcc      720
```

gaggacgtgg gagtctatta ctgctggcag gggacccact tcccggggac tttcggagga 780

ggcaccaaag tcgagattaa gaccactacc ccagcaccga ggccacccac cccggctcct 840

accatcgcct cccagcctct gtccctgcgt ccggaggcat gtagacccgc agctggtggg 900

gccgtgcata cccggggtct tgacttcgcc tgcgatatct acatttgggc ccctctggct 960

ggtacttgcg gggtcctgct gctttcactc gtgatcactc tttactgtaa gcgcggtcgg 1020

aagaagctgc tgtacatctt taagcaaccc ttcatgaggc ctgtgcagac tactcaagag 1080

gaggacggct gttcatgccg gttcccagag gaggaggaag gcggctgcga actgcgcgtg 1140

aaattcagcc gcagcgcaga tgctccagcc tacaagcagg ggcagaacca gctctacaac 1200

gaactcaatc ttggtcggag agaggagtac gacgtgctgg acaagcggag aggacgggac 1260

ccagaaatgg gcgggaagcc gcgcagaaag aatccccaag agggcctgta caacgagctc 1320

caaaaggata agatggcaga agcctatagc gagattggta tgaaagggga acgcagaaga 1380

ggcaaaggcc acgacggact gtaccaggga ctcagcaccg ccaccaagga cacctatgac 1440

gctcttcaca tgcaggccct gccgcctcgg 1470

<210> 432
<211> 490
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 432
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Ile Gln Leu Val Gln Ser Gly Ala Glu Val
20 25 30

Lys Lys Pro Gly Glu Ser Leu Arg Ile Ser Cys Lys Gly Ser Gly Phe
35 40 45

Asn Ile Glu Asp Tyr Tyr Ile His Trp Val Arg Gln Met Pro Gly Lys
50 55 60

Gly Leu Glu Trp Met Gly Arg Ile Asp Pro Glu Asn Asp Glu Thr Lys
65 70 75 80

Tyr Gly Pro Ile Phe Gln Gly His Val Thr Ile Ser Ala Asp Thr Ser
85 90 95

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                                                    _SL
Ile Asn Thr Val Tyr Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr
            100                 105                 110

Ala Met Tyr Tyr Cys Ala Phe Arg Gly Gly Val Tyr Trp Gly Gln Gly
        115                 120                 125

Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
    130                 135                 140

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr
145                 150                 155                 160

Gln Ser Pro Leu Ser Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile
                165                 170                 175

Ser Cys Lys Ser Ser Gln Ser Leu Leu Asp Ser Asp Gly Lys Thr Tyr
            180                 185                 190

Leu Asn Trp Leu Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile
        195                 200                 205

Ser Leu Val Ser Lys Leu Asp Ser Gly Val Pro Asp Arg Phe Ser Gly
    210                 215                 220

Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala
225                 230                 235                 240

Glu Asp Val Gly Val Tyr Tyr Cys Trp Gln Gly Thr His Phe Pro Gly
                245                 250                 255

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Thr Thr Thr Pro Ala
            260                 265                 270

Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser
        275                 280                 285

Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr
    290                 295                 300

Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala
305                 310                 315                 320

Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys
                325                 330                 335

Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met
            340                 345                 350
```

```
Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe
        355                 360                 365

Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg
    370                 375                 380

Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn
385                 390                 395                 400

Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg
                405                 410                 415

Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro
            420                 425                 430

Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala
        435                 440                 445

Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His
    450                 455                 460

Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp
465                 470                 475                 480

Ala Leu His Met Gln Ala Leu Pro Pro Arg
                485                 490
```

<210> 433
<211> 246
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 433

```
Asp Val Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Leu Gly
1               5                   10                  15

Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser Gln Ser Leu Leu Asp Ser
            20                  25                  30

Asp Gly Lys Thr Tyr Leu Asn Trp Leu Gln Gln Arg Pro Gly Gln Ser
        35                  40                  45

Pro Arg Arg Leu Ile Ser Leu Val Ser Lys Leu Asp Ser Gly Val Pro
    50                  55                  60
```

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Trp Gln Gly
85 90 95

Thr His Phe Pro Gly Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
115 120 125

Gly Gly Gly Ser Glu Ile Gln Leu Val Gln Ser Gly Ala Glu Val Lys
130 135 140

Lys Pro Gly Glu Ser Leu Arg Ile Ser Cys Lys Gly Ser Gly Phe Asn
145 150 155 160

Ile Glu Asp Tyr Tyr Ile His Trp Val Arg Gln Met Pro Gly Lys Gly
165 170 175

Leu Glu Trp Met Gly Arg Ile Asp Pro Glu Asn Asp Glu Thr Lys Tyr
180 185 190

Gly Pro Ile Phe Gln Gly His Val Thr Ile Ser Ala Asp Thr Ser Ile
195 200 205

Asn Thr Val Tyr Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala
210 215 220

Met Tyr Tyr Cys Ala Phe Arg Gly Gly Val Tyr Trp Gly Gln Gly Thr
225 230 235 240

Thr Val Thr Val Ser Ser
245

<210> 434
<211> 738
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 434
gacgtcgtca tgacccagag cccgctgtca ctgcctgtga ccctgggcca gccggcgtcc 60

attagctgca aatcctcgca atccctgctc gactcagacg gaaaaacgta cttgaactgg 120

ctccaacagc gccctgggca atccccaagg cggcttatct cactcgtcag caagctcgat 180

agcggtgtcc cagacagatt ttcgggctcg ggatcgggca ctgatttcac tctgaagatc 240

tcgcgggtgg aagccgagga tgtgggagtg tactattgct ggcagggcac tcacttcccc 300

gggacgtttg gcggaggaac taaggtcgag atcaaaggag gaggtggatc aggcggaggt 360

gggagcggag gaggaggaag cggtggtgga ggttccgaaa tccagctggt gcaatcagga 420

gccgaggtga agaagccggg agaatccctg cgcatctcgt gcaagggctc gggcttcaac 480

atcgaggatt actacatcca ctgggtgcgg cagatgccgg gaaaggggtt ggaatggatg 540

ggacgcattg acccggaaaa tgatgaaacc aaatacgggc caatcttcca aggccacgtg 600

accattagcg ctgacacttc catcaacacc gtgtaccttc agtggtcctc actgaaggcg 660

tcggacactg ccatgtacta ctgtgcattc agaggagggg tctactgggg acagggcacc 720

accgtgaccg tgagctcc 738

<210> 435
<211> 831
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 435
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgacgtcg tcatgaccca gagcccgctg tcactgcctg tgaccctggg ccagccggcg 120

tccattagct gcaaatcctc gcaatccctg ctcgactcag acggaaaaac gtacttgaac 180

tggctccaac agcgccctgg gcaatcccca aggcggctta tctcactcgt cagcaagctc 240

gatagcggtg tcccagacag attttcgggc tcgggatcgg gcactgattt cactctgaag 300

atctcgcggg tggaagccga ggatgtggga gtgtactatt gctggcaggg cactcacttc 360

cccgggacgt ttggcggagg aactaaggtc gagatcaaag gaggaggtgg atcaggcgga 420

ggtgggagcg gaggaggagg aagcggtggt ggaggttccg aaatccagct ggtgcaatca 480

ggagccgagg tgaagaagcc gggagaatcc ctgcgcatct cgtgcaaggg ctcgggcttc 540

aacatcgagg attactacat ccactgggtg cggcagatgc cgggaaaggg gttggaatgg 600

atgggacgca ttgacccgga aaatgatgaa accaaatacg ggccaatctt ccaaggccac 660

gtgaccatta gcgctgacac ttccatcaac accgtgtacc ttcagtggtc ctcactgaag 720

gcgtcggaca ctgccatgta ctactgtgca ttcagaggag gggtctactg gggacagggc 780

accaccgtga ccgtgagctc cggctcgcat caccatcatc accaccatca c 831

<210> 436
<211> 277
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 436
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Asp Val Val Met Thr Gln Ser Pro Leu Ser Leu
20 25 30

Pro Val Thr Leu Gly Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser Gln
35 40 45

Ser Leu Leu Asp Ser Asp Gly Lys Thr Tyr Leu Asn Trp Leu Gln Gln
50 55 60

Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Ser Leu Val Ser Lys Leu
65 70 75 80

Asp Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
85 90 95

Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr
100 105 110

Tyr Cys Trp Gln Gly Thr His Phe Pro Gly Thr Phe Gly Gly Gly Thr
115 120 125

Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
130 135 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Gln Leu Val Gln Ser
145 150 155 160

Gly Ala Glu Val Lys Lys Pro Gly Glu Ser Leu Arg Ile Ser Cys Lys
165 170 175

Gly Ser Gly Phe Asn Ile Glu Asp Tyr Tyr Ile His Trp Val Arg Gln
180 185 190

Met Pro Gly Lys Gly Leu Glu Trp Met Gly Arg Ile Asp Pro Glu Asn
195 200 205

Asp Glu Thr Lys Tyr Gly Pro Ile Phe Gln Gly His Val Thr Ile Ser
210 215 220

Ala Asp Thr Ser Ile Asn Thr Val Tyr Leu Gln Trp Ser Ser Leu Lys
225 230 235 240

Ala Ser Asp Thr Ala Met Tyr Tyr Cys Ala Phe Arg Gly Gly Val Tyr
245 250 255

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Ser His His His
260 265 270

His His His His His
275

<210> 437
<211> 1470
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 437
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgacgtcg tcatgaccca atcccctctc tccctgccgg tcaccctggg tcagccggcg 120

tcgatctcat gcaaaagctc acagtccctg ctggattcgg acggaaaaac ctacttgaac 180

tggctccaac agaggccggg tcagtcccct cgcagactga tctcgctggt gagcaagctc 240

gactcgggtg tgccggatcg gttctccggg tcaggatcgg gcaccgactt tacgctcaag 300

atttcgagag tggaggccga ggatgtggga gtgtactatt gctggcaggg cacgcatttc 360

cccgggacct ttggaggcgg gactaaggtg gaaatcaagg gaggtggcgg atcaggcgga 420

ggaggcagcg gcggaggtgg atcaggaggc ggagggtcag agatccagct ggtccaaagc 480

ggagcagagg tgaagaagcc aggcgagtcc cttcgcattt cgtgcaaagg gagcggcttc 540

aacattgaag attactacat ccactgggtg cggcaaatgc caggaaaggg tctggaatgg 600

atgggacgga tcgacccaga aaatgatgaa actaagtacg gaccgatctt ccaaggacac 660

gtcactatct ccgcggacac ttcgatcaac accgtgtacc tccagtggag cagcttgaaa 720

gcctccgaca ccgctatgta ctactgtgcc ttccgcggag gagtctactg gggacagggg 780

actactgtga ccgtgtcgtc caccactacc ccagcaccga ggccacccac cccggctcct 840

accatcgcct cccagcctct gtccctgcgt ccggaggcat gtagacccgc agctggtggg 900

gccgtgcata cccggggtct tgacttcgcc tgcgatatct acatttgggc ccctctggct 960

ggtacttgcg gggtcctgct gctttcactc gtgatcactc tttactgtaa gcgcggtcgg 1020

aagaagctgc tgtacatctt taagcaaccc ttcatgaggc ctgtgcagac tactcaagag 1080

gaggacggct gttcatgccg gttcccagag gaggaggaag gcggctgcga actgcgcgtg 1140

aaattcagcc gcagcgcaga tgctccagcc tacaagcagg ggcagaacca gctctacaac 1200

gaactcaatc ttggtcggag agaggagtac gacgtgctgg acaagcggag aggacgggac 1260

ccagaaatgg gcgggaagcc gcgcagaaag aatccccaag agggcctgta caacgagctc 1320

caaaaggata agatggcaga agcctatagc gagattggta tgaaagggga acgcagaaga 1380

ggcaaaggcc acgacggact gtaccaggga ctcagcaccg ccaccaagga cacctatgac 1440

gctcttcaca tgcaggccct gccgcctcgg 1470

<210> 438
<211> 490
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 438
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Asp Val Val Met Thr Gln Ser Pro Leu Ser Leu
20 25 30

Pro Val Thr Leu Gly Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser Gln
35 40 45

Ser Leu Leu Asp Ser Asp Gly Lys Thr Tyr Leu Asn Trp Leu Gln Gln
50 55 60

Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Ser Leu Val Ser Lys Leu
65 70 75 80

Asp Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
85 90 95

Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr
100 105 110

Tyr Cys Trp Gln Gly Thr His Phe Pro Gly Thr Phe Gly Gly Gly Thr
115 120 125

```
                                                _SL
Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Gln Leu Val Gln Ser
145                 150                 155                 160

Gly Ala Glu Val Lys Lys Pro Gly Glu Ser Leu Arg Ile Ser Cys Lys
                165                 170                 175

Gly Ser Gly Phe Asn Ile Glu Asp Tyr Tyr Ile His Trp Val Arg Gln
            180                 185                 190

Met Pro Gly Lys Gly Leu Glu Trp Met Gly Arg Ile Asp Pro Glu Asn
        195                 200                 205

Asp Glu Thr Lys Tyr Gly Pro Ile Phe Gln Gly His Val Thr Ile Ser
    210                 215                 220

Ala Asp Thr Ser Ile Asn Thr Val Tyr Leu Gln Trp Ser Ser Leu Lys
225                 230                 235                 240

Ala Ser Asp Thr Ala Met Tyr Tyr Cys Ala Phe Arg Gly Gly Val Tyr
                245                 250                 255

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Thr Thr Thr Pro Ala
            260                 265                 270

Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser
        275                 280                 285

Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr
    290                 295                 300

Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala
305                 310                 315                 320

Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys
                325                 330                 335

Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met
            340                 345                 350

Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe
        355                 360                 365

Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg
    370                 375                 380
```

Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn
385 390 395 400

Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg
405 410 415

Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro
420 425 430

Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala
435 440 445

Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His
450 455 460

Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp
465 470 475 480

Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 439
<211> 246
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 439
Glu Ile Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Thr Val Lys Ile Ser Cys Lys Gly Ser Gly Phe Asn Ile Glu Asp Tyr
20 25 30

Tyr Ile His Trp Val Gln Gln Ala Pro Gly Lys Gly Leu Glu Trp Met
35 40 45

Gly Arg Ile Asp Pro Glu Asn Asp Glu Thr Lys Tyr Gly Pro Ile Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

```
Ala Phe Arg Gly Gly Val Tyr Trp Gly Gln Gly Thr Thr Val Thr Val
            100                 105                 110

Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
        115                 120                 125

Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln Ser Pro Leu Ser
    130                 135                 140

Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser
145                 150                 155                 160

Gln Ser Leu Leu Asp Ser Asp Gly Lys Thr Tyr Leu Asn Trp Leu Gln
                165                 170                 175

Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Ser Leu Val Ser Lys
            180                 185                 190

Leu Asp Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr
        195                 200                 205

Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Val Gly Val
    210                 215                 220

Tyr Tyr Cys Trp Gln Gly Thr His Phe Pro Gly Thr Phe Gly Gly Gly
225                 230                 235                 240

Thr Lys Val Glu Ile Lys
                245
```

<210> 440
<211> 738
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 440

```
gaaatccagc tcgtgcagag cggagccgag gtcaagaaac cgggtgctac cgtgaagatt       60

tcatgcaagg gatcgggctt caacatcgag gattactaca tccactgggt gcagcaggca      120

ccaggaaaag gacttgaatg gatgggccgg atcgacccgg aaaatgacga gactaagtac      180

ggccctatct tccaaggacg ggtgacgatc accgcagaca ctagcaccaa caccgtctat      240

atggaactct cgtccctgag gtccgaagat actgccgtgt actactgtgc gtttcgcgga      300

ggtgtgtact ggggacaggg taccaccgtc accgtgtcat cgggcggtgg aggctccggt      360
```

ggaggagggt caggaggcgg tggaagcgga ggaggcggca gcgacgtggt catgactcaa 420

tcgccgctgt cgctgcccgt cactctggga caacccgcgt ccatcagctg caaatcctcg 480

cagtcactgc ttgactccga tggaaagacc tacctcaact ggctgcagca acgcccaggc 540

caatccccaa gacgcctgat ctcgttggtg tcaaagctgg actcaggggt gccggaccgg 600

ttctccggga gcgggtcggg cacggatttc actctcaaga tctccagagt ggaagccgag 660

gatgtgggag tctactactg ctggcaggga acccatttcc ctggaacttt tggcggagga 720

actaaggtcg agattaaa 738

<210> 441
<211> 831
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 441
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaaatcc agctcgtgca gagcggagcc gaggtcaaga aaccgggtgc taccgtgaag 120

atttcatgca agggatcggg cttcaacatc gaggattact acatccactg ggtgcagcag 180

gcaccaggaa aaggacttga atggatgggc cggatcgacc cggaaaatga cgagactaag 240

tacggcccta tcttccaagg acgggtgacg atcaccgcag acactagcac caacaccgtc 300

tatatggaac tctcgtccct gaggtccgaa gatactgccg tgtactactg tgcgtttcgc 360

ggaggtgtgt actggggaca gggtaccacc gtcaccgtgt catcgggcgg tggaggctcc 420

ggtggaggag ggtcaggagg cggtggaagc ggaggaggcg gcagcgacgt ggtcatgact 480

caatcgccgc tgtcgctgcc cgtcactctg ggacaacccg cgtccatcag ctgcaaatcc 540

tcgcagtcac tgcttgactc cgatggaaag acctacctca actggctgca gcaacgccca 600

ggccaatccc caagacgcct gatctcgttg gtgtcaaagc tggactcagg ggtgccggac 660

cggttctccg ggagcgggtc gggcacggat ttcactctca agatctccag agtggaagcc 720

gaggatgtgg gagtctacta ctgctggcag ggaacccatt tccctggaac ttttggcgga 780

ggaactaagg tcgagattaa agggagccac catcatcatc accaccacca c 831

<210> 442
<211> 277
<212> PRT
<213> Artificial Sequence

<220>
<221> source

_SL

<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 442

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15

His Ala Ala Arg Pro Glu Ile Gln Leu Val Gln Ser Gly Ala Glu Val
            20                  25                  30

Lys Lys Pro Gly Ala Thr Val Lys Ile Ser Cys Lys Gly Ser Gly Phe
        35                  40                  45

Asn Ile Glu Asp Tyr Tyr Ile His Trp Val Gln Gln Ala Pro Gly Lys
    50                  55                  60

Gly Leu Glu Trp Met Gly Arg Ile Asp Pro Glu Asn Asp Glu Thr Lys
65                  70                  75                  80

Tyr Gly Pro Ile Phe Gln Gly Arg Val Thr Ile Thr Ala Asp Thr Ser
                85                  90                  95

Thr Asn Thr Val Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Phe Arg Gly Gly Val Tyr Trp Gly Gln Gly
        115                 120                 125

Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
    130                 135                 140

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr
145                 150                 155                 160

Gln Ser Pro Leu Ser Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile
                165                 170                 175

Ser Cys Lys Ser Ser Gln Ser Leu Leu Asp Ser Asp Gly Lys Thr Tyr
            180                 185                 190

Leu Asn Trp Leu Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile
        195                 200                 205

Ser Leu Val Ser Lys Leu Asp Ser Gly Val Pro Asp Arg Phe Ser Gly
    210                 215                 220

Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala
225                 230                 235                 240
```

Glu Asp Val Gly Val Tyr Tyr Cys Trp Gln Gly Thr His Phe Pro Gly
245 250 255

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Ser His His His
260 265 270

His His His His His
275

<210> 443
<211> 1470
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 443
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaaatcc agctcgtgca gagcggagcc gaggtcaaga aaccgggtgc taccgtgaag 120

atttcatgca agggatcggg cttcaacatc gaggattact acatccactg ggtgcagcag 180

gcaccaggaa aaggacttga atggatgggc cggatcgacc cggaaaatga cgagactaag 240

tacggcccta tcttccaagg acgggtgacg atcaccgcag acactagcac caacaccgtc 300

tatatggaac tctcgtccct gaggtccgaa gatactgccg tgtactactg tgcgtttcgc 360

ggaggtgtgt actggggaca gggtaccacc gtcaccgtgt catcgggcgg tggaggctcc 420

ggtggaggag ggtcaggagg cggtggaagc ggaggaggcg gcagcgacgt ggtcatgact 480

caatcgccgc tgtcgctgcc cgtcactctg ggacaacccg cgtccatcag ctgcaaatcc 540

tcgcagtcac tgcttgactc cgatggaaag acctacctca actggctgca gcaacgccca 600

ggccaatccc caagacgcct gatctcgttg gtgtcaaagc tggactcagg ggtgccggac 660

cggttctccg ggagcgggtc gggcacggat ttcactctca agatctccag agtggaagcc 720

gaggatgtgg gagtctacta ctgctggcag ggaacccatt tccctggaac ttttggcgga 780

ggaactaagg tcgagattaa aaccactacc ccagcaccga ggccacccac cccggctcct 840

accatcgcct cccagcctct gtccctgcgt ccggaggcat gtagacccgc agctggtggg 900

gccgtgcata cccggggtct tgacttcgcc tgcgatatct acatttgggc ccctctggct 960

ggtacttgcg gggtcctgct gctttcactc gtgatcactc tttactgtaa gcgcggtcgg 1020

aagaagctgc tgtacatctt taagcaaccc ttcatgaggc ctgtgcagac tactcaagag 1080

gaggacggct gttcatgccg gttcccagag gaggaggaag gcggctgcga actgcgcgtg 1140

aaattcagcc gcagcgcaga tgctccagcc tacaagcagg ggcagaacca gctctacaac 1200

gaactcaatc ttggtcggag agaggagtac gacgtgctgg acaagcggag aggacgggac 1260

ccagaaatgg gcgggaagcc gcgcagaaag aatccccaag agggcctgta caacgagctc 1320

caaaaggata agatggcaga agcctatagc gagattggta tgaaagggga acgcagaaga 1380

ggcaaaggcc acgacggact gtaccaggga ctcagcaccg ccaccaagga cacctatgac 1440

gctcttcaca tgcaggccct gccgcctcgg 1470

<210> 444
<211> 490
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 444
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Ile Gln Leu Val Gln Ser Gly Ala Glu Val
20 25 30

Lys Lys Pro Gly Ala Thr Val Lys Ile Ser Cys Lys Gly Ser Gly Phe
35 40 45

Asn Ile Glu Asp Tyr Tyr Ile His Trp Val Gln Gln Ala Pro Gly Lys
50 55 60

Gly Leu Glu Trp Met Gly Arg Ile Asp Pro Glu Asn Asp Glu Thr Lys
65 70 75 80

Tyr Gly Pro Ile Phe Gln Gly Arg Val Thr Ile Thr Ala Asp Thr Ser
85 90 95

Thr Asn Thr Val Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Ala Phe Arg Gly Gly Val Tyr Trp Gly Gln Gly
115 120 125

Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
130 135 140

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr
145 150 155 160

```
                                                _SL
Gln Ser Pro Leu Ser Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile
                165                 170                 175

Ser Cys Lys Ser Ser Gln Ser Leu Leu Asp Ser Asp Gly Lys Thr Tyr
            180                 185                 190

Leu Asn Trp Leu Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile
        195                 200                 205

Ser Leu Val Ser Lys Leu Asp Ser Gly Val Pro Asp Arg Phe Ser Gly
    210                 215                 220

Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala
225                 230                 235                 240

Glu Asp Val Gly Val Tyr Tyr Cys Trp Gln Gly Thr His Phe Pro Gly
                245                 250                 255

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Thr Thr Thr Pro Ala
            260                 265                 270

Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser
        275                 280                 285

Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr
    290                 295                 300

Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala
305                 310                 315                 320

Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys
                325                 330                 335

Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met
            340                 345                 350

Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe
        355                 360                 365

Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg
    370                 375                 380

Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn
385                 390                 395                 400

Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg
                405                 410                 415
```

```
Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro
            420                 425                 430

Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala
        435                 440                 445

Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His
    450                 455                 460

Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp
465                 470                 475                 480

Ala Leu His Met Gln Ala Leu Pro Pro Arg
                485                 490
```

<210> 445
<211> 246
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 445

```
Glu Ile Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1               5                   10                  15

Ser Leu Arg Ile Ser Cys Lys Gly Ser Gly Phe Asn Ile Glu Asp Tyr
            20                  25                  30

Tyr Ile His Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
        35                  40                  45

Gly Arg Ile Asp Pro Glu Asn Asp Glu Thr Lys Tyr Gly Pro Ile Phe
    50                  55                  60

Gln Gly His Val Thr Ile Ser Ala Asp Thr Ser Ile Asn Thr Val Tyr
65                  70                  75                  80

Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
                85                  90                  95

Ala Phe Arg Gly Gly Val Tyr Trp Gly Gln Gly Thr Thr Val Thr Val
            100                 105                 110

Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
        115                 120                 125
```

```
Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln Ser Pro Asp Ser
    130                 135                 140

Leu Ala Val Ser Leu Gly Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser
145                 150                 155                 160

Gln Ser Leu Leu Asp Ser Asp Gly Lys Thr Tyr Leu Asn Trp Leu Gln
                165                 170                 175

Gln Lys Pro Gly Gln Pro Pro Lys Arg Leu Ile Ser Leu Val Ser Lys
            180                 185                 190

Leu Asp Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr
        195                 200                 205

Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val
    210                 215                 220

Tyr Tyr Cys Trp Gln Gly Thr His Phe Pro Gly Thr Phe Gly Gly Gly
225                 230                 235                 240

Thr Lys Val Glu Ile Lys
                245
```

<210> 446
<211> 738
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 446
gaaatccagc tggtgcagtc aggcgccgag gtcaagaagc cgggagagtc gctgagaatc 60

tcgtgcaagg gctcggggtt caacatcgag gactactaca ttcactgggt caggcagatg 120

ccgggaaagg gactggaatg gatgggccgg atcgacccag aaaatgacga aaccaaatac 180

gggccgattt ttcaaggcca cgtgactatc agcgcagaca cgagcatcaa cactgtctac 240

ctccagtggt cctcgcttaa ggccagcgat accgctatgt actactgcgc attcagaggc 300

ggggtgtact ggggacaagg aaccactgtg accgtgagca gcggaggtgg cggctcggga 360

ggaggtggga gcggaggagg aggttccggc ggtggaggat cagatgtcgt gatgacccag 420

tccccggact ccctcgctgt ctcactgggc gagcgcgcga ccatcaactg caaatcgagc 480

cagtcgctgt tggactccga tggaaagact tatctgaatt ggctgcaaca gaaaccagga 540

caacctccca agcggctcat ctcgcttgtg tcaaaactcg attcgggagt gccagaccgc 600

ttctcggggt ccgggagcgg aactgacttt actttgacca tttcctcact gcaagcggag 660

gatgtggccg tgtattactg ttggcagggc acgcatttcc ctggaacctt cggtggcgga 720

actaaggtgg aaatcaag 738

<210> 447
<211> 834
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 447
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaaatcc agctggtgca gtcaggcgcc gaggtcaaga agccgggaga gtcgctgaga 120

atctcgtgca agggctcggg gttcaacatc gaggactact acattcactg ggtcaggcag 180

atgccgggaa agggactgga atggatgggc cggatcgacc cagaaaatga cgaaaccaaa 240

tacgggccga tttttcaagg ccacgtgact atcagcgcag acacgagcat caacactgtc 300

tacctccagt ggtcctcgct taaggccagc gataccgcta tgtactactg cgcattcaga 360

ggcggggtgt actggggaca aggaaccact gtgaccgtga gcagcggagg tggcggctcg 420

ggaggaggtg ggagcggagg aggaggttcc ggcggtggag gatcagatgt cgtgatgacc 480

cagtccccgg actccctcgc tgtctcactg ggcgagcgcg cgaccatcaa ctgcaaatcg 540

agccagtcgc tgttggactc cgatggaaag acttatctga attggctgca acagaaacca 600

ggacaacctc ccaagcggct catctcgctt gtgtcaaaac tcgattcggg agtgccagac 660

cgcttctcgg ggtccgggag cggaactgac tttactttga ccatttcctc actgcaagcg 720

gaggatgtgg ccgtgtatta ctgttggcag ggcacgcatt tccctggaac cttcggtggc 780

ggaactaagg tggaaatcaa gggatcacac caccatcatc accatcacca ccat 834

<210> 448
<211> 278
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 448
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

_SL
His Ala Ala Arg Pro Glu Ile Gln Leu Val Gln Ser Gly Ala Glu Val
            20   25   30

Lys Lys Pro Gly Glu Ser Leu Arg Ile Ser Cys Lys Gly Ser Gly Phe
        35   40   45

Asn Ile Glu Asp Tyr Tyr Ile His Trp Val Arg Gln Met Pro Gly Lys
    50   55   60

Gly Leu Glu Trp Met Gly Arg Ile Asp Pro Glu Asn Asp Glu Thr Lys
65   70   75   80

Tyr Gly Pro Ile Phe Gln Gly His Val Thr Ile Ser Ala Asp Thr Ser
                85   90   95

Ile Asn Thr Val Tyr Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr
            100   105   110

Ala Met Tyr Tyr Cys Ala Phe Arg Gly Gly Val Tyr Trp Gly Gln Gly
        115   120   125

Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
    130   135   140

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr
145   150   155   160

Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly Glu Arg Ala Thr Ile
                165   170   175

Asn Cys Lys Ser Ser Gln Ser Leu Leu Asp Ser Asp Gly Lys Thr Tyr
            180   185   190

Leu Asn Trp Leu Gln Gln Lys Pro Gly Gln Pro Pro Lys Arg Leu Ile
        195   200   205

Ser Leu Val Ser Lys Leu Asp Ser Gly Val Pro Asp Arg Phe Ser Gly
    210   215   220

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala
225   230   235   240

Glu Asp Val Ala Val Tyr Tyr Cys Trp Gln Gly Thr His Phe Pro Gly
                245   250   255

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Ser His His His
            260   265   270

His His His His His His
275

<210> 449
<211> 1470
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 449
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgagattc agctcgtgca atcgggagcg gaagtcaaga agccaggaga gtccttgcgg 120

atctcatgca agggtagcgg ctttaacatc gaggattact acatccactg ggtgaggcag 180

atgccgggga agggactcga atggatggga cggatcgacc cagaaaacga cgaaactaag 240

tacggtccga tcttccaagg ccatgtgact attagcgccg atacttcaat caataccgtg 300

tatctgcaat ggtcctcatt gaaagcctca gataccgcga tgtactactg tgctttcaga 360

ggaggggtct actggggaca gggaactacc gtgactgtct cgtccggcgg aggcgggtca 420

ggaggtggcg gcagcggagg aggagggtcc ggcggaggtg ggtccgacgt cgtgatgacc 480

cagagccctg acagcctggc agtgagcctg ggcgaaagag ctaccattaa ctgcaaatcg 540

tcgcagagcc tgctggactc ggacggaaaa acgtacctca attggctgca gcaaaagcct 600

ggccagccac cgaagcgcct tatctcactg gtgtcgaagc tggattcggg agtgcccgat 660

cgcttctccg gctcgggatc gggtactgac ttcaccctca ctatctcctc gcttcaagca 720

gaggacgtgg ccgtctacta ctgctggcag ggaacccact ttccgggaac cttcggcgga 780

gggacgaaag tggagatcaa gaccactacc ccagcaccga ggccacccac cccggctcct 840

accatcgcct cccagcctct gtccctgcgt ccggaggcat gtagacccgc agctggtggg 900

gccgtgcata cccggggtct tgacttcgcc tgcgatatct acatttgggc ccctctggct 960

ggtacttgcg gggtcctgct gctttcactc gtgatcactc tttactgtaa gcgcggtcgg 1020

aagaagctgc tgtacatctt taagcaaccc ttcatgaggc ctgtgcagac tactcaagag 1080

gaggacggct gttcatgccg gttcccagag gaggaggaag gcggctgcga actgcgcgtg 1140

aaattcagcc gcagcgcaga tgctccagcc tacaagcagg ggcagaacca gctctacaac 1200

gaactcaatc ttggtcggag agaggagtac gacgtgctgg acaagcggag aggacgggac 1260

ccagaaatgg gcgggaagcc gcgcagaaag aatccccaag agggcctgta caacgagctc 1320

caaaaggata agatggcaga agcctatagc gagattggta tgaaagggga acgcagaaga 1380

ggcaaaggcc acgacggact gtaccaggga ctcagcaccg ccaccaagga cacctatgac 1440

gctcttcaca tgcaggccct gccgcctcgg 1470

<210> 450
<211> 490
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 450
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Ile Gln Leu Val Gln Ser Gly Ala Glu Val
20 25 30

Lys Lys Pro Gly Glu Ser Leu Arg Ile Ser Cys Lys Gly Ser Gly Phe
35 40 45

Asn Ile Glu Asp Tyr Tyr Ile His Trp Val Arg Gln Met Pro Gly Lys
50 55 60

Gly Leu Glu Trp Met Gly Arg Ile Asp Pro Glu Asn Asp Glu Thr Lys
65 70 75 80

Tyr Gly Pro Ile Phe Gln Gly His Val Thr Ile Ser Ala Asp Thr Ser
85 90 95

Ile Asn Thr Val Tyr Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr
100 105 110

Ala Met Tyr Tyr Cys Ala Phe Arg Gly Gly Val Tyr Trp Gly Gln Gly
115 120 125

Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
130 135 140

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr
145 150 155 160

Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly Glu Arg Ala Thr Ile
165 170 175

Asn Cys Lys Ser Ser Gln Ser Leu Leu Asp Ser Asp Gly Lys Thr Tyr
180 185 190

```
                                                    _SL
Leu Asn Trp Leu Gln Gln Lys Pro Gly Gln Pro Pro Lys Arg Leu Ile
        195                 200                 205

Ser Leu Val Ser Lys Leu Asp Ser Gly Val Pro Asp Arg Phe Ser Gly
    210                 215                 220

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala
225                 230                 235                 240

Glu Asp Val Ala Val Tyr Tyr Cys Trp Gln Gly Thr His Phe Pro Gly
                245                 250                 255

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Thr Thr Thr Pro Ala
            260                 265                 270

Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser
        275                 280                 285

Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr
    290                 295                 300

Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala
305                 310                 315                 320

Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys
                325                 330                 335

Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met
            340                 345                 350

Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe
        355                 360                 365

Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg
    370                 375                 380

Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn
385                 390                 395                 400

Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg
                405                 410                 415

Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro
            420                 425                 430

Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala
        435                 440                 445
```

Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His
450 455 460

Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp
465 470 475 480

Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 451
<211> 246
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 451
Asp Val Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser Gln Ser Leu Leu Asp Ser
20 25 30

Asp Gly Lys Thr Tyr Leu Asn Trp Leu Gln Gln Lys Pro Gly Gln Pro
35 40 45

Pro Lys Arg Leu Ile Ser Leu Val Ser Lys Leu Asp Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile
65 70 75 80

Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Trp Gln Gly
85 90 95

Thr His Phe Pro Gly Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
115 120 125

Gly Gly Gly Ser Glu Ile Gln Leu Val Gln Ser Gly Ala Glu Val Lys
130 135 140

Lys Pro Gly Glu Ser Leu Arg Ile Ser Cys Lys Gly Ser Gly Phe Asn
145 150 155 160

```
Ile Glu Asp Tyr Tyr Ile His Trp Val Arg Gln Met Pro Gly Lys Gly
                165                 170                 175

Leu Glu Trp Met Gly Arg Ile Asp Pro Glu Asn Asp Glu Thr Lys Tyr
            180                 185                 190

Gly Pro Ile Phe Gln Gly His Val Thr Ile Ser Ala Asp Thr Ser Ile
        195                 200                 205

Asn Thr Val Tyr Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala
    210                 215                 220

Met Tyr Tyr Cys Ala Phe Arg Gly Gly Val Tyr Trp Gly Gln Gly Thr
225                 230                 235                 240

Thr Val Thr Val Ser Ser
                245
```

<210> 452
<211> 738
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 452

```
gacgtggtga tgacccaatc gccagattcc ctggcagtgt ccctgggcga acgcgccact       60

attaactgca aatcgtcaca gtccttgctt gattccgacg gaaagaccta cctcaattgg      120

ctccagcaga agccaggaca accgccaaag agactgatct ccctggtgtc aaagctggac      180

tcgggagtgc ctgatcggtt ctcgggtagc gggagcggca ccgacttcac tctgaccatc      240

tcgtcactcc aggctgagga cgtggccgtg tattactgtt ggcagggtac tcactttccg      300

ggcactttcg gaggcggcac caaggtggag attaaaggag gaggcggaag cggaggtgga      360

ggatcgggag gtggtgggag cggcggagga gggagcgaga tccagctcgt ccaatcggga      420

gcggaagtga agaagcccgg agagtcactt agaatctcat gcaaggggtc gggcttcaac      480

atcgaggatt actacatcca ttgggtccgc cagatgcctg gtaaaggact ggaatggatg      540

gggaggattg acccggaaaa cgacgaaact aagtacggac cgatctttca agggcacgtg      600

actatctccg ctgatacctc aatcaatact gtctacctcc agtggtcctc gctgaaagca      660

agcgacaccg cgatgtacta ctgcgccttc cggggaggag tgtactgggg ccaaggcacc      720

acggtcacgg tcagctcc                                                    738
```

<210> 453
<211> 834
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 453
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgacgtgg tgatgaccca atcgccagat tccctggcag tgtccctggg cgaacgcgcc 120

actattaact gcaaatcgtc acagtccttg cttgattccg acggaaagac ctacctcaat 180

tggctccagc agaagccagg acaaccgcca aagagactga tctccctggt gtcaaagctg 240

gactcgggag tgcctgatcg gttctcgggt agcgggagcg gcaccgactt cactctgacc 300

atctcgtcac tccaggctga ggacgtggcc gtgtattact gttggcaggg tactcacttt 360

ccgggcactt tcggaggcgg caccaaggtg gagattaaag gaggaggcgg aagcggaggt 420

ggaggatcgg gaggtggtgg gagcggcgga ggagggagcg agatccagct cgtccaatcg 480

ggagcggaag tgaagaagcc cggagagtca cttagaatct catgcaaggg gtcgggcttc 540

aacatcgagg attactacat ccattgggtc cgccagatgc ctggtaaagg actggaatgg 600

atggggagga ttgacccgga aaacgacgaa actaagtacg gaccgatctt tcaagggcac 660

gtgactatct ccgctgatac ctcaatcaat actgtctacc tccagtggtc ctcgctgaaa 720

gcaagcgaca ccgcgatgta ctactgcgcc ttccggggag gagtgtactg gggccaaggc 780

accacggtca cggtcagctc cggctcccat caccaccacc atcaccatca tcac 834

<210> 454
<211> 278
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 454
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Asp Val Val Met Thr Gln Ser Pro Asp Ser Leu
20 25 30

Ala Val Ser Leu Gly Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser Gln
35 40 45

_SL
Ser Leu Leu Asp Ser Asp Gly Lys Thr Tyr Leu Asn Trp Leu Gln Gln
50 55 60

Lys Pro Gly Gln Pro Pro Lys Arg Leu Ile Ser Leu Val Ser Lys Leu
65 70 75 80

Asp Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
85 90 95

Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr
100 105 110

Tyr Cys Trp Gln Gly Thr His Phe Pro Gly Thr Phe Gly Gly Gly Thr
115 120 125

Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
130 135 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Gln Leu Val Gln Ser
145 150 155 160

Gly Ala Glu Val Lys Lys Pro Gly Glu Ser Leu Arg Ile Ser Cys Lys
165 170 175

Gly Ser Gly Phe Asn Ile Glu Asp Tyr Tyr Ile His Trp Val Arg Gln
180 185 190

Met Pro Gly Lys Gly Leu Glu Trp Met Gly Arg Ile Asp Pro Glu Asn
195 200 205

Asp Glu Thr Lys Tyr Gly Pro Ile Phe Gln Gly His Val Thr Ile Ser
210 215 220

Ala Asp Thr Ser Ile Asn Thr Val Tyr Leu Gln Trp Ser Ser Leu Lys
225 230 235 240

Ala Ser Asp Thr Ala Met Tyr Tyr Cys Ala Phe Arg Gly Gly Val Tyr
245 250 255

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Ser His His His
260 265 270

His His His His His His
275

<210> 455
<211> 1470
<212> DNA

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 455
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgacgtgg tgatgactca gtcgcctgac tcgctggctg tgtcccttgg agagcgggcc 120

actatcaatt gcaagtcatc ccagtcgctg ctggattccg acgggaaaac ctacctcaat 180

tggctgcagc aaaaaccggg acagcctcca aagcggctca tcagcctggt gtccaagttg 240

gacagcggcg tgccagaccg cttctccggt tcgggaagcg gtactgattt cacgctgacc 300

atctcatccc tccaagcgga ggatgtggca gtctactact gttggcaggg cacgcatttt 360

ccgggcactt ttggaggagg gaccaaggtc gaaatcaagg gaggaggtgg ctcgggcgga 420

ggaggctcgg gaggaggagg atcaggaggc ggtggaagcg agattcaact ggtccagagc 480

ggcgcagaag tcaagaagcc gggtgaatcg ctcagaatct cgtgcaaagg atcgggattc 540

aacatcgagg actactacat tcactgggtc agacaaatgc cgggcaaagg gctggaatgg 600

atggggagga tcgaccccga aaacgatgaa accaagtacg gaccaatctt ccaagggcac 660

gtgaccattt cggcggacac ctcaatcaac actgtgtacc tccagtggag ctcacttaag 720

gccagcgata ccgccatgta ctattgcgct ttccgcggag gggtgtactg gggacagggc 780

actactgtga ccgtgtcatc caccactacc ccagcaccga ggccacccac cccggctcct 840

accatcgcct cccagcctct gtccctgcgt ccggaggcat gtagacccgc agctggtggg 900

gccgtgcata cccggggtct tgacttcgcc tgcgatatct acatttgggc ccctctggct 960

ggtacttgcg gggtcctgct gctttcactc gtgatcactc tttactgtaa gcgcggtcgg 1020

aagaagctgc tgtacatctt taagcaaccc ttcatgaggc ctgtgcagac tactcaagag 1080

gaggacggct gttcatgccg gttcccagag gaggaggaag gcggctgcga actgcgcgtg 1140

aaattcagcc gcagcgcaga tgctccagcc tacaagcagg ggcagaacca gctctacaac 1200

gaactcaatc ttggtcggag agaggagtac gacgtgctgg acaagcggag aggacgggac 1260

ccagaaatgg gcgggaagcc gcgcagaaag aatccccaag agggcctgta caacgagctc 1320

caaaaggata agatggcaga agcctatagc gagattggta tgaaagggga acgcagaaga 1380

ggcaaaggcc acgacggact gtaccaggga ctcagcaccg ccaccaagga cacctatgac 1440

gctcttcaca tgcaggccct gccgcctcgg 1470

<210> 456
<211> 490
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 456

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15

His Ala Ala Arg Pro Asp Val Val Met Thr Gln Ser Pro Asp Ser Leu
            20                  25                  30

Ala Val Ser Leu Gly Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser Gln
        35                  40                  45

Ser Leu Leu Asp Ser Asp Gly Lys Thr Tyr Leu Asn Trp Leu Gln Gln
    50                  55                  60

Lys Pro Gly Gln Pro Pro Lys Arg Leu Ile Ser Leu Val Ser Lys Leu
65                  70                  75                  80

Asp Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
                85                  90                  95

Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr
            100                 105                 110

Tyr Cys Trp Gln Gly Thr His Phe Pro Gly Thr Phe Gly Gly Gly Thr
        115                 120                 125

Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Gln Leu Val Gln Ser
145                 150                 155                 160

Gly Ala Glu Val Lys Lys Pro Gly Glu Ser Leu Arg Ile Ser Cys Lys
                165                 170                 175

Gly Ser Gly Phe Asn Ile Glu Asp Tyr Tyr Ile His Trp Val Arg Gln
            180                 185                 190

Met Pro Gly Lys Gly Leu Glu Trp Met Gly Arg Ile Asp Pro Glu Asn
        195                 200                 205

Asp Glu Thr Lys Tyr Gly Pro Ile Phe Gln Gly His Val Thr Ile Ser
    210                 215                 220
```

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                                                    _SL
Ala Asp Thr Ser Ile Asn Thr Val Tyr Leu Gln Trp Ser Ser Leu Lys
225                 230                 235                 240

Ala Ser Asp Thr Ala Met Tyr Tyr Cys Ala Phe Arg Gly Gly Val Tyr
                245                 250                 255

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Thr Thr Thr Pro Ala
            260                 265                 270

Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser
        275                 280                 285

Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr
    290                 295                 300

Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala
305                 310                 315                 320

Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys
                325                 330                 335

Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met
            340                 345                 350

Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe
        355                 360                 365

Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg
    370                 375                 380

Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn
385                 390                 395                 400

Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg
                405                 410                 415

Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro
            420                 425                 430

Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala
        435                 440                 445

Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His
    450                 455                 460

Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp
465                 470                 475                 480
```

Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 457
<211> 246
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 457
Asp Val Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Leu Gly
1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser Gln Ser Leu Leu Asp Ser
20 25 30

Asp Gly Lys Thr Tyr Leu Asn Trp Leu Gln Gln Arg Pro Gly Gln Ser
35 40 45

Pro Arg Arg Leu Ile Ser Leu Val Ser Lys Leu Asp Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Trp Gln Gly
85 90 95

Thr His Phe Pro Gly Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
115 120 125

Gly Gly Gly Ser Glu Ile Gln Leu Val Gln Ser Gly Ala Glu Val Lys
130 135 140

Lys Pro Gly Ala Thr Val Lys Ile Ser Cys Lys Gly Ser Gly Phe Asn
145 150 155 160

Ile Glu Asp Tyr Tyr Ile His Trp Val Gln Gln Ala Pro Gly Lys Gly
165 170 175

Leu Glu Trp Met Gly Arg Ile Asp Pro Glu Asn Asp Glu Thr Lys Tyr
180 185 190

Gly Pro Ile Phe Gln Gly Arg Val Thr Ile Thr Ala Asp Thr Ser Thr
195 200 205

Asn Thr Val Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala
210 215 220

Val Tyr Tyr Cys Ala Phe Arg Gly Gly Val Tyr Trp Gly Gln Gly Thr
225 230 235 240

Thr Val Thr Val Ser Ser
245

<210> 458
<211> 738
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 458
gatgtggtca tgacgcagtc accactgtcc ctccccgtga cccttggaca gccagcgtcg 60

attagctgca agtcatccca atccctgctc gattcggatg gaaagaccta tctcaactgg 120

ctgcagcaaa gacccggtca gagccctagg agactcatct cgttggtgtc aaagctggac 180

agcggagtgc cggaccggtt ttccggttcg ggatcgggga cggacttcac tctgaagatt 240

tcacgggtgg aagctgagga tgtgggagtg tactactgct ggcagggaac ccatttccct 300

ggcacttttg gcggaggaac taaggtcgaa atcaagggag gaggtggctc gggaggaggc 360

ggatcgggcg gaggcgggag cggcggagga gggtccgaaa tccaacttgt ccagtcagga 420

gccgaagtga agaaaccggg agccaccgtc aaaatcagct gtaagggatc gggattcaat 480

atcgaggact actacatcca ctgggtgcag caagctccgg gcaaaggact ggagtggatg 540

gggcgcatcg acccagagaa cgacgaaacc aaatacggcc cgatcttcca agggcgggtg 600

accatcaccg cggacacctc aactaacact gtgtacatgg agctgagctc cctgcgctcc 660

gaagatactg cagtctacta ctgcgccttc cgcggtggtg tgtactgggg acagggcacc 720

actgtgactg tcagctcg 738

<210> 459
<211> 831
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

polynucleotide"

<400> 459
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgatgtgg tcatgacgca gtcaccactg tccctccccg tgacccttgg acagccagcg 120

tcgattagct gcaagtcatc ccaatccctg ctcgattcgg atggaaagac ctatctcaac 180

tggctgcagc aaagacccgg tcagagccct aggagactca tctcgttggt gtcaaagctg 240

gacagcggag tgccggaccg gttttccggt tcgggatcgg ggacggactt cactctgaag 300

atttcacggg tggaagctga ggatgtggga gtgtactact gctggcaggg aacccatttc 360

cctggcactt ttggcggagg aactaaggtc gaaatcaagg gaggaggtgg ctcgggagga 420

ggcggatcgg gcggaggcgg gagcggcgga ggagggtccg aaatccaact tgtccagtca 480

ggagccgaag tgaagaaacc gggagccacc gtcaaaatca gctgtaaggg atcgggattc 540

aatatcgagg actactacat ccactgggtg cagcaagctc cgggcaaagg actggagtgg 600

atggggcgca tcgacccaga gaacgacgaa accaaatacg gcccgatctt ccaagggcgg 660

gtgaccatca ccgcggacac ctcaactaac actgtgtaca tggagctgag ctccctgcgc 720

tccgaagata ctgcagtcta ctactgcgcc ttccgcggtg gtgtgtactg gggacagggc 780

accactgtga ctgtcagctc ggggtcccac catcatcacc accaccatca c 831

<210> 460
<211> 277
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 460
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Asp Val Val Met Thr Gln Ser Pro Leu Ser Leu
20 25 30

Pro Val Thr Leu Gly Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser Gln
35 40 45

Ser Leu Leu Asp Ser Asp Gly Lys Thr Tyr Leu Asn Trp Leu Gln Gln
50 55 60

Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Ser Leu Val Ser Lys Leu
65 70 75 80

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                                                _SL
Asp Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
                85                  90                  95

Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr
            100                 105                 110

Tyr Cys Trp Gln Gly Thr His Phe Pro Gly Thr Phe Gly Gly Gly Thr
        115                 120                 125

Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Gln Leu Val Gln Ser
145                 150                 155                 160

Gly Ala Glu Val Lys Lys Pro Gly Ala Thr Val Lys Ile Ser Cys Lys
                165                 170                 175

Gly Ser Gly Phe Asn Ile Glu Asp Tyr Tyr Ile His Trp Val Gln Gln
            180                 185                 190

Ala Pro Gly Lys Gly Leu Glu Trp Met Gly Arg Ile Asp Pro Glu Asn
        195                 200                 205

Asp Glu Thr Lys Tyr Gly Pro Ile Phe Gln Gly Arg Val Thr Ile Thr
    210                 215                 220

Ala Asp Thr Ser Thr Asn Thr Val Tyr Met Glu Leu Ser Ser Leu Arg
225                 230                 235                 240

Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Phe Arg Gly Gly Val Tyr
                245                 250                 255

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Ser His His His
            260                 265                 270

His His His His His
        275


<210> 461
<211> 1470
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 461
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atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgatgtgg tcatgacgca gtcaccactg tccctccccg tgacccttgg acagccagcg 120

tcgattagct gcaagtcatc ccaatccctg ctcgattcgg atggaaagac ctatctcaac 180

tggctgcagc aaagacccgg tcagagccct aggagactca tctcgttggt gtcaaagctg 240

gacagcggag tgccggaccg gttttccggt tcgggatcgg ggacggactt cactctgaag 300

atttcacggg tggaagctga ggatgtggga gtgtactact gctggcaggg aacccatttc 360

cctggcactt ttggcggagg aactaaggtc gaaatcaagg gaggaggtgg ctcgggagga 420

ggcggatcgg gcggaggcgg gagcggcgga ggagggtccg aaatccaact tgtccagtca 480

ggagccgaag tgaagaaacc gggagccacc gtcaaaatca gctgtaaggg atcgggattc 540

aatatcgagg actactacat ccactgggtg cagcaagctc cgggcaaagg actggagtgg 600

atggggcgca tcgacccaga gaacgacgaa accaaatacg gcccgatctt ccaagggcgg 660

gtgaccatca ccgcggacac ctcaactaac actgtgtaca tggagctgag ctccctgcgc 720

tccgaagata ctgcagtcta ctactgcgcc ttccgcggtg gtgtgtactg gggacagggc 780

accactgtga ctgtcagctc gaccactacc ccagcaccga ggccacccac cccggctcct 840

accatcgcct cccagcctct gtccctgcgt ccggaggcat gtagacccgc agctggtggg 900

gccgtgcata cccggggtct tgacttcgcc tgcgatatct acatttgggc ccctctggct 960

ggtacttgcg gggtcctgct gctttcactc gtgatcactc tttactgtaa gcgcggtcgg 1020

aagaagctgc tgtacatctt taagcaaccc ttcatgaggc ctgtgcagac tactcaagag 1080

gaggacggct gttcatgccg gttcccagag gaggaggaag gcggctgcga actgcgcgtg 1140

aaattcagcc gcagcgcaga tgctccagcc tacaagcagg ggcagaacca gctctacaac 1200

gaactcaatc ttggtcggag agaggagtac gacgtgctgg acaagcggag aggacgggac 1260

ccagaaatgg gcgggaagcc gcgcagaaag aatccccaag agggcctgta caacgagctc 1320

caaaaggata agatggcaga agcctatagc gagattggta tgaaagggga acgcagaaga 1380

ggcaaaggcc acgacggact gtaccaggga ctcagcaccg ccaccaagga cacctatgac 1440

gctcttcaca tgcaggccct gccgcctcgg 1470

<210> 462
<211> 490
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 462
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu

```
                                                _SL
1               5                   10                  15

His Ala Ala Arg Pro Asp Val Val Met Thr Gln Ser Pro Leu Ser Leu
            20                  25                  30

Pro Val Thr Leu Gly Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser Gln
        35                  40                  45

Ser Leu Leu Asp Ser Asp Gly Lys Thr Tyr Leu Asn Trp Leu Gln Gln
    50                  55                  60

Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Ser Leu Val Ser Lys Leu
65                  70                  75                  80

Asp Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
                85                  90                  95

Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr
            100                 105                 110

Tyr Cys Trp Gln Gly Thr His Phe Pro Gly Thr Phe Gly Gly Gly Thr
        115                 120                 125

Lys Val Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Gln Leu Val Gln Ser
145                 150                 155                 160

Gly Ala Glu Val Lys Lys Pro Gly Ala Thr Val Lys Ile Ser Cys Lys
                165                 170                 175

Gly Ser Gly Phe Asn Ile Glu Asp Tyr Tyr Ile His Trp Val Gln Gln
            180                 185                 190

Ala Pro Gly Lys Gly Leu Glu Trp Met Gly Arg Ile Asp Pro Glu Asn
        195                 200                 205

Asp Glu Thr Lys Tyr Gly Pro Ile Phe Gln Gly Arg Val Thr Ile Thr
    210                 215                 220

Ala Asp Thr Ser Thr Asn Thr Val Tyr Met Glu Leu Ser Ser Leu Arg
225                 230                 235                 240

Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Phe Arg Gly Gly Val Tyr
                245                 250                 255
```

```
                                                _SL
Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Thr Thr Thr Pro Ala
            260                 265                 270

Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser
        275                 280                 285

Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr
    290                 295                 300

Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala
305                 310                 315                 320

Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys
                325                 330                 335

Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met
            340                 345                 350

Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe
        355                 360                 365

Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg
    370                 375                 380

Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn
385                 390                 395                 400

Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg
                405                 410                 415

Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro
            420                 425                 430

Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala
        435                 440                 445

Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His
    450                 455                 460

Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp
465                 470                 475                 480

Ala Leu His Met Gln Ala Leu Pro Pro Arg
                485                 490
```

<210> 463
<211> 243
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 463

```
Glu Ile Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Lys Pro Gly Ala
1               5                  10                  15

Ser Val Lys Leu Ser Cys Thr Gly Ser Gly Phe Asn Ile Glu Asp Tyr
            20                  25                  30

Tyr Ile His Trp Val Lys Gln Arg Thr Glu Gln Gly Leu Glu Trp Ile
        35                  40                  45

Gly Arg Ile Asp Pro Glu Asn Asp Glu Thr Lys Tyr Gly Pro Ile Phe
    50                  55                  60

Gln Gly Arg Ala Thr Ile Thr Ala Asp Thr Ser Ser Asn Thr Val Tyr
65                  70                  75                  80

Leu Gln Leu Ser Ser Leu Thr Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Phe Arg Gly Gly Val Tyr Trp Gly Pro Gly Thr Thr Leu Thr Val
            100                 105                 110

Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
        115                 120                 125

Ser His Met Asp Val Val Met Thr Gln Ser Pro Leu Thr Leu Ser Val
    130                 135                 140

Ala Ile Gly Gln Ser Ala Ser Ile Ser Cys Lys Ser Ser Gln Ser Leu
145                 150                 155                 160

Leu Asp Ser Asp Gly Lys Thr Tyr Leu Asn Trp Leu Leu Gln Arg Pro
                165                 170                 175

Gly Gln Ser Pro Lys Arg Leu Ile Ser Leu Val Ser Lys Leu Asp Ser
            180                 185                 190

Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr
        195                 200                 205

Leu Arg Ile Ser Arg Val Glu Ala Glu Asp Leu Gly Ile Tyr Tyr Cys
    210                 215                 220
```

Trp Gln Gly Thr His Phe Pro Gly Thr Phe Gly Gly Gly Thr Lys Leu
225 230 235 240

Glu Ile Lys

<210> 464
<211> 729
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 464
gagatccagc tccaacagag cggagccgaa ctggtcaaac cgggagcgtc ggtgaagttg 60

tcatgcactg gatcgggctt caacatcgag gattactaca tccactgggt caagcaacgc 120

accgagcagg ggctggaatg gatcggacgg atcgaccccg aaaacgatga aaccaagtac 180

gggcctatct tccaaggacg ggccaccatt acggctgaca cgtcaagcaa taccgtctac 240

ctccagcttt ccagcctgac ctccgaggac actgccgtgt actactgcgc cttcagagga 300

ggcgtgtact ggggaccagg aaccactttg accgtgtcca gcggaggcgg tggatcagga 360

ggaggaggct caggcggtgg cggctcgcac atggacgtgg tcatgactca gtccccgctg 420

accctgtcgg tggcaattgg acagagcgca tccatctcgt gcaagagctc acagtcgctg 480

ctggattccg acggaaagac ttatctgaac tggctgctcc aaagaccagg gcaatcaccg 540

aaacgcctta tctccctggt gtcgaaactc gactcgggtg tgccggatcg gtttaccggt 600

agcgggtccg gcacggactt cactctccgc atttcgaggg tggaagcgga ggatctcggg 660

atctactact gttggcaggg aacccacttc cctgggactt ttggaggcgg aactaagctg 720

gaaatcaag 729

<210> 465
<211> 822
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 465
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgagatcc agctccaaca gagcggagcc gaactggtca aaccgggagc gtcggtgaag 120

ttgtcatgca ctggatcggg cttcaacatc gaggattact acatccactg ggtcaagcaa 180

cgcaccgagc aggggctgga atggatcgga cggatcgacc ccgaaaacga tgaaaccaag 240

tacgggccta tcttccaagg acgggccacc attacggctg acacgtcaag caataccgtc 300

tacctccagc tttccagcct gacctccgag gacactgccg tgtactactg cgccttcaga 360

ggaggcgtgt actggggacc aggaaccact ttgaccgtgt ccagcggagg cggtggatca 420

ggaggaggag gctcaggcgg tggcggctcg cacatggacg tggtcatgac tcagtccccg 480

ctgaccctgt cggtggcaat tggacagagc gcatccatct cgtgcaagag ctcacagtcg 540

ctgctggatt ccgacggaaa gacttatctg aactggctgc tccaaagacc agggcaatca 600

ccgaaacgcc ttatctccct ggtgtcgaaa ctcgactcgg gtgtgccgga tcggtttacc 660

ggtagcgggt ccggcacgga cttcactctc cgcatttcga gggtggaagc ggaggatctc 720

gggatctact actgttggca gggaacccac ttccctggga cttttggagg cggaactaag 780

ctggaaatca agggtagcca tcaccatcac caccaccatc at 822

<210> 466
<211> 274
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 466
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Ile Gln Leu Gln Gln Ser Gly Ala Glu Leu
20 25 30

Val Lys Pro Gly Ala Ser Val Lys Leu Ser Cys Thr Gly Ser Gly Phe
35 40 45

Asn Ile Glu Asp Tyr Tyr Ile His Trp Val Lys Gln Arg Thr Glu Gln
50 55 60

Gly Leu Glu Trp Ile Gly Arg Ile Asp Pro Glu Asn Asp Glu Thr Lys
65 70 75 80

Tyr Gly Pro Ile Phe Gln Gly Arg Ala Thr Ile Thr Ala Asp Thr Ser
85 90 95

Ser Asn Thr Val Tyr Leu Gln Leu Ser Ser Leu Thr Ser Glu Asp Thr
100 105 110

_SL
Ala Val Tyr Tyr Cys Ala Phe Arg Gly Gly Val Tyr Trp Gly Pro Gly
        115   120   125

Thr Thr Leu Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
    130   135   140

Ser Gly Gly Gly Gly Ser His Met Asp Val Val Met Thr Gln Ser Pro
145   150   155   160

Leu Thr Leu Ser Val Ala Ile Gly Gln Ser Ala Ser Ile Ser Cys Lys
                165   170   175

Ser Ser Gln Ser Leu Leu Asp Ser Asp Gly Lys Thr Tyr Leu Asn Trp
            180   185   190

Leu Leu Gln Arg Pro Gly Gln Ser Pro Lys Arg Leu Ile Ser Leu Val
        195   200   205

Ser Lys Leu Asp Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser
    210   215   220

Gly Thr Asp Phe Thr Leu Arg Ile Ser Arg Val Glu Ala Glu Asp Leu
225   230   235   240

Gly Ile Tyr Tyr Cys Trp Gln Gly Thr His Phe Pro Gly Thr Phe Gly
                245   250   255

Gly Gly Thr Lys Leu Glu Ile Lys Gly Ser His His His His His His
            260   265   270

His His

<210> 467
<211> 1461
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 467
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgagatcc agctccaaca gagcggagcc gaactggtca aaccgggagc gtcggtgaag 120

ttgtcatgca ctggatcggg cttcaacatc gaggattact acatccactg ggtcaagcaa 180

cgcaccgagc aggggctgga atggatcgga cggatcgacc ccgaaaacga tgaaaccaag 240

tacgggccta tcttccaagg acgggccacc attacggctg acacgtcaag caataccgtc 300

tacctccagc tttccagcct gacctccgag gacactgccg tgtactactg cgccttcaga 360

ggaggcgtgt actggggacc aggaaccact ttgaccgtgt ccagcggagg cggtggatca 420

ggaggaggag gctcaggcgg tggcggctcg cacatggacg tggtcatgac tcagtccccg 480

ctgaccctgt cggtggcaat tggacagagc gcatccatct cgtgcaagag ctcacagtcg 540

ctgctggatt ccgacggaaa gacttatctg aactggctgc tccaaagacc agggcaatca 600

ccgaaacgcc ttatctccct ggtgtcgaaa ctcgactcgg gtgtgccgga tcggtttacc 660

ggtagcgggt ccggcacgga cttcactctc cgcatttcga gggtggaagc ggaggatctc 720

gggatctact actgttggca gggaacccac ttccctggga cttttggagg cggaactaag 780

ctggaaatca agaccactac cccagcaccg aggccaccca ccccggctcc taccatcgcc 840

tcccagcctc tgtccctgcg tccggaggca tgtagacccg cagctggtgg ggccgtgcat 900

acccggggtc ttgacttcgc ctgcgatatc tacatttggg cccctctggc tggtacttgc 960

ggggtcctgc tgctttcact cgtgatcact ctttactgta agcgcggtcg gaagaagctg 1020

ctgtacatct ttaagcaacc cttcatgagg cctgtgcaga ctactcaaga ggaggacggc 1080

tgttcatgcc ggttcccaga ggaggaggaa ggcggctgcg aactgcgcgt gaaattcagc 1140

cgcagcgcag atgctccagc ctacaagcag gggcagaacc agctctacaa cgaactcaat 1200

cttggtcgga gagaggagta cgacgtgctg gacaagcgga gaggacggga cccagaaatg 1260

ggcgggaagc cgcgcagaaa gaatccccaa gagggcctgt acaacgagct ccaaaaggat 1320

aagatggcag aagcctatag cgagattggt atgaaagggg aacgcagaag aggcaaaggc 1380

cacgacggac tgtaccaggg actcagcacc gccaccaagg acacctatga cgctcttcac 1440

atgcaggccc tgccgcctcg g 1461

<210> 468
<211> 487
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 468
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Ile Gln Leu Gln Gln Ser Gly Ala Glu Leu
20 25 30

Val Lys Pro Gly Ala Ser Val Lys Leu Ser Cys Thr Gly Ser Gly Phe

_SL

35 40 45

Asn Ile Glu Asp Tyr Tyr Ile His Trp Val Lys Gln Arg Thr Glu Gln
50 55 60

Gly Leu Glu Trp Ile Gly Arg Ile Asp Pro Glu Asn Asp Glu Thr Lys
65 70 75 80

Tyr Gly Pro Ile Phe Gln Gly Arg Ala Thr Ile Thr Ala Asp Thr Ser
85 90 95

Ser Asn Thr Val Tyr Leu Gln Leu Ser Ser Leu Thr Ser Glu Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Ala Phe Arg Gly Gly Val Tyr Trp Gly Pro Gly
115 120 125

Thr Thr Leu Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
130 135 140

Ser Gly Gly Gly Gly Ser His Met Asp Val Val Met Thr Gln Ser Pro
145 150 155 160

Leu Thr Leu Ser Val Ala Ile Gly Gln Ser Ala Ser Ile Ser Cys Lys
165 170 175

Ser Ser Gln Ser Leu Leu Asp Ser Asp Gly Lys Thr Tyr Leu Asn Trp
180 185 190

Leu Leu Gln Arg Pro Gly Gln Ser Pro Lys Arg Leu Ile Ser Leu Val
195 200 205

Ser Lys Leu Asp Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser
210 215 220

Gly Thr Asp Phe Thr Leu Arg Ile Ser Arg Val Glu Ala Glu Asp Leu
225 230 235 240

Gly Ile Tyr Tyr Cys Trp Gln Gly Thr His Phe Pro Gly Thr Phe Gly
245 250 255

Gly Gly Thr Lys Leu Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro
260 265 270

Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro
275 280 285

_SL
Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu
290 295 300

Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys
305 310 315 320

Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly
325 330 335

Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val
340 345 350

Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu
355 360 365

Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp
370 375 380

Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn
385 390 395 400

Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg
405 410 415

Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly
420 425 430

Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu
435 440 445

Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu
450 455 460

Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His
465 470 475 480

Met Gln Ala Leu Pro Pro Arg
485

<210> 469
<211> 240
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 469

```
                                                 _SL
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asn
            20                  25                  30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile
        35                  40                  45

Tyr Ala Ala Ser Asn Leu Gln Ser Gly Val Pro Ser Arg Phe Thr Gly
    50                  55                  60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Ile Val Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His His Ser Tyr Pro Leu
                85                  90                  95

Thr Ser Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Gly Ser Thr
            100                 105                 110

Ser Gly Ser Gly Lys Pro Gly Ser Gly Glu Gly Ser Glu Val Gln Val
        115                 120                 125

Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu
    130                 135                 140

Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr Ala Met Ser Trp
145                 150                 155                 160

Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser Ala Ile Ser
                165                 170                 175

Gly Ser Gly Gly Ser Thr Asn Tyr Ala Asp Ser Val Lys Gly Arg Phe
            180                 185                 190

Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln Met Asn
        195                 200                 205

Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Gly Ser Ser
    210                 215                 220

Gly Trp Ser Glu Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
225                 230                 235                 240
```

<210> 470
<211> 720
<212> DNA

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 470
gatatccaaa tgactcagag cccttcatcc ctgagcgcca gcgtcggaga cagggtgacc 60

atcacgtgcc gggcatccca aggcattaga aataacttgg cgtggtatca gcaaaaacca 120

ggaaaggccc cgaagcgcct gatctacgcg gcctccaacc ttcagtcagg agtgccctcg 180

cgcttcaccg ggagcggtag cggaactgag tttaccctta tcgtgtcgtc cctgcagcca 240

gaggacttcg cgacctacta ctgcctccag catcactcgt acccgttgac ttcgggaggc 300

ggaaccaagg tcgaaatcaa acgcactggc tcgacgtcag ggtccggtaa accgggatcg 360

ggagaaggat cggaagtcca agtgctggag agcggaggcg gactcgtgca acctggcggg 420

tcgctgcggc tcagctgtgc cgcgtcgggt tttactttca gctcgtacgc tatgtcatgg 480

gtgcggcagg ctccgggaaa ggggctggaa tgggtgtccg ctatttccgg ctcgggtgga 540

agcaccaatt acgccgactc cgtgaaggga cgcttcacca tctcacggga taactccaag 600

aatactctgt acctccagat gaactcgctg agagccgagg acaccgcagt gtactactgc 660

gcagggtcaa gcggctggtc cgaatactgg ggacagggca ccctcgtcac tgtcagctcc 720

<210> 471
<211> 807
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 471
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgatatcc aaatgactca gagcccttca tccctgagcg ccagcgtcgg agacagggtg 120

accatcacgt gccgggcatc ccaaggcatt agaaataact tggcgtggta tcagcaaaaa 180

ccaggaaagg ccccgaagcg cctgatctac gcggcctcca accttcagtc aggagtgccc 240

tcgcgcttca ccgggagcgg tagcggaact gagtttaccc ttatcgtgtc gtccctgcag 300

ccagaggact tcgcgaccta ctactgcctc agcatcact cgtacccgtt gacttcggga 360

ggcggaacca aggtcgaaat caaacgcact ggctcgacgt cagggtccgg taaaccggga 420

tcgggagaag gatcggaagt ccaagtgctg gagagcggag gcggactcgt gcaacctggc 480

gggtcgctgc ggctcagctg tgccgcgtcg ggttttactt tcagctcgta cgctatgtca 540

tgggtgcggc aggctccggg aaaggggctg gaatgggtgt ccgctatttc cggctcgggt 600

ggaagcacca attacgccga ctccgtgaag ggacgcttca ccatctcacg ggataactcc 660

aagaatactc tgtacctcca gatgaactcg ctgagagccg aggacaccgc agtgtactac 720

tgcgcagggt caagcggctg gtccgaatac tggggacagg gcaccctcgt cactgtcagc 780

tcccatcacc atcaccacca ccatcac 807

<210> 472
<211> 269
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 472

Met	Ala	Leu	Pro	Val	Thr	Ala	Leu	Leu	Leu	Pro	Leu	Ala	Leu	Leu	Leu
1				5				10					15		
His	Ala	Ala	Arg	Pro	Asp	Ile	Gln	Met	Thr	Gln	Ser	Pro	Ser	Ser	Leu
		20					25					30			
Ser	Ala	Ser	Val	Gly	Asp	Arg	Val	Thr	Ile	Thr	Cys	Arg	Ala	Ser	Gln
	35					40					45				
Gly	Ile	Arg	Asn	Asn	Leu	Ala	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Lys	Ala
50					55					60					
Pro	Lys	Arg	Leu	Ile	Tyr	Ala	Ala	Ser	Asn	Leu	Gln	Ser	Gly	Val	Pro
65				70					75					80	
Ser	Arg	Phe	Thr	Gly	Ser	Gly	Ser	Gly	Thr	Glu	Phe	Thr	Leu	Ile	Val
			85					90					95		
Ser	Ser	Leu	Gln	Pro	Glu	Asp	Phe	Ala	Thr	Tyr	Tyr	Cys	Leu	Gln	His
		100					105					110			
His	Ser	Tyr	Pro	Leu	Thr	Ser	Gly	Gly	Gly	Thr	Lys	Val	Glu	Ile	Lys
	115					120					125				
Arg	Thr	Gly	Ser	Thr	Ser	Gly	Ser	Gly	Lys	Pro	Gly	Ser	Gly	Glu	Gly
130					135					140					
Ser	Glu	Val	Gln	Val	Leu	Glu	Ser	Gly	Gly	Gly	Leu	Val	Gln	Pro	Gly
145				150					155					160	
Gly	Ser	Leu	Arg	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Phe	Thr	Phe	Ser	Ser
			165					170					175		

Tyr Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp
180 185 190

Val Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Asn Tyr Ala Asp Ser
195 200 205

Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu
210 215 220

Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr
225 230 235 240

Cys Ala Gly Ser Ser Gly Trp Ser Glu Tyr Trp Gly Gln Gly Thr Leu
245 250 255

Val Thr Val Ser Ser His His His His His His His His
260 265

<210> 473
<211> 1452
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 473
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgatatcc aaatgactca gagcccttca tccctgagcg ccagcgtcgg agacagggtg 120

accatcacgt gccgggcatc ccaaggcatt agaaataact tggcgtggta tcagcaaaaa 180

ccaggaaagg ccccgaagcg cctgatctac gcggcctcca accttcagtc aggagtgccc 240

tcgcgcttca ccgggagcgg tagcggaact gagtttaccc ttatcgtgtc gtccctgcag 300

ccagaggact tcgcgaccta ctactgcctc cagcatcact cgtacccgtt gacttcggga 360

ggcggaacca aggtcgaaat caaacgcact ggctcgacgt cagggtccgg taaaccggga 420

tcgggagaag gatcggaagt ccaagtgctg gagagcggag gcggactcgt gcaacctggc 480

gggtcgctgc ggctcagctg tgccgcgtcg ggttttactt tcagctcgta cgctatgtca 540

tgggtgcggc aggctccggg aaaggggctg gaatgggtgt ccgctatttc cggctcgggt 600

ggaagcacca attacgccga ctccgtgaag ggacgcttca ccatctcacg ggataactcc 660

aagaatactc tgtacctcca gatgaactcg ctgagagccg aggacaccgc agtgtactac 720

tgcgcagggt caagcggctg gtccgaatac tggggacagg gcaccctcgt cactgtcagc 780

_SL

tccaccacta ccccagcacc gaggccaccc accccggctc ctaccatcgc ctcccagcct 840

ctgtccctgc gtccggaggc atgtagaccc gcagctggtg gggccgtgca tacccggggt 900

cttgacttcg cctgcgatat ctacatttgg gcccctctgg ctggtacttg cggggtcctg 960

ctgctttcac tcgtgatcac tctttactgt aagcgcggtc ggaagaagct gctgtacatc 1020

tttaagcaac ccttcatgag gcctgtgcag actactcaag aggaggacgg ctgttcatgc 1080

cggttcccag aggaggagga aggcggctgc gaactgcgcg tgaaattcag ccgcagcgca 1140

gatgctccag cctacaagca ggggcagaac cagctctaca acgaactcaa tcttggtcgg 1200

agagaggagt acgacgtgct ggacaagcgg agaggacggg acccagaaat gggcgggaag 1260

ccgcgcagaa agaatcccca agagggcctg tacaacgagc tccaaaagga taagatggca 1320

gaagcctata gcgagattgg tatgaaaggg gaacgcagaa gaggcaaagg ccacgacgga 1380

ctgtaccagg gactcagcac cgccaccaag gacacctatg acgctcttca catgcaggcc 1440

ctgccgcctc gg 1452

<210> 474
<211> 484
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 474
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu
20 25 30

Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln
35 40 45

Gly Ile Arg Asn Asn Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala
50 55 60

Pro Lys Arg Leu Ile Tyr Ala Ala Ser Asn Leu Gln Ser Gly Val Pro
65 70 75 80

Ser Arg Phe Thr Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Ile Val
85 90 95

Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His
100 105 110

```
His Ser Tyr Pro Leu Thr Ser Gly Gly Gly Thr Lys Val Glu Ile Lys
        115                 120                 125

Arg Thr Gly Ser Thr Ser Gly Ser Gly Lys Pro Gly Ser Gly Glu Gly
    130                 135                 140

Ser Glu Val Gln Val Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly
145                 150                 155                 160

Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser
                165                 170                 175

Tyr Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp
            180                 185                 190

Val Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Asn Tyr Ala Asp Ser
        195                 200                 205

Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu
    210                 215                 220

Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr
225                 230                 235                 240

Cys Ala Gly Ser Ser Gly Trp Ser Glu Tyr Trp Gly Gln Gly Thr Leu
                245                 250                 255

Val Thr Val Ser Ser Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro
            260                 265                 270

Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys
        275                 280                 285

Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala
    290                 295                 300

Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu
305                 310                 315                 320

Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys
                325                 330                 335

Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr
            340                 345                 350

Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly
        355                 360                 365
```

Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala
370 375 380

Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg
385 390 395 400

Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu
405 410 415

Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn
420 425 430

Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met
435 440 445

Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly
450 455 460

Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala
465 470 475 480

Leu Pro Pro Arg

<210> 475
<211> 1482
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 475
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtgc aactcgtcca gtccggtgca gaagtcaaga agccaggaga atcactcaag 120

attagctgca aaggcagcgg ctactccttc acttcctact ggatcggctg ggtgcgccag 180

atgcccggaa agggactgga gtggatggga atcatctacc ctggcgatag cgacaccaga 240

tactccccga gctttcaagg ccaagtgacc atttcggccg acaagtcgat ctccaccgcg 300

tatctgcagt ggagctcact gaaggcttcg gacaccgcca tgtactactg tgcccggctg 360

gggggaagcc tgcccgatta cggaatggac gtgtggggcc agggaaccat ggtcactgtg 420

tcctccgcct ccgggggtgg aggctccggt ggaggggggt ccggtggtgg aggatcagaa 480

attgtgctga cccagtctcc gctgtccttg cctgtgaccc cgggcgaacc cgcaagcatc 540

tcctgccggt cgtcgcagtc cctgcttcac tccaacggct acaactacct cgattggtac 600

ctccagaagc ctggacagag cccacagctg ttgatctacc tgggctcgaa ccgggcctca 660

ggagtgccgg acaggttctc cggctccggg tcgggaaccg acttcacgct gaagatctcc 720

cgcgtggagg ccgaggacgt gggcgtgtac tattgcatgc aggcgctgca gacccttatt 780

acattcggac aggggactaa ggtcgatatc aagaccacta ccccagcacc gaggccaccc 840

accccggctc ctaccatcgc ctcccagcct ctgtccctgc gtccggaggc atgtagaccc 900

gcagctggtg gggccgtgca tacccggggt cttgacttcg cctgcgatat ctacatttgg 960

gcccctctgg ctggtacttg cggggtcctg ctgctttcac tcgtgatcac tctttactgt 1020

aagcgcggtc ggaagaagct gctgtacatc tttaagcaac ccttcatgag gcctgtgcag 1080

actactcaag aggaggacgg ctgttcatgc cggttcccag aggaggagga aggcggctgc 1140

gaactgcgcg tgaaattcag ccgcagcgca gatgctccag cctacaagca ggggcagaac 1200

cagctctaca acgaactcaa tcttggtcgg agagaggagt acgacgtgct ggacaagcgg 1260

agaggacggg acccagaaat gggcgggaag ccgcgcagaa agaatcccca agagggcctg 1320

tacaacgagc tccaaaagga taagatggca gaagcctata gcgagattgg tatgaaaggg 1380

gaacgcagaa gaggcaaagg ccacgacgga ctgtaccagg gactcagcac cgccaccaag 1440

gacacctatg acgctcttca catgcaggcc ctgccgcctc gg 1482

<210> 476
<211> 494
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 476

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
            20                  25                  30

Lys Lys Pro Gly Glu Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr
        35                  40                  45

Ser Phe Thr Ser Tyr Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys
    50                  55                  60

Gly Leu Glu Trp Met Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg
65                  70                  75                  80
```

```
Tyr Ser Pro Ser Phe Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser
                85                  90                  95

Ile Ser Thr Ala Tyr Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr
            100                 105                 110

Ala Met Tyr Tyr Cys Ala Arg Leu Gly Gly Ser Leu Pro Asp Tyr Gly
        115                 120                 125

Met Asp Val Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Ala Ser
    130                 135                 140

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu
145                 150                 155                 160

Ile Val Leu Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly Glu
                165                 170                 175

Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser Asn
            180                 185                 190

Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro
        195                 200                 205

Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro Asp
    210                 215                 220

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser
225                 230                 235                 240

Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala Leu
                245                 250                 255

Gln Thr Leu Ile Thr Phe Gly Gln Gly Thr Lys Val Asp Ile Lys Thr
            260                 265                 270

Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser
        275                 280                 285

Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly
    290                 295                 300

Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp
305                 310                 315                 320

Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile
                325                 330                 335
```

```
Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys
            340                 345                 350

Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys
        355                 360                 365

Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val
    370                 375                 380

Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn
385                 390                 395                 400

Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val
                405                 410                 415

Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg
            420                 425                 430

Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys
        435                 440                 445

Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg
    450                 455                 460

Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys
465                 470                 475                 480

Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
                485                 490
```

<210> 477
<211> 271
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 477

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
            20                  25                  30

Lys Lys Pro Gly Glu Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr
        35                  40                  45
```

```
Ser Phe Thr Ser Tyr Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys
    50                  55                  60

Gly Leu Glu Trp Met Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg
65                  70                  75                  80

Tyr Ser Pro Ser Phe Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser
                85                  90                  95

Ile Ser Thr Ala Tyr Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr
            100                 105                 110

Ala Met Tyr Tyr Cys Ala Arg Leu Gly Gly Ser Leu Pro Asp Tyr Gly
        115                 120                 125

Met Asp Val Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Ala Ser
    130                 135                 140

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu
145                 150                 155                 160

Ile Val Leu Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly Glu
                165                 170                 175

Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser Asn
            180                 185                 190

Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro
        195                 200                 205

Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro Asp
    210                 215                 220

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser
225                 230                 235                 240

Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala Leu
                245                 250                 255

Gln Thr Leu Ile Thr Phe Gly Gln Gly Thr Lys Val Asp Ile Lys
            260                 265                 270
```

<210> 478
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 478
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15

Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
20 25 30

Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
35 40 45

Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe
50 55 60

Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65 70 75 80

Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
85 90 95

Ala Arg Leu Gly Gly Ser Leu Pro Asp Tyr Gly Met Asp Val Trp Gly
100 105 110

Gln Gly Thr Met Val Thr Val Ser Ser
115 120

<210> 479
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 479
Glu Ile Val Leu Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser
20 25 30

Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala
85 90 95

Leu Gln Thr Leu Ile Thr Phe Gly Gln Gly Thr Lys Val Asp Ile Lys
100 105 110

<210> 480
<211> 1485
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 480
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtcc aactcgtcca atcaggagct gaagtcaaga agcctggagc atccgtgaga 120

gtgtcctgta aagcctccgg ctacatcttc accaactact acgtgcactg ggtcagacag 180

gccccgggcc agggactgga atggatggga atcatttccc cgtccggcgg atcgcctact 240

tacgcgcaac ggctgcaggg ccgcgtgacc atgactcggg atctctccac ttcaaccgtg 300

tacatggaac tgtccagcct tacatcggag gatactgccg tgtacttctg cgcgagggag 360

tcccggctga ggggcaaccg cctcgggctg cagtcaagca tcttcgatca ctggggccag 420

ggcaccctcg tgaccgtgtc cagcgcctcg gggggaggag gctccggggg cggaggttcg 480

ggcggtggtg gatctgacat tcgcatgact cagtccccac cttcactgtc cgctagcgtg 540

ggggaccgcg tgacgattcc gtgccaagcc agccaggaca tcaacaacca tctgaactgg 600

tatcagcaga agcccggaaa ggccccgcag ctgctgatct acgacacctc gaatctggag 660

atcggcgtgc catcccggtt ctccggttcg ggaagcggaa ccgactttac cctgactatc 720

tcctccttgc aacccgagga cattgccacc tactactgcc agcagtacga aaaccttccc 780

ctgaccttcg ggggtggaac caaagtggag atcaagacca ctaccccagc accgaggcca 840

cccaccccgg ctcctaccat cgcctcccag cctctgtccc tgcgtccgga ggcatgtaga 900

cccgcagctg gtggggccgt gcatacccgg ggtcttgact tcgcctgcga tatctacatt 960

tgggcccctc tggctggtac ttgcggggtc ctgctgcttt cactcgtgat cactctttac 1020

tgtaagcgcg gtcggaagaa gctgctgtac atctttaagc aacccttcat gaggcctgtg 1080

cagactactc aagaggagga cggctgttca tgccggttcc cagaggagga ggaaggcggc 1140

_SL

tgcgaactgc gcgtgaaatt cagccgcagc gcagatgctc cagcctacaa gcaggggcag 1200

aaccagctct acaacgaact caatcttggt cggagagagg agtacgacgt gctggacaag 1260

cggagaggac gggacccaga aatgggcggg aagccgcgca gaaagaatcc ccaagagggc 1320

ctgtacaacg agctccaaaa ggataagatg gcagaagcct atagcgagat tggtatgaaa 1380

ggggaacgca gaagaggcaa aggccacgac ggactgtacc agggactcag caccgccacc 1440

aaggacacct atgacgctct tcacatgcag gccctgccgc ctcgg 1485

<210> 481
<211> 495
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 481

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
20 25 30

Lys Lys Pro Gly Ala Ser Val Arg Val Ser Cys Lys Ala Ser Gly Tyr
35 40 45

Ile Phe Thr Asn Tyr Tyr Val His Trp Val Arg Gln Ala Pro Gly Gln
50 55 60

Gly Leu Glu Trp Met Gly Ile Ile Ser Pro Ser Gly Gly Ser Pro Thr
65 70 75 80

Tyr Ala Gln Arg Leu Gln Gly Arg Val Thr Met Thr Arg Asp Leu Ser
85 90 95

Thr Ser Thr Val Tyr Met Glu Leu Ser Ser Leu Thr Ser Glu Asp Thr
100 105 110

Ala Val Tyr Phe Cys Ala Arg Glu Ser Arg Leu Arg Gly Asn Arg Leu
115 120 125

Gly Leu Gln Ser Ser Ile Phe Asp His Trp Gly Gln Gly Thr Leu Val
130 135 140

Thr Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
145 150 155 160

```
Gly Gly Gly Gly Ser Asp Ile Arg Met Thr Gln Ser Pro Pro Ser Leu
                165                 170                 175

Ser Ala Ser Val Gly Asp Arg Val Thr Ile Pro Cys Gln Ala Ser Gln
            180                 185                 190

Asp Ile Asn Asn His Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala
        195                 200                 205

Pro Gln Leu Leu Ile Tyr Asp Thr Ser Asn Leu Glu Ile Gly Val Pro
    210                 215                 220

Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile
225                 230                 235                 240

Ser Ser Leu Gln Pro Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Tyr
                245                 250                 255

Glu Asn Leu Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            260                 265                 270

Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala
        275                 280                 285

Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly
    290                 295                 300

Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile
305                 310                 315                 320

Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val
                325                 330                 335

Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe
            340                 345                 350

Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly
        355                 360                 365

Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg
    370                 375                 380

Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln
385                 390                 395                 400

Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp
                405                 410                 415
```

Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro
420 425 430

Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp
435 440 445

Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg
450 455 460

Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr
465 470 475 480

Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490 495

<210> 482
<211> 272
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 482
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
20 25 30

Lys Lys Pro Gly Ala Ser Val Arg Val Ser Cys Lys Ala Ser Gly Tyr
35 40 45

Ile Phe Thr Asn Tyr Tyr Val His Trp Val Arg Gln Ala Pro Gly Gln
50 55 60

Gly Leu Glu Trp Met Gly Ile Ile Ser Pro Ser Gly Gly Ser Pro Thr
65 70 75 80

Tyr Ala Gln Arg Leu Gln Gly Arg Val Thr Met Thr Arg Asp Leu Ser
85 90 95

Thr Ser Thr Val Tyr Met Glu Leu Ser Ser Leu Thr Ser Glu Asp Thr
100 105 110

Ala Val Tyr Phe Cys Ala Arg Glu Ser Arg Leu Arg Gly Asn Arg Leu
115 120 125

```
Gly Leu Gln Ser Ser Ile Phe Asp His Trp Gly Gln Gly Thr Leu Val
    130                 135                 140

Thr Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
145                 150                 155                 160

Gly Gly Gly Gly Ser Asp Ile Arg Met Thr Gln Ser Pro Pro Ser Leu
                165                 170                 175

Ser Ala Ser Val Gly Asp Arg Val Thr Ile Pro Cys Gln Ala Ser Gln
            180                 185                 190

Asp Ile Asn Asn His Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala
        195                 200                 205

Pro Gln Leu Leu Ile Tyr Asp Thr Ser Asn Leu Glu Ile Gly Val Pro
    210                 215                 220

Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile
225                 230                 235                 240

Ser Ser Leu Gln Pro Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Tyr
                245                 250                 255

Glu Asn Leu Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            260                 265                 270
```

<210> 483
<211> 127
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 483

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15

Ser Val Arg Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Asn Tyr
            20                  25                  30

Tyr Val His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

Gly Ile Ile Ser Pro Ser Gly Gly Ser Pro Thr Tyr Ala Gln Arg Leu
    50                  55                  60
```

Gln Gly Arg Val Thr Met Thr Arg Asp Leu Ser Thr Ser Thr Val Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Thr Ser Glu Asp Thr Ala Val Tyr Phe Cys
85 90 95

Ala Arg Glu Ser Arg Leu Arg Gly Asn Arg Leu Gly Leu Gln Ser Ser
100 105 110

Ile Phe Asp His Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 484
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 484
Asp Ile Arg Met Thr Gln Ser Pro Pro Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Pro Cys Gln Ala Ser Gln Asp Ile Asn Asn His
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Gln Leu Leu Ile
35 40 45

Tyr Asp Thr Ser Asn Leu Glu Ile Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Tyr Glu Asn Leu Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 485
<211> 1479
<212> DNA
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 485
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtgc aattggtgca gtcaggagga ggattggtgc aacccggagg atcgctgaga 120

ctgtcatgtg ctgccagcgg gttcacattc tcctcctacg caatgtcctg ggtccgccag 180

gcgccgggca aaggactgga atgggtgtcc gccatctcgg ggtcgggcgg ctccacctat 240

tacgctgact ccgtgaaggg acgcttcacc attagcagag ataactccaa gaacaccctc 300

tacctccaaa tgaacagcct tagggctgag gacaccgccg tctattactg cgccaaggag 360

gacacgatcc ggggacctaa ctactattac tacggaatgg atgtctgggg ccagggtacc 420

actgtgaccg tgtcctcggc ctcgggaggc ggaggatcag ggggtggtgg ctctgggggg 480

ggtggcagcg aaactactct gacccagtcc ccctcatccg tgtcagcgtc cgtgggcgat 540

cgggtgtcga tcacttgccg ggcctcccaa gacatcgaca cctggctcgc gtggtaccag 600

ctgaagccag gaaaggcccc taagctgctg atgtacgcag cctccaatct gcaaggaggg 660

gtgccctccc gcttttccgg gtccggcagc ggaaccgact tcattctgac tatctcgagc 720

ctccagccgg aggatttcgc cacctactac tgccagcagg cctccatctt cccgccgact 780

ttcggtggcg gaaccaaggt cgacattaag accactaccc cagcaccgag gccacccacc 840

ccggctccta ccatcgcctc ccagcctctg tccctgcgtc cggaggcatg tagacccgca 900

gctggtgggg ccgtgcatac ccggggtctt gacttcgcct gcgatatcta catttgggcc 960

cctctggctg gtacttgcgg ggtcctgctg ctttcactcg tgatcactct ttactgtaag 1020

cgcggtcgga agaagctgct gtacatcttt aagcaaccct tcatgaggcc tgtgcagact 1080

actcaagagg aggacggctg ttcatgccgg ttcccagagg aggaggaagg cggctgcgaa 1140

ctgcgcgtga aattcagccg cagcgcagat gctccagcct acaagcaggg gcagaaccag 1200

ctctacaacg aactcaatct tggtcggaga gaggagtacg acgtgctgga caagcggaga 1260

ggacgggacc cagaaatggg cgggaagccg cgcagaaaga atccccaaga gggcctgtac 1320

aacgagctcc aaaaggataa gatggcagaa gcctatagcg agattggtat gaaaggggaa 1380

cgcagaagag gcaaaggcca cgacggactg taccagggac tcagcaccgc caccaaggac 1440

acctatgacg ctcttcacat gcaggccctg ccgcctcgg 1479

<210> 486
<211> 493
<212> PRT
<213> Artificial Sequence

<220>
<221> source

_SL
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 486
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Gly Gly Leu
20 25 30

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
35 40 45

Thr Phe Ser Ser Tyr Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys
50 55 60

Gly Leu Glu Trp Val Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr
65 70 75 80

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser
85 90 95

Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Ala Lys Glu Asp Thr Ile Arg Gly Pro Asn Tyr
115 120 125

Tyr Tyr Tyr Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val
130 135 140

Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
145 150 155 160

Gly Gly Ser Glu Thr Thr Leu Thr Gln Ser Pro Ser Ser Val Ser Ala
165 170 175

Ser Val Gly Asp Arg Val Ser Ile Thr Cys Arg Ala Ser Gln Asp Ile
180 185 190

Asp Thr Trp Leu Ala Trp Tyr Gln Leu Lys Pro Gly Lys Ala Pro Lys
195 200 205

Leu Leu Met Tyr Ala Ala Ser Asn Leu Gln Gly Gly Val Pro Ser Arg
210 215 220

Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Ile Leu Thr Ile Ser Ser
225 230 235 240

```
Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ala Ser Ile
                245                 250                 255

Phe Pro Pro Thr Phe Gly Gly Gly Thr Lys Val Asp Ile Lys Thr Thr
            260                 265                 270

Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln
        275                 280                 285

Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala
    290                 295                 300

Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala
305                 310                 315                 320

Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr
                325                 330                 335

Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln
            340                 345                 350

Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser
        355                 360                 365

Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys
    370                 375                 380

Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln
385                 390                 395                 400

Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu
                405                 410                 415

Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg
            420                 425                 430

Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met
        435                 440                 445

Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly
    450                 455                 460

Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp
465                 470                 475                 480

Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
                485                 490
```

<210> 487
<211> 270
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 487
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Gly Gly Leu
20 25 30

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
35 40 45

Thr Phe Ser Ser Tyr Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys
50 55 60

Gly Leu Glu Trp Val Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr
65 70 75 80

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser
85 90 95

Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Ala Lys Glu Asp Thr Ile Arg Gly Pro Asn Tyr
115 120 125

Tyr Tyr Tyr Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val
130 135 140

Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
145 150 155 160

Gly Gly Ser Glu Thr Thr Leu Thr Gln Ser Pro Ser Ser Val Ser Ala
165 170 175

Ser Val Gly Asp Arg Val Ser Ile Thr Cys Arg Ala Ser Gln Asp Ile
180 185 190

Asp Thr Trp Leu Ala Trp Tyr Gln Leu Lys Pro Gly Lys Ala Pro Lys
195 200 205

```
Leu Leu Met Tyr Ala Ala Ser Asn Leu Gln Gly Gly Val Pro Ser Arg
    210                 215                 220

Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Ile Leu Thr Ile Ser Ser
225                 230                 235                 240

Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ala Ser Ile
                245                 250                 255

Phe Pro Pro Thr Phe Gly Gly Gly Thr Lys Val Asp Ile Lys
            260                 265                 270
```

<210> 488
<211> 125
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 488

```
Gln Val Gln Leu Val Gln Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Glu Asp Thr Ile Arg Gly Pro Asn Tyr Tyr Tyr Tyr Gly Met
            100                 105                 110

Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120                 125
```

<210> 489
<211> 107

<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 489

Glu	Thr	Thr	Leu	Thr	Gln	Ser	Pro	Ser	Ser	Val	Ser	Ala	Ser	Val	Gly
1				5				10					15		
Asp	Arg	Val	Ser	Ile	Thr	Cys	Arg	Ala	Ser	Gln	Asp	Ile	Asp	Thr	Trp
		20					25					30			
Leu	Ala	Trp	Tyr	Gln	Leu	Lys	Pro	Gly	Lys	Ala	Pro	Lys	Leu	Leu	Met
	35					40					45				
Tyr	Ala	Ala	Ser	Asn	Leu	Gln	Gly	Gly	Val	Pro	Ser	Arg	Phe	Ser	Gly
50					55					60					
Ser	Gly	Ser	Gly	Thr	Asp	Phe	Ile	Leu	Thr	Ile	Ser	Ser	Leu	Gln	Pro
65				70					75					80	
Glu	Asp	Phe	Ala	Thr	Tyr	Tyr	Cys	Gln	Gln	Ala	Ser	Ile	Phe	Pro	Pro
			85					90					95		
Thr	Phe	Gly	Gly	Gly	Thr	Lys	Val	Asp	Ile	Lys					
		100					105								

<210> 490
<211> 1482
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 490

atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtgc agctcgtcca atccggtgca gaagtgaaga agcctggcga atccctgaag 120

atctcatgca aaggctcggg atacagcttc acctcatatt ggattggatg ggtcagacag 180

atgccaggaa agggtctgga gtggatggga atcatctacc cgggagacag cgatacccgg 240

tactccccga gcttccaggg acaggtcacc atctcggccg acaagtccat tactactgcc 300

tacttgcaat ggtcctcgct gcgcgcctcc gatagcgcca tgtactactg cgcgagaggc 360

ggctactccg actacgacta ctacttcgat ttctggggac aggggacact cgtgactgtg 420

tcctccgcgt cgggtggcgg cggctcgggt ggaggaggaa gcggaggggg aggctccgaa 480

attgtgatga cccagtcacc cctgtcgctc cctgtgactc ctggggaacc ggcctccatc 540

tcctgccgga gctcacagag cctgctgcac tccaacggat acaactacct cgattggtac 600

cttcagaagc ccggccagtc gccccagctg ctgatctacc tggggtccaa ccgggctagc 660

ggcgtgccgg accgcttctc cggttccggg tctggaaccg acttcacgct gaaaatctcc 720

agggtggagg ccgaggacgt gggagtgtat tactgtatgc aggccctgca aacccccttc 780

acctttggcg ggggcaccaa ggtcgagatt aagaccacta ccccagcacc gaggccaccc 840

accccggctc ctaccatcgc ctcccagcct ctgtccctgc gtccggaggc atgtagaccc 900

gcagctggtg gggccgtgca tacccggggt cttgacttcg cctgcgatat ctacatttgg 960

gcccctctgg ctggtacttg cggggtcctg ctgctttcac tcgtgatcac tctttactgt 1020

aagcgcggtc ggaagaagct gctgtacatc tttaagcaac ccttcatgag gcctgtgcag 1080

actactcaag aggaggacgg ctgttcatgc cggttcccag aggaggagga aggcggctgc 1140

gaactgcgcg tgaaattcag ccgcagcgca gatgctccag cctacaagca ggggcagaac 1200

cagctctaca acgaactcaa tcttggtcgg agagaggagt acgacgtgct ggacaagcgg 1260

agaggacggg acccagaaat gggcgggaag ccgcgcagaa agaatcccca agagggcctg 1320

tacaacgagc tccaaaagga taagatggca gaagcctata gcgagattgg tatgaaaggg 1380

gaacgcagaa gaggcaaagg ccacgacgga ctgtaccagg gactcagcac cgccaccaag 1440

gacacctatg acgctcttca catgcaggcc ctgccgcctc gg 1482

<210> 491
<211> 494
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 491
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
20 25 30

Lys Lys Pro Gly Glu Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr
35 40 45

Ser Phe Thr Ser Tyr Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys
50 55 60

```
                                                    _SL
Gly Leu Glu Trp Met Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg
65                  70                  75                  80

Tyr Ser Pro Ser Phe Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser
                85                  90                  95

Ile Thr Thr Ala Tyr Leu Gln Trp Ser Ser Leu Arg Ala Ser Asp Ser
            100                 105                 110

Ala Met Tyr Tyr Cys Ala Arg Gly Gly Tyr Ser Asp Tyr Asp Tyr Tyr
        115                 120                 125

Phe Asp Phe Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser
    130                 135                 140

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu
145                 150                 155                 160

Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly Glu
                165                 170                 175

Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser Asn
            180                 185                 190

Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro
        195                 200                 205

Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro Asp
    210                 215                 220

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser
225                 230                 235                 240

Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala Leu
                245                 250                 255

Gln Thr Pro Phe Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Thr
            260                 265                 270

Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser
        275                 280                 285

Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly
    290                 295                 300

Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp
305                 310                 315                 320
```

Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Ser Leu Val Ile
325 330 335

Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys
340 345 350

Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys
355 360 365

Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val
370 375 380

Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn
385 390 395 400

Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val
405 410 415

Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg
420 425 430

Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys
435 440 445

Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg
450 455 460

Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys
465 470 475 480

Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 492
<211> 271
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 492
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
20 25 30

```
Lys Lys Pro Gly Glu Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr
        35                  40                  45

Ser Phe Thr Ser Tyr Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys
    50                  55                  60

Gly Leu Glu Trp Met Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg
65                  70                  75                  80

Tyr Ser Pro Ser Phe Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser
                85                  90                  95

Ile Thr Thr Ala Tyr Leu Gln Trp Ser Ser Leu Arg Ala Ser Asp Ser
            100                 105                 110

Ala Met Tyr Tyr Cys Ala Arg Gly Gly Tyr Ser Asp Tyr Asp Tyr Tyr
        115                 120                 125

Phe Asp Phe Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser
    130                 135                 140

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu
145                 150                 155                 160

Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly Glu
                165                 170                 175

Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser Asn
            180                 185                 190

Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro
        195                 200                 205

Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro Asp
    210                 215                 220

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser
225                 230                 235                 240

Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala Leu
                245                 250                 255

Gln Thr Pro Phe Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            260                 265                 270
```

<210> 493
<211> 121

<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 493
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15

Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
20 25 30

Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
35 40 45

Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe
50 55 60

Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Thr Thr Ala Tyr
65 70 75 80

Leu Gln Trp Ser Ser Leu Arg Ala Ser Asp Ser Ala Met Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Tyr Ser Asp Tyr Asp Tyr Tyr Phe Asp Phe Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 494
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 494
Glu Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser
20 25 30

Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala
85 90 95

Leu Gln Thr Pro Phe Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 495
<211> 1452
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 495
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtgc aactcgtcca aagcggtgga gatctcgccc agcccggaag atcccttaga 120

ctctcatgtg ccgccagcgg gttcaccttc gacgactacg ctatgcattg ggtgcgccag 180

gccccgggga agggactgga atgggtggcc gtgatttggc cggacggcgg acagaagtac 240

tacggagaca gcgtgaaagg gcggttcacc gtgtcgaggg acaacccgaa gaataccctc 300

taccttcaaa tgaactccct gcgcgccgag gacaccgcga tctactactg cgtgcgccac 360

tttaacgcat gggattactg gggacagggg actctggtca ctgtgtcctc cgcctctggc 420

ggcggaggtt ccggcggtgg tggctccggt ggaggaggat cggacatcca gctgacccag 480

tccccttcct cactgtcggc gtacgtggga ggccgggtca ctatcacgtg ccaggcatcc 540

cagggcattt cccagttcct gaactggttc cagcagaagc ccggaaaggc ccctaagctg 600

ttgatttccg atgctagcaa cctggaaccc ggcgtgccgt cacggttcag cggctccggg 660

tcgggcaccg acttcacctt caccatcact aacctccaac cggaggacat cgccacctat 720

tactgccagc agtacgatga tctgccactg actttcggcg gcggaaccaa ggtcgaaatc 780

aagaccacta ccccagcacc gaggccaccc accccggctc ctaccatcgc ctcccagcct 840

ctgtccctgc gtccggaggc atgtagaccc gcagctggtg gggccgtgca tacccggggt 900

cttgacttcg cctgcgatat ctacatttgg gcccctctgg ctggtacttg cggggtcctg 960

ctgctttcac tcgtgatcac tctttactgt aagcgcggtc ggaagaagct gctgtacatc 1020

tttaagcaac ccttcatgag gcctgtgcag actactcaag aggaggacgg ctgttcatgc 1080

cggttcccag aggaggagga aggcggctgc gaactgcgcg tgaaattcag ccgcagcgca 1140

gatgctccag cctacaagca ggggcagaac cagctctaca acgaactcaa tcttggtcgg 1200

agagaggagt acgacgtgct ggacaagcgg agaggacggg acccagaaat gggcgggaag 1260

ccgcgcagaa agaatcccca agagggcctg tacaacgagc tccaaaagga taagatggca 1320

gaagcctata gcgagattgg tatgaaaggg gaacgcagaa gaggcaaagg ccacgacgga 1380

ctgtaccagg gactcagcac cgccaccaag gacacctatg acgctcttca catgcaggcc 1440

ctgccgcctc gg 1452

<210> 496
<211> 484
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 496

Met	Ala	Leu	Pro	Val	Thr	Ala	Leu	Leu	Leu	Pro	Leu	Ala	Leu	Leu	Leu
1				5				10					15		
His	Ala	Ala	Arg	Pro	Gln	Val	Gln	Leu	Val	Gln	Ser	Gly	Gly	Asp	Leu
			20					25					30		
Ala	Gln	Pro	Gly	Arg	Ser	Leu	Arg	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Phe
		35					40					45			
Thr	Phe	Asp	Asp	Tyr	Ala	Met	His	Trp	Val	Arg	Gln	Ala	Pro	Gly	Lys
	50					55					60				
Gly	Leu	Glu	Trp	Val	Ala	Val	Ile	Trp	Pro	Asp	Gly	Gly	Gln	Lys	Tyr
65					70					75					80
Tyr	Gly	Asp	Ser	Val	Lys	Gly	Arg	Phe	Thr	Val	Ser	Arg	Asp	Asn	Pro
				85					90					95	
Lys	Asn	Thr	Leu	Tyr	Leu	Gln	Met	Asn	Ser	Leu	Arg	Ala	Glu	Asp	Thr
			100					105					110		
Ala	Ile	Tyr	Tyr	Cys	Val	Arg	His	Phe	Asn	Ala	Trp	Asp	Tyr	Trp	Gly
		115					120					125			
Gln	Gly	Thr	Leu	Val	Thr	Val	Ser	Ser	Ala	Ser	Gly	Gly	Gly	Gly	Ser
	130					135					140				

```
                                                    _SL
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln
145                 150                 155                 160

Ser Pro Ser Ser Leu Ser Ala Tyr Val Gly Gly Arg Val Thr Ile Thr
                165                 170                 175

Cys Gln Ala Ser Gln Gly Ile Ser Gln Phe Leu Asn Trp Phe Gln Gln
            180                 185                 190

Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Ser Asp Ala Ser Asn Leu
        195                 200                 205

Glu Pro Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
    210                 215                 220

Phe Thr Phe Thr Ile Thr Asn Leu Gln Pro Glu Asp Ile Ala Thr Tyr
225                 230                 235                 240

Tyr Cys Gln Gln Tyr Asp Asp Leu Pro Leu Thr Phe Gly Gly Gly Thr
                245                 250                 255

Lys Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro
            260                 265                 270

Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys
        275                 280                 285

Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala
    290                 295                 300

Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu
305                 310                 315                 320

Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys
                325                 330                 335

Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr
            340                 345                 350

Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly
        355                 360                 365

Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala
    370                 375                 380

Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg
385                 390                 395                 400
```

```
Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu
                405                 410                 415

Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn
            420                 425                 430

Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met
        435                 440                 445

Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly
    450                 455                 460

Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala
465                 470                 475                 480

Leu Pro Pro Arg
```

<210> 497
<211> 261
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 497

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Gly Asp Leu
            20                  25                  30

Ala Gln Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
        35                  40                  45

Thr Phe Asp Asp Tyr Ala Met His Trp Val Arg Gln Ala Pro Gly Lys
    50                  55                  60

Gly Leu Glu Trp Val Ala Val Ile Trp Pro Asp Gly Gly Gln Lys Tyr
65                  70                  75                  80

Tyr Gly Asp Ser Val Lys Gly Arg Phe Thr Val Ser Arg Asp Asn Pro
                85                  90                  95

Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
            100                 105                 110
```

```
Ala Ile Tyr Tyr Cys Val Arg His Phe Asn Ala Trp Asp Tyr Trp Gly
        115                 120                 125

Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Gly Gly Gly Gly Ser
    130                 135                 140

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln
145                 150                 155                 160

Ser Pro Ser Ser Leu Ser Ala Tyr Val Gly Gly Arg Val Thr Ile Thr
                165                 170                 175

Cys Gln Ala Ser Gln Gly Ile Ser Gln Phe Leu Asn Trp Phe Gln Gln
            180                 185                 190

Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Ser Asp Ala Ser Asn Leu
        195                 200                 205

Glu Pro Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
    210                 215                 220

Phe Thr Phe Thr Ile Thr Asn Leu Gln Pro Glu Asp Ile Ala Thr Tyr
225                 230                 235                 240

Tyr Cys Gln Gln Tyr Asp Asp Leu Pro Leu Thr Phe Gly Gly Gly Thr
                245                 250                 255

Lys Val Glu Ile Lys
            260
```

<210> 498
<211> 116
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 498

```
Gln Val Gln Leu Val Gln Ser Gly Gly Asp Leu Ala Gln Pro Gly Arg
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
            20                  25                  30

Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
```

```
Ala Val Ile Trp Pro Asp Gly Gly Gln Lys Tyr Tyr Gly Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Val Ser Arg Asp Asn Pro Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Ile Tyr Tyr Cys
                85                  90                  95

Val Arg His Phe Asn Ala Trp Asp Tyr Trp Gly Gln Gly Thr Leu Val
            100                 105                 110

Thr Val Ser Ser
        115
```

<210> 499
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 499

```
Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Tyr Val Gly
1               5                   10                  15

Gly Arg Val Thr Ile Thr Cys Gln Ala Ser Gln Gly Ile Ser Gln Phe
            20                  25                  30

Leu Asn Trp Phe Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Ser Asp Ala Ser Asn Leu Glu Pro Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Thr Asn Leu Gln Pro
65                  70                  75                  80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Tyr Asp Asp Leu Pro Leu
                85                  90                  95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            100                 105
```

<210> 500
<211> 1476
<212> DNA

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 500
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtgc aactcgtcca atccggtggt ggtgtcgtgc aaccaggaaa gtctcttcgc 120

ctctcatgcg ctgccagcgg attcacgttt tccatcttcg ctatgcactg ggtgcggcag 180

gccccgggaa agggactgga atgggtggca accatttcat acgatggatc aaacgcgttc 240

tacgccgact ccgtggaagg aaggttcacc atctcgagag acaactccaa ggactcgctg 300

tatctgcaaa tggactccct gcgccctgag gataccgccg tctactactg cgtgaaggcc 360

ggcgacgggg gatacgacgt gttcgattcg tggggccagg gaactctggt caccgtgtcc 420

agcgcgagcg ggggaggcgg atcgggtggt ggagggtccg ggggaggagg ctccgagatc 480

gtgatgactc agtcgccgct ctccctcccc gtgaccccg gagagccagc tagcatttca 540

tgtcggagct cccagtccct gctgcactcc aacggctaca attacctgga ttggtacttg 600

cagaagcctg ggcagagccc tcagctgctg atctacctcg gctcgaacag agcctccggc 660

gtgccggacc ggttttccgg gagcggcagc ggcaccgatt tcaccttgaa aatctcccgc 720

gtggaagccg aggacgtggg cgtgtactat tgcatgcagg ccctgcagac tcccaccttc 780

ggcccgggaa ctaaggtcga catcaagacc actaccccag caccgaggcc acccaccccg 840

gctcctacca tcgcctccca gcctctgtcc ctgcgtccgg aggcatgtag acccgcagct 900

ggtggggccg tgcatacccg gggtcttgac ttcgcctgcg atatctacat ttgggccct 960

ctggctggta cttgcggggt cctgctgctt tcactcgtga tcactcttta ctgtaagcgc 1020

ggtcggaaga agctgctgta catctttaag caacccttca tgaggcctgt gcagactact 1080

caagaggagg acggctgttc atgccggttc ccagaggagg aggaaggcgg ctgcgaactg 1140

cgcgtgaaat tcagccgcag cgcagatgct ccagcctaca agcaggggca gaaccagctc 1200

tacaacgaac tcaatcttgg tcggagagag gagtacgacg tgctggacaa gcggagagga 1260

cgggacccag aaatgggcgg gaagccgcgc agaaagaatc cccaagaggg cctgtacaac 1320

gagctccaaa aggataagat ggcagaagcc tatagcgaga ttggtatgaa aggggaacgc 1380

agaagaggca aaggccacga cggactgtac cagggactca gcaccgccac caaggacacc 1440

tatgacgctc ttcacatgca ggccctgccg cctcgg 1476

<210> 501
<211> 492
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 501

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Gly Gly Val
            20                  25                  30

Val Gln Pro Gly Lys Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
        35                  40                  45

Thr Phe Ser Ile Phe Ala Met His Trp Val Arg Gln Ala Pro Gly Lys
    50                  55                  60

Gly Leu Glu Trp Val Ala Thr Ile Ser Tyr Asp Gly Ser Asn Ala Phe
65                  70                  75                  80

Tyr Ala Asp Ser Val Glu Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser
                85                  90                  95

Lys Asp Ser Leu Tyr Leu Gln Met Asp Ser Leu Arg Pro Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Val Lys Ala Gly Asp Gly Gly Tyr Asp Val Phe
        115                 120                 125

Asp Ser Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile
145                 150                 155                 160

Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly Glu Pro
                165                 170                 175

Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser Asn Gly
            180                 185                 190

Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Gln
        195                 200                 205

Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro Asp Arg
    210                 215                 220
```

```
                                                    _SL
Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg
225                 230                 235                 240

Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala Leu Gln
                245                 250                 255

Thr Pro Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys Thr Thr Thr
            260                 265                 270

Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro
        275                 280                 285

Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val
    290                 295                 300

His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro
305                 310                 315                 320

Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu
                325                 330                 335

Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro
            340                 345                 350

Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys
        355                 360                 365

Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe
    370                 375                 380

Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu
385                 390                 395                 400

Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp
                405                 410                 415

Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys
            420                 425                 430

Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala
        435                 440                 445

Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys
    450                 455                 460

Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr
465                 470                 475                 480
```

Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 502
<211> 269
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 502
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Gly Gly Val
20 25 30

Val Gln Pro Gly Lys Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
35 40 45

Thr Phe Ser Ile Phe Ala Met His Trp Val Arg Gln Ala Pro Gly Lys
50 55 60

Gly Leu Glu Trp Val Ala Thr Ile Ser Tyr Asp Gly Ser Asn Ala Phe
65 70 75 80

Tyr Ala Asp Ser Val Glu Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser
85 90 95

Lys Asp Ser Leu Tyr Leu Gln Met Asp Ser Leu Arg Pro Glu Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Val Lys Ala Gly Asp Gly Gly Tyr Asp Val Phe
115 120 125

Asp Ser Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Gly
130 135 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile
145 150 155 160

Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly Glu Pro
165 170 175

Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser Asn Gly
180 185 190

```
Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Gln
        195                 200                 205

Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro Asp Arg
    210                 215                 220

Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg
225                 230                 235                 240

Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala Leu Gln
                245                 250                 255

Thr Pro Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys
            260                 265
```

<210> 503
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 503

```
Gln Val Gln Leu Val Gln Ser Gly Gly Gly Val Val Gln Pro Gly Lys
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ile Phe
            20                  25                  30

Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ala Thr Ile Ser Tyr Asp Gly Ser Asn Ala Phe Tyr Ala Asp Ser Val
    50                  55                  60

Glu Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asp Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asp Ser Leu Arg Pro Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Val Lys Ala Gly Asp Gly Gly Tyr Asp Val Phe Asp Ser Trp Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser
        115                 120
```

<210> 504
<211> 111
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 504
Glu Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser
20 25 30

Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala
85 90 95

Leu Gln Thr Pro Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys
100 105 110

<210> 505
<211> 1467
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 505
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaagtgc aattggtgga atctggagga ggattggtgc aacctggagg atctctgaga 120

ctgtcatgtg ccgccagcgg cttcacattt tcctcctacg cgatgtcatg ggtccgccag 180

gcaccgggga aaggactgga atgggtgtcc gccatttcgg gatcgggagg ctcgacctac 240

tacgccgaca gcgtgaaggg aagattcact atctcccggg ataactccaa gaatactctg 300

tatctccaaa tgaactccct gagggccgag gatactgccg tgtactactg cgctaaggaa 360

accgactact acggctcagg aaccttcgac tactggggcc agggcaccct cgtgaccgtg 420

tcctcggcct ccggcggcgg aggttcgggg gggggcggtt ccgggggagg gggcagcgac 480

atccagatga cccagtcccc aagctccctt tccgcgtccg tgggagatcg cgtgaccatt 540

tcgtgccggg ctagccaggg catcggtatc tatcttgcgt ggtaccagca gcggagcgga 600

aagccgcccc agctgctgat ccacggcgcc tcaactctgc aatccggggt ccccagccgg 660

ttcagcggta gcgggtcggg taccgacttt accctgacta tctcctccct ccaaccggag 720

gacttcgcct cctactggtg ccagcagtcc aacaacttcc ctcccacctt cggccaggga 780

acgaaggtcg agattaagac cactacccca gcaccgaggc cacccacccc ggctcctacc 840

atcgcctccc agcctctgtc cctgcgtccg gaggcatgta gacccgcagc tggtggggcc 900

gtgcataccc ggggtcttga cttcgcctgc gatatctaca tttgggcccc tctggctggt 960

acttgcgggg tcctgctgct ttcactcgtg atcactcttt actgtaagcg cggtcggaag 1020

aagctgctgt acatctttaa gcaacccttc atgaggcctg tgcagactac tcaagaggag 1080

gacggctgtt catgccggtt cccagaggag gaggaaggcg gctgcgaact gcgcgtgaaa 1140

ttcagccgca gcgcagatgc tccagcctac aagcaggggc agaaccagct ctacaacgaa 1200

ctcaatcttg gtcggagaga ggagtacgac gtgctggaca agcggagagg acgggaccca 1260

gaaatgggcg ggaagccgcg cagaaagaat ccccaagagg gcctgtacaa cgagctccaa 1320

aaggataaga tggcagaagc ctatagcgag attggtatga aaggggaacg cagaagaggc 1380

aaaggccacg acggactgta ccagggactc agcaccgcca ccaaggacac ctatgacgct 1440

cttcacatgc aggccctgcc gcctcgg 1467

<210> 506
<211> 489
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 506

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
20 25 30

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
35 40 45

Thr Phe Ser Ser Tyr Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys

_SL

50 55 60

Gly Leu Glu Trp Val Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr
65 70 75 80

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser
85 90 95

Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Ala Lys Glu Thr Asp Tyr Tyr Gly Ser Gly Thr
115 120 125

Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser
130 135 140

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp
145 150 155 160

Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp
165 170 175

Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Gly Ile Gly Ile Tyr Leu
180 185 190

Ala Trp Tyr Gln Gln Arg Ser Gly Lys Pro Pro Gln Leu Leu Ile His
195 200 205

Gly Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
210 215 220

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
225 230 235 240

Asp Phe Ala Ser Tyr Trp Cys Gln Gln Ser Asn Asn Phe Pro Pro Thr
245 250 255

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Thr Thr Thr Pro Ala Pro
260 265 270

Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu
275 280 285

Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg
290 295 300

_SL
Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly
305 310 315 320

Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys
325 330 335

Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg
340 345 350

Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro
355 360 365

Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser
370 375 380

Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu
385 390 395 400

Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg
405 410 415

Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln
420 425 430

Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr
435 440 445

Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp
450 455 460

Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala
465 470 475 480

Leu His Met Gln Ala Leu Pro Pro Arg
485

<210> 507
<211> 266
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 507
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

```
                                                _SL
His Ala Ala Arg Pro Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
            20                  25                  30

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
        35                  40                  45

Thr Phe Ser Ser Tyr Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys
    50                  55                  60

Gly Leu Glu Trp Val Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr
65                  70                  75                  80

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser
                85                  90                  95

Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Lys Glu Thr Asp Tyr Tyr Gly Ser Gly Thr
        115                 120                 125

Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser
    130                 135                 140

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp
145                 150                 155                 160

Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp
                165                 170                 175

Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Gly Ile Gly Ile Tyr Leu
            180                 185                 190

Ala Trp Tyr Gln Gln Arg Ser Gly Lys Pro Pro Gln Leu Leu Ile His
        195                 200                 205

Gly Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
    210                 215                 220

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
225                 230                 235                 240

Asp Phe Ala Ser Tyr Trp Cys Gln Gln Ser Asn Asn Phe Pro Pro Thr
                245                 250                 255

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
            260                 265
```

<210> 508
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 508
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Glu Thr Asp Tyr Tyr Gly Ser Gly Thr Phe Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 509
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 509
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Gly Ile Gly Ile Tyr
20 25 30

```
                                            _SL
Leu Ala Trp Tyr Gln Gln Arg Ser Gly Lys Pro Pro Gln Leu Leu Ile
        35                  40                  45

His Gly Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Ser Tyr Trp Cys Gln Gln Ser Asn Asn Phe Pro Pro
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
            100                 105
```

<210> 510
<211> 1467
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 510

```
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg       60

ccccaagtcc aactcgtcca gtccggtgca gaagtcaaga agccaggagc ctccgtgaga      120

gtgtcgtgca aagcgtccgg ctacatgttc accgactttt tcattcactg ggtgcgccag      180

gcgcccggac agggtctgga gtggatgggg tggatcaacc ctaactccgg cgtgactaaa      240

tacgcccaga agttccaggg ccgcgtgacc atgacccgga acactagcat ctccaccgcc      300

tacatggaac tgtcatccct ccggtccgag gataccgccg tgtactactg cgccacctgg      360

tacagcagcg gttggtacgg catcgcgaac atttggggac aggggactat ggtcaccgtg      420

tcatccgcct ccgggggagg agggtccggc ggcggaggtt ctggaggagg cggctcggac      480

atccagttga cgcagagccc ctcgtcgctg agcgcctccg tgggcgacag agtgaccatt      540

acctgtcaag cttcccatga tatctcgaac tacctccact ggtatcagca gaagccggga      600

aaggctccca agctgctgat ctacgacgcc tccaatctgg aaaccggagt gccgagccgg      660

ttcactggat cagggagcgg cactgacttc accctgacaa ttaggtcgct gcagccggag      720

gatgtggcag cctactactg ccaacagtca gacgaccttc ctcacacttt cggacaaggg      780

actaaggtcg acatcaagac cactacccca gcaccgaggc cacccacccc ggctcctacc      840

atcgcctccc agcctctgtc cctgcgtccg gaggcatgta gacccgcagc tggtggggcc      900

gtgcataccc ggggtcttga cttcgcctgc gatatctaca tttgggcccc tctggctggt      960
```

acttgcgggg tcctgctgct ttcactcgtg atcactcttt actgtaagcg cggtcggaag 1020

aagctgctgt acatctttaa gcaacccttc atgaggcctg tgcagactac tcaagaggag 1080

gacggctgtt catgccggtt cccagaggag gaggaaggcg gctgcgaact gcgcgtgaaa 1140

ttcagccgca gcgcagatgc tccagcctac aagcaggggc agaaccagct ctacaacgaa 1200

ctcaatcttg gtcggagaga ggagtacgac gtgctggaca agcggagagg acgggaccca 1260

gaaatgggcg ggaagccgcg cagaaagaat ccccaagagg gcctgtacaa cgagctccaa 1320

aaggataaga tggcagaagc ctatagcgag attggtatga aaggggaacg cagaagaggc 1380

aaaggccacg acggactgta ccagggactc agcaccgcca ccaaggacac ctatgacgct 1440

cttcacatgc aggccctgcc gcctcgg 1467

<210> 511
<211> 489
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 511
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
20 25 30

Lys Lys Pro Gly Ala Ser Val Arg Val Ser Cys Lys Ala Ser Gly Tyr
35 40 45

Met Phe Thr Asp Phe Phe Ile His Trp Val Arg Gln Ala Pro Gly Gln
50 55 60

Gly Leu Glu Trp Met Gly Trp Ile Asn Pro Asn Ser Gly Val Thr Lys
65 70 75 80

Tyr Ala Gln Lys Phe Gln Gly Arg Val Thr Met Thr Arg Asn Thr Ser
85 90 95

Ile Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Ala Thr Trp Tyr Ser Ser Gly Trp Tyr Gly Ile
115 120 125

Ala Asn Ile Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Ala Ser

_SL

130 135 140

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp
145 150 155 160

Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp
165 170 175

Arg Val Thr Ile Thr Cys Gln Ala Ser His Asp Ile Ser Asn Tyr Leu
180 185 190

His Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
195 200 205

Asp Ala Ser Asn Leu Glu Thr Gly Val Pro Ser Arg Phe Thr Gly Ser
210 215 220

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Arg Ser Leu Gln Pro Glu
225 230 235 240

Asp Val Ala Ala Tyr Tyr Cys Gln Gln Ser Asp Asp Leu Pro His Thr
245 250 255

Phe Gly Gln Gly Thr Lys Val Asp Ile Lys Thr Thr Thr Pro Ala Pro
260 265 270

Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu
275 280 285

Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg
290 295 300

Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly
305 310 315 320

Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys
325 330 335

Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg
340 345 350

Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro
355 360 365

Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser
370 375 380

_SL
Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu
385 390 395 400

Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg
405 410 415

Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln
420 425 430

Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr
435 440 445

Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp
450 455 460

Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala
465 470 475 480

Leu His Met Gln Ala Leu Pro Pro Arg
485

<210> 512
<211> 266
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 512
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
20 25 30

Lys Lys Pro Gly Ala Ser Val Arg Val Ser Cys Lys Ala Ser Gly Tyr
35 40 45

Met Phe Thr Asp Phe Phe Ile His Trp Val Arg Gln Ala Pro Gly Gln
50 55 60

Gly Leu Glu Trp Met Gly Trp Ile Asn Pro Asn Ser Gly Val Thr Lys
65 70 75 80

Tyr Ala Gln Lys Phe Gln Gly Arg Val Thr Met Thr Arg Asn Thr Ser
85 90 95

```
                                                _SL
Ile Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
            100                 105                 110


Ala Val Tyr Tyr Cys Ala Thr Trp Tyr Ser Ser Gly Trp Tyr Gly Ile
        115                 120                 125


Ala Asn Ile Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Ala Ser
    130                 135                 140


Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp
145                 150                 155                 160


Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp
                165                 170                 175


Arg Val Thr Ile Thr Cys Gln Ala Ser His Asp Ile Ser Asn Tyr Leu
            180                 185                 190


His Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
        195                 200                 205


Asp Ala Ser Asn Leu Glu Thr Gly Val Pro Ser Arg Phe Thr Gly Ser
    210                 215                 220


Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Arg Ser Leu Gln Pro Glu
225                 230                 235                 240


Asp Val Ala Ala Tyr Tyr Cys Gln Gln Ser Asp Asp Leu Pro His Thr
                245                 250                 255


Phe Gly Gln Gly Thr Lys Val Asp Ile Lys
            260                 265


<210> 513
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 513
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15


Ser Val Arg Val Ser Cys Lys Ala Ser Gly Tyr Met Phe Thr Asp Phe
            20                  25                  30
```

```
                                                _SL
Phe Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

Gly Trp Ile Asn Pro Asn Ser Gly Val Thr Lys Tyr Ala Gln Lys Phe
    50                  55                  60

Gln Gly Arg Val Thr Met Thr Arg Asn Thr Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Thr Trp Tyr Ser Ser Gly Trp Tyr Gly Ile Ala Asn Ile Trp Gly
            100                 105                 110

Gln Gly Thr Met Val Thr Val Ser Ser
        115                 120
```

<210> 514
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 514

```
Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Gln Ala Ser His Asp Ile Ser Asn Tyr
            20                  25                  30

Leu His Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Asp Ala Ser Asn Leu Glu Thr Gly Val Pro Ser Arg Phe Thr Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Arg Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Val Ala Ala Tyr Tyr Cys Gln Gln Ser Asp Asp Leu Pro His
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Val Asp Ile Lys
            100                 105
```

<210> 515
<211> 1464
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 515
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtgc aactcgtcca gtccggtgca gaagtgaaaa agccaggaga aagcctcaag 120

atcagctgca agggatctgg gtacagcttc accaactact ggatcggctg ggtgcgccag 180

atgcccggaa agggactgga gtggatgggc attatctacc ctggggactc cgacacccgg 240

tattccccga gcttccaagg acaggtcacc atctccgccg ataagtcgat tagcactgcg 300

tacttgcagt ggtcaagcct gaaggcctcg gacaccgcca tgtactactg cgcgagacac 360

gggccctcgt cctggggcga atttgactac tggggccagg gaacgcttgt gaccgtgtcg 420

tccgcgtccg ggggtggagg atcaggagga ggaggctccg gtggtggcgg tagcgacatc 480

cggctgactc agtccccttc ctcactctcc gcctccgtgg gggaccgcgt gaccattacc 540

tgtcgggcat cacagtccat cagctcatac ctgaactggt atcagcagaa gccggggaag 600

gccccgaaac tcctgatcta cgccgcctcc tccctgcaat ccggcgtgcc ctcgaggttc 660

tccggctccg gctcgggaac cgatttcact ctgacaatta gcagcctgca gcctgaggat 720

ttcgctacct actactgcca gcagtcctac tcgactccgc tgactttcgg cgggggaacc 780

aaggtcgaca tcaagaccac taccccagca ccgaggccac ccaccccggc tcctaccatc 840

gcctcccagc ctctgtccct gcgtccggag gcatgtagac ccgcagctgg tggggccgtg 900

catacccggg gtcttgactt cgcctgcgat atctacattt gggcccctct ggctggtact 960

tgcggggtcc tgctgctttc actcgtgatc actctttact gtaagcgcgg tcggaagaag 1020

ctgctgtaca tctttaagca acccttcatg aggcctgtgc agactactca agaggaggac 1080

ggctgttcat gccggttccc agaggaggag gaaggcggct gcgaactgcg cgtgaaattc 1140

agccgcagcg cagatgctcc agcctacaag caggggcaga accagctcta caacgaactc 1200

aatcttggtc ggagagagga gtacgacgtg ctggacaagc ggagaggacg ggacccagaa 1260

atgggcggga agccgcgcag aaagaatccc caagagggcc tgtacaacga gctccaaaag 1320

gataagatgg cagaagccta tagcgagatt ggtatgaaag gggaacgcag aagaggcaaa 1380

ggccacgacg gactgtacca gggactcagc accgccacca aggacaccta tgacgctctt 1440

cacatgcagg ccctgccgcc tcgg 1464

<210> 516

<211> 488
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 516

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
            20                  25                  30

Lys Lys Pro Gly Glu Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr
        35                  40                  45

Ser Phe Thr Asn Tyr Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys
    50                  55                  60

Gly Leu Glu Trp Met Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg
65                  70                  75                  80

Tyr Ser Pro Ser Phe Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser
                85                  90                  95

Ile Ser Thr Ala Tyr Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr
            100                 105                 110

Ala Met Tyr Tyr Cys Ala Arg His Gly Pro Ser Ser Trp Gly Glu Phe
        115                 120                 125

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile
145                 150                 155                 160

Arg Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg
                165                 170                 175

Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn
            180                 185                 190

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala
        195                 200                 205

Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly
```

_SL

210 215 220

Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
225 230 235 240

Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe
245 250 255

Gly Gly Gly Thr Lys Val Asp Ile Lys Thr Thr Thr Pro Ala Pro Arg
260 265 270

Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg
275 280 285

Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly
290 295 300

Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr
305 310 315 320

Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg
325 330 335

Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro
340 345 350

Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu
355 360 365

Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala
370 375 380

Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu
385 390 395 400

Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly
405 410 415

Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu
420 425 430

Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser
435 440 445

Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly
450 455 460

                                                _SL
Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu
465   470   475   480

His Met Gln Ala Leu Pro Pro Arg
                485

<210> 517
<211> 265
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 517
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1   5   10   15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
            20   25   30

Lys Lys Pro Gly Glu Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr
        35   40   45

Ser Phe Thr Asn Tyr Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys
    50   55   60

Gly Leu Glu Trp Met Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg
65   70   75   80

Tyr Ser Pro Ser Phe Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser
                85   90   95

Ile Ser Thr Ala Tyr Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr
            100   105   110

Ala Met Tyr Tyr Cys Ala Arg His Gly Pro Ser Ser Trp Gly Glu Phe
        115   120   125

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Gly
    130   135   140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile
145   150   155   160

Arg Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg
                165   170   175

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                                                _SL
Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn
            180                 185                 190


Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala
        195                 200                 205


Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly
    210                 215                 220


Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
225                 230                 235                 240


Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe
                245                 250                 255


Gly Gly Gly Thr Lys Val Asp Ile Lys
            260                 265


<210> 518
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 518
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1               5                   10                  15


Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Asn Tyr
            20                  25                  30


Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
        35                  40                  45


Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe
    50                  55                  60


Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80


Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
                85                  90                  95


Ala Arg His Gly Pro Ser Ser Trp Gly Glu Phe Asp Tyr Trp Gly Gln
            100                 105                 110
```

Gly Thr Leu Val Thr Val Ser Ser
        115   120

<210> 519
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 519
Asp Ile Arg Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1   5   10   15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr
            20   25   30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35   40   45

Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu
                85   90   95

Thr Phe Gly Gly Gly Thr Lys Val Asp Ile Lys
            100   105

<210> 520
<211> 750
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 520
caagtgcaac tcgtccagtc cggtgcagaa gtcaagaagc caggagaatc actcaagatt 60

agctgcaaag gcagcggcta ctccttcact tcctactgga tcggctgggt gcgccagatg 120

cccggaaagg gactggagtg gatgggaatc atctaccctg gcgatagcga caccagatac 180

tccccgagct ttcaaggcca agtgaccatt tcggccgaca agtcgatctc caccgcgtat 240

ctgcagtgga gctcactgaa ggcttcggac accgccatgt actactgtgc ccggctgggg 300

ggaagcctgc ccgattacgg aatggacgtg tggggccagg gaaccatggt cactgtgtcc 360

tccgcctccg ggggtggagg ctccggtgga ggggggtccg gtggtggagg atcagaaatt 420

gtgctgaccc agtctccgct gtccttgcct gtgaccccgg gcgaacccgc aagcatctcc 480

tgccggtcgt cgcagtccct gcttcactcc aacggctaca actacctcga ttggtacctc 540

cagaagcctg gacagagccc acagctgttg atctacctgg gctcgaaccg ggcctcagga 600

gtgccggaca ggttctccgg ctccgggtcg ggaaccgact tcacgctgaa gatctcccgc 660

gtggaggccg aggacgtggg cgtgtactat tgcatgcagg cgctgcagac ccttattaca 720

ttcggacagg ggactaaggt cgatatcaag 750

<210> 521
<211> 250
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 521

Gln	Val	Gln	Leu	Val	Gln	Ser	Gly	Ala	Glu	Val	Lys	Lys	Pro	Gly	Glu
1				5				10				15			
Ser	Leu	Lys	Ile	Ser	Cys	Lys	Gly	Ser	Gly	Tyr	Ser	Phe	Thr	Ser	Tyr
			20					25				30			
Trp	Ile	Gly	Trp	Val	Arg	Gln	Met	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Met
		35					40					45			
Gly	Ile	Ile	Tyr	Pro	Gly	Asp	Ser	Asp	Thr	Arg	Tyr	Ser	Pro	Ser	Phe
	50					55					60				
Gln	Gly	Gln	Val	Thr	Ile	Ser	Ala	Asp	Lys	Ser	Ile	Ser	Thr	Ala	Tyr
65					70					75					80
Leu	Gln	Trp	Ser	Ser	Leu	Lys	Ala	Ser	Asp	Thr	Ala	Met	Tyr	Tyr	Cys
				85					90					95	
Ala	Arg	Leu	Gly	Gly	Ser	Leu	Pro	Asp	Tyr	Gly	Met	Asp	Val	Trp	Gly
			100					105				110			
Gln	Gly	Thr	Met	Val	Thr	Val	Ser	Ser	Ala	Ser	Gly	Gly	Gly	Gly	Ser
		115					120					125			
Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Glu	Ile	Val	Leu	Thr	Gln
	130					135					140				

```
Ser Pro Leu Ser Leu Pro Val Thr Pro Gly Glu Pro Ala Ser Ile Ser
145                 150                 155                 160

Cys Arg Ser Ser Gln Ser Leu Leu His Ser Asn Gly Tyr Asn Tyr Leu
                165                 170                 175

Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Gln Leu Leu Ile Tyr
            180                 185                 190

Leu Gly Ser Asn Arg Ala Ser Gly Val Pro Asp Arg Phe Ser Gly Ser
        195                 200                 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
    210                 215                 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Ala Leu Gln Thr Leu Ile Thr
225                 230                 235                 240

Phe Gly Gln Gly Thr Lys Val Asp Ile Lys
                245                 250
```

<210> 522
<211> 753
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 522
caagtccaac tcgtccaatc aggagctgaa gtcaagaagc ctggagcatc cgtgagagtg 60

tcctgtaaag cctccggcta catcttcacc aactactacg tgcactgggt cagacaggcc 120

ccgggccagg gactggaatg gatgggaatc atttccccgt ccggcggatc gcctacttac 180

gcgcaacggc tgcagggccg cgtgaccatg actcgggatc tctccacttc aaccgtgtac 240

atggaactgt ccagccttac atcggaggat actgccgtgt acttctgcgc gagggagtcc 300

cggctgaggg gcaaccgcct cgggctgcag tcaagcatct tcgatcactg gggccagggc 360

accctcgtga ccgtgtccag cgcctcgggg ggaggaggct ccgggggcgg aggttcgggc 420

ggtggtggat ctgacattcg catgactcag tccccacctt cactgtccgc tagcgtgggg 480

gaccgcgtga cgattccgtg ccaagccagc caggacatca acaaccatct gaactggtat 540

cagcagaagc ccggaaaggc cccgcagctg ctgatctacg acacctcgaa tctggagatc 600

ggcgtgccat cccggttctc cggttcggga agcggaaccg actttaccct gactatctcc 660

tccttgcaac ccgaggacat tgccacctac tactgccagc agtacgaaaa ccttcccctg 720

accttcgggg gtggaaccaa agtggagatc aag 753

<210> 523
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 523

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15

Ser Val Arg Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Asn Tyr
            20                  25                  30

Tyr Val His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

Gly Ile Ile Ser Pro Ser Gly Gly Ser Pro Thr Tyr Ala Gln Arg Leu
    50                  55                  60

Gln Gly Arg Val Thr Met Thr Arg Asp Leu Ser Thr Ser Thr Val Tyr
65                  70                  75                  80

Met Glu Leu Ser Ser Leu Thr Ser Glu Asp Thr Ala Val Tyr Phe Cys
                85                  90                  95

Ala Arg Glu Ser Arg Leu Arg Gly Asn Arg Leu Gly Leu Gln Ser Ser
            100                 105                 110

Ile Phe Asp His Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala
        115                 120                 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
    130                 135                 140

Asp Ile Arg Met Thr Gln Ser Pro Pro Ser Leu Ser Ala Ser Val Gly
145                 150                 155                 160

Asp Arg Val Thr Ile Pro Cys Gln Ala Ser Gln Asp Ile Asn Asn His
                165                 170                 175

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Gln Leu Leu Ile
            180                 185                 190
```

Tyr Asp Thr Ser Asn Leu Glu Ile Gly Val Pro Ser Arg Phe Ser Gly
195 200 205

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
210 215 220

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Tyr Glu Asn Leu Pro Leu
225 230 235 240

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
245 250

<210> 524
<211> 750
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 524
caagtgcagc tcgtccaatc cggtgcagaa gtgaagaagc ctggcgaatc cctgaagatc 60

tcatgcaaag gctcgggata cagcttcacc tcatattgga ttggatgggt cagacagatg 120

ccaggaaagg gtctggagtg gatgggaatc atctacccgg gagacagcga tacccggtac 180

tccccgagct tccagggaca ggtcaccatc tcggccgaca agtccattac tactgcctac 240

ttgcaatggt cctcgctgcg cgcctccgat agcgccatgt actactgcgc gagaggcggc 300

tactccgact acgactacta cttcgatttc tggggacagg ggacactcgt gactgtgtcc 360

tccgcgtcgg gtggcggcgg ctcgggtgga ggaggaagcg gagggggagg ctccgaaatt 420

gtgatgaccc agtcaccccct gtcgctccct gtgactcctg gggaaccggc ctccatctcc 480

tgccggagct cacagagcct gctgcactcc aacggataca actacctcga ttggtacctt 540

cagaagcccg gccagtcgcc ccagctgctg atctacctgg ggtccaaccg ggctagcggc 600

gtgccggacc gcttctccgg ttccgggtct ggaaccgact tcacgctgaa aatctccagg 660

gtggaggccg aggacgtggg agtgtattac tgtatgcagg ccctgcaaac ccccttcacc 720

tttggcgggg gcaccaaggt cgagattaag 750

<210> 525
<211> 250
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

_SL

polypeptide"

<400> 525

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1               5                   10                  15

Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
            20                  25                  30

Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
        35                  40                  45

Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe
    50                  55                  60

Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Thr Thr Ala Tyr
65                  70                  75                  80

Leu Gln Trp Ser Ser Leu Arg Ala Ser Asp Ser Ala Met Tyr Tyr Cys
                85                  90                  95

Ala Arg Gly Gly Tyr Ser Asp Tyr Asp Tyr Tyr Phe Asp Phe Trp Gly
            100                 105                 110

Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Gly Gly Gly Gly Ser
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Met Thr Gln
    130                 135                 140

Ser Pro Leu Ser Leu Pro Val Thr Pro Gly Glu Pro Ala Ser Ile Ser
145                 150                 155                 160

Cys Arg Ser Ser Gln Ser Leu Leu His Ser Asn Gly Tyr Asn Tyr Leu
                165                 170                 175

Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Gln Leu Leu Ile Tyr
            180                 185                 190

Leu Gly Ser Asn Arg Ala Ser Gly Val Pro Asp Arg Phe Ser Gly Ser
        195                 200                 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
    210                 215                 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Ala Leu Gln Thr Pro Phe Thr
225                 230                 235                 240
```

_SL
Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
245 250

<210> 526
<211> 720
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 526
caagtgcaac tcgtccaaag cggtggagat ctcgcccagc ccggaagatc ccttagactc 60

tcatgtgccg ccagcgggtt caccttcgac gactacgcta tgcattgggt gcgccaggcc 120

ccggggaagg gactggaatg ggtggccgtg atttggccgg acggcggaca gaagtactac 180

ggagacagcg tgaaagggcg gttcaccgtg tcgagggaca acccgaagaa taccctctac 240

cttcaaatga actccctgcg cgccgaggac accgcgatct actactgcgt gcgccacttt 300

aacgcatggg attactgggg acaggggact ctggtcactg tgtcctccgc ctctggcggc 360

ggaggttccg gcggtggtgg ctccggtgga ggaggatcgg acatccagct gacccagtcc 420

ccttcctcac tgtcggcgta cgtgggaggc cgggtcacta tcacgtgcca ggcatcccag 480

ggcatttccc agttcctgaa ctggttccag cagaagcccg gaaaggcccc taagctgttg 540

atttccgatg ctagcaacct ggaacccggc gtgccgtcac ggttcagcgg ctccgggtcg 600

ggcaccgact tcaccttcac catcactaac ctccaaccgg aggacatcgc cacctattac 660

tgccagcagt acgatgatct gccactgact ttcggcggcg gaaccaaggt cgaaatcaag 720

<210> 527
<211> 240
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 527
Gln Val Gln Leu Val Gln Ser Gly Gly Asp Leu Ala Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
20 25 30

Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

```
                                                _SL
Ala Val Ile Trp Pro Asp Gly Gly Gln Lys Tyr Tyr Gly Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Val Ser Arg Asp Asn Pro Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Ile Tyr Tyr Cys
                85                  90                  95

Val Arg His Phe Asn Ala Trp Asp Tyr Trp Gly Gln Gly Thr Leu Val
            100                 105                 110

Thr Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125

Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu
    130                 135                 140

Ser Ala Tyr Val Gly Gly Arg Val Thr Ile Thr Cys Gln Ala Ser Gln
145                 150                 155                 160

Gly Ile Ser Gln Phe Leu Asn Trp Phe Gln Gln Lys Pro Gly Lys Ala
                165                 170                 175

Pro Lys Leu Leu Ile Ser Asp Ala Ser Asn Leu Glu Pro Gly Val Pro
            180                 185                 190

Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile
        195                 200                 205

Thr Asn Leu Gln Pro Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Tyr
    210                 215                 220

Asp Asp Leu Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
225                 230                 235                 240
```

<210> 528
<211> 744
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 528
caagtgcaac tcgtccaatc cggtggtggt gtcgtgcaac caggaaagtc tcttcgcctc 60

tcatgcgctg ccagcggatt cacgttttcc atcttcgcta tgcactgggt gcggcaggcc 120

ccgggaaagg gactggaatg ggtggcaacc atttcatacg atggatcaaa cgcgttctac 180

gccgactccg tggaaggaag gttcaccatc tcgagagaca actccaagga ctcgctgtat 240

ctgcaaatgg actccctgcg ccctgaggat accgccgtct actactgcgt gaaggccggc 300

gacgggggat acgacgtgtt cgattcgtgg ggccagggaa ctctggtcac cgtgtccagc 360

gcgagcgggg gaggcggatc gggtggtgga gggtccgggg gaggaggctc cgagatcgtg 420

atgactcagt cgccgctctc cctccccgtg acccccggag agccagctag catttcatgt 480

cggagctccc agtccctgct gcactccaac ggctacaatt acctggattg gtacttgcag 540

aagcctgggc agagccctca gctgctgatc tacctcggct cgaacagagc ctccggcgtg 600

ccggaccggt tttccgggag cggcagcggc accgatttca ccttgaaaat ctcccgcgtg 660

gaagccgagg acgtgggcgt gtactattgc atgcaggccc tgcagactcc caccttcggc 720

ccgggaacta aggtcgacat caag 744

<210> 529
<211> 248
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 529

Gln Val Gln Leu Val Gln Ser Gly Gly Gly Val Val Gln Pro Gly Lys
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ile Phe
20 25 30

Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Thr Ile Ser Tyr Asp Gly Ser Asn Ala Phe Tyr Ala Asp Ser Val
50 55 60

Glu Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asp Ser Leu Tyr
65 70 75 80

Leu Gln Met Asp Ser Leu Arg Pro Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Val Lys Ala Gly Asp Gly Gly Tyr Asp Val Phe Asp Ser Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly

_SL

115 120 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Met Thr Gln Ser
130 135 140

Pro Leu Ser Leu Pro Val Thr Pro Gly Glu Pro Ala Ser Ile Ser Cys
145 150 155 160

Arg Ser Ser Gln Ser Leu Leu His Ser Asn Gly Tyr Asn Tyr Leu Asp
165 170 175

Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Gln Leu Leu Ile Tyr Leu
180 185 190

Gly Ser Asn Arg Ala Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly
195 200 205

Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp
210 215 220

Val Gly Val Tyr Tyr Cys Met Gln Ala Leu Gln Thr Pro Thr Phe Gly
225 230 235 240

Pro Gly Thr Lys Val Asp Ile Lys
245

<210> 530
<211> 735
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 530
gaagtgcaat tggtggaatc tggaggagga ttggtgcaac ctggaggatc tctgagactg 60

tcatgtgccg ccagcggctt cacattttcc tcctacgcga tgtcatgggt ccgccaggca 120

ccggggaaag gactggaatg ggtgtccgcc atttcgggat cgggaggctc gacctactac 180

gccgacagcg tgaagggaag attcactatc tcccgggata actccaagaa tactctgtat 240

ctccaaatga actccctgag ggccgaggat actgccgtgt actactgcgc taaggaaacc 300

gactactacg gctcaggaac cttcgactac tggggccagg gcaccctcgt gaccgtgtcc 360

tcggcctccg gcggcggagg ttcgggggggg ggcggttccg ggggaggggg cagcgacatc 420

cagatgaccc agtccccaag ctccctttcc gcgtccgtgg gagatcgcgt gaccatttcg 480

tgccgggcta gccagggcat cggtatctat cttgcgtggt accagcagcg gagcggaaag 540

ccgccccagc tgctgatcca cggcgcctca actctgcaat ccggggtccc cagccggttc 600

agcggtagcg ggtcgggtac cgactttacc ctgactatct cctccctcca accggaggac 660

ttcgcctcct actggtgcca gcagtccaac aacttccctc ccaccttcgg ccagggaacg 720

aaggtcgaga ttaag 735

<210> 531
<211> 245
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 531
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Glu Thr Asp Tyr Tyr Gly Ser Gly Thr Phe Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln
130 135 140

Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Ser
145 150 155 160

Cys Arg Ala Ser Gln Gly Ile Gly Ile Tyr Leu Ala Trp Tyr Gln Gln
165 170 175

Arg Ser Gly Lys Pro Pro Gln Leu Leu Ile His Gly Ala Ser Thr Leu
180 185 190

Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
195 200 205

Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Ser Tyr
210 215 220

Trp Cys Gln Gln Ser Asn Asn Phe Pro Pro Thr Phe Gly Gln Gly Thr
225 230 235 240

Lys Val Glu Ile Lys
245

<210> 532
<211> 732
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 532
caagtgcaac tcgtccagtc cggtgcagaa gtgaaaaagc caggagaaag cctcaagatc 60

agctgcaagg gatctgggta cagcttcacc aactactgga tcggctgggt gcgccagatg 120

cccggaaagg gactggagtg gatgggcatt atctaccctg gggactccga cacccggtat 180

tccccgagct tccaaggaca ggtcaccatc tccgccgata agtcgattag cactgcgtac 240

ttgcagtggt caagcctgaa ggcctcggac accgccatgt actactgcgc gagacacggg 300

ccctcgtcct ggggcgaatt tgactactgg ggccagggaa cgcttgtgac cgtgtcgtcc 360

gcgtccgggg gtggaggatc aggaggagga ggctccggtg gtggcggtag cgacatccgg 420

ctgactcagt ccccttcctc actctccgcc tccgtggggg accgcgtgac cattacctgt 480

cgggcatcac agtccatcag ctcatacctg aactggtatc agcagaagcc ggggaaggcc 540

ccgaaactcc tgatctacgc cgcctcctcc ctgcaatccg gcgtgccctc gaggttctcc 600

ggctccggct cgggaaccga tttcactctg acaattagca gcctgcagcc tgaggatttc 660

gctacctact actgccagca gtcctactcg actccgctga ctttcggcgg gggaaccaag 720

gtcgacatca ag 732

<210> 533
<211> 244
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 533

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Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1               5                  10                  15

Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Asn Tyr
            20                  25                  30

Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
        35                  40                  45

Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe
    50                  55                  60

Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80

Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
                85                  90                  95

Ala Arg His Gly Pro Ser Ser Trp Gly Glu Phe Asp Tyr Trp Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Arg Leu Thr Gln Ser
    130                 135                 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145                 150                 155                 160

Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys
                165                 170                 175

Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln
            180                 185                 190

Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
        195                 200                 205

Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr
    210                 215                 220
```

Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys
225 230 235 240

Val Asp Ile Lys

<210> 534
<211> 244
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 534
Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Arg Ile Asn Pro Asn Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Arg Tyr Tyr Gly Met Asp Val Trp Gly Gln Gly Thr Met
100 105 110

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
115 120 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser
130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Ile Ser Cys
145 150 155 160

Arg Ala Ser Gln Ser Val Ser Ser Asn Phe Ala Trp Tyr Gln Gln Arg
165 170 175

Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Asp Ala Ser Asn Arg Ala
180 185 190

Thr Gly Ile Pro Pro Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
195 200 205

Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp Phe Ala Ala Tyr Tyr
210 215 220

Cys His Gln Arg Ser Asn Trp Leu Tyr Thr Phe Gly Gln Gly Thr Lys
225 230 235 240

Val Asp Ile Lys

<210> 535
<211> 488
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 535
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Val
20 25 30

Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
35 40 45

Thr Phe Thr Gly Tyr Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln
50 55 60

Gly Leu Glu Trp Met Gly Arg Ile Asn Pro Asn Ser Gly Gly Thr Asn
65 70 75 80

Tyr Ala Gln Lys Phe Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser
85 90 95

Ile Ser Thr Ala Tyr Met Glu Leu Ser Arg Leu Arg Ser Glu Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Ala Arg Gly Arg Tyr Tyr Gly Met Asp Val Trp
115 120 125

```
Gly Gln Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile
145                 150                 155                 160

Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg
                165                 170                 175

Ala Thr Ile Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Asn Phe Ala
            180                 185                 190

Trp Tyr Gln Gln Arg Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Asp
        195                 200                 205

Ala Ser Asn Arg Ala Thr Gly Ile Pro Pro Arg Phe Ser Gly Ser Gly
    210                 215                 220

Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp
225                 230                 235                 240

Phe Ala Ala Tyr Tyr Cys His Gln Arg Ser Asn Trp Leu Tyr Thr Phe
                245                 250                 255

Gly Gln Gly Thr Lys Val Asp Ile Lys Thr Thr Thr Pro Ala Pro Arg
            260                 265                 270

Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg
        275                 280                 285

Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly
    290                 295                 300

Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr
305                 310                 315                 320

Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg
                325                 330                 335

Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro
            340                 345                 350

Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu
        355                 360                 365

Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala
    370                 375                 380
```

```
Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu
385                 390                 395                 400

Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly
                405                 410                 415

Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu
            420                 425                 430

Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser
        435                 440                 445

Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly
    450                 455                 460

Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu
465                 470                 475                 480

His Met Gln Ala Leu Pro Pro Arg
                485
```

<210> 536
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 536

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr
            20                  25                  30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

Gly Trp Ile Asn Pro Asn Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe
    50                  55                  60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
```

Ala Arg Asp Leu Arg Arg Thr Val Val Thr Pro Arg Ala Tyr Tyr Gly
100 105 110

Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly
115 120 125

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
130 135 140

Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser
145 150 155 160

Val Gly Asp Arg Val Thr Ile Thr Cys Gln Ala Ser Gln Asp Ile Ser
165 170 175

Asn Ser Leu Asn Trp Tyr Gln Gln Lys Ala Gly Lys Ala Pro Lys Leu
180 185 190

Leu Ile Tyr Asp Ala Ser Thr Leu Glu Thr Gly Val Pro Ser Arg Phe
195 200 205

Ser Gly Ser Gly Ser Gly Thr Asp Phe Ser Phe Thr Ile Ser Ser Leu
210 215 220

Gln Pro Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln His Asp Asn Leu
225 230 235 240

Pro Leu Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
245 250

<210> 537
<211> 497
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 537
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
20 25 30

Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
35 40 45

```
Thr Phe Thr Gly Tyr Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln
    50                  55                  60

Gly Leu Glu Trp Met Gly Trp Ile Asn Pro Asn Ser Gly Gly Thr Asn
65                  70                  75                  80

Tyr Ala Gln Lys Phe Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser
                85                  90                  95

Ile Ser Thr Ala Tyr Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Arg Asp Leu Arg Arg Thr Val Val Thr Pro
        115                 120                 125

Arg Ala Tyr Tyr Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr
    130                 135                 140

Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
145                 150                 155                 160

Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro Ser
                165                 170                 175

Thr Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Gln Ala
            180                 185                 190

Ser Gln Asp Ile Ser Asn Ser Leu Asn Trp Tyr Gln Gln Lys Ala Gly
        195                 200                 205

Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Thr Leu Glu Thr Gly
    210                 215                 220

Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Ser Phe
225                 230                 235                 240

Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala Thr Tyr Tyr Cys Gln
                245                 250                 255

Gln His Asp Asn Leu Pro Leu Thr Phe Gly Gln Gly Thr Lys Val Glu
            260                 265                 270

Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr
        275                 280                 285

Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala
```

_SL
290 295 300

Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile
305 310 315 320

Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser
325 330 335

Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr
340 345 350

Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu
355 360 365

Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu
370 375 380

Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln
385 390 395 400

Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu
405 410 415

Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly
420 425 430

Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln
435 440 445

Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu
450 455 460

Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr
465 470 475 480

Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro
485 490 495

Arg

<210> 538
<211> 246
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

_SL

polypeptide"

<400> 538

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15

Pro Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr
            20                  25                  30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

Gly Trp Ile Asn Pro Asn Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe
    50                  55                  60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Gly Glu Trp Asp Gly Ser Tyr Tyr Tyr Asp Tyr Trp Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115                 120                 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Leu
    130                 135                 140

Thr Gln Thr Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr
145                 150                 155                 160

Ile Thr Cys Arg Ala Ser Gln Ser Ile Asn Thr Tyr Leu Asn Trp Tyr
                165                 170                 175

Gln His Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser
            180                 185                 190

Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
        195                 200                 205

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
    210                 215                 220

Thr Tyr Tyr Cys Gln Gln Ser Phe Ser Pro Leu Thr Phe Gly Gly Gly
225                 230                 235                 240
```

Thr Lys Leu Glu Ile Lys
245

<210> 539
<211> 490
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 539
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
20 25 30

Lys Lys Pro Gly Ala Pro Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
35 40 45

Thr Phe Thr Gly Tyr Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln
50 55 60

Gly Leu Glu Trp Met Gly Trp Ile Asn Pro Asn Ser Gly Gly Thr Asn
65 70 75 80

Tyr Ala Gln Lys Phe Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser
85 90 95

Ile Ser Thr Ala Tyr Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Ala Arg Gly Glu Trp Asp Gly Ser Tyr Tyr Tyr
115 120 125

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
130 135 140

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
145 150 155 160

Ser Asp Ile Val Leu Thr Gln Thr Pro Ser Ser Leu Ser Ala Ser Val
165 170 175

Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Asn Thr
180 185 190

```
                                                    _SL
Tyr Leu Asn Trp Tyr Gln His Lys Pro Gly Lys Ala Pro Lys Leu Leu
        195                 200                 205

Ile Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser
    210                 215                 220

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln
225                 230                 235                 240

Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Phe Ser Pro Leu
                245                 250                 255

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Thr Thr Thr Pro Ala
            260                 265                 270

Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser
        275                 280                 285

Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr
    290                 295                 300

Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala
305                 310                 315                 320

Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys
                325                 330                 335

Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met
            340                 345                 350

Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe
        355                 360                 365

Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg
    370                 375                 380

Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn
385                 390                 395                 400

Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg
                405                 410                 415

Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro
            420                 425                 430

Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala
        435                 440                 445
```

Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His
450 455 460

Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp
465 470 475 480

Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 540
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 540
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Trp Met His Trp Val Arg Gln Val Pro Gly Lys Gly Leu Val Trp Val
35 40 45

Ser Arg Ile Asn Thr Asp Gly Ser Thr Thr Thr Tyr Ala Asp Ser Val
50 55 60

Glu Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Asp Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Val Gly Gly His Trp Ala Val Trp Gly Gln Gly Thr Thr Val Thr Val
100 105 110

Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
115 120 125

Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Thr
130 135 140

Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser
145 150 155 160

```
Gln Ser Ile Ser Asp Arg Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys
                165                 170                 175

Ala Pro Lys Leu Leu Ile Tyr Lys Ala Ser Ser Leu Glu Ser Gly Val
            180                 185                 190

Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr
        195                 200                 205

Ile Ser Ser Leu Gln Pro Asp Asp Phe Ala Val Tyr Tyr Cys Gln Gln
    210                 215                 220

Tyr Gly His Leu Pro Met Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu
225                 230                 235                 240

Ile Lys
```

<210> 541
<211> 486
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 541

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15

His Ala Ala Arg Pro Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu
            20                  25                  30

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
        35                  40                  45

Thr Phe Ser Ser Tyr Trp Met His Trp Val Arg Gln Val Pro Gly Lys
    50                  55                  60

Gly Leu Val Trp Val Ser Arg Ile Asn Thr Asp Gly Ser Thr Thr Thr
65                  70                  75                  80

Tyr Ala Asp Ser Val Glu Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala
                85                  90                  95

Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Asp Asp Asp Thr
            100                 105                 110
```

```
Ala Val Tyr Tyr Cys Val Gly Gly His Trp Ala Val Trp Gly Gln Gly
        115                 120                 125

Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
    130                 135                 140

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr
145                 150                 155                 160

Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile
                165                 170                 175

Thr Cys Arg Ala Ser Gln Ser Ile Ser Asp Arg Leu Ala Trp Tyr Gln
            180                 185                 190

Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Lys Ala Ser Ser
        195                 200                 205

Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr
    210                 215                 220

Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Asp Asp Phe Ala Val
225                 230                 235                 240

Tyr Tyr Cys Gln Gln Tyr Gly His Leu Pro Met Tyr Thr Phe Gly Gln
                245                 250                 255

Gly Thr Lys Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro
            260                 265                 270

Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu
        275                 280                 285

Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
    290                 295                 300

Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly
305                 310                 315                 320

Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg
                325                 330                 335

Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln
            340                 345                 350

Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu
        355                 360                 365
```

Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
370 375 380

Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
385 390 395 400

Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
405 410 415

Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
420 425 430

Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
435 440 445

Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
450 455 460

Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
465 470 475 480

Gln Ala Leu Pro Pro Arg
485

<210> 542
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 542
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Glu Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Asn Pro Asn Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

```
Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Ser Gly Trp Asp Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr
            100                 105                 110

Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115                 120                 125

Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln Ser Pro Ser
    130                 135                 140

Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala
145                 150                 155                 160

Ser Gln Ser Ile Arg Tyr Tyr Leu Ser Trp Tyr Gln Gln Lys Pro Gly
                165                 170                 175

Lys Ala Pro Lys Leu Leu Ile Tyr Thr Ala Ser Ile Leu Gln Asn Gly
            180                 185                 190

Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
        195                 200                 205

Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Leu
    210                 215                 220

Gln Thr Tyr Thr Thr Pro Asp Phe Gly Pro Gly Thr Lys Val Glu Ile
225                 230                 235                 240

Lys
```

<210> 543
<211> 485
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 543

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
            20                  25                  30
```

```
Glu Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
        35                  40                  45

Thr Phe Thr Asp Tyr Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln
    50                  55                  60

Gly Leu Glu Trp Met Gly Trp Ile Asn Pro Asn Ser Gly Gly Thr Asn
65                  70                  75                  80

Tyr Ala Gln Lys Phe Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser
                85                  90                  95

Ile Ser Thr Ala Tyr Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Ser Gly Trp Asp Phe Asp Tyr Trp Gly Gln
        115                 120                 125

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
    130                 135                 140

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Met
145                 150                 155                 160

Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr
                165                 170                 175

Ile Thr Cys Arg Ala Ser Gln Ser Ile Arg Tyr Tyr Leu Ser Trp Tyr
            180                 185                 190

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Thr Ala Ser
        195                 200                 205

Ile Leu Gln Asn Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
    210                 215                 220

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
225                 230                 235                 240

Thr Tyr Tyr Cys Leu Gln Thr Tyr Thr Thr Pro Asp Phe Gly Pro Gly
                245                 250                 255

Thr Lys Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr
            260                 265                 270

Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala
```

_SL

275 280 285

Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe
290 295 300

Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val
305 310 315 320

Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys
325 330 335

Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr
340 345 350

Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu
355 360 365

Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro
370 375 380

Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly
385 390 395 400

Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro
405 410 415

Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr
420 425 430

Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly
435 440 445

Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln
450 455 460

Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln
465 470 475 480

Ala Leu Pro Pro Arg
485

<210> 544
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

polypeptide"

<400> 544

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

Gly Ile Ile Asn Pro Ser Gly Gly Ser Thr Ser Tyr Ala Gln Lys Phe
    50                  55                  60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Ser Thr Val Tyr
65                  70                  75                  80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Tyr Arg Leu Ile Ala Val Ala Gly Asp Tyr Tyr Tyr Tyr Gly
            100                 105                 110

Met Asp Val Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Gly Gly
        115                 120                 125

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
    130                 135                 140

Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Val Ser Ala Ser
145                 150                 155                 160

Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Val Gly
                165                 170                 175

Arg Trp Leu Ala Trp Tyr Gln Gln Lys Pro Gly Thr Ala Pro Lys Leu
            180                 185                 190

Leu Ile Tyr Ala Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe
        195                 200                 205

Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asn Asn Leu
    210                 215                 220

Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ala Asn Ser Phe
225                 230                 235                 240
```

_SL
Pro Leu Thr Phe Gly Gly Gly Thr Arg Leu Glu Ile Lys
245 250

<210> 545
<211> 497
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 545
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
20 25 30

Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
35 40 45

Thr Phe Thr Ser Tyr Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln
50 55 60

Gly Leu Glu Trp Met Gly Ile Ile Asn Pro Ser Gly Gly Ser Thr Ser
65 70 75 80

Tyr Ala Gln Lys Phe Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser
85 90 95

Thr Ser Thr Val Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Ala Arg Tyr Arg Leu Ile Ala Val Ala Gly Asp
115 120 125

Tyr Tyr Tyr Tyr Gly Met Asp Val Trp Gly Gln Gly Thr Met Val Thr
130 135 140

Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
145 150 155 160

Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser
165 170 175

Ser Val Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala
180 185 190

```
                                                 _SL
Ser Gln Gly Val Gly Arg Trp Leu Ala Trp Tyr Gln Gln Lys Pro Gly
        195                 200                 205

Thr Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Thr Leu Gln Ser Gly
    210                 215                 220

Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
225                 230                 235                 240

Thr Ile Asn Asn Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln
                245                 250                 255

Gln Ala Asn Ser Phe Pro Leu Thr Phe Gly Gly Gly Thr Arg Leu Glu
            260                 265                 270

Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr
        275                 280                 285

Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala
    290                 295                 300

Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile
305                 310                 315                 320

Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser
                325                 330                 335

Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr
            340                 345                 350

Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu
        355                 360                 365

Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu
    370                 375                 380

Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln
385                 390                 395                 400

Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu
                405                 410                 415

Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly
            420                 425                 430

Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln
        435                 440                 445
```

Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu
450 455 460

Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr
465 470 475 480

Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro
485 490 495

Arg

<210> 546
<211> 250
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 546
Gln Val Gln Leu Val Gln Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Val Ile Ser Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Trp Lys Val Ser Ser Ser Ser Pro Ala Phe Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
115 120 125

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val
130 135 140

Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala
145 150 155 160

Ile Leu Ser Cys Arg Ala Ser Gln Ser Val Tyr Thr Lys Tyr Leu Gly
165 170 175

Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Asp
180 185 190

Ala Ser Thr Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly Ser Gly
195 200 205

Ser Gly Thr Asp Phe Thr Leu Thr Ile Asn Arg Leu Glu Pro Glu Asp
210 215 220

Phe Ala Val Tyr Tyr Cys Gln His Tyr Gly Gly Ser Pro Leu Ile Thr
225 230 235 240

Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys
245 250

<210> 547
<211> 494
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 547
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Gly Gly Val
20 25 30

Val Gln Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
35 40 45

Thr Phe Ser Ser Tyr Ala Met His Trp Val Arg Gln Ala Pro Gly Lys
50 55 60

Gly Leu Glu Trp Val Ala Val Ile Ser Tyr Asp Gly Ser Asn Lys Tyr
65 70 75 80

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser
85 90 95

```
Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Arg Trp Lys Val Ser Ser Ser Ser Pro Ala
        115                 120                 125

Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly
    130                 135                 140

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
145                 150                 155                 160

Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser
                165                 170                 175

Pro Gly Glu Arg Ala Ile Leu Ser Cys Arg Ala Ser Gln Ser Val Tyr
            180                 185                 190

Thr Lys Tyr Leu Gly Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg
        195                 200                 205

Leu Leu Ile Tyr Asp Ala Ser Thr Arg Ala Thr Gly Ile Pro Asp Arg
    210                 215                 220

Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asn Arg
225                 230                 235                 240

Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln His Tyr Gly Gly
                245                 250                 255

Ser Pro Leu Ile Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys Thr
            260                 265                 270

Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser
        275                 280                 285

Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly
    290                 295                 300

Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp
305                 310                 315                 320

Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile
                325                 330                 335

Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys
            340                 345                 350
```

```
Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys
        355                 360                 365

Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val
    370                 375                 380

Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn
385                 390                 395                 400

Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val
                405                 410                 415

Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg
            420                 425                 430

Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys
        435                 440                 445

Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg
    450                 455                 460

Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys
465                 470                 475                 480

Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
                485                 490
```

<210> 548
<211> 246
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 548

```
Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15

Ser Val Lys Val Ser Cys Lys Thr Ser Gly Tyr Pro Phe Thr Gly Tyr
            20                  25                  30

Ser Leu His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

Gly Trp Ile Asn Pro Asn Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe
    50                  55                  60
```

```
Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Asp His Tyr Gly Gly Asn Ser Leu Phe Tyr Trp Gly Gln Gly
            100                 105                 110

Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
        115                 120                 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr
    130                 135                 140

Gln Ser Pro Ser Ser Ile Ser Ala Ser Val Gly Asp Thr Val Ser Ile
145                 150                 155                 160

Thr Cys Arg Ala Ser Gln Asp Ser Gly Thr Trp Leu Ala Trp Tyr Gln
                165                 170                 175

Gln Lys Pro Gly Lys Ala Pro Asn Leu Leu Met Tyr Asp Ala Ser Thr
            180                 185                 190

Leu Glu Asp Gly Val Pro Ser Arg Phe Ser Gly Ser Ala Ser Gly Thr
        195                 200                 205

Glu Phe Thr Leu Thr Val Asn Arg Leu Gln Pro Glu Asp Ser Ala Thr
    210                 215                 220

Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Pro Leu Thr Phe Gly Gly Gly
225                 230                 235                 240

Thr Lys Val Asp Ile Lys
                245
```

<210> 549
<211> 490
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 549

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15
```

```
His Ala Ala Arg Pro Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Val
            20                  25                  30

Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Thr Ser Gly Tyr
        35                  40                  45

Pro Phe Thr Gly Tyr Ser Leu His Trp Val Arg Gln Ala Pro Gly Gln
    50                  55                  60

Gly Leu Glu Trp Met Gly Trp Ile Asn Pro Asn Ser Gly Gly Thr Asn
65                  70                  75                  80

Tyr Ala Gln Lys Phe Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser
                85                  90                  95

Ile Ser Thr Ala Tyr Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Arg Asp His Tyr Gly Gly Asn Ser Leu Phe
        115                 120                 125

Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly
    130                 135                 140

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
145                 150                 155                 160

Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Ile Ser Ala Ser Val Gly
                165                 170                 175

Asp Thr Val Ser Ile Thr Cys Arg Ala Ser Gln Asp Ser Gly Thr Trp
            180                 185                 190

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Asn Leu Leu Met
        195                 200                 205

Tyr Asp Ala Ser Thr Leu Glu Asp Gly Val Pro Ser Arg Phe Ser Gly
    210                 215                 220

Ser Ala Ser Gly Thr Glu Phe Thr Leu Thr Val Asn Arg Leu Gln Pro
225                 230                 235                 240

Glu Asp Ser Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Pro Leu
                245                 250                 255

Thr Phe Gly Gly Gly Thr Lys Val Asp Ile Lys Thr Thr Thr Pro Ala
```

_SL

260 265 270

Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser
275 280 285

Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr
290 295 300

Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala
305 310 315 320

Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys
325 330 335

Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met
340 345 350

Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe
355 360 365

Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg
370 375 380

Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn
385 390 395 400

Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg
405 410 415

Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro
420 425 430

Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala
435 440 445

Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His
450 455 460

Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp
465 470 475 480

Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 550
<211> 248
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 550
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Glu Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Gly Gly Ser Thr Gly Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Ser Thr Val His
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Tyr Ser Ser Ser Ser Asp Ala Phe Asp Ile Trp Gly
100 105 110

Gln Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
115 120 125

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln
130 135 140

Met Thr Gln Ser Pro Pro Ser Leu Ser Ala Ser Val Gly Asp Arg Val
145 150 155 160

Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Ala Leu Ala Trp
165 170 175

Tyr Gln Gln Lys Pro Gly Thr Pro Pro Lys Leu Leu Ile Tyr Asp Ala
180 185 190

Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser
195 200 205

Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe
210 215 220

```
                                                _SL
Ala Thr Tyr Tyr Cys Gln Gln Phe Ser Ser Tyr Pro Leu Thr Phe Gly
225                 230                 235                 240


Gly Gly Thr Arg Leu Glu Ile Lys
                245


<210> 551
<211> 492
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 551
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15


His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
            20                  25                  30


Lys Lys Pro Gly Ala Ser Val Glu Val Ser Cys Lys Ala Ser Gly Tyr
        35                  40                  45


Thr Phe Thr Ser Tyr Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln
    50                  55                  60


Gly Leu Glu Trp Met Gly Ile Ile Asn Pro Ser Gly Gly Ser Thr Gly
65                  70                  75                  80


Tyr Ala Gln Lys Phe Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser
                85                  90                  95


Thr Ser Thr Val His Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
            100                 105                 110


Ala Val Tyr Tyr Cys Ala Arg Gly Gly Tyr Ser Ser Ser Ser Asp Ala
        115                 120                 125


Phe Asp Ile Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Gly Gly
    130                 135                 140


Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
145                 150                 155                 160


Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Pro Ser Leu Ser Ala Ser
                165                 170                 175
```

_SL

```
Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser
            180                 185                 190

Ser Ala Leu Ala Trp Tyr Gln Gln Lys Pro Gly Thr Pro Pro Lys Leu
        195                 200                 205

Leu Ile Tyr Asp Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe
    210                 215                 220

Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu
225                 230                 235                 240

Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Phe Ser Ser Tyr
                245                 250                 255

Pro Leu Thr Phe Gly Gly Gly Thr Arg Leu Glu Ile Lys Thr Thr Thr
            260                 265                 270

Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro
        275                 280                 285

Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val
    290                 295                 300

His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro
305                 310                 315                 320

Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu
                325                 330                 335

Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro
            340                 345                 350

Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys
        355                 360                 365

Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe
    370                 375                 380

Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu
385                 390                 395                 400

Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp
                405                 410                 415

Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys
            420                 425                 430
```

```
Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala
        435                 440                 445


Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys
    450                 455                 460


Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr
465                 470                 475                 480


Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
                485                 490


<210> 552
<211> 255
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 552
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15


Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30


Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45


Gly Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Leu
    50                  55                  60


Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80


Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Val Ala Gly Gly Ile Tyr Tyr Tyr Tyr Gly Met Asp Val Trp
            100                 105                 110


Gly Gln Gly Thr Thr Ile Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125


Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile
    130                 135                 140
```

```
Val Met Thr Gln Thr Pro Asp Ser Leu Ala Val Ser Leu Gly Glu Arg
145                 150                 155                 160

Ala Thr Ile Ser Cys Lys Ser Ser His Ser Val Leu Tyr Asn Arg Asn
                165                 170                 175

Asn Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
            180                 185                 190

Lys Leu Leu Phe Tyr Trp Ala Ser Thr Arg Lys Ser Gly Val Pro Asp
        195                 200                 205

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
    210                 215                 220

Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Phe Cys Gln Gln Thr Gln
225                 230                 235                 240

Thr Phe Pro Leu Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Asn
                245                 250                 255


<210> 553
<211> 499
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 553
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
            20                  25                  30

Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
        35                  40                  45

Thr Phe Thr Ser Tyr Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln
    50                  55                  60

Gly Leu Glu Trp Met Gly Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn
65                  70                  75                  80

Tyr Ala Gln Lys Leu Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser
                85                  90                  95
```

```
Thr Ser Thr Ala Tyr Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Arg Val Ala Gly Gly Ile Tyr Tyr Tyr Tyr
        115                 120                 125

Gly Met Asp Val Trp Gly Gln Gly Thr Thr Ile Thr Val Ser Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
145                 150                 155                 160

Gly Gly Ser Asp Ile Val Met Thr Gln Thr Pro Asp Ser Leu Ala Val
                165                 170                 175

Ser Leu Gly Glu Arg Ala Thr Ile Ser Cys Lys Ser Ser His Ser Val
            180                 185                 190

Leu Tyr Asn Arg Asn Asn Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys
        195                 200                 205

Pro Gly Gln Pro Pro Lys Leu Leu Phe Tyr Trp Ala Ser Thr Arg Lys
    210                 215                 220

Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
225                 230                 235                 240

Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Phe
                245                 250                 255

Cys Gln Gln Thr Gln Thr Phe Pro Leu Thr Phe Gly Gln Gly Thr Arg
            260                 265                 270

Leu Glu Ile Asn Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala
        275                 280                 285

Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg
    290                 295                 300

Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys
305                 310                 315                 320

Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu
                325                 330                 335

Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu
            340                 345                 350
```

```
Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln
        355                 360                 365

Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly
    370                 375                 380

Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr
385                 390                 395                 400

Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg
                405                 410                 415

Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met
            420                 425                 430

Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu
        435                 440                 445

Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys
    450                 455                 460

Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu
465                 470                 475                 480

Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu
                485                 490                 495

Pro Pro Arg
```

<210> 554
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 554

```
Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr
            20                  25                  30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45
```

```
Gly Trp Ile Asn Pro Asn Ser Gly Gly Thr Asn Tyr Ala Gln Asn Phe
    50                  55                  60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Arg Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Ser Gly Trp Asp Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr
            100                 105                 110

Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115                 120                 125

Gly Ser Gly Gly Gly Gly Ser Asp Ile Arg Met Thr Gln Ser Pro Ser
    130                 135                 140

Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala
145                 150                 155                 160

Ser Gln Ser Ile Arg Tyr Tyr Leu Ser Trp Tyr Gln Gln Lys Pro Gly
                165                 170                 175

Lys Ala Pro Lys Leu Leu Ile Tyr Thr Ala Ser Ile Leu Gln Asn Gly
            180                 185                 190

Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
        195                 200                 205

Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Leu
    210                 215                 220

Gln Thr Tyr Thr Thr Pro Asp Phe Gly Pro Gly Thr Lys Val Glu Ile
225                 230                 235                 240

Lys
```

<210> 555
<211> 485
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 555
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Val
20 25 30

Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
35 40 45

Thr Phe Thr Gly Tyr Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln
50 55 60

Gly Leu Glu Trp Met Gly Trp Ile Asn Pro Asn Ser Gly Gly Thr Asn
65 70 75 80

Tyr Ala Gln Asn Phe Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser
85 90 95

Ile Ser Thr Ala Tyr Met Glu Leu Arg Arg Leu Arg Ser Asp Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Ala Ser Gly Trp Asp Phe Asp Tyr Trp Gly Gln
115 120 125

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
130 135 140

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Arg Met
145 150 155 160

Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr
165 170 175

Ile Thr Cys Arg Ala Ser Gln Ser Ile Arg Tyr Tyr Leu Ser Trp Tyr
180 185 190

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Thr Ala Ser
195 200 205

Ile Leu Gln Asn Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
210 215 220

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
225 230 235 240

Thr Tyr Tyr Cys Leu Gln Thr Tyr Thr Thr Pro Asp Phe Gly Pro Gly

_SL

245 250 255

Thr Lys Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr
260 265 270

Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala
275 280 285

Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe
290 295 300

Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val
305 310 315 320

Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys
325 330 335

Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr
340 345 350

Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu
355 360 365

Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro
370 375 380

Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly
385 390 395 400

Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro
405 410 415

Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr
420 425 430

Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly
435 440 445

Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln
450 455 460

Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln
465 470 475 480

Ala Leu Pro Pro Arg
485

<210> 556
<211> 246
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 556

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr
            20                  25                  30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

Gly Arg Ile Asn Pro Asn Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe
    50                  55                  60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Thr Thr Thr Ser Tyr Ala Phe Asp Ile Trp Gly Gln Gly Thr
            100                 105                 110

Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln
    130                 135                 140

Ser Pro Ser Thr Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr
145                 150                 155                 160

Cys Arg Ala Ser Gln Ser Ile Ser Thr Trp Leu Ala Trp Tyr Gln Gln
                165                 170                 175

Lys Pro Gly Lys Ala Pro Asn Leu Leu Ile Tyr Lys Ala Ser Thr Leu
            180                 185                 190

Glu Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu
        195                 200                 205
```

_SL
Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Asp Asp Phe Ala Thr Tyr
    210   215   220

Tyr Cys Gln Gln Tyr Asn Thr Tyr Ser Pro Tyr Thr Phe Gly Gln Gly
225   230   235   240

Thr Lys Leu Glu Ile Lys
                245

<210> 557
<211> 490
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 557
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1   5   10   15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
            20   25   30

Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
        35   40   45

Thr Phe Thr Gly Tyr Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln
    50   55   60

Gly Leu Glu Trp Met Gly Arg Ile Asn Pro Asn Ser Gly Gly Thr Asn
65   70   75   80

Tyr Ala Gln Lys Phe Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser
                85   90   95

Thr Ser Thr Ala Tyr Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr
            100   105   110

Ala Val Tyr Tyr Cys Ala Arg Thr Thr Thr Ser Tyr Ala Phe Asp Ile
        115   120   125

Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser
    130   135   140

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp
145   150   155   160

_SL
Ile Gln Leu Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly Asp
165 170 175

Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Thr Trp Leu
180 185 190

Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Asn Leu Leu Ile Tyr
195 200 205

Lys Ala Ser Thr Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
210 215 220

Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Asp
225 230 235 240

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Thr Tyr Ser Pro Tyr
245 250 255

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Thr Thr Thr Pro Ala
260 265 270

Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser
275 280 285

Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr
290 295 300

Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala
305 310 315 320

Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys
325 330 335

Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met
340 345 350

Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe
355 360 365

Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg
370 375 380

Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn
385 390 395 400

Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg
405 410 415

```
Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro
            420                 425                 430

Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala
        435                 440                 445

Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His
    450                 455                 460

Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp
465                 470                 475                 480

Ala Leu His Met Gln Ala Leu Pro Pro Arg
                485                 490
```

<210> 558
<211> 249
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 558

```
Gln Val Gln Leu Val Gln Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Glu Ala Ser Gly Phe Ile Phe Ser Asp Tyr
            20                  25                  30

Tyr Met Gly Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Tyr Ile Gly Arg Ser Gly Ser Ser Met Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Phe Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Ala Ser Pro Val Val Ala Ala Thr Glu Asp Phe Gln His Trp Gly
            100                 105                 110

Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
        115                 120                 125
```

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val
130 135 140

Met Thr Gln Thr Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala
145 150 155 160

Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Thr Ser Asn Tyr Leu Ala
165 170 175

Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Leu Phe Gly
180 185 190

Ala Ser Thr Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly Ser Gly
195 200 205

Ser Gly Thr Asp Phe Thr Leu Thr Ile Asn Arg Leu Glu Pro Glu Asp
210 215 220

Phe Ala Met Tyr Tyr Cys Gln Gln Tyr Gly Ser Ala Pro Val Thr Phe
225 230 235 240

Gly Gln Gly Thr Lys Leu Glu Ile Lys
245

<210> 559
<211> 493
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 559
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Gly Gly Leu
20 25 30

Val Lys Pro Gly Gly Ser Leu Arg Leu Ser Cys Glu Ala Ser Gly Phe
35 40 45

Ile Phe Ser Asp Tyr Tyr Met Gly Trp Ile Arg Gln Ala Pro Gly Lys
50 55 60

Gly Leu Glu Trp Val Ser Tyr Ile Gly Arg Ser Gly Ser Ser Met Tyr
65 70 75 80

```
Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Phe Ser Arg Asp Asn Ala
                85                  90                  95

Lys Asn Ser Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Ala Ser Pro Val Val Ala Ala Thr Glu Asp
        115                 120                 125

Phe Gln His Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly
    130                 135                 140

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
145                 150                 155                 160

Gly Ser Asp Ile Val Met Thr Gln Thr Pro Ala Thr Leu Ser Leu Ser
                165                 170                 175

Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Thr
            180                 185                 190

Ser Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg
        195                 200                 205

Leu Leu Leu Phe Gly Ala Ser Thr Arg Ala Thr Gly Ile Pro Asp Arg
    210                 215                 220

Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asn Arg
225                 230                 235                 240

Leu Glu Pro Glu Asp Phe Ala Met Tyr Tyr Cys Gln Gln Tyr Gly Ser
                245                 250                 255

Ala Pro Val Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Thr Thr
            260                 265                 270

Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln
        275                 280                 285

Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala
    290                 295                 300

Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala
305                 310                 315                 320

Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr
                325                 330                 335
```

```
Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln
            340                 345                 350

Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser
        355                 360                 365

Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys
    370                 375                 380

Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln
385                 390                 395                 400

Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu
                405                 410                 415

Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg
            420                 425                 430

Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met
        435                 440                 445

Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly
    450                 455                 460

Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp
465                 470                 475                 480

Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
                485                 490


<210> 560
<211> 249
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 560
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Arg Ala Pro Gly Ala
1               5                   10                  15

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Phe Thr Phe Arg Gly Tyr
            20                  25                  30

Tyr Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45
```

```
Gly Ile Ile Asn Pro Ser Gly Gly Ser Arg Ala Tyr Ala Gln Lys Phe
    50                  55                  60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Ser Thr Val Tyr
65                  70                  75                  80

Met Glu Leu Ser Ser Leu Arg Ser Asp Asp Thr Ala Met Tyr Tyr Cys
                85                  90                  95

Ala Arg Thr Ala Ser Cys Gly Gly Asp Cys Tyr Tyr Leu Asp Tyr Trp
            100                 105                 110

Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile
    130                 135                 140

Gln Met Thr Gln Ser Pro Pro Thr Leu Ser Ala Ser Val Gly Asp Arg
145                 150                 155                 160

Val Thr Ile Thr Cys Arg Ala Ser Glu Asn Val Asn Ile Trp Leu Ala
                165                 170                 175

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Lys
            180                 185                 190

Ser Ser Ser Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly
        195                 200                 205

Ser Gly Ala Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Asp Asp
    210                 215                 220

Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Gln Ser Tyr Pro Leu Thr Phe
225                 230                 235                 240

Gly Gly Gly Thr Lys Val Asp Ile Lys
                245
```

<210> 561
<211> 493
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 561
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
20 25 30

Arg Ala Pro Gly Ala Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Phe
35 40 45

Thr Phe Arg Gly Tyr Tyr Ile His Trp Val Arg Gln Ala Pro Gly Gln
50 55 60

Gly Leu Glu Trp Met Gly Ile Ile Asn Pro Ser Gly Gly Ser Arg Ala
65 70 75 80

Tyr Ala Gln Lys Phe Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser
85 90 95

Thr Ser Thr Val Tyr Met Glu Leu Ser Ser Leu Arg Ser Asp Asp Thr
100 105 110

Ala Met Tyr Tyr Cys Ala Arg Thr Ala Ser Cys Gly Gly Asp Cys Tyr
115 120 125

Tyr Leu Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly
130 135 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
145 150 155 160

Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Pro Thr Leu Ser Ala
165 170 175

Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Glu Asn Val
180 185 190

Asn Ile Trp Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys
195 200 205

Leu Leu Ile Tyr Lys Ser Ser Ser Leu Ala Ser Gly Val Pro Ser Arg
210 215 220

Phe Ser Gly Ser Gly Ser Gly Ala Glu Phe Thr Leu Thr Ile Ser Ser
225 230 235 240

Leu Gln Pro Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Gln Ser

_SL

```
                245                 250                 255

Tyr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Asp Ile Lys Thr Thr
            260                 265                 270

Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln
        275                 280                 285

Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala
    290                 295                 300

Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala
305                 310                 315                 320

Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr
                325                 330                 335

Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln
            340                 345                 350

Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser
        355                 360                 365

Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys
    370                 375                 380

Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln
385                 390                 395                 400

Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu
                405                 410                 415

Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg
            420                 425                 430

Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met
        435                 440                 445

Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly
    450                 455                 460

Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp
465                 470                 475                 480

Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
                485                 490
```

<210> 562
<211> 244
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 562

```
Gln Val Gln Leu Val Gln Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
            20                  25                  30

Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Gly Ile Ser Trp Asn Ser Gly Ser Ile Gly Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Asp Gly Ser Ser Ser Trp Ser Trp Gly Tyr Phe Asp Tyr Trp
            100                 105                 110

Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Ser Ser Glu Leu Thr Gln Asp
    130                 135                 140

Pro Ala Val Ser Val Ala Leu Gly Gln Thr Val Arg Thr Thr Cys Gln
145                 150                 155                 160

Gly Asp Ala Leu Arg Ser Tyr Tyr Ala Ser Trp Tyr Gln Gln Lys Pro
                165                 170                 175

Gly Gln Ala Pro Met Leu Val Ile Tyr Gly Lys Asn Asn Arg Pro Ser
            180                 185                 190

Gly Ile Pro Asp Arg Phe Ser Gly Ser Asp Ser Gly Asp Thr Ala Ser
        195                 200                 205
```

_SL
Leu Thr Ile Thr Gly Ala Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys
210 215 220

Asn Ser Arg Asp Ser Ser Gly Tyr Pro Val Phe Gly Thr Gly Thr Lys
225 230 235 240

Val Thr Val Leu

<210> 563
<211> 488
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 563
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Gly Gly Leu
20 25 30

Val Gln Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
35 40 45

Thr Phe Asp Asp Tyr Ala Met His Trp Val Arg Gln Ala Pro Gly Lys
50 55 60

Gly Leu Glu Trp Val Ser Gly Ile Ser Trp Asn Ser Gly Ser Ile Gly
65 70 75 80

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala
85 90 95

Lys Asn Ser Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Ala Lys Asp Gly Ser Ser Ser Trp Ser Trp Gly
115 120 125

Tyr Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly
130 135 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ser Ser
145 150 155 160

```
                                                _SL
Glu Leu Thr Gln Asp Pro Ala Val Ser Val Ala Leu Gly Gln Thr Val
                165                 170                 175

Arg Thr Thr Cys Gln Gly Asp Ala Leu Arg Ser Tyr Tyr Ala Ser Trp
            180                 185                 190

Tyr Gln Gln Lys Pro Gly Gln Ala Pro Met Leu Val Ile Tyr Gly Lys
        195                 200                 205

Asn Asn Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser Asp Ser
    210                 215                 220

Gly Asp Thr Ala Ser Leu Thr Ile Thr Gly Ala Gln Ala Glu Asp Glu
225                 230                 235                 240

Ala Asp Tyr Tyr Cys Asn Ser Arg Asp Ser Ser Gly Tyr Pro Val Phe
                245                 250                 255

Gly Thr Gly Thr Lys Val Thr Val Leu Thr Thr Thr Pro Ala Pro Arg
            260                 265                 270

Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg
        275                 280                 285

Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly
    290                 295                 300

Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr
305                 310                 315                 320

Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg
                325                 330                 335

Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro
            340                 345                 350

Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu
        355                 360                 365

Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala
    370                 375                 380

Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu
385                 390                 395                 400

Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly
                405                 410                 415
```

```
Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu
            420                 425                 430

Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser
        435                 440                 445

Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly
    450                 455                 460

Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu
465                 470                 475                 480

His Met Gln Ala Leu Pro Pro Arg
                485
```

<210> 564
<211> 246
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 564

```
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
            20                  25                  30

Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Gly Ile Ser Trp Asn Ser Gly Ser Thr Gly Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Leu Tyr Tyr Cys
                85                  90                  95

Ala Lys Asp Ser Ser Ser Trp Tyr Gly Gly Gly Ser Ala Phe Asp Ile
            100                 105                 110

Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser
        115                 120                 125
```

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ser Ser Glu Leu Thr Gln
130 135 140

Glu Pro Ala Val Ser Val Ala Leu Gly Gln Thr Val Arg Ile Thr Cys
145 150 155 160

Gln Gly Asp Ser Leu Arg Ser Tyr Tyr Ala Ser Trp Tyr Gln Gln Lys
165 170 175

Pro Gly Gln Ala Pro Val Leu Val Ile Phe Gly Arg Ser Arg Arg Pro
180 185 190

Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser Ser Ser Gly Asn Thr Ala
195 200 205

Ser Leu Ile Ile Thr Gly Ala Gln Ala Glu Asp Glu Ala Asp Tyr Tyr
210 215 220

Cys Asn Ser Arg Asp Asn Thr Ala Asn His Tyr Val Phe Gly Thr Gly
225 230 235 240

Thr Lys Leu Thr Val Leu
245

<210> 565
<211> 490
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 565
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
20 25 30

Val Gln Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
35 40 45

Thr Phe Asp Asp Tyr Ala Met His Trp Val Arg Gln Ala Pro Gly Lys
50 55 60

Gly Leu Glu Trp Val Ser Gly Ile Ser Trp Asn Ser Gly Ser Thr Gly
65 70 75 80

```
Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala
                85                  90                  95

Lys Asn Ser Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
            100                 105                 110

Ala Leu Tyr Tyr Cys Ala Lys Asp Ser Ser Ser Trp Tyr Gly Gly Gly
        115                 120                 125

Ser Ala Phe Asp Ile Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
    130                 135                 140

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ser
145                 150                 155                 160

Ser Glu Leu Thr Gln Glu Pro Ala Val Ser Val Ala Leu Gly Gln Thr
                165                 170                 175

Val Arg Ile Thr Cys Gln Gly Asp Ser Leu Arg Ser Tyr Tyr Ala Ser
            180                 185                 190

Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Phe Gly
        195                 200                 205

Arg Ser Arg Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser Ser
    210                 215                 220

Ser Gly Asn Thr Ala Ser Leu Ile Ile Thr Gly Ala Gln Ala Glu Asp
225                 230                 235                 240

Glu Ala Asp Tyr Tyr Cys Asn Ser Arg Asp Asn Thr Ala Asn His Tyr
                245                 250                 255

Val Phe Gly Thr Gly Thr Lys Leu Thr Val Leu Thr Thr Thr Pro Ala
            260                 265                 270

Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser
        275                 280                 285

Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr
    290                 295                 300

Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala
305                 310                 315                 320

Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys
                325                 330                 335
```

Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met
340 345 350

Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe
355 360 365

Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg
370 375 380

Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn
385 390 395 400

Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg
405 410 415

Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro
420 425 430

Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala
435 440 445

Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His
450 455 460

Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp
465 470 475 480

Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 566
<211> 246
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 566
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
20 25 30

Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

```
Ser Gly Ile Ser Trp Asn Ser Gly Ser Thr Gly Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Leu Tyr Tyr Cys
                85                  90                  95

Ala Lys Asp Ser Ser Ser Trp Tyr Gly Gly Gly Ser Ala Phe Asp Ile
            100                 105                 110

Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ser Ser Glu Leu Thr Gln
    130                 135                 140

Asp Pro Ala Val Ser Val Ala Leu Gly Gln Thr Val Arg Ile Thr Cys
145                 150                 155                 160

Gln Gly Asp Ser Leu Arg Ser Tyr Tyr Ala Ser Trp Tyr Gln Gln Lys
                165                 170                 175

Pro Gly Gln Ala Pro Val Leu Val Ile Tyr Gly Lys Asn Asn Arg Pro
            180                 185                 190

Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser Ser Ser Gly Asn Thr Ala
        195                 200                 205

Ser Leu Thr Ile Thr Gly Ala Gln Ala Glu Asp Glu Ala Asp Tyr Tyr
    210                 215                 220

Cys Asn Ser Arg Gly Ser Ser Gly Asn His Tyr Val Phe Gly Thr Gly
225                 230                 235                 240

Thr Lys Val Thr Val Leu
                245
```

<210> 567
<211> 490
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 567
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
20 25 30

Val Gln Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
35 40 45

Thr Phe Asp Asp Tyr Ala Met His Trp Val Arg Gln Ala Pro Gly Lys
50 55 60

Gly Leu Glu Trp Val Ser Gly Ile Ser Trp Asn Ser Gly Ser Thr Gly
65 70 75 80

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala
85 90 95

Lys Asn Ser Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
100 105 110

Ala Leu Tyr Tyr Cys Ala Lys Asp Ser Ser Ser Trp Tyr Gly Gly Gly
115 120 125

Ser Ala Phe Asp Ile Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
130 135 140

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ser
145 150 155 160

Ser Glu Leu Thr Gln Asp Pro Ala Val Ser Val Ala Leu Gly Gln Thr
165 170 175

Val Arg Ile Thr Cys Gln Gly Asp Ser Leu Arg Ser Tyr Tyr Ala Ser
180 185 190

Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Tyr Gly
195 200 205

Lys Asn Asn Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser Ser
210 215 220

Ser Gly Asn Thr Ala Ser Leu Thr Ile Thr Gly Ala Gln Ala Glu Asp
225 230 235 240

Glu Ala Asp Tyr Tyr Cys Asn Ser Arg Gly Ser Ser Gly Asn His Tyr

_SL

245 250 255

Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu Thr Thr Thr Pro Ala
260 265 270

Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser
275 280 285

Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr
290 295 300

Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala
305 310 315 320

Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys
325 330 335

Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met
340 345 350

Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe
355 360 365

Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg
370 375 380

Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn
385 390 395 400

Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg
405 410 415

Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro
420 425 430

Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala
435 440 445

Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His
450 455 460

Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp
465 470 475 480

Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 568
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 568

```
Gln Val Gln Leu Val Gln Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30

Trp Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Val Trp Val
        35                  40                  45

Ser Arg Ile Asn Ser Asp Gly Ser Ser Thr Ser Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Val Arg Thr Gly Trp Val Gly Ser Tyr Tyr Tyr Tyr Met Asp Val Trp
            100                 105                 110

Gly Lys Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile
    130                 135                 140

Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly Glu Arg
145                 150                 155                 160

Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Asn Tyr Leu
                165                 170                 175

Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Arg Leu Leu Ile Tyr
            180                 185                 190

Asp Val Ser Thr Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly Gly
        195                 200                 205
```

_SL
Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu
    210   215   220

Asp Phe Ala Val Tyr Tyr Cys Gln Gln Arg Ser Asn Trp Pro Pro Trp
225   230   235   240

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
                245   250

<210> 569
<211> 495
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 569
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1   5   10   15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Gly Gly Leu
            20   25   30

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
        35   40   45

Thr Phe Ser Ser Tyr Trp Met His Trp Val Arg Gln Ala Pro Gly Lys
    50   55   60

Gly Leu Val Trp Val Ser Arg Ile Asn Ser Asp Gly Ser Ser Thr Ser
65   70   75   80

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala
                85   90   95

Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
            100   105   110

Ala Val Tyr Tyr Cys Val Arg Thr Gly Trp Val Gly Ser Tyr Tyr Tyr
        115   120   125

Tyr Met Asp Val Trp Gly Lys Gly Thr Thr Val Thr Val Ser Ser Gly
    130   135   140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
145   150   155   160

```
                                                _SL
Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu
                165                 170                 175

Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val
            180                 185                 190

Ser Ser Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
        195                 200                 205

Arg Leu Leu Ile Tyr Asp Val Ser Thr Arg Ala Thr Gly Ile Pro Ala
    210                 215                 220

Arg Phe Ser Gly Gly Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
225                 230                 235                 240

Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Arg Ser
                245                 250                 255

Asn Trp Pro Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
            260                 265                 270

Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala
        275                 280                 285

Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly
    290                 295                 300

Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile
305                 310                 315                 320

Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val
                325                 330                 335

Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe
            340                 345                 350

Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly
        355                 360                 365

Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg
    370                 375                 380

Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln
385                 390                 395                 400

Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp
                405                 410                 415
```

```
Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro
            420                 425                 430

Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp
        435                 440                 445

Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg
    450                 455                 460

Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr
465                 470                 475                 480

Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
                485                 490                 495

<210> 570
<211> 250
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 570
Gln Val Gln Leu Val Gln Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30

Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ala Val Ile Ser Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Gly Tyr Ser Arg Tyr Tyr Tyr Tyr Gly Met Asp Val Trp Gly
            100                 105                 110

Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
        115                 120                 125
```

```
Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val
    130                 135                 140

Met Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala
145                 150                 155                 160

Ile Leu Ser Cys Arg Ala Ser Gln Ser Val Tyr Thr Lys Tyr Leu Gly
                165                 170                 175

Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Asp
            180                 185                 190

Ala Ser Thr Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly Ser Gly
        195                 200                 205

Ser Gly Thr Asp Phe Thr Leu Thr Ile Asn Arg Leu Glu Pro Glu Asp
    210                 215                 220

Phe Ala Val Tyr Tyr Cys Gln His Tyr Gly Gly Ser Pro Leu Ile Thr
225                 230                 235                 240

Phe Gly Gln Gly Thr Lys Val Asp Ile Lys
                245                 250
```

<210> 571
<211> 494
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 571

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Gly Gly Val
            20                  25                  30

Val Gln Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
        35                  40                  45

Thr Phe Ser Ser Tyr Gly Met His Trp Val Arg Gln Ala Pro Gly Lys
    50                  55                  60

Gly Leu Glu Trp Val Ala Val Ile Ser Tyr Asp Gly Ser Asn Lys Tyr
65                  70                  75                  80
```

```
Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser
                85                  90                  95

Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Lys Gly Tyr Ser Arg Tyr Tyr Tyr Tyr Gly
        115                 120                 125

Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly
    130                 135                 140

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
145                 150                 155                 160

Gly Ser Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser
                165                 170                 175

Pro Gly Glu Arg Ala Ile Leu Ser Cys Arg Ala Ser Gln Ser Val Tyr
            180                 185                 190

Thr Lys Tyr Leu Gly Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg
        195                 200                 205

Leu Leu Ile Tyr Asp Ala Ser Thr Arg Ala Thr Gly Ile Pro Asp Arg
    210                 215                 220

Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asn Arg
225                 230                 235                 240

Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln His Tyr Gly Gly
                245                 250                 255

Ser Pro Leu Ile Thr Phe Gly Gln Gly Thr Lys Val Asp Ile Lys Thr
            260                 265                 270

Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser
        275                 280                 285

Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly
    290                 295                 300

Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp
305                 310                 315                 320

Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile
                325                 330                 335
```

Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys
340 345 350

Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys
355 360 365

Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val
370 375 380

Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn
385 390 395 400

Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val
405 410 415

Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg
420 425 430

Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys
435 440 445

Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg
450 455 460

Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys
465 470 475 480

Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 572
<211> 249
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 572
Gln Val Gln Leu Val Gln Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

```
Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Arg Glu Ala Ala Ala Gly His Asp Trp Tyr Phe Asp Leu Trp
            100                 105                 110

Gly Arg Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile
    130                 135                 140

Arg Val Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg
145                 150                 155                 160

Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn
                165                 170                 175

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala
            180                 185                 190

Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly
        195                 200                 205

Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
    210                 215                 220

Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Ile Pro Leu Thr Phe
225                 230                 235                 240

Gly Gln Gly Thr Lys Val Glu Ile Lys
                245
```

<210> 573
<211> 493
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 573
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Gly Gly Leu
20 25 30

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
35 40 45

Thr Phe Ser Ser Tyr Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys
50 55 60

Gly Leu Glu Trp Val Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr
65 70 75 80

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser
85 90 95

Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Ala Lys Arg Glu Ala Ala Ala Gly His Asp Trp
115 120 125

Tyr Phe Asp Leu Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser Gly
130 135 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
145 150 155 160

Gly Gly Ser Asp Ile Arg Val Thr Gln Ser Pro Ser Ser Leu Ser Ala
165 170 175

Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile
180 185 190

Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys
195 200 205

Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg
210 215 220

Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser
225 230 235 240

Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser

_SL

245 250 255

Ile Pro Leu Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Thr Thr
260 265 270

Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln
275 280 285

Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala
290 295 300

Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala
305 310 315 320

Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr
325 330 335

Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln
340 345 350

Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser
355 360 365

Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys
370 375 380

Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln
385 390 395 400

Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu
405 410 415

Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg
420 425 430

Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met
435 440 445

Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly
450 455 460

Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp
465 470 475 480

Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 574
<211> 239
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 574

```
Gln Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Glu Lys Pro Gly Ala
1               5                   10                  15

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ser Phe Thr Gly Tyr
            20                  25                  30

Thr Met Asn Trp Val Lys Gln Ser His Gly Lys Ser Leu Glu Trp Ile
        35                  40                  45

Gly Leu Ile Thr Pro Tyr Asn Gly Ala Ser Ser Tyr Asn Gln Lys Phe
    50                  55                  60

Arg Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser Thr Ala Tyr
65                  70                  75                  80

Met Asp Leu Leu Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys
                85                  90                  95

Ala Arg Gly Gly Tyr Asp Gly Arg Gly Phe Asp Tyr Trp Gly Gln Gly
            100                 105                 110

Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
        115                 120                 125

Ser Gly Gly Gly Gly Ser Asp Ile Glu Leu Thr Gln Ser Pro Ala Ile
    130                 135                 140

Met Ser Ala Ser Pro Gly Glu Lys Val Thr Met Thr Cys Ser Ala Ser
145                 150                 155                 160

Ser Ser Val Ser Tyr Met His Trp Tyr Gln Gln Lys Ser Gly Thr Ser
                165                 170                 175

Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Leu Ala Ser Gly Val Pro
            180                 185                 190

Gly Arg Phe Ser Gly Ser Gly Ser Gly Asn Ser Tyr Ser Leu Thr Ile
        195                 200                 205
```

_SL
Ser Ser Val Glu Ala Glu Asp Asp Ala Thr Tyr Tyr Cys Gln Gln Trp
210 215 220

Ser Gly Tyr Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Ile
225 230 235

<210> 575
<211> 383
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 575
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Gln Gln Ser Gly Pro Glu Leu
20 25 30

Glu Lys Pro Gly Ala Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr
35 40 45

Ser Phe Thr Gly Tyr Thr Met Asn Trp Val Lys Gln Ser His Gly Lys
50 55 60

Ser Leu Glu Trp Ile Gly Leu Ile Thr Pro Tyr Asn Gly Ala Ser Ser
65 70 75 80

Tyr Asn Gln Lys Phe Arg Gly Lys Ala Thr Leu Thr Val Asp Lys Ser
85 90 95

Ser Ser Thr Ala Tyr Met Asp Leu Leu Ser Leu Thr Ser Glu Asp Ser
100 105 110

Ala Val Tyr Phe Cys Ala Arg Gly Gly Tyr Asp Gly Arg Gly Phe Asp
115 120 125

Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly
130 135 140

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Glu Leu Thr
145 150 155 160

Gln Ser Pro Ala Ile Met Ser Ala Ser Pro Gly Glu Lys Val Thr Met
165 170 175

```
                                                _SL
Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met His Trp Tyr Gln Gln
            180                 185                 190

Lys Ser Gly Thr Ser Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Leu
        195                 200                 205

Ala Ser Gly Val Pro Gly Arg Phe Ser Gly Ser Gly Ser Gly Asn Ser
    210                 215                 220

Tyr Ser Leu Thr Ile Ser Ser Val Glu Ala Glu Asp Asp Ala Thr Tyr
225                 230                 235                 240

Tyr Cys Gln Gln Trp Ser Gly Tyr Pro Leu Thr Phe Gly Ala Gly Thr
                245                 250                 255

Lys Leu Glu Ile Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala
            260                 265                 270

Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg
        275                 280                 285

Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys
    290                 295                 300

Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu
305                 310                 315                 320

Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu
                325                 330                 335

Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln
            340                 345                 350

Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly
        355                 360                 365

Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala
    370                 375                 380


<210> 576
<211> 732
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 576
```

caagtccaac tgcagcagtc aggagcggaa gtgaagaaac caggagcgtc agtcaaagtg 60

tcgtgcaagg ctagcggcta caccttcacc ggctactaca tgcactgggt tcgacaggct 120

ccagggcagg gtctggagtg gatgggccgc atcaacccga attccggtgg gactaactac 180

gcccagaagt tccagggaag agtgaccatg actagggaca cgtcgatcag cactgcgtac 240

atggaactga gccgcctgcg gtccgaggat actgccgtct actactgcgc acgcggaagg 300

tactatggaa tggacgtgtg gggccaaggg actatggtga ctgtgagctc gggaggggga 360

ggctccggtg gcgggggatc aggaggagga ggatcagggg gaggaggttc cgaaattgtc 420

ctcacccaga gcccggcaac cctctcactt tccccgggag agcgcgcaac catctcttgc 480

cgggctagcc aatccgtgtc gtccaatttc gcctggtacc agcaacggcc gggacaagcc 540

cctagactcc tgatctacga cgccagcaac agagcgactg gaattcctcc acgcttttcg 600

ggatcaggct ccggtaccga cttcaccctg actatctcgt cgctcgaacc cgaggatttc 660

gccgcctact actgtcatca gcggtcgaac tggttgtata cgtttggcca gggcaccaag 720

gtggatatca ag 732

<210> 577
<211> 1464
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 577
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtcc aactgcagca gtcaggagcg gaagtgaaga aaccaggagc gtcagtcaaa 120

gtgtcgtgca aggctagcgg ctacaccttc accggctact acatgcactg ggttcgacag 180

gctccagggc agggtctgga gtggatgggc cgcatcaacc cgaattccgg tgggactaac 240

tacgcccaga agttccaggg aagagtgacc atgactaggg acacgtcgat cagcactgcg 300

tacatggaac tgagccgcct gcggtccgag gatactgccg tctactactg cgcacgcgga 360

aggtactatg gaatggacgt gtggggccaa gggactatgg tgactgtgag ctcgggaggg 420

ggaggctccg gtggcggggg atcaggagga ggaggatcag ggggaggagg ttccgaaatt 480

gtcctcaccc agagcccggc aaccctctca ctttccccgg gagagcgcgc aaccatctct 540

tgccgggcta gccaatccgt gtcgtccaat ttcgcctggt accagcaacg gccgggacaa 600

gcccctagac tcctgatcta cgacgccagc aacagagcga ctggaattcc tccacgcttt 660

tcgggatcag gctccggtac cgacttcacc ctgactatct cgtcgctcga acccgaggat 720

ttcgccgcct actactgtca tcagcggtcg aactggttgt atacgtttgg ccagggcacc 780

aaggtggata tcaagaccac taccccagca ccgaggccac ccaccccggc tcctaccatc 840

gcctcccagc ctctgtccct gcgtccggag gcatgtagac ccgcagctgg tggggccgtg 900

catacccggg gtcttgactt cgcctgcgat atctacattt gggcccctct ggctggtact 960

tgcggggtcc tgctgctttc actcgtgatc actctttact gtaagcgcgg tcggaagaag 1020

ctgctgtaca tctttaagca acccttcatg aggcctgtgc agactactca agaggaggac 1080

ggctgttcat gccggttccc agaggaggag gaaggcggct gcgaactgcg cgtgaaattc 1140

agccgcagcg cagatgctcc agcctacaag caggggcaga accagctcta caacgaactc 1200

aatcttggtc ggagagagga gtacgacgtg ctggacaagc ggagaggacg ggacccagaa 1260

atgggcggga agccgcgcag aaagaatccc caagagggcc tgtacaacga gctccaaaag 1320

gataagatgg cagaagccta tagcgagatt ggtatgaaag gggaacgcag aagaggcaaa 1380

ggccacgacg gactgtacca gggactcagc accgccacca aggacaccta tgacgctctt 1440

cacatgcagg ccctgccgcc tcgg 1464

<210> 578
<211> 759
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 578
caagtccaac tcgtccagtc aggagcagaa gtcaagaaac caggtgctag cgtgaaagtg 60

tcgtgcaagg cgtcgggata cactttcacc ggatactaca tgcactgggt ccgccaggcc 120

cccggacaag gactggaatg gatgggctgg atcaacccga atagcggggg aactaattac 180

gcccagaagt ttcagggacg agtgaccatg acccgcgata cctctatctc gaccgcctac 240

atggagctct ccagactgcg ctccgacgat actgcagtgt actactgcgc ccgggacctg 300

aggcggactg tggttactcc tcgcgcctat tatggcatgg acgtgtgggg ccaaggaact 360

actgtgactg tgagctcggg aggcggtggg tcaggcggag gagggtcggg cggtggtggc 420

tcgggagggg gaggaagcga cattcaactt acgcagagcc cgtcaaccct gtcagcgtca 480

gtgggagatc gggtgaccat cacgtgtcag gccagccagg atatctccaa ctcgctcaac 540

tggtaccagc aaaaggcggg taaagctccg aagctgctga tctacgacgc ttccaccctc 600

gagactggag tcccatccag attttccggg tcaggaagcg gcaccgattt ctccttcacc 660

atttcgtcct tgcaaccgga ggacatcgca acctactact gccagcagca tgacaacttg 720

cctctgacgt tcgggcaggg caccaaggtg gaaatcaag 759

<210> 579
<211> 1491
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 579
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtcc aactcgtcca gtcaggagca gaagtcaaga aaccaggtgc tagcgtgaaa 120

gtgtcgtgca aggcgtcggg atacactttc accggatact acatgcactg ggtccgccag 180

gcccccggac aaggactgga atggatgggc tggatcaacc cgaatagcgg gggaactaat 240

tacgcccaga agtttcaggg acgagtgacc atgacccgcg atacctctat ctcgaccgcc 300

tacatggagc tctccagact gcgctccgac gatactgcag tgtactactg cgcccgggac 360

ctgaggcgga ctgtggttac tcctcgcgcc tattatggca tggacgtgtg gggccaagga 420

actactgtga ctgtgagctc gggaggcggt gggtcaggcg gaggagggtc gggcggtggt 480

ggctcgggag ggggaggaag cgacattcaa cttacgcaga gcccgtcaac cctgtcagcg 540

tcagtgggag atcgggtgac catcacgtgt caggccagcc aggatatctc caactcgctc 600

aactggtacc agcaaaaggc gggtaaagct ccgaagctgc tgatctacga cgcttccacc 660

ctcgagactg gagtcccatc cagattttcc gggtcaggaa gcggcaccga tttctccttc 720

accatttcgt ccttgcaacc ggaggacatc gcaacctact actgccagca gcatgacaac 780

ttgcctctga cgttcgggca gggcaccaag gtggaaatca agaccactac cccagcaccg 840

aggccaccca ccccggctcc taccatcgcc tcccagcctc tgtccctgcg tccggaggca 900

tgtagacccg cagctggtgg ggccgtgcat acccggggtc ttgacttcgc ctgcgatatc 960

tacatttggg cccctctggc tggtacttgc ggggtcctgc tgctttcact cgtgatcact 1020

ctttactgta agcgcggtcg gaagaagctg ctgtacatct ttaagcaacc cttcatgagg 1080

cctgtgcaga ctactcaaga ggaggacggc tgttcatgcc ggttcccaga ggaggaggaa 1140

ggcggctgcg aactgcgcgt gaaattcagc cgcagcgcag atgctccagc ctacaagcag 1200

gggcagaacc agctctacaa cgaactcaat cttggtcgga gagaggagta cgacgtgctg 1260

gacaagcgga gaggacggga cccagaaatg ggcgggaagc cgcgcagaaa gaatccccaa 1320

gagggcctgt acaacgagct ccaaaaggat aagatggcag aagcctatag cgagattggt 1380

atgaaagggg aacgcagaag aggcaaaggc cacgacggac tgtaccaggg actcagcacc 1440

gccaccaagg acacctatga cgctcttcac atgcaggccc tgccgcctcg g 1491

<210> 580
<211> 738
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 580
caagtccaac tcgtccaatc aggagcggaa gtcaaaaagc ccggagctcc agtgaaagtg 60

tcatgcaagg cctccggcta caccttcacc ggttactata tgcactgggt gcggcaggcc 120

ccgggccagg ggttggaatg gatgggatgg atcaatccaa actcgggtgg gactaactac 180

gcccagaagt tccaaggacg ggtgaccatg actagggaca cctcgatctc caccgcatac 240

atggagctta gcagactccg ctccgacgat accgcagtct actattgcgc gcggggagag 300

tgggacggat cgtactacta cgattactgg ggccagggaa ctctggtgac tgtttcctcg 360

ggtggaggag gttcaggcgg aggcggctcg ggcgggggag gatctggagg aggagggtcc 420

gacattgtgc tgacccaaac tccttcgtcc ctgtcggcca gcgtgggcga ccgcgtgacg 480

attacgtgca gagctagcca atccatcaat acttacctca actggtacca gcataagccg 540

gggaaagcac caaagctgct gatctacgcc gcctcatcct tgcagagcgg tgtgccttca 600

cgctttagcg gatcgggatc gggaacggat ttcaccctga ctatcagctc cctccagccg 660

gaggattttg cgacctacta ctgtcagcag agcttctcac cgctgacttt cggcggcggg 720

accaagctgg aaatcaag 738

<210> 581
<211> 1470
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 581
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtcc aactcgtcca atcaggagcg gaagtcaaaa agcccggagc tccagtgaaa 120

gtgtcatgca aggcctccgg ctacaccttc accggttact atatgcactg ggtgcggcag 180

gccccgggcc aggggttgga atggatggga tggatcaatc caaactcggg tgggactaac 240

tacgcccaga agttccaagg acgggtgacc atgactaggg acacctcgat ctccaccgca 300

tacatggagc ttagcagact ccgctccgac gataccgcag tctactattg cgcgcgggga 360

gagtgggacg gatcgtacta ctacgattac tggggccagg gaactctggt gactgtttcc 420

tcgggtggag gaggttcagg cggaggcggc tcgggcgggg gaggatctgg aggaggaggg 480

tccgacattg tgctgaccca aactccttcg tccctgtcgg ccagcgtggg cgaccgcgtg 540

acgattacgt gcagagctag ccaatccatc aatacttacc tcaactggta ccagcataag 600

ccggggaaag caccaaagct gctgatctac gccgcctcat ccttgcagag cggtgtgcct 660

tcacgcttta gcggatcggg atcgggaacg gatttcaccc tgactatcag ctccctccag 720

ccggaggatt ttgcgaccta ctactgtcag cagagcttct caccgctgac tttcggcggc 780

gggaccaagc tggaaatcaa gaccactacc ccagcaccga ggccacccac cccggctcct 840

accatcgcct cccagcctct gtccctgcgt ccggaggcat gtagacccgc agctggtggg 900

gccgtgcata cccggggtct tgacttcgcc tgcgatatct acatttgggc ccctctggct 960

ggtacttgcg gggtcctgct gctttcactc gtgatcactc tttactgtaa gcgcggtcgg 1020

aagaagctgc tgtacatctt taagcaaccc ttcatgaggc ctgtgcagac tactcaagag 1080

gaggacggct gttcatgccg gttcccagag gaggaggaag gcggctgcga actgcgcgtg 1140

aaattcagcc gcagcgcaga tgctccagcc tacaagcagg ggcagaacca gctctacaac 1200

gaactcaatc ttggtcggag agaggagtac gacgtgctgg acaagcggag aggacgggac 1260

ccagaaatgg gcgggaagcc gcgcagaaag aatccccaag agggcctgta caacgagctc 1320

caaaaggata agatggcaga agcctatagc gagattggta tgaaagggga acgcagaaga 1380

ggcaaaggcc acgacggact gtaccaggga ctcagcaccg ccaccaagga cacctatgac 1440

gctcttcaca tgcaggccct gccgcctcgg 1470

<210> 582
<211> 726
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 582
caagtgcaac tcgttgaatc aggtggaggt ttggtgcaac ccggaggatc tctcagactg 60

tcgtgtgcgg cgtccgggtt caccttttcg tcctactgga tgcactgggt gcgccaggtg 120

ccgggaaaag gactggtgtg ggtgtccaga atcaacaccg acgggtcaac gactacctac 180

gcagatagcg tggaaggtcg gttcaccatt tcgcgggaca acgctaaaaa cactctgtac 240

cttcagatga attcactgcg cgatgacgac accgcagtct actactgcgt cggtggacac 300

tgggcggtct ggggacaggg aactacggtg actgtgtcca gcggcggggg aggaagcggc 360

ggaggggga gcggaggcgg aggatcagga ggaggcggct ccgatatcca gatgacccag 420

tcgccatcga ccctctccgc tagcgtgggg gatagggtca ctatcacttg ccgagccagc 480

caatccatta gcgaccggct tgcctggtac caacagaaac ctggaaaggc cccgaagctg 540

ctcatctaca aggcctcgtc actggagtcg ggagtcccgt cccgcttttc cggctcgggc 600

tcaggcaccg agttcactct gaccatctcg agcctgcagc cggacgattt cgccgtgtat 660

tactgccagc aatacggaca tctcccaatg tacacgttcg gtcagggcac caaggtcgaa 720

atcaag 726

<210> 583
<211> 1458
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 583
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtgc aactcgttga atcaggtgga ggtttggtgc aacccggagg atctctcaga 120

ctgtcgtgtg cggcgtccgg gttcaccttt tcgtcctact ggatgcactg ggtgcgccag 180

gtgccgggaa aaggactggt gtgggtgtcc agaatcaaca ccgacgggtc aacgactacc 240

tacgcagata gcgtggaagg tcggttcacc atttcgcggg acaacgctaa aaacactctg 300

taccttcaga tgaattcact gcgcgatgac gacaccgcag tctactactg cgtcggtgga 360

cactgggcgg tctggggaca gggaactacg gtgactgtgt ccagcggcgg gggaggaagc 420

ggcggagggg ggagcggagg cggaggatca ggaggaggcg gctccgatat ccagatgacc 480

cagtcgccat cgaccctctc cgctagcgtg ggggataggg tcactatcac ttgccgagcc 540

agccaatcca ttagcgaccg gcttgcctgg taccaacaga aacctggaaa ggccccgaag 600

ctgctcatct acaaggcctc gtcactggag tcgggagtcc cgtcccgctt ttccggctcg 660

ggctcaggca ccgagttcac tctgaccatc tcgagcctgc agccggacga tttcgccgtg 720

tattactgcc agcaatacgg acatctccca atgtacacgt tcggtcaggg caccaaggtc 780

gaaatcaaga ccactacccc agcaccgagg ccacccaccc cggctcctac catcgcctcc 840

cagcctctgt ccctgcgtcc ggaggcatgt agacccgcag ctggtggggc cgtgcatacc 900

cggggtcttg acttcgcctg cgatatctac atttgggccc ctctggctgg tacttgcggg 960

gtcctgctgc tttcactcgt gatcactctt tactgtaagc gcggtcggaa gaagctgctg 1020

tacatcttta agcaaccctt catgaggcct gtgcagacta ctcaagagga ggacggctgt 1080

tcatgccggt tcccagagga ggaggaaggc ggctgcgaac tgcgcgtgaa attcagccgc 1140

agcgcagatg ctccagccta caagcagggg cagaaccagc tctacaacga actcaatctt 1200

ggtcggagag aggagtacga cgtgctggac aagcggagag gacgggaccc agaaatgggc 1260

gggaagccgc gcagaaagaa tccccaagag ggcctgtaca acgagctcca aaaggataag 1320

atggcagaag cctatagcga gattggtatg aaaggggaac gcagaagagg caaaggccac 1380

gacggactgt accagggact cagcaccgcc accaaggaca cctatgacgc tcttcacatg 1440

caggccctgc cgcctcgg 1458

<210> 584
<211> 723
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 584
caagtccaac tcgttcaatc aggcgcagaa gtcgaaaagc ccggagcatc agtcaaagtc 60

tcttgcaagg cttccggcta caccttcacg gactactaca tgcactgggt gcgccaggct 120

ccaggccagg gactggagtg gatgggatgg atcaacccga attccggggg aactaactac 180

gcccagaagt ttcagggccg ggtgactatg actcgcgata cctcgatctc gactgcgtac 240

atggagctca gccgcctccg gtcggacgat accgccgtgt actattgtgc gtcgggatgg 300

gacttcgact actgggggca gggcactctg gtcactgtgt caagcggagg aggtggatca 360

ggtggaggtg gaagcggggg aggaggttcc ggcggcggag gatcagatat cgtgatgacg 420

caatcgcctt cctcgttgtc cgcatccgtg ggagacaggg tgaccattac ttgcagagcg 480

tcccagtcca ttcggtacta cctgtcgtgg taccagcaga agccggggaa agccccaaaa 540

ctgcttatct atactgcctc gatcctccaa aacggcgtgc catcaagatt cagcggttcg 600

ggcagcggga ccgactttac cctgactatc agcagcctgc agccggaaga tttcgccacg 660

tactactgcc tgcaaaccta caccaccccg gacttcggac ctggaaccaa ggtggagatc 720

aag 723

<210> 585
<211> 1455
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 585
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtcc aactcgttca atcaggcgca gaagtcgaaa agcccggagc atcagtcaaa 120

gtctcttgca aggcttccgg ctacaccttc acggactact acatgcactg ggtgcgccag 180

gctccaggcc agggactgga gtggatggga tggatcaacc cgaattccgg gggaactaac 240

tacgcccaga agtttcaggg ccgggtgact atgactcgcg atacctcgat ctcgactgcg 300

tacatggagc tcagccgcct ccggtcggac gataccgccg tgtactattg tgcgtcggga 360

tgggacttcg actactgggg gcagggcact ctggtcactg tgtcaagcgg aggaggtgga 420

tcaggtggag gtggaagcgg gggaggaggt tccggcggcg gaggatcaga tatcgtgatg 480

acgcaatcgc cttcctcgtt gtccgcatcc gtgggagaca gggtgaccat tacttgcaga 540

gcgtcccagt ccattcggta ctacctgtcg tggtaccagc agaagccggg gaaagcccca 600

aaactgctta tctatactgc ctcgatcctc caaaacggcg tgccatcaag attcagcggt 660

tcgggcagcg ggaccgactt taccctgact atcagcagcc tgcagccgga agatttcgcc 720

acgtactact gcctgcaaac ctacaccacc ccggacttcg gacctggaac caaggtggag 780

atcaagacca ctaccccagc accgaggcca cccaccccgg ctcctaccat cgcctcccag 840

cctctgtccc tgcgtccgga ggcatgtaga cccgcagctg gtggggccgt gcatacccgg 900

ggtcttgact tcgcctgcga tatctacatt tgggcccctc tggctggtac ttgcggggtc 960

ctgctgcttt cactcgtgat cactctttac tgtaagcgcg gtcggaagaa gctgctgtac 1020

atctttaagc aacccttcat gaggcctgtg cagactactc aagaggagga cggctgttca 1080

tgccggttcc cagaggagga ggaaggcggc tgcgaactgc gcgtgaaatt cagccgcagc 1140

gcagatgctc cagcctacaa gcaggggcag aaccagctct acaacgaact caatcttggt 1200

cggagagagg agtacgacgt gctggacaag cggagaggac gggacccaga aatgggcggg 1260

aagccgcgca gaaagaatcc ccaagagggc ctgtacaacg agctccaaaa ggataagatg 1320

gcagaagcct atagcgagat tggtatgaaa ggggaacgca gaagaggcaa aggccacgac 1380

ggactgtacc agggactcag caccgccacc aaggacacct atgacgctct tcacatgcag 1440

gccctgccgc ctcgg 1455

<210> 586
<211> 759
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 586
caagtgcaac tcgtccagtc aggtgcagaa gtgaagaaac ccggagcgtc agtcaaagtg 60

tcatgcaagg cgtcaggcta caccttcacc agctactaca tgcactgggt gcggcaggcc 120

ccaggccaag gcttggagtg gatgggaatc attaacccgt caggaggctc cacctcctac 180

gcccagaagt ttcagggaag agtgacgatg actcgggata cgtcgacctc gaccgtgtac 240

atggaactga gctcgctgcg ctccgaggac actgctgtgt actactgcgc acggtacaga 300

ctcattgccg tggcaggaga ctactactac tatggcatgg acgtctgggg gcagggcact 360

atggtcactg tgtcgtccgg cggaggaggc tcgggtggag gaggtagcgg aggaggggga 420

agcggagggg ggggctccga tatccagatg actcagtcgc cttcctccgt gtcggcctcg 480

gttggagatc gcgtcaccat cacttgtcga gcttcccaag gagtcggtag gtggctggcg 540

tggtaccagc aaaagccggg aactgccccg aagctcctga tctacgcggc tagcaccctg 600

cagtcgggag tgccatcccg cttcagcgga tctgggtcag gtaccgactt cacccttacg 660

atcaacaatc tccagccgga ggactttgcc acctattact gccaacaggc caacagcttc 720

cctctgactt tcggaggggg cactcgcctg gaaatcaag 759

<210> 587
<211> 1491
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 587
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtgc aactcgtcca gtcaggtgca gaagtgaaga aacccggagc gtcagtcaaa 120

gtgtcatgca aggcgtcagg ctacaccttc accagctact acatgcactg ggtgcggcag 180

gccccaggcc aaggcttgga gtggatggga atcattaacc cgtcaggagg ctccacctcc 240

tacgcccaga agtttcaggg aagagtgacg atgactcggg atacgtcgac ctcgaccgtg 300

tacatggaac tgagctcgct gcgctccgag gacactgctg tgtactactg cgcacggtac 360

agactcattg ccgtggcagg agactactac tactatggca tggacgtctg ggggcagggc 420

actatggtca ctgtgtcgtc cggcggagga ggctcgggtg gaggaggtag cggaggaggg 480

ggaagcggag gggggggctc cgatatccag atgactcagt cgccttcctc cgtgtcggcc 540

tcggttggag atcgcgtcac catcacttgt cgagcttccc aaggagtcgg taggtggctg 600

gcgtggtacc agcaaaagcc gggaactgcc ccgaagctcc tgatctacgc ggctagcacc 660

ctgcagtcgg gagtgccatc ccgcttcagc ggatctgggt caggtaccga cttcaccctt 720

acgatcaaca atctccagcc ggaggacttt gccacctatt actgccaaca ggccaacagc 780

ttccctctga ctttcggagg gggcactcgc ctggaaatca agaccactac cccagcaccg 840

aggccaccca ccccggctcc taccatcgcc tcccagcctc tgtccctgcg tccggaggca 900

tgtagacccg cagctggtgg ggccgtgcat acccggggtc ttgacttcgc ctgcgatatc 960

tacatttggg cccctctggc tggtacttgc ggggtcctgc tgctttcact cgtgatcact 1020

ctttactgta agcgcggtcg gaagaagctg ctgtacatct ttaagcaacc cttcatgagg 1080

cctgtgcaga ctactcaaga ggaggacggc tgttcatgcc ggttcccaga ggaggaggaa 1140

ggcggctgcg aactgcgcgt gaaattcagc cgcagcgcag atgctccagc ctacaagcag 1200

gggcagaacc agctctacaa cgaactcaat cttggtcgga gagaggagta cgacgtgctg 1260

gacaagcgga gaggacggga cccagaaatg ggcgggaagc cgcgcagaaa gaatccccaa 1320

gagggcctgt acaacgagct ccaaaaggat aagatggcag aagcctatag cgagattggt 1380

atgaaagggg aacgcagaag aggcaaaggc cacgacggac tgtaccaggg actcagcacc 1440

gccaccaagg acacctatga cgctcttcac atgcaggccc tgccgcctcg g 1491

<210> 588
<211> 750
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 588
caagtgcaat tggttcaatc aggaggagga gtggtgcaac ctggaagatc tctcagactg 60

tcgtgtgcgg catcgggatt cactttctca tcatacgcaa tgcactgggt ccgccaggcc 120

ccgggcaaag gcttggaatg ggtggcggtc atttcatacg acggctcgaa caagtactac 180

gctgacagcg tgaagggacg ctttactatt tcccgggaca attcgaagaa cactctgtac 240

ctccagatga actcccttag ggctgaggac accgccgtct actactgcgc acgctggaaa 300

gtgtcgtcca gctccccagc ttttgactac tggggacagg gaacccttgt gaccgtgtcg 360

tccggtggag ggggaagcgg cggaggggga tcaggtggcg gcggatcggg aggcggggga 420

tcagaaatcg tgctgactca gtccccggcc acgctgtctc tcagcccggg agagagagcg 480

atcctgtcct gccgcgcctc gcagagcgtg tacactaagt acctggggtg gtaccagcag 540

aaaccgggtc aagcgcctcg gctgctgatc tacgatgcct ccacccgggc caccggaatc 600

cccgatcggt tctccggcag cggctcggga actgatttca cgctgaccat caatcgcctg 660

gagccggaag atttcgccgt ctattactgc cagcattacg gcgggagccc actcatcacc 720

ttcggtcaag gaacccgact cgaaatcaag 750

<210> 589
<211> 1482
<212> DNA

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 589
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtgc aattggttca atcaggagga ggagtggtgc aacctggaag atctctcaga 120

ctgtcgtgtg cggcatcggg attcactttc tcatcatacg caatgcactg ggtccgccag 180

gccccgggca aaggcttgga atgggtggcg gtcatttcat acgacggctc gaacaagtac 240

tacgctgaca gcgtgaaggg acgctttact atttcccggg acaattcgaa gaacactctg 300

tacctccaga tgaactccct tagggctgag gacaccgccg tctactactg cgcacgctgg 360

aaagtgtcgt ccagctcccc agcttttgac tactggggac agggaaccct tgtgaccgtg 420

tcgtccggtg gaggggaag cggcggaggg ggatcaggtg gcggcggatc gggaggcggg 480

ggatcagaaa tcgtgctgac tcagtccccg gccacgctgt ctctcagccc gggagagaga 540

gcgatcctgt cctgccgcgc ctcgcagagc gtgtacacta agtacctggg gtggtaccag 600

cagaaaccgg gtcaagcgcc tcggctgctg atctacgatg cctccacccg ggccaccgga 660

atccccgatc ggttctccgg cagcggctcg ggaactgatt tcacgctgac catcaatcgc 720

ctggagccgg aagatttcgc cgtctattac tgccagcatt acggcgggag cccactcatc 780

accttcggtc aaggaacccg actcgaaatc aagaccacta ccccagcacc gaggccaccc 840

accccggctc ctaccatcgc ctcccagcct ctgtccctgc gtccggaggc atgtagaccc 900

gcagctggtg gggccgtgca tacccggggt cttgacttcg cctgcgatat ctacatttgg 960

gcccctctgg ctggtacttg cggggtcctg ctgctttcac tcgtgatcac tctttactgt 1020

aagcgcggtc ggaagaagct gctgtacatc tttaagcaac ccttcatgag gcctgtgcag 1080

actactcaag aggaggacgg ctgttcatgc cggttcccag aggaggagga aggcggctgc 1140

gaactgcgcg tgaaattcag ccgcagcgca gatgctccag cctacaagca ggggcagaac 1200

cagctctaca acgaactcaa tcttggtcgg agagaggagt acgacgtgct ggacaagcgg 1260

agaggacggg acccagaaat gggcgggaag ccgcgcagaa agaatcccca agagggcctg 1320

tacaacgagc tccaaaagga taagatggca gaagcctata gcgagattgg tatgaaaggg 1380

gaacgcagaa gaggcaaagg ccacgacgga ctgtaccagg gactcagcac cgccaccaag 1440

gacacctatg acgctcttca catgcaggcc ctgccgcctc gg 1482

<210> 590
<211> 738
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 590
caagtccaac tccagcagtc aggtgcagaa gtcaaaaagc caggagcatc cgtgaaggtt 60

tcgtgcaaga cttccggcta ccctttttacc gggtactccc tccattgggt gagacaagca 120

ccgggccagg gactggagtg gatgggatgg atcaacccaa attcgggcgg caccaactat 180

gcgcagaagt tccagggacg ggtgaccatg actcgcgaca cttcgatctc cactgcctac 240

atggagctgt cccgcttgag atctgacgac acggccgtct actactgcgc ccgggatcac 300

tacggaggta attcgctgtt ctactggggg cagggaaccc ttgtgactgt gtcctcgggt 360

ggtggagggt caggaggcgg aggctcaggg ggaggaggta gcggaggagg cggatcagac 420

atccaactga cccagtcacc atcctccatc tcggctagcg tcggagacac cgtgtcgatt 480

acttgtaggg cctcccaaga ctcagggacg tggctggcgt ggtatcagca aaaaccgggc 540

aaagctccga acctgttgat gtacgacgcc agcaccctcg aagatggagt gcctagccgc 600

ttcagcggaa gcgcctcggg cactgaattc acgctgactg tgaatcggct ccagccggag 660

gattcggcga cctactactg ccagcagtac aacagctacc ccctgacctt tggaggcggg 720

accaaggtgg atatcaag 738

<210> 591
<211> 1470
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 591
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtcc aactccagca gtcaggtgca gaagtcaaaa agccaggagc atccgtgaag 120

gtttcgtgca agacttccgg ctacccttttt accgggtact ccctccattg ggtgagacaa 180

gcaccgggcc agggactgga gtggatggga tggatcaacc caaattcggg cggcaccaac 240

tatgcgcaga agttccaggg acgggtgacc atgactcgcg acacttcgat ctccactgcc 300

tacatggagc tgtcccgctt gagatctgac gacacggccg tctactactg cgcccgggat 360

cactacggag gtaattcgct gttctactgg gggcagggaa cccttgtgac tgtgtcctcg 420

ggtggtggag ggtcaggagg cggaggctca gggggaggag gtagcggagg aggcggatca 480

gacatccaac tgacccagtc accatcctcc atctcggcta gcgtcggaga caccgtgtcg 540

attacttgta gggcctccca agactcaggg acgtggctgg cgtggtatca gcaaaaaccg 600

ggcaaagctc cgaacctgtt gatgtacgac gccagcaccc tcgaagatgg agtgcctagc 660

cgcttcagcg gaagcgcctc gggcactgaa ttcacgctga ctgtgaatcg gctccagccg 720

gaggattcgg cgacctacta ctgccagcag tacaacagct acccccctgac ctttggaggc 780

gggaccaagg tggatatcaa gaccactacc ccagcaccga ggccacccac cccggctcct 840

accatcgcct cccagcctct gtccctgcgt ccggaggcat gtagacccgc agctggtggg 900

gccgtgcata cccggggtct tgacttcgcc tgcgatatct acatttgggc ccctctggct 960

ggtacttgcg gggtcctgct gctttcactc gtgatcactc tttactgtaa gcgcggtcgg 1020

aagaagctgc tgtacatctt taagcaaccc ttcatgaggc ctgtgcagac tactcaagag 1080

gaggacggct gttcatgccg gttcccagag gaggaggaag gcggctgcga actgcgcgtg 1140

aaattcagcc gcagcgcaga tgctccagcc tacaagcagg ggcagaacca gctctacaac 1200

gaactcaatc ttggtcggag agaggagtac gacgtgctgg acaagcggag aggacgggac 1260

ccagaaatgg gcgggaagcc gcgcagaaag aatccccaag agggcctgta caacgagctc 1320

caaaaggata agatggcaga agcctatagc gagattggta tgaaagggga acgcagaaga 1380

ggcaaaggcc acgacggact gtaccaggga ctcagcaccg ccaccaagga cacctatgac 1440

gctcttcaca tgcaggccct gccgcctcgg 1470

<210> 592
<211> 744
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 592
caagtgcaac tcgtccagtc aggtgcagaa gtgaagaaac caggagcgtc cgtcgaagtg 60

tcgtgtaagg cgtccggcta cactttcacc tcgtactaca tgcactgggt gcggcaggcc 120

ccgggacaag gcctcgaatg gatgggaatc atcaacccga gcggaggctc gactggttac 180

gcccagaagt tccagggaag ggtgacgatg acccgcgata cctcgacttc gaccgttcat 240

atggagctct cgtccctgcg gagcgaggac actgctgtct actattgcgc gcggggagga 300

tactctagct cctccgatgc atttgacatt tggggccagg gaactatggt gaccgtgtca 360

tcaggcggag gtggatcagg aggaggaggg tcgggagggg gaggcagcgg cgggggtggg 420

tcggacattc agatgacgca gtcccctcct agcctgagcg cctcggtggg tgacagagtg 480

accatcactt gcagagcctc gcaagacatc tcctccgcat tggcttggta ccagcaaaag 540

ccgggcactc cgccgaaact gctcatctac gatgcctcct cactggagtc aggagtccca 600

tctcgcttct cggggtcagg aagcggcacc gattttaccc ttaccatctc cagcctgcag 660

cccgaggact tcgccacgta ctactgccaa cagttcagct cctacccact gaccttcggg 720

ggcggaactc gcctggaaat caag 744

<210> 593
<211> 1476
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 593
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtgc aactcgtcca gtcaggtgca gaagtgaaga aaccaggagc gtccgtcgaa 120

gtgtcgtgta aggcgtccgg ctacactttc acctcgtact acatgcactg ggtgcggcag 180

gccccgggac aaggcctcga atggatggga atcatcaacc cgagcggagg ctcgactggt 240

tacgcccaga agttccaggg aagggtgacg atgacccgcg atacctcgac ttcgaccgtt 300

catatggagc tctcgtccct gcggagcgag gacactgctg tctactattg cgcgcgggga 360

ggatactcta gctcctccga tgcatttgac atttggggcc agggaactat ggtgaccgtg 420

tcatcaggcg gaggtggatc aggaggagga gggtcgggag ggggaggcag cggcgggggt 480

gggtcggaca ttcagatgac gcagtcccct cctagcctga gcgcctcggt gggtgacaga 540

gtgaccatca cttgcagagc ctcgcaagac atctcctccg cattggcttg gtaccagcaa 600

aagccgggca ctccgccgaa actgctcatc tacgatgcct cctcactgga gtcaggagtc 660

ccatctcgct tctcggggtc aggaagcggc accgatttta cccttaccat ctccagcctg 720

cagcccgagg acttcgccac gtactactgc caacagttca gctcctaccc actgaccttc 780

gggggcggaa ctcgcctgga aatcaagacc actaccccag caccgaggcc acccaccccg 840

gctcctacca tcgcctccca gcctctgtcc ctgcgtccgg aggcatgtag acccgcagct 900

ggtggggccg tgcatacccg gggtcttgac ttcgcctgcg atatctacat ttgggccccc 960

ctggctggta cttgcggggt cctgctgctt tcactcgtga tcactcttta ctgtaagcgc 1020

ggtcggaaga agctgctgta catctttaag caacccttca tgaggcctgt gcagactact 1080

caagaggagg acggctgttc atgccggttc ccagaggagg aggaaggcgg ctgcgaactg 1140

cgcgtgaaat tcagccgcag cgcagatgct ccagcctaca agcaggggca gaaccagctc 1200

tacaacgaac tcaatcttgg tcggagagag gagtacgacg tgctggacaa gcggagagga 1260

cgggacccag aaatgggcgg gaagccgcgc agaaagaatc cccaagaggg cctgtacaac 1320

gagctccaaa aggataagat ggcagaagcc tatagcgaga ttggtatgaa aggggaacgc 1380

agaagaggca aaggccacga cggactgtac cagggactca gcaccgccac caaggacacc 1440

tatgacgctc ttcacatgca ggccctgccg cctcgg 1476

<210> 594
<211> 765
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 594
caagtgcaac tcgtccagag cggagcagaa gtcaagaagc caggagcgtc agtgaaagtg 60

tcatgcaagg ccagcggcta tacctttact tcgtatggga tctcctgggt gcggcaggca 120

ccgggccaag gactggagtg gatgggatgg atctcagcct acaacggtaa caccaactac 180

gcccagaagc tgcaaggacg cgtgaccatg actactgata cgagcacctc cactgcctac 240

atggaattgc ggtcccttcg gtcggacgat actgctgtgt actactgcgc aagagtcgcc 300

ggagggatct actactacta cggcatggac gtctggggac agggaaccac cattacggtg 360

tcgagcggag ggggaggctc ggggggagga ggaagcggag gtggcggctc cgggggcggc 420

ggatcggaca ttgtgatgac ccagactcct gactccctgg ctgtttcgtt gggagagcgc 480

gcgactatct cgtgtaagtc cagccactca gtcctgtaca atcgcaataa caagaactac 540

ctcgcgtggt accagcaaaa accgggtcag ccgcctaaac tcctgttcta ctgggcctcc 600

accagaaaga gcggggtgcc agatcgattc tctggatcag gatcaggtac cgactttacg 660

ctgaccatct cgtccctgca gccggaggat ttcgcgactt acttctgcca gcagactcag 720

actttccccc tcaccttcgg tcaaggcacc aggctggaaa tcaat 765

<210> 595
<211> 1497
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 595
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtgc aactcgtcca gagcggagca gaagtcaaga agccaggagc gtcagtgaaa 120

gtgtcatgca aggccagcgg ctataccttt acttcgtatg ggatctcctg ggtgcggcag 180

gcaccgggcc aaggactgga gtggatggga tggatctcag cctacaacgg taacaccaac 240

tacgcccaga agctgcaagg acgcgtgacc atgactactg atacgagcac ctccactgcc 300

tacatggaat tgcggtccct tcggtcggac gatactgctg tgtactactg cgcaagagtc 360

gccggaggga tctactacta ctacggcatg gacgtctggg gacagggaac caccattacg 420

gtgtcgagcg gaggggggagg ctcgggggga ggaggaagcg gaggtggcgg ctccgggggc 480

ggcggatcgg acattgtgat gacccagact cctgactccc tggctgtttc gttgggagag 540

cgcgcgacta tctcgtgtaa gtccagccac tcagtcctgt acaatcgcaa taacaagaac 600

tacctcgcgt ggtaccagca aaaaccgggt cagccgccta aactcctgtt ctactgggcc 660

tccaccagaa agagcggggt gccagatcga ttctctggat caggatcagg taccgacttt 720

acgctgacca tctcgtccct gcagccggag gatttcgcga cttacttctg ccagcagact 780

cagactttcc ccctcacctt cggtcaaggc accaggctgg aaatcaatac cactacccca 840

gcaccgaggc cacccacccc ggctcctacc atcgcctccc agcctctgtc cctgcgtccg 900

gaggcatgta gacccgcagc tggtggggcc gtgcataccc ggggtcttga cttcgcctgc 960

gatatctaca tttgggcccc tctggctggt acttgcgggg tcctgctgct ttcactcgtg 1020

atcactcttt actgtaagcg cggtcggaag aagctgctgt acatctttaa gcaacccttc 1080

atgaggcctg tgcagactac tcaagaggag gacggctgtt catgccggtt cccagaggag 1140

gaggaaggcg gctgcgaact gcgcgtgaaa ttcagccgca gcgcagatgc tccagcctac 1200

aagcaggggc agaaccagct ctacaacgaa ctcaatcttg gtcggagaga ggagtacgac 1260

gtgctggaca agcggagagg acgggaccca gaaatgggcg ggaagccgcg cagaaagaat 1320

ccccaagagg gcctgtacaa cgagctccaa aaggataaga tggcagaagc ctatagcgag 1380

attggtatga aaggggaacg cagaagaggc aaaggccacg acggactgta ccagggactc 1440

agcaccgcca ccaaggacac ctatgacgct cttcacatgc aggccctgcc gcctcgg 1497

<210> 596
<211> 723
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 596
caagtccaat tgcagcagag cggagcagaa gtgaagaagc caggagcgtc agtcaaagtg 60

tcgtgtaagg cgtcaggata caccttcacg ggatactaca tgcactgggt gcgccaggcc 120

ccgggccaag gactcgagtg gatgggctgg atcaacccta actctggagg caccaactac 180

gcccagaatt tccaaggcag agtgaccatg acccgggaca cctccatctc gactgcctat 240

atggaactgc ggcggctgcg ctcggacgat actgctgtgt attactgcgc cagcggctgg 300

gactttgact actggggaca gggtactctg gtgactgttt cctcgggagg aggcggatcg 360

ggtggaggag gtagcggggg agggggtcg ggaggcggag gcagcgatat tcgcatgact 420

caatcgccgt cctccctgag cgctagcgtg ggagatcgag tcaccatcac ttgcagagcg 480

tcacagtcga ttcgctacta cctgtcctgg taccagcaga aaccgggaaa ggcaccaaag 540

cttctgatct acacggcctc catcctgcaa aatggtgtcc catcaaggtt ctccgggtca 600

gggagcggca ctgacttcac tctcaccatc tcctcactcc agcccgagga ctttgcaacc 660

tactactgcc tccagacgta caccaccccg gatttcggtc ctggaaccaa ggtggaaatc 720

aaa 723

<210> 597
<211> 1455
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 597
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtcc aattgcagca gagcggagca gaagtgaaga agccaggagc gtcagtcaaa 120

gtgtcgtgta aggcgtcagg atacaccttc acgggatact acatgcactg ggtgcgccag 180

gccccgggcc aaggactcga gtggatgggc tggatcaacc ctaactctgg aggcaccaac 240

tacgcccaga atttccaagg cagagtgacc atgacccggg acacctccat ctcgactgcc 300

tatatggaac tgcggcggct gcgctcggac gatactgctg tgtattactg cgccagcggc 360

tgggactttg actactgggg acagggtact ctggtgactg tttcctcggg aggaggcgga 420

tcgggtggag gaggtagcgg gggaggggcg tcgggaggcg gaggcagcga tattcgcatg 480

actcaatcgc cgtcctccct gagcgctagc gtgggagatc gagtcaccat cacttgcaga 540

gcgtcacagt cgattcgcta ctacctgtcc tggtaccagc agaaaccggg aaaggcacca 600

aagcttctga tctacacggc ctccatcctg caaaatggtg tcccatcaag gttctccggg 660

tcagggagcg gcactgactt cactctcacc atctcctcac tccagcccga ggactttgca 720

acctactact gcctccagac gtacaccacc ccggatttcg gtcctggaac caaggtggaa 780

atcaaaacca ctaccccagc accgaggcca cccaccccgg ctcctaccat cgcctcccag 840

cctctgtccc tgcgtccgga ggcatgtaga cccgcagctg gtggggccgt gcatacccgg 900

ggtcttgact tcgcctgcga tatctacatt tgggcccctc tggctggtac ttgcggggtc 960

ctgctgcttt cactcgtgat cactctttac tgtaagcgcg gtcggaagaa gctgctgtac 1020

atctttaagc aacccttcat gaggcctgtg cagactactc aagaggagga cggctgttca 1080

tgccggttcc cagaggagga ggaaggcggc tgcgaactgc gcgtgaaatt cagccgcagc 1140

gcagatgctc cagcctacaa gcaggggcag aaccagctct acaacgaact caatcttggt 1200

cggagagagg agtacgacgt gctggacaag cggagaggac gggacccaga aatgggcggg 1260

aagccgcgca gaaagaatcc ccaagagggc ctgtacaacg agctccaaaa ggataagatg 1320

gcagaagcct atagcgagat tggtatgaaa ggggaacgca gaagaggcaa aggccacgac 1380

ggactgtacc agggactcag caccgccacc aaggacacct atgacgctct tcacatgcag 1440

gccctgccgc ctcgg 1455

<210> 598
<211> 738
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 598
caagtccaac tcgtccaaag cggagcagaa gtcaaaaagc caggagcgtc ggtgaaagtg 60

tcttgcaaag ccagcggcta caccttcacg ggttactaca tgcactgggt gcgccaggcg 120

ccgggccagg ggctggagtg gatgggccgg attaacccta acagcggggg aactaattac 180

gctcagaagt tccagggtag agtcaccatg actacggaca cttccacttc caccgcctat 240

atggaactgc gctccctccg ctcagatgat actgccgtgt attactgcgc gcggactacc 300

acgtcatacg catttgacat ctggggccag ggaactatgg tgaccgtgag ctcgggcgga 360

ggcggttcag ggggaggagg aagcggagga ggaggatcgg gaggaggtgg ctccgatatc 420

cagctgactc agtccccgag caccctgtcg gcgtcggtgg gggacagggt taccatcacc 480

tgtagagctt cccaatccat ttcgacttgg ctggcctggt accagcaaaa gccgggaaag 540

gcccctaatt tgcttatcta caaggcatcg accctcgaaa gcggtgtgcc ctcccggttt 600

tcgggatcag gatcagggac cgagttcacc ctgaccatct catccctcca gccggacgac 660

ttcgccactt actactgcca gcagtacaac acctactcgc catacacttt cggccaaggc 720

accaagctgg agatcaag 738

<210> 599
<211> 1470
<212> DNA
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 599
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtcc aactcgtcca aagcggagca gaagtcaaaa agccaggagc gtcggtgaaa 120

gtgtcttgca aagccagcgg ctacaccttc acgggttact acatgcactg ggtgcgccag 180

gcgccgggcc aggggctgga gtggatgggc cggattaacc ctaacagcgg gggaactaat 240

tacgctcaga agttccaggg tagagtcacc atgactacgg acacttccac ttccaccgcc 300

tatatggaac tgcgctccct ccgctcagat gatactgccg tgtattactg cgcgcggact 360

accacgtcat acgcatttga catctggggc cagggaacta tggtgaccgt gagctcgggc 420

ggaggcggtt caggggggagg aggaagcgga ggaggaggat cgggaggagg tggctccgat 480

atccagctga ctcagtcccc gagcaccctg tcggcgtcgg tgggggacag ggttaccatc 540

acctgtagag cttcccaatc catttcgact tggctggcct ggtaccagca aaagccggga 600

aaggccccta atttgcttat ctacaaggca tcgaccctcg aaagcggtgt gccctcccgg 660

ttttcgggat caggatcagg gaccgagttc accctgacca tctcatccct ccagccggac 720

gacttcgcca cttactactg ccagcagtac aacacctact cgccatacac tttcggccaa 780

ggcaccaagc tggagatcaa gaccactacc ccagcaccga ggccacccac cccggctcct 840

accatcgcct cccagcctct gtccctgcgt ccggaggcat gtagacccgc agctggtggg 900

gccgtgcata cccggggtct tgacttcgcc tgcgatatct acatttgggc ccctctggct 960

ggtacttgcg gggtcctgct gctttcactc gtgatcactc tttactgtaa gcgcggtcgg 1020

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gaggacggct gttcatgccg gttcccagag gaggaggaag gcggctgcga actgcgcgtg 1140

aaattcagcc gcagcgcaga tgctccagcc tacaagcagg ggcagaacca gctctacaac 1200

gaactcaatc ttggtcggag agaggagtac gacgtgctgg acaagcggag aggacgggac 1260

ccagaaatgg gcgggaagcc gcgcagaaag aatccccaag agggcctgta caacgagctc 1320

caaaaggata agatggcaga agcctatagc gagattggta tgaaaggggа acgcagaaga 1380

ggcaaaggcc acgacggact gtaccaggga ctcagcaccg ccaccaagga cacctatgac 1440

gctcttcaca tgcaggccct gccgcctcgg 1470

<210> 600
<211> 747
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

polynucleotide"

<400> 600
caagttcaac tcgtgcaatc aggtggagga ctcgtcaaac ccggaggatc attgagactg 60

tcatgcgaag cgagcggttt tatcttctcc gattactata tgggatggat tcggcaggcc 120

ccgggaaagg gactcgaatg ggtgtcatac atcggaaggt caggctcgtc catgtactac 180

gcagactcgg tgaaaggcag attcaccttt agccgggaca acgccaagaa ttccctctac 240

ttgcagatga acagcctgcg agccgaggat actgctgtct actactgtgc cgcgtcgccg 300

gtggtggcag ctactgaaga tttccagcac tggggacagg gaactctggt cacggtgtcg 360

agcggtgggg gcggaagcgg aggcggagga tcgggcggcg gaggttcggg gggggggagg 420

tctgacatcg tgatgaccca aaccccagcc accctgagcc tctcccctgg agagcgcgcg 480

actctttcgt gccgcgcttc ccagtcagtg accagcaatt acttggcttg gtaccaacag 540

aagccgggac aggcgccacg gctgctgctt tttggtgcca gcactcgcgc caccggaatc 600

ccggatcgct tctcgggctc agggtccggg acggacttca ccctgactat caaccggctg 660

gaacctgagg acttcgcgat gtactactgc cagcagtacg gctccgcacc agtcactttc 720

ggacaaggca ccaagctgga gatcaag 747

<210> 601
<211> 1479
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 601
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagttc aactcgtgca atcaggtgga ggactcgtca aacccggagg atcattgaga 120

ctgtcatgcg aagcgagcgg ttttatcttc tccgattact atatgggatg gattcggcag 180

gccccgggaa agggactcga atgggtgtca tacatcggaa ggtcaggctc gtccatgtac 240

tacgcagact cggtgaaagg cagattcacc tttagccggg acaacgccaa gaattccctc 300

tacttgcaga tgaacagcct gcgagccgag gatactgctg tctactactg tgccgcgtcg 360

ccggtggtgg cagctactga agatttccag cactggggac agggaactct ggtcacggtg 420

tcgagcggtg ggggcggaag cggaggcgga ggatcgggcg gcggaggttc gggggggggga 480

gggtctgaca tcgtgatgac ccaaacccca gccaccctga gcctctcccc tggagagcgc 540

gcgactcttt cgtgccgcgc ttcccagtca gtgaccagca attacttggc ttggtaccaa 600

cagaagccgg gacaggcgcc acggctgctg ctttttggtg ccagcactcg cgccaccgga 660

atcccggatc gcttctcggg ctcagggtcc gggacggact tcaccctgac tatcaaccgg 720

ctggaacctg aggacttcgc gatgtactac tgccagcagt acggctccgc accagtcact 780

ttcggacaag gcaccaagct ggagatcaag accactaccc cagcaccgag gccacccacc 840

ccggctccta ccatcgcctc ccagcctctg tccctgcgtc cggaggcatg tagacccgca 900

gctggtgggg ccgtgcatac ccggggtctt gacttcgcct gcgatatcta catttgggcc 960

cctctggctg gtacttgcgg ggtcctgctg ctttcactcg tgatcactct ttactgtaag 1020

cgcggtcgga agaagctgct gtacatcttt aagcaaccct tcatgaggcc tgtgcagact 1080

actcaagagg aggacggctg ttcatgccgg ttcccagagg aggaggaagg cggctgcgaa 1140

ctgcgcgtga aattcagccg cagcgcagat gctccagcct acaagcaggg gcagaaccag 1200

ctctacaacg aactcaatct tggtcggaga gaggagtacg acgtgctgga caagcggaga 1260

ggacgggacc cagaaatggg cgggaagccg cgcagaaaga atccccaaga gggcctgtac 1320

aacgagctcc aaaaggataa gatggcagaa gcctatagcg agattggtat gaaaggggaa 1380

cgcagaagag gcaaaggcca cgacggactg taccagggac tcagcaccgc caccaaggac 1440

acctatgacg ctcttcacat gcaggccctg ccgcctcgg 1479

<210> 602
<211> 747
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 602
caagtccaac tcgtccagtc gggagcagaa gttagagcac caggagcgtc agtgaaaatc 60

tcatgcaagg cctcgggctt cacgttccgc ggatactaca tccactgggt gcgccaagcc 120

ccgggtcagg gattggagtg gatgggaatc attaacccat caggagggag ccgggcttac 180

gcgcagaagt tccagggacg cgtcactatg acccgagata cttccacctc gactgtgtac 240

atggaactct cgtccctgag gtccgacgac actgcgatgt attactgtgc tcggactgcc 300

agctgcggtg gggactgtta ctacctcgat tactggggcc agggaactct ggtgaccgtg 360

tccagcggag gtggcgggtc aggggtggc ggaagcggag gcggcggttc aggcggagga 420

ggctcggaca tccaaatgac gcaatcgccg cctaccctga gcgcttccgt gggagatcgg 480

gtgaccatta cttgcagagc atccgagaac gtcaatatct ggctggcctg gtaccaacag 540

aagccgggga aggcccctaa actgctgatc tacaagtcga gcagccttgc ctctggagtg 600

ccctcccgct tctcgggctc gggatcagga gcggaattca ccctcaccat ctcctccctg 660

cagccagatg actttgccac ctactactgc cagcagtacc agagctatcc gttgaccttt 720

ggggggaggca ctaaagtgga catcaag 747

<210> 603
<211> 1479
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 603
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtcc aactcgtcca gtcgggagca gaagttagag caccaggagc gtcagtgaaa 120

atctcatgca aggcctcggg cttcacgttc cgcggatact acatccactg ggtgcgccaa 180

gccccgggtc agggattgga gtggatggga atcattaacc catcaggagg gagccgggct 240

tacgcgcaga agttccaggg acgcgtcact atgacccgag atacttccac ctcgactgtg 300

tacatggaac tctcgtccct gaggtccgac gacactgcga tgtattactg tgctcggact 360

gccagctgcg gtggggactg ttactacctc gattactggg gccagggaac tctggtgacc 420

gtgtccagcg gaggtggcgg gtcaggggt ggcggaagcg gaggcggcgg ttcaggcgga 480

ggaggctcgg acatccaaat gacgcaatcg ccgcctaccc tgagcgcttc cgtgggagat 540

cgggtgacca ttacttgcag agcatccgag aacgtcaata tctggctggc ctggtaccaa 600

cagaagccgg ggaaggcccc taaactgctg atctacaagt cgagcagcct tgcctctgga 660

gtgccctccc gcttctcggg ctcgggatca ggagcggaat tcaccctcac catctcctcc 720

ctgcagccag atgactttgc cacctactac tgccagcagt accagagcta tccgttgacc 780

tttgggggag gcactaaagt ggacatcaag accactaccc cagcaccgag gccacccacc 840

ccggctccta ccatcgcctc ccagcctctg tccctgcgtc cggaggcatg tagacccgca 900

gctggtgggg ccgtgcatac ccggggtctt gacttcgcct gcgatatcta catttgggcc 960

cctctggctg gtacttgcgg ggtcctgctg ctttcactcg tgatcactct ttactgtaag 1020

cgcggtcgga agaagctgct gtacatcttt aagcaaccct tcatgaggcc tgtgcagact 1080

actcaagagg aggacggctg ttcatgccgg ttcccagagg aggaggaagg cggctgcgaa 1140

ctgcgcgtga aattcagccg cagcgcagat gctccagcct acaagcaggg gcagaaccag 1200

ctctacaacg aactcaatct tggtcggaga gaggagtacg acgtgctgga caagcggaga 1260

ggacgggacc cagaaatggg cgggaagccg cgcagaaaga atccccaaga gggcctgtac 1320

aacgagctcc aaaaggataa gatggcagaa gcctatagcg agattggtat gaaaggggaa 1380

cgcagaagag gcaaaggcca cgacggactg taccagggac tcagcaccgc caccaaggac 1440

acctatgacg ctcttcacat gcaggccctg ccgcctcgg 1479

<210> 604
<211> 732
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 604
caagttcaac tcgttcaatc aggtggagga ctcgtgcaac caggaagatc actcagactc 60

agctgcgccg cgtcgggatt cactttcgat gactacgcaa tgcactgggt gcggcaggcc 120

ccgggcaaag gactggaatg ggtgagcgga attagctgga actcggggtc catcgggtac 180

gccgactcgg tgaagggacg ctttacgatc tcccgggaca atgccaagaa ctccctgtat 240

ttgcagatga actccttgag ggctgaggac accgccgtgt actactgcgc taaagatgga 300

tcatcgtcct ggtcctgggg atacttcgat tactggggcc agggcactct ggtgaccgtg 360

tcgtcaggcg gtggagggtc gggcggagga ggtagcggag gcggagggag cagctctgaa 420

ctgacccaag acccggcggt gtcggtcgcc cttggtcaga ctgtgcggac tacctgtcag 480

ggggacgcgc tgcgctcgta ctacgcttca tggtaccagc agaagcccgg acaggcacct 540

atgctggtca tctacggaaa gaataaccgc ccatccggca tcccggatcg cttctcgggt 600

tcggacagcg gcgacaccgc atccctgacg atcactggag cgcaggccga ggatgaagcc 660

gactactact gcaattcccg agattcaagc ggctaccctg tgtttgggac cggaactaag 720

gtcaccgtcc tg 732

<210> 605
<211> 1464
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 605
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagttc aactcgttca atcaggtgga ggactcgtgc aaccaggaag atcactcaga 120

ctcagctgcg ccgcgtcggg attcactttc gatgactacg caatgcactg ggtgcggcag 180

gccccgggca aaggactgga atgggtgagc ggaattagct ggaactcggg gtccatcggg 240

tacgccgact cggtgaaggg acgctttacg atctcccggg acaatgccaa gaactccctg 300

tatttgcaga tgaactcctt gagggctgag gacaccgccg tgtactactg cgctaaagat 360

ggatcatcgt cctggtcctg gggatacttc gattactggg gccagggcac tctggtgacc 420

gtgtcgtcag gcggtggagg gtcgggcgga ggaggtagcg gaggcggagg gagcagctct 480

gaactgaccc aagacccggc ggtgtcggtc gcccttggtc agactgtgcg gactacctgt 540

caggggacg cgctgcgctc gtactacgct tcatggtacc agcagaagcc cggacaggca 600

cctatgctgg tcatctacgg aaagaataac cgcccatccg gcatcccgga tcgcttctcg 660

ggttcggaca gcggcgacac cgcatccctg acgatcactg gagcgcaggc cgaggatgaa 720

gccgactact actgcaattc ccgagattca agcggctacc ctgtgtttgg gaccggaact 780

aaggtcaccg tcctgaccac taccccagca ccgaggccac ccaccccggc tcctaccatc 840

gcctcccagc ctctgtccct gcgtccggag gcatgtagac ccgcagctgg tggggccgtg 900

catacccggg gtcttgactt cgcctgcgat atctacattt gggcccctct ggctggtact 960

tgcggggtcc tgctgctttc actcgtgatc actctttact gtaagcgcgg tcggaagaag 1020

ctgctgtaca tctttaagca acccttcatg aggcctgtgc agactactca agaggaggac 1080

ggctgttcat gccggttccc agaggaggag gaaggcggct gcgaactgcg cgtgaaattc 1140

agccgcagcg cagatgctcc agcctacaag caggggcaga accagctcta caacgaactc 1200

aatcttggtc ggagagagga gtacgacgtg ctggacaagc ggagaggacg ggacccagaa 1260

atgggcggga agccgcgcag aaagaatccc caagagggcc tgtacaacga gctccaaaag 1320

gataagatgg cagaagccta tagcgagatt ggtatgaaag gggaacgcag aagaggcaaa 1380

ggccacgacg gactgtacca gggactcagc accgccacca aggacaccta tgacgctctt 1440

cacatgcagg ccctgccgcc tcgg 1464

<210> 606
<211> 738
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 606
gaagtgcaac tcgtggaatc tggtggagga cttgtgcaac ctggaagatc gttgagactc 60

tcatgtgctg cctccgggtt cacctttgac gactacgcca tgcactgggt gcgccaggca 120

ccaggaaagg gtctggagtg ggtttcgggt atctcgtgga actccgggag cactggctac 180

gctgattcgg tgaaaggccg gtttaccatc tcccgagaca atgcgaagaa ttccctctat 240

ctgcagatga acagcctccg ggccgaggat actgccctgt actactgcgc caaggatagc 300

tcatcatggt acggaggtgg atcggctttc gatatctggg gccagggcac gatggtcacc 360

gtgtcctcgg ggggcggagg ctccggggga ggaggtagcg gaggaggagg atcgagctca 420

gagttgactc aagaacccgc agtgtccgtg gcactgggcc aaaccgtcag gatcacttgc 480

cagggagaca gcctgaggtc gtactacgcg tcctggtacc agcagaagcc gggacaggcc 540

ccggtcctgg tcattttcgg acgctcaaga cgcccatcgg gcatcccgga ccggttcagc 600

ggaagctcct cgggaaacac cgcgtcactt atcattaccg gcgcacaggc tgaggacgaa 660

gcggattact actgcaactc ccgcgacaat actgccaacc attacgtgtt cgggaccgga 720

acgaaactga ctgtcctg 738

<210> 607
<211> 1470
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 607
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaagtgc aactcgtgga atctggtgga ggacttgtgc aacctggaag atcgttgaga 120

ctctcatgtg ctgcctccgg gttcaccttt gacgactacg ccatgcactg ggtgcgccag 180

gcaccaggaa agggtctgga gtgggtttcg ggtatctcgt ggaactccgg gagcactggc 240

tacgctgatt cggtgaaagg ccggtttacc atctcccgag acaatgcgaa gaattccctc 300

tatctgcaga tgaacagcct ccgggccgag gatactgccc tgtactactg cgccaaggat 360

agctcatcat ggtacggagg tggatcggct ttcgatatct ggggccaggg cacgatggtc 420

accgtgtcct cgggggcgg aggctccggg ggaggaggta gcggaggagg aggatcgagc 480

tcagagttga ctcaagaacc cgcagtgtcc gtggcactgg gccaaaccgt caggatcact 540

tgccagggag acagcctgag gtcgtactac gcgtcctggt accagcagaa gccgggacag 600

gccccggtcc tggtcatttt cggacgctca agacgcccat cgggcatccc ggaccggttc 660

agcggaagct cctcgggaaa caccgcgtca cttatcatta ccggcgcaca ggctgaggac 720

gaagcggatt actactgcaa ctcccgcgac aatactgcca accattacgt gttcgggacc 780

ggaacgaaac tgactgtcct gaccactacc ccagcaccga ggccacccac cccggctcct 840

accatcgcct cccagcctct gtccctgcgt ccggaggcat gtagacccgc agctggtggg 900

gccgtgcata cccggggtct tgacttcgcc tgcgatatct acatttgggc ccctctggct 960

ggtacttgcg gggtcctgct gctttcactc gtgatcactc tttactgtaa gcgcggtcgg 1020

aagaagctgc tgtacatctt taagcaaccc ttcatgaggc ctgtgcagac tactcaagag 1080

gaggacggct gttcatgccg gttcccagag gaggaggaag gcggctgcga actgcgcgtg 1140

aaattcagcc gcagcgcaga tgctccagcc tacaagcagg ggcagaacca gctctacaac 1200

gaactcaatc ttggtcggag agaggagtac gacgtgctgg acaagcggag aggacgggac 1260

ccagaaatgg gcgggaagcc gcgcagaaag aatccccaag agggcctgta caacgagctc 1320

caaaaggata agatggcaga agcctatagc gagattggta tgaaagggga acgcagaaga 1380

ggcaaaggcc acgacggact gtaccaggga ctcagcaccg ccaccaagga cacctatgac 1440

gctcttcaca tgcaggccct gccgcctcgg 1470

<210> 608
<211> 738
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 608
gaagttcaat tggtggaatc tggaggagga cttgtgcaac ccggtagatc tctgagactg 60

tcctgtgcgg catcgggatt caccttcgac gactacgcta tgcactgggt gagacaagcc 120

cctggaaaag gactggagtg ggtgtcaggc atctcctgga atagcgggtc cactggatac 180

gccgattcgg tcaagggtcg cttcaccatt tcccgggaca atgccaagaa ctccctgtac 240

cttcaaatga actccctccg ggccgaggat accgccctct actactgcgc caaagacagc 300

tcgtcatggt atggcggagg gtcggcattt gacatctggg gacagggaac tatggtgact 360

gtgtcatcag gaggcggcgg aagcggcggc ggcgggtccg gcggaggagg gtcgtccagc 420

gaactcaccc aagatccagc agtgagcgtc gcgctgggcc agaccgtcag gatcacgtgc 480

cagggagatt cactgcgctc atactacgcg tcctggtacc agcagaagcc ggggcaggcc 540

ccggtcctcg tgatctacgg aaagaacaac cgcccgtcgg gtatcccaga ccgcttttcg 600

ggtagctcca gcggaaatac ggctagcctg accatcactg gagcacaggc tgaggatgaa 660

gcggactact actgcaattc gcggggctca tcggggaacc attacgtgtt cggaactggt 720

accaaggtga ctgtcctg 738

<210> 609
<211> 1470
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 609

atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaagttc aattggtgga atctggagga ggacttgtgc aacccggtag atctctgaga 120

ctgtcctgtg cggcatcggg attcaccttc gacgactacg ctatgcactg ggtgagacaa 180

gcccctggaa aaggactgga gtgggtgtca ggcatctcct ggaatagcgg gtccactgga 240

tacgccgatt cggtcaaggg tcgcttcacc atttcccggg acaatgccaa gaactccctg 300

taccttcaaa tgaactccct ccgggccgag gataccgccc tctactactg cgccaaagac 360

agctcgtcat ggtatggcgg agggtcggca tttgacatct ggggacaggg aactatggtg 420

actgtgtcat caggaggcgg cggaagcggc ggcggcgggt ccggcggagg agggtcgtcc 480

agcgaactca cccaagatcc agcagtgagc gtcgcgctgg gccagaccgt caggatcacg 540

tgccagggag attcactgcg ctcatactac gcgtcctggt accagcagaa gccggggcag 600

gccccggtcc tcgtgatcta cggaaagaac aaccgcccgt cgggtatccc agaccgcttt 660

tcgggtagct ccagcggaaa tacggctagc ctgaccatca ctggagcaca ggctgaggat 720

gaagcggact actactgcaa ttcgcggggc tcatcgggga accattacgt gttcggaact 780

ggtaccaagg tgactgtcct gaccactacc ccagcaccga ggccacccac cccggctcct 840

accatcgcct cccagcctct gtccctgcgt ccggaggcat gtagacccgc agctggtggg 900

gccgtgcata cccggggtct tgacttcgcc tgcgatatct acatttgggc ccctctggct 960

ggtacttgcg gggtcctgct gctttcactc gtgatcactc tttactgtaa gcgcggtcgg 1020

aagaagctgc tgtacatctt taagcaaccc ttcatgaggc ctgtgcagac tactcaagag 1080

gaggacggct gttcatgccg gttcccagag gaggaggaag gcggctgcga actgcgcgtg 1140

aaattcagcc gcagcgcaga tgctccagcc tacaagcagg ggcagaacca gctctacaac 1200

gaactcaatc ttggtcggag agaggagtac gacgtgctgg acaagcggag aggacgggac 1260

ccagaaatgg gcgggaagcc gcgcagaaag aatccccaag agggcctgta caacgagctc 1320

caaaaggata agatggcaga agcctatagc gagattggta tgaaagggga acgcagaaga 1380

ggcaaaggcc acgacggact gtaccaggga ctcagcaccg ccaccaagga cacctatgac 1440

gctcttcaca tgcaggccct gccgcctcgg 1470

<210> 610
<211> 753
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 610
caagtgcagc tcgttcaatc aggcggagga ctcgttcaac caggaggatc attgcgactc 60

tcatgtgcgg cctctggatt cacgtttagc tcatattgga tgcactgggt gcggcaggcg 120

ccggggaaag gtctggtgtg ggtcagccgc atcaactcag acggctcctc gacttcgtac 180

gccgactccg tgaagggacg ctttaccatt tcccgcgaca acgccaagaa tacccttac 240

cttcagatga actccctccg cgctgaggat accgccgtgt actactgcgt gaggactggc 300

tgggtcggca gctactacta ctacatggac gtgtggggca aaggaactac tgtcaccgtg 360

tcaagcggcg gtggaggttc cggcggggga ggatcggggg ggggcggatc gggtggcgga 420

ggatcggaga tcgtgttgac ccagtcgccg ggaaccctgt cgctgtcgcc tggggagaga 480

gcaactctgt cctgccgggc ttcccagtcg gtgtcgagca attacctggc atggtaccaa 540

cagaagccgg gacagccgcc acgcctgctg atctatgacg tgtcaactcg ggcaactgga 600

atccctgcgc ggttcagcgg cggagggagc ggtaccgatt tcaccctgac tatttcctcc 660

ctcgaaccag aagatttcgc cgtctactac tgccagcaga gaagcaactg gccgccctgg 720

acgttcggac aaggaaccaa ggtcgaaatc aag 753

<210> 611
<211> 1485
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 611
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtgc agctcgttca atcaggcgga ggactcgttc aaccaggagg atcattgcga 120

ctctcatgtg cggcctctgg attcacgttt agctcatatt ggatgcactg ggtgcggcag 180

gcgccgggga aaggtctggt gtgggtcagc cgcatcaact cagacggctc ctcgacttcg 240

tacgccgact ccgtgaaggg acgctttacc atttcccgcg acaacgccaa gaataccctt 300

taccttcaga tgaactccct ccgcgctgag gataccgccg tgtactactg cgtgaggact 360

ggctgggtcg gcagctacta ctactacatg gacgtgtggg gcaaaggaac tactgtcacc 420

gtgtcaagcg gcggtggagg ttccggcggg ggaggatcgg gggggggcgg atcgggtggc 480

ggaggatcgg agatcgtgtt gacccagtcg ccgggaaccc tgtcgctgtc gcctggggag 540

agagcaactc tgtcctgccg ggcttcccag tcggtgtcga gcaattacct ggcatggtac 600

caacagaagc cgggacagcc gccacgcctg ctgatctatg acgtgtcaac tcgggcaact 660

ggaatccctg cgcggttcag cggcggaggg agcggtaccg atttcaccct gactatttcc 720

tccctcgaac cagaagattt cgccgtctac tactgccagc agagaagcaa ctggccgccc 780

tggacgttcg gacaaggaac caaggtcgaa atcaagacca ctaccccagc accgaggcca 840

cccaccccgg ctcctaccat cgcctcccag cctctgtccc tgcgtccgga ggcatgtaga 900

cccgcagctg gtggggccgt gcatacccgg ggtcttgact tcgcctgcga tatctacatt 960

tgggcccctc tggctggtac ttgcggggtc ctgctgcttt cactcgtgat cactctttac 1020

tgtaagcgcg gtcggaagaa gctgctgtac atctttaagc aacccttcat gaggcctgtg 1080

cagactactc aagaggagga cggctgttca tgccggttcc cagaggagga ggaaggcggc 1140

tgcgaactgc gcgtgaaatt cagccgcagc gcagatgctc cagcctacaa gcaggggcag 1200

aaccagctct acaacgaact caatcttggt cggagagagg agtacgacgt gctggacaag 1260

cggagaggac gggacccaga aatgggcggg aagccgcgca gaaagaatcc ccaagagggc 1320

ctgtacaacg agctccaaaa ggataagatg gcagaagcct atagcgagat tggtatgaaa 1380

ggggaacgca gaagaggcaa aggccacgac ggactgtacc agggactcag caccgccacc 1440

aaggacacct atgacgctct tcacatgcag gccctgccgc ctcgg 1485

<210> 612
<211> 750
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 612
caagtgcaat tggttcaatc aggaggagga gtcgtgcagc ccggaagatc gttgagactg 60

tcatgtgccg cgagcggctt tactttctca agctacggaa tgcattgggt gcgacaggct 120

ccgggaaaag gactggaatg ggtcgcagtg atctcatacg acggctcgaa caagtactac 180

gccgactccg tcaagggtcg gttcacgatt tcgcgcgata attccaagaa cactctgtac 240

ctccaaatga acagcctccg ggcagaggac accgccgtct actactgcgc taagggatac 300

tcgcgctact actactatgg aatggatgtg tggggccagg gaactaccgt gacggtgtcg 360

tccggcggcg gtgggtcggg cggaggcgga tcaggtggag gtggaagcgg aggaggaggg 420

agcgaaatcg tcatgactca gtcccctgct acccctttctc tgtcgccggg agaaagagcc 480

atcctgagct gccgggcctc ccagagcgtg tacaccaaat acctgggatg gtaccagcag 540

aagccggggc aggcaccaag gctcctgatc tacgatgcgt ccacccgcgc gactggtatc 600

ccagaccgct tttccggctc ggggtcaggg actgacttca cccttactat caatcggctc 660

gagcctgagg atttcgccgt gtattactgc cagcactacg gagggtcccc gctgattacc 720

ttcggccaag gcaccaaagt ggacatcaag 750

<210> 613
<211> 1482
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 613
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtgc aattggttca atcaggagga ggagtcgtgc agcccggaag atcgttgaga 120

ctgtcatgtg ccgcgagcgg ctttactttc tcaagctacg gaatgcattg ggtgcgacag 180

gctccgggaa aaggactgga atgggtcgca gtgatctcat acgacggctc gaacaagtac 240

tacgccgact ccgtcaaggg tcggttcacg atttcgcgcg ataattccaa gaacactctg 300

tacctccaaa tgaacagcct ccgggcagag gacaccgccg tctactactg cgctaaggga 360

tactcgcgct actactacta tggaatggat gtgtggggcc agggaactac cgtgacggtg 420

tcgtccggcg gcggtgggtc gggcggaggc ggatcaggtg gaggtggaag cggaggagga 480

gggagcgaaa tcgtcatgac tcagtcccct gctacccttt ctctgtcgcc gggagaaaga 540

gccatcctga gctgccgggc ctcccagagc gtgtacacca aatacctggg atggtaccag 600

cagaagccgg ggcaggcacc aaggctcctg atctacgatg cgtccacccg cgcgactggt 660

atcccagacc gcttttccgg ctcggggtca gggactgact tcacccttac tatcaatcgg 720

ctcgagcctg aggatttcgc cgtgtattac tgccagcact acggagggtc cccgctgatt 780

accttcggcc aaggcaccaa agtggacatc aagaccacta ccccagcacc gaggccaccc 840

accccggctc ctaccatcgc ctcccagcct ctgtccctgc gtccggaggc atgtagaccc 900

gcagctggtg gggccgtgca tacccggggt cttgacttcg cctgcgatat ctacatttgg 960

gcccctctgg ctggtacttg cggggtcctg ctgctttcac tcgtgatcac tctttactgt 1020

aagcgcggtc ggaagaagct gctgtacatc tttaagcaac ccttcatgag gcctgtgcag 1080

actactcaag aggaggacgg ctgttcatgc cggttcccag aggaggagga aggcggctgc 1140

gaactgcgcg tgaaattcag ccgcagcgca gatgctccag cctacaagca ggggcagaac 1200

cagctctaca acgaactcaa tcttggtcgg agagaggagt acgacgtgct ggacaagcgg 1260

agaggacggg acccagaaat gggcgggaag ccgcgcagaa agaatcccca agagggcctg 1320

tacaacgagc tccaaaagga taagatggca gaagcctata gcgagattgg tatgaaaggg 1380

gaacgcagaa gaggcaaagg ccacgacgga ctgtaccagg gactcagcac cgccaccaag 1440

gacacctatg acgctcttca catgcaggcc ctgccgcctc gg 1482

<210> 614

<211> 747
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 614
caagtgcaac ttgttcaatc aggaggagga ctcgttcaac ccggaggatc actgcgactc 60

tcatgtgcag cgtcggggtt caccttctcc agctacgcaa tgtcctgggt gcgccaagcc 120

cctggaaaag gcctggagtg ggtgtcggcc atctctggga gcgggggatc aacttactac 180

gctgactccg tcaagggccg ctttaccatc tcccgggaca acagcaagaa cactctctat 240

ctccagatga actcgctgag agccgaagat accgctgtct actactgcgc gaagagagaa 300

gctgccgcag ggcacgattg gtacttcgac ttgtggggca ggggcaccct tgtgaccgtg 360

tcctccggtg gaggcggatc aggaggtggg ggatcgggtg gaggaggaag cggaggcggc 420

ggttcggaca ttcgcgtcac ccagtcaccg agctccctca gcgcatcggt gggcgaccgg 480

gtcactatca cttgccgggc gtcccagtcg atctcatcgt atctgaattg gtaccagcag 540

aaaccgggaa aggcgccgaa gctgttgatc tacgctgcca gctccctgca gtcgggtgtg 600

ccatcacgct tttccggctc gggatcggga accgatttca ctctgacgat ctctagcctg 660

cagccagaag atttcgccac ttactactgc cagcagtcct acagcatccc tctgactttc 720

ggacaaggga cgaaagtgga gattaag 747

<210> 615
<211> 1479
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 615
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtgc aacttgttca atcaggagga ggactcgttc aacccggagg atcactgcga 120

ctctcatgtg cagcgtcggg gttcaccttc tccagctacg caatgtcctg ggtgcgccaa 180

gcccctggaa aaggcctgga gtgggtgtcg gccatctctg ggagcggggg atcaacttac 240

tacgctgact ccgtcaaggg ccgctttacc atctcccggg acaacagcaa gaacactctc 300

tatctccaga tgaactcgct gagagccgaa gataccgctg tctactactg cgcgaagaga 360

gaagctgccg cagggcacga ttggtacttc gacttgtggg gcaggggcac ccttgtgacc 420

gtgtcctccg gtggaggcgg atcaggaggt gggggatcgg gtggaggagg aagcggaggc 480

ggcggttcgg acattcgcgt cacccagtca ccgagctccc tcagcgcatc ggtgggcgac 540

cgggtcacta tcacttgccg ggcgtcccag tcgatctcat cgtatctgaa ttggtaccag 600

cagaaaccgg gaaaggcgcc gaagctgttg atctacgctg ccagctccct gcagtcgggt 660

gtgccatcac gcttttccgg ctcgggatcg ggaaccgatt tcactctgac gatctctagc 720

ctgcagccag aagatttcgc cacttactac tgccagcagt cctacagcat ccctctgact 780

ttcggacaag ggacgaaagt ggagattaag accactaccc cagcaccgag gccacccacc 840

ccggctccta ccatcgcctc ccagcctctg tccctgcgtc cggaggcatg tagacccgca 900

gctggtgggg ccgtgcatac ccggggtctt gacttcgcct gcgatatcta catttgggcc 960

cctctggctg gtacttgcgg ggtcctgctg ctttcactcg tgatcactct ttactgtaag 1020

cgcggtcgga agaagctgct gtacatcttt aagcaaccct tcatgaggcc tgtgcagact 1080

actcaagagg aggacggctg ttcatgccgg ttcccagagg aggaggaagg cggctgcgaa 1140

ctgcgcgtga aattcagccg cagcgcagat gctccagcct acaagcaggg gcagaaccag 1200

ctctacaacg aactcaatct tggtcggaga gaggagtacg acgtgctgga caagcggaga 1260

ggacgggacc cagaaatggg cgggaagccg cgcagaaaga atccccaaga gggcctgtac 1320

aacgagctcc aaaaggataa gatggcagaa gcctatagcg agattggtat gaaaggggaa 1380

cgcagaagag gcaaaggcca cgacggactg taccagggac tcagcaccgc caccaaggac 1440

acctatgacg ctcttcacat gcaggccctg ccgcctcgg 1479

<210> 616
<211> 741
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 616
caagtccaac tcgttcagtc atgggcagaa gtcaagaaac ccggtgcaag cgtcaaagtg 60

tcgtgtaagg cctccggcta cactttcact tcctactaca tgcactgggt gcgccaagcc 120

ccgggacagg gccttgaatg gatgggcatc atcaacccat caggaggttc cacgagctac 180

gcgcagaagt tccaggggag agtgacgatg actagagata cctccacgag caccgtctac 240

atggagctgt cgaatctgcg gtcagaggac actgctgtgt attactgcgc gcgctccccg 300

cgggtgacca ctggctactt tgactactgg ggacaaggga ccctggtgac cgtcagctcg 360

ggaggcggag gatcgggagg tggagggtcc ggtggaggcg gctctggagg aggcgggtcg 420

gacattcaat tgacccagag cccatccacc ctctcagcct cggtgggga tagggtgact 480

atcacttgcc gggcctccca gtcaatttcc agctggctgg cttggtacca gcaaaagcct 540

ggaaaggcac cgaagctcct gatctacaag gcctcatctc tggaatcagg agtgccttcg 600

cgcttcagcg gaagcggctc gggaactgag tttaccctga ccatctcgag cctgcagcca 660

gatgacttcg cgacctatta ctgccagcag tactcgtcct acccgttgac tttcggagga 720

ggtacccgcc tcgaaatcaa a 741

<210> 617
<211> 1473
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 617
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtcc aactcgttca gtcatgggca gaagtcaaga aacccggtgc aagcgtcaaa 120

gtgtcgtgta aggcctccgg ctacactttc acttcctact acatgcactg ggtgcgccaa 180

gccccgggac agggccttga atggatgggc atcatcaacc catcaggagg ttccacgagc 240

tacgcgcaga agttccaggg gagagtgacg atgactagag atacctccac gagcaccgtc 300

tacatggagc tgtcgaatct gcggtcagag gacactgctg tgtattactg cgcgcgctcc 360

ccgcgggtga ccactggcta ctttgactac tggggacaag ggaccctggt gaccgtcagc 420

tcgggaggcg gaggatcggg aggtggaggg tccggtggag gcggctctgg aggaggcggg 480

tcggacattc aattgaccca gagcccatcc accctctcag cctcggtggg ggatagggtg 540

actatcactt gccgggcctc ccagtcaatt tccagctggc tggcttggta ccagcaaaag 600

cctggaaagg caccgaagct cctgatctac aaggcctcat ctctggaatc aggagtgcct 660

tcgcgcttca gcggaagcgg ctcgggaact gagtttaccc tgaccatctc gagcctgcag 720

ccagatgact tcgcgaccta ttactgccag cagtactcgt cctacccgtt gactttcgga 780

ggaggtaccc gcctcgaaat caaaaccact accccagcac cgaggccacc caccccggct 840

cctaccatcg cctcccagcc tctgtccctg cgtccggagg catgtagacc cgcagctggt 900

ggggccgtgc atacccgggg tcttgacttc gcctgcgata tctacatttg ggcccctctg 960

gctggtactt gcggggtcct gctgctttca ctcgtgatca ctctttactg taagcgcggt 1020

cggaagaagc tgctgtacat ctttaagcaa cccttcatga ggcctgtgca gactactcaa 1080

gaggaggacg gctgttcatg ccggttccca gaggaggagg aaggcggctg cgaactgcgc 1140

gtgaaattca gccgcagcgc agatgctcca gcctacaagc aggggcagaa ccagctctac 1200

aacgaactca atcttggtcg gagagaggag tacgacgtgc tggacaagcg gagaggacgg 1260

gacccagaaa tgggcgggaa gccgcgcaga aagaatcccc aagagggcct gtacaacgag 1320

ctccaaaagg ataagatggc agaagcctat agcgagattg gtatgaaagg ggaacgcaga 1380

agaggcaaag gccacgacgg actgtaccag ggactcagca ccgccaccaa ggacacctat 1440

gacgctcttc acatgcaggc cctgccgcct cgg 1473

<210> 618
<211> 759
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 618
caagtccaac tcgtccagtc cggtgcagaa gtcagaaggc caggagcaag cgtgaagatc 60

tcgtgtagag cgtcaggaga caccagcact cgccattaca tccactggct gcgccaggct 120

ccgggccaag ggccggagtg gatgggtgtg atcaacccga ctacgggacc ggctaccgga 180

agccctgcgt acgcacagat gctgcaggga cgggtgacta tgacccgcga tactagcact 240

aggaccgtgt acatggaact ccgctcgttg cggttcgaag ataccgccgt ctactactgc 300

gcccggtccg tggtgggccg aagcgcccct tactacttcg attactgggg acagggcact 360

ctggtgaccg ttagctccgg tgggggaggc tcgggtggag gcggatcggg aggaggaggc 420

agcggtggag ggggatcgga cattcagatg acccagtcac cctcctccct ctcagcctcg 480

gtcggggacc gggtgaccat tacgtgcaga gcctcacaag ggatctcgga ctactccgcc 540

tggtaccagc agaaaccggg aaaagcgcca aagctcctga tctacgccgc gagcaccctg 600

caatcaggag tgccatcgcg cttttctgga tcgggctcag ggactgactt cacgctgact 660

atctcctacc ttcagtccga ggatttcgct acctactact gccaacagta ttactcctat 720

cccctgacct ttggcggagg cactaaggtg gacatcaag 759

<210> 619
<211> 1491
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 619
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtcc aactcgtcca gtccggtgca gaagtcagaa ggccaggagc aagcgtgaag 120

atctcgtgta gagcgtcagg agacaccagc actcgccatt acatccactg gctgcgccag 180

gctccgggcc aagggccgga gtggatgggt gtgatcaacc cgactacggg accggctacc 240

ggaagccctg cgtacgcaca gatgctgcag ggacgggtga ctatgacccg cgatactagc 300

actaggaccg tgtacatgga actccgctcg ttgcggttcg aagataccgc cgtctactac 360

tgcgcccggt ccgtggtggg ccgaagcgcc ccttactact tcgattactg gggacagggc 420

actctggtga ccgttagctc cggtggggga ggctcgggtg gaggcggatc gggaggagga 480

ggcagcggtg gaggggggatc ggacattcag atgacccagt caccctcctc cctctcagcc 540

tcggtcgggg accgggtgac cattacgtgc agagcctcac aagggatctc ggactactcc 600

gcctggtacc agcagaaacc gggaaaagcg ccaaagctcc tgatctacgc cgcgagcacc 660

ctgcaatcag gagtgccatc gcgcttttct ggatcgggct cagggactga cttcacgctg 720

actatctcct accttcagtc cgaggatttc gctacctact actgccaaca gtattactcc 780

tatcccctga cctttggcgg aggcactaag gtggacatca agaccactac cccagcaccg 840

aggccaccca ccccggctcc taccatcgcc tcccagcctc tgtccctgcg tccggaggca 900

tgtagacccg cagctggtgg ggccgtgcat acccggggtc ttgacttcgc ctgcgatatc 960

tacatttggg cccctctggc tggtacttgc ggggtcctgc tgctttcact cgtgatcact 1020

ctttactgta agcgcggtcg gaagaagctg ctgtacatct ttaagcaacc cttcatgagg 1080

cctgtgcaga ctactcaaga ggaggacggc tgttcatgcc ggttcccaga ggaggaggaa 1140

ggcggctgcg aactgcgcgt gaaattcagc cgcagcgcag atgctccagc ctacaagcag 1200

gggcagaacc agctctacaa cgaactcaat cttggtcgga gagaggagta cgacgtgctg 1260

gacaagcgga gaggacggga cccagaaatg ggcgggaagc cgcgcagaaa gaatccccaa 1320

gagggcctgt acaacgagct ccaaaaggat aagatggcag aagcctatag cgagattggt 1380

atgaaagggg aacgcagaag aggcaaaggc cacgacggac tgtaccaggg actcagcacc 1440

gccaccaagg acacctatga cgctcttcac atgcaggccc tgccgcctcg g 1491

<210> 620
<211> 747
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 620
caagtccaac tccagcaatc gggagcagaa gtcaagaaac caggcgcatc ggtgaaagtg 60

tcgtgtaagg cgtcagggta caccttcacc aactactata tgcactgggt gcgccaggct 120

ccaggccagg ggttggagtg gatggggatc atcaatccgt caggtggcta caccacttac 180

gctcagaagt tccagggacg cctcactatg actcgcgata ctagcacctc cacggtgtac 240

atggaactgt catcgctgag gtccgaagat accgccgtct actactgcgc acggatcaga 300

tcctgcggag gagattgtta ctactttgac aactggggac agggcaccct tgttactgtg 360

tcatcgggag gaggggggaag cggaggaggt ggatcaggcg gcggtggcag cgggggcgga 420

ggatcggaca ttcagctgac tcagtccccc tccactttgt cggccagcgt gggagacaga 480

gtgaccatca cttgccgggc gtccgagaac gtcaatatct ggctggcctg gtaccagcaa 540

aagcctggaa aagccccgaa gctgctcatc tataagtcat ccagcctggc gtctggtgtg 600

ccgtcgcggt tctccggcag cgggagcgga gccgagttca ctctcaccat ttcgagcctt 660

caaccggacg atttcgccac ctactactgc cagcagtacc aatcctaccc tctgacgttt 720

ggaggtggaa ccaaggtgga catcaag 747

<210> 621
<211> 1479
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 621
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtcc aactccagca atcgggagca gaagtcaaga aaccaggcgc atcggtgaaa 120

gtgtcgtgta aggcgtcagg gtacaccttc accaactact atatgcactg ggtgcgccag 180

gctccaggcc aggggttgga gtggatgggg atcatcaatc cgtcaggtgg ctacaccact 240

tacgctcaga agttccaggg acgcctcact atgactcgcg atactagcac ctccacggtg 300

tacatggaac tgtcatcgct gaggtccgaa gataccgccg tctactactg cgcacggatc 360

agatcctgcg gaggagattg ttactacttt gacaactggg gacagggcac ccttgttact 420

gtgtcatcgg gaggaggggg aagcggagga ggtggatcag gcggcggtgg cagcgggggc 480

ggaggatcgg acattcagct gactcagtcc ccctccactt tgtcggccag cgtgggagac 540

agagtgacca tcacttgccg ggcgtccgag aacgtcaata tctggctggc ctggtaccag 600

caaaagcctg gaaaagcccc gaagctgctc atctataagt catccagcct ggcgtctggt 660

gtgccgtcgc ggttctccgg cagcgggagc ggagccgagt tcactctcac catttcgagc 720

cttcaaccgg acgatttcgc cacctactac tgccagcagt accaatccta ccctctgacg 780

tttggaggtg gaaccaaggt ggacatcaag accactaccc cagcaccgag gccacccacc 840

ccggctccta ccatcgcctc ccagcctctg tccctgcgtc cggaggcatg tagacccgca 900

gctggtgggg ccgtgcatac ccggggtctt gacttcgcct gcgatatcta catttgggcc 960

cctctggctg gtacttgcgg ggtcctgctg ctttcactcg tgatcactct ttactgtaag 1020

cgcggtcgga agaagctgct gtacatcttt aagcaaccct tcatgaggcc tgtgcagact 1080

actcaagagg aggacggctg ttcatgccgg ttcccagagg aggaggaagg cggctgcgaa 1140

ctgcgcgtga aattcagccg cagcgcagat gctccagcct acaagcaggg gcagaaccag 1200

ctctacaacg aactcaatct tggtcggaga gaggagtacg acgtgctgga caagcggaga 1260

ggacgggacc cagaaatggg cgggaagccg cgcagaaaga atccccaaga gggcctgtac 1320

aacgagctcc aaaaggataa gatggcagaa gcctatagcg agattggtat gaaaggggaa 1380

cgcagaagag gcaaaggcca cgacggactg taccagggac tcagcaccgc caccaaggac 1440

acctatgacg ctcttcacat gcaggccctg ccgcctcgg 1479

<210> 622
<211> 738
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 622
caaatcactc tgaaagaatc tggaccggcc ctggttaagc cgactcaaac gctcaccctt 60

acttgcacct tcagcggatt ctcactcagc actgctggtg tgcacgtcgg atggattaga 120

cagccgcctg gaaaggccct ggaatggctc gccctcatct cctgggccga tgacaagaga 180

tacaggccct cgcttcgatc ccggttggac attacccggg tgacctcgaa agatcaggtg 240

gtgctctcaa tgaccaatat gcagccggag gacaccgcta cgtactactg cgcactgcaa 300

ggatttgacg gctacgaggc taactgggga ccaggtactc tggtcaccgt gagctccggc 360

gggggaggat caggcggggg ggggtcagga ggcggaggct ccggtggagg aggatcggat 420

atcgtcatga cccagtcccc aagctcgctg agcgcgtcag cgggcgaccg cgtgactatc 480

acttgccggg ccagccgcgg catctcctcc gcactggcgt ggtaccagca gaagcctgga 540

aaaccgccaa agctcctgat ctatgatgcc tccagcctgg agtcaggtgt ccccagccgc 600

ttctcgggtt cgggctcggg aaccgacttc actttgacca tcgactcgct ggaaccggaa 660

gatttcgcaa cctactactg tcagcagtcc tactcgaccc cttggacttt tggacaaggg 720

acgaaggtgg acatcaag 738

<210> 623
<211> 1470
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 623
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaaatca ctctgaaaga atctggaccg gccctggtta agccgactca aacgctcacc 120

cttacttgca ccttcagcgg attctcactc agcactgctg gtgtgcacgt cggatggatt 180

agacagccgc ctggaaaggc cctggaatgg ctcgccctca tctcctgggc cgatgacaag 240

agatacaggc cctcgcttcg atcccggttg gacattaccc gggtgacctc gaaagatcag 300

gtggtgctct caatgaccaa tatgcagccg gaggacaccg ctacgtacta ctgcgcactg 360

caaggatttg acggctacga ggctaactgg ggaccaggta ctctggtcac cgtgagctcc 420

ggcgggggag gatcaggcgg gggggggtca ggaggcggag gctccggtgg aggaggatcg 480

gatatcgtca tgacccagtc cccaagctcg ctgagcgcgt cagcgggcga ccgcgtgact 540

atcacttgcc gggccagccg cggcatctcc tccgcactgg cgtggtacca gcagaagcct 600

ggaaaaccgc caaagctcct gatctatgat gcctccagcc tggagtcagg tgtccccagc 660

cgcttctcgg gttcgggctc gggaaccgac ttcactttga ccatcgactc gctggaaccg 720

gaagatttcg caacctacta ctgtcagcag tcctactcga ccccttggac ttttggacaa 780

gggacgaagg tggacatcaa gaccactacc ccagcaccga ggccacccac cccggctcct 840

accatcgcct cccagcctct gtccctgcgt ccggaggcat gtagacccgc agctggtggg 900

gccgtgcata cccggggtct tgacttcgcc tgcgatatct acatttgggc ccctctggct 960

ggtacttgcg gggtcctgct gctttcactc gtgatcactc tttactgtaa gcgcggtcgg 1020

aagaagctgc tgtacatctt taagcaaccc ttcatgaggc ctgtgcagac tactcaagag 1080

gaggacggct gttcatgccg gttcccagag gaggaggaag gcggctgcga actgcgcgtg 1140

aaattcagcc gcagcgcaga tgctccagcc tacaagcagg ggcagaacca gctctacaac 1200

gaactcaatc ttggtcggag agaggagtac gacgtgctgg acaagcggag aggacgggac 1260

ccagaaatgg gcgggaagcc gcgcagaaag aatccccaag agggcctgta caacgagctc 1320

caaaaggata agatggcaga agcctatagc gagattggta tgaaagggga acgcagaaga 1380

ggcaaaggcc acgacggact gtaccaggga ctcagcaccg ccaccaagga cacctatgac 1440

gctcttcaca tgcaggccct gccgcctcgg 1470

<210> 624
<211> 717
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 624
caagtccagc tccagcagtc gggcccagag ttggagaagc ctggggcgag cgtgaagatc 60

tcatgcaaag cctcaggcta ctcctttact ggatacacga tgaattgggt gaaacagtcg 120

catggaaagt cactggaatg gatcggtctg attacgccct acaacggcgc ctccagctac 180

aaccagaagt tcaggggaaa ggcgaccctt actgtcgaca agtcgtcaag caccgcctac 240

atggacctcc tgtccctgac ctccgaagat agcgcggtct acttttgtgc acgcggaggt 300

tacgatggac ggggattcga ctactggggc cagggaacca ctgtcaccgt gtcgagcgga 360

ggcggaggga gcggaggagg aggcagcgga ggtggagggt cggatatcga actcactcag 420

tccccagcaa tcatgtccgc ttcaccggga gaaaaggtga ccatgacttg ctcggcctcc 480

tcgtccgtgt catacatgca ctggtaccaa caaaaatcgg ggacctcccc taagagatgg 540

atctacgata ccagcaaact ggcttcaggc gtgccgggac gcttctcggg ttcggggagc 600

ggaaattcgt attcgttgac catttcgtcc gtggaagccg aggacgacgc aacttattac 660

tgccaacagt ggtcaggcta cccgctcact ttcggagccg gcactaagct ggagatc 717

<210> 625
<211> 1149
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 625
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtcc agctccagca gtcgggccca gagttggaga agcctggggc gagcgtgaag 120

atctcatgca aagcctcagg ctactccttt actggataca cgatgaattg ggtgaaacag 180

tcgcatggaa agtcactgga atggatcggt ctgattacgc cctacaacgg cgcctccagc 240

tacaaccaga agttcagggg aaaggcgacc cttactgtcg acaagtcgtc aagcaccgcc 300

tacatggacc tcctgtccct gacctccgaa gatagcgcgg tctacttttg tgcacgcgga 360

ggttacgatg gacggggatt cgactactgg ggccagggaa ccactgtcac cgtgtcgagc 420

ggaggcggag ggagcggagg aggaggcagc ggaggtggag ggtcggatat cgaactcact 480

cagtccccag caatcatgtc cgcttcaccg ggagaaaagg tgaccatgac ttgctcggcc 540

tcctcgtccg tgtcatacat gcactggtac caacaaaaat cggggacctc ccctaagaga 600

tggatctacg ataccagcaa actggcttca ggcgtgccgg gacgcttctc gggttcgggg 660

agcggaaatt cgtattcgtt gaccatttcg tccgtggaag ccgaggacga cgcaacttat 720

tactgccaac agtggtcagg ctacccgctc actttcggag ccggcactaa gctggagatc 780

accactaccc cagcaccgag gccacccacc ccggctccta ccatcgcctc ccagcctctg 840

tccctgcgtc cggaggcatg tagacccgca gctggtgggg ccgtgcatac ccggggtctt 900

gacttcgcct gcgatatcta catttgggcc cctctggctg gtacttgcgg ggtcctgctg 960

ctttcactcg tgatcactct ttactgtaag cgcggtcgga agaagctgct gtacatcttt 1020

aagcaaccct tcatgaggcc tgtgcagact actcaagagg aggacggctg ttcatgccgg 1080

ttcccagagg aggaggaagg cggctgcgaa ctgcgcgtga aattcagccg cagcgcagat 1140

gctccagcc 1149

<210> 626
<211> 249
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 626

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Thr Phe Ser Asn Tyr
20 25 30

Trp Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Ala Thr Tyr Arg Gly His Ser Asp Thr Tyr Tyr Asn Gln Lys Phe
50 55 60

Lys Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Ala Ile Tyr Asn Gly Tyr Asp Val Leu Asp Asn Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
115 120 125

```
                                                _SL
Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln
    130                 135                 140

Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
145                 150                 155                 160

Thr Ile Thr Cys Ser Ala Ser Gln Asp Ile Ser Asn Tyr Leu Asn Trp
                165                 170                 175

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Tyr Thr
            180                 185                 190

Ser Asn Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser
        195                 200                 205

Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe
    210                 215                 220

Ala Thr Tyr Tyr Cys Gln Gln Tyr Arg Lys Leu Pro Trp Thr Phe Gly
225                 230                 235                 240

Gln Gly Thr Lys Leu Glu Ile Lys Arg
                245
```

<210> 627
<211> 249
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 627

```
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Ser Ala Ser Gln Asp Ile Ser Asn Tyr
            20                  25                  30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Tyr Thr Ser Asn Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
```

_SL
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Arg Lys Leu Pro Trp
85 90 95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg Gly Gly Gly Gly
100 105 110

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
130 135 140

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Thr Phe Ser Asn Tyr
145 150 155 160

Trp Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
165 170 175

Gly Ala Thr Tyr Arg Gly His Ser Asp Thr Tyr Tyr Asn Gln Lys Phe
180 185 190

Lys Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
195 200 205

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
210 215 220

Ala Arg Gly Ala Ile Tyr Asn Gly Tyr Asp Val Leu Asp Asn Trp Gly
225 230 235 240

Gln Gly Thr Leu Val Thr Val Ser Ser
245

<210> 628
<211> 239
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 628
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe Ala Leu Ser Asn His
20 25 30

_SL
Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45

Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr Ala Ala Ser Val Lys
    50   55   60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg Asn Thr Leu Tyr Leu
65   70   75   80

Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Ile Tyr Tyr Cys Ser
                85   90   95

Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln Gly Thr Thr Val Thr
            100   105   110

Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly Gly Arg Ala Ser Gly
        115   120   125

Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser
    130   135   140

Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser
145   150   155   160

Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro
                165   170   175

Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser
            180   185   190

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
        195   200   205

Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr
    210   215   220

Ser Thr Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
225   230   235

<210> 629
<211> 717
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 629

_SL

gaagtgcaat tggtggaatc agggggagga cttgtgcagc ctggaggatc gctgagactg 60

tcatgtgccg tgtccggctt tgccctgtcc aaccacggga tgtcctgggt ccgccgcgcg 120

cctggaaagg gcctcgaatg ggtgtcgggt attgtgtaca gcggtagcac ctactatgcc 180

gcatccgtga aggggagatt caccatcagc cgggacaact ccaggaacac tctgtacctc 240

caaatgaatt cgctgaggcc agaggacact gccatctact actgctccgc gcatggcgga 300

gagtccgacg tctggggaca ggggaccacc gtgaccgtgt ctagcgcgtc cggcggaggc 360

ggcagcgggg gtcgggcatc agggggcggc ggatcggaca tccagctcac ccagtccccg 420

agctcgctgt ccgcctccgt gggagatcgg gtcaccatca cgtgccgcgc cagccagtcg 480

atttcctcct acctgaactg gtaccaacag aagcccggaa aagccccgaa gcttctcatc 540

tacgccgcct cgagcctgca gtcaggagtg ccctcacggt tctccggctc cggttccggt 600

actgatttca ccctgaccat ttcctccctg caaccggagg acttcgctac ttactactgc 660

cagcagtcgt actccacccc ctacactttc ggacaaggca ccaaggtcga aatcaag 717

<210> 630
<211> 115
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 630

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe Ala Leu Ser Asn His
20 25 30

Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr Ala Ala Ser Val Lys
50 55 60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg Asn Thr Leu Tyr Leu
65 70 75 80

Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Ile Tyr Tyr Cys Ser
85 90 95

Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser
        115

<210> 631
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 631
Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1   5   10   15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr
            20   25   30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35   40   45

Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Tyr
                85   90   95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
            100   105

<210> 632
<211> 483
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 632
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1   5   10   15

His Ala Ala Arg Pro Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
            20   25   30

```
                                                    _SL
Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe
        35                  40                  45

Ala Leu Ser Asn His Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys
    50                  55                  60

Gly Leu Glu Trp Val Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr
65                  70                  75                  80

Ala Ala Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg
                85                  90                  95

Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala
            100                 105                 110

Ile Tyr Tyr Cys Ser Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln
        115                 120                 125

Gly Thr Thr Val Thr Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly
    130                 135                 140

Gly Arg Ala Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser
145                 150                 155                 160

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
                165                 170                 175

Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys
            180                 185                 190

Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln
        195                 200                 205

Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
    210                 215                 220

Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr
225                 230                 235                 240

Cys Gln Gln Ser Tyr Ser Thr Pro Tyr Thr Phe Gly Gln Gly Thr Lys
                245                 250                 255

Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala
            260                 265                 270

Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg
        275                 280                 285
```

```
Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys
    290                 295                 300

Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu
305                 310                 315                 320

Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu
                325                 330                 335

Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln
            340                 345                 350

Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly
        355                 360                 365

Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr
    370                 375                 380

Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg
385                 390                 395                 400

Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met
                405                 410                 415

Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu
            420                 425                 430

Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys
        435                 440                 445

Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu
    450                 455                 460

Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu
465                 470                 475                 480

Pro Pro Arg
```

<210> 633
<211> 1449
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 633
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaagtgc aattggtgga atcaggggga ggacttgtgc agcctggagg atcgctgaga 120

ctgtcatgtg ccgtgtccgg ctttgccctg tccaaccacg ggatgtcctg ggtccgccgc 180

gcgcctggaa agggcctcga atgggtgtcg ggtattgtgt acagcggtag cacctactat 240

gccgcatccg tgaaggggag attcaccatc agccgggaca actccaggaa cactctgtac 300

ctccaaatga attcgctgag gccagaggac actgccatct actactgctc cgcgcatggc 360

ggagagtccg acgtctgggg acaggggacc accgtgaccg tgtctagcgc gtccggcgga 420

ggcggcagcg ggggtcgggc atcaggggc ggcggatcgg acatccagct cacccagtcc 480

ccgagctcgc tgtccgcctc cgtgggagat cgggtcacca tcacgtgccg cgccagccag 540

tcgatttcct cctacctgaa ctggtaccaa cagaagcccg gaaaagcccc gaagcttctc 600

atctacgccg cctcgagcct gcagtcagga gtgccctcac ggttctccgg ctccggttcc 660

ggtactgatt tcaccctgac catttcctcc ctgcaaccgg aggacttcgc tacttactac 720

tgccagcagt cgtactccac cccctacact ttcggacaag gcaccaaggt cgaaatcaag 780

accactaccc cagcaccgag gccacccacc ccggctccta ccatcgcctc ccagcctctg 840

tccctgcgtc cggaggcatg tagacccgca gctggtgggg ccgtgcatac ccggggtctt 900

gacttcgcct gcgatatcta catttgggcc cctctggctg gtacttgcgg ggtcctgctg 960

ctttcactcg tgatcactct ttactgtaag cgcggtcgga agaagctgct gtacatcttt 1020

aagcaaccct tcatgaggcc tgtgcagact actcaagagg aggacggctg ttcatgccgg 1080

ttcccagagg aggaggaagg cggctgcgaa ctgcgcgtga aattcagccg cagcgcagat 1140

gctccagcct acaagcaggg gcagaaccag ctctacaacg aactcaatct tggtcggaga 1200

gaggagtacg acgtgctgga caagcggaga ggacgggacc cagaaatggg cgggaagccg 1260

cgcagaaaga atccccaaga gggcctgtac aacgagctcc aaaaggataa gatggcagaa 1320

gcctatagcg agattggtat gaaaggggaa cgcagaagag gcaaaggcca cgacggactg 1380

taccagggac tcagcaccgc caccaaggac acctatgacg ctcttcacat gcaggccctg 1440

ccgcctcgg 1449

<210> 634
<211> 246
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 634

```
                                                    _SL
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asn Tyr
            20                  25                  30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Gly Trp Val
        35                  40                  45

Ser Gly Ile Ser Arg Ser Gly Glu Asn Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Asp Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ser Pro Ala His Tyr Tyr Gly Gly Met Asp Val Trp Gly Gln
            100                 105                 110

Gly Thr Thr Val Thr Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Arg Ala Ser Gly Gly Gly Gly Ser Asp Ile Val Leu Thr Gln Ser
    130                 135                 140

Pro Gly Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
145                 150                 155                 160

Arg Ala Ser Gln Ser Ile Ser Ser Ser Phe Leu Ala Trp Tyr Gln Gln
                165                 170                 175

Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Arg Arg
            180                 185                 190

Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
        195                 200                 205

Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu Asp Ser Ala Val Tyr
    210                 215                 220

Tyr Cys Gln Gln Tyr His Ser Ser Pro Ser Trp Thr Phe Gly Gln Gly
225                 230                 235                 240

Thr Lys Leu Glu Ile Lys
                245
```

<210> 635
<211> 738
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 635
caagtgcaac tcgtggaatc tggtggagga ctcgtgcaac ccggaagatc gcttagactg 60

tcgtgtgccg ccagcgggtt cactttctcg aactacgcga tgtcctgggt ccgccaggca 120

cccggaaagg gactcggttg ggtgtccggc atttcccggt ccggcgaaaa tacctactac 180

gccgactccg tgaagggccg cttcaccatc tcaagggaca acagcaaaaa caccctgtac 240

ttgcaaatga actccctgcg ggatgaagat acagccgtgt actattgcgc ccggtcgcct 300

gcccattact acggcggaat ggacgtctgg ggacagggaa ccactgtgac tgtcagcagc 360

gcgtcgggtg gcggcggctc aggggtcgg gcctccgggg ggggagggtc cgacatcgtg 420

ctgacccagt ccccgggaac cctgagcctg agcccgggag agcgcgcgac cctgtcatgc 480

cgggcatccc agagcattag ctcctccttt ctcgcctggt atcagcagaa gcccggacag 540

gccccgaggc tgctgatcta cggcgctagc agaagggcta ccggaatccc agaccggttc 600

tccggctccg gttccgggac cgatttcacc cttactatct cgcgcctgga acctgaggac 660

tccgccgtct actactgcca gcagtaccac tcatccccgt cgtggacgtt cggacagggc 720

accaagctgg agattaag 738

<210> 636
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 636
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asn Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Gly Trp Val
35 40 45

Ser Gly Ile Ser Arg Ser Gly Glu Asn Thr Tyr Tyr Ala Asp Ser Val

_SL
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Asp Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Pro Ala His Tyr Tyr Gly Gly Met Asp Val Trp Gly Gln
100 105 110

Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 637
<211> 109
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 637
Asp Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Ile Ser Ser Ser
20 25 30

Phe Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45

Ile Tyr Gly Ala Ser Arg Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
50 55 60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65 70 75 80

Pro Glu Asp Ser Ala Val Tyr Tyr Cys Gln Gln Tyr His Ser Ser Pro
85 90 95

Ser Trp Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 638
<211> 490
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 638
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu
20 25 30

Val Gln Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
35 40 45

Thr Phe Ser Asn Tyr Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys
50 55 60

Gly Leu Gly Trp Val Ser Gly Ile Ser Arg Ser Gly Glu Asn Thr Tyr
65 70 75 80

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser
85 90 95

Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Asp Glu Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Ala Arg Ser Pro Ala His Tyr Tyr Gly Gly Met
115 120 125

Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Gly
130 135 140

Gly Gly Gly Ser Gly Gly Arg Ala Ser Gly Gly Gly Gly Ser Asp Ile
145 150 155 160

Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly Glu Arg
165 170 175

Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Ile Ser Ser Ser Phe Leu
180 185 190

Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr
195 200 205

Gly Ala Ser Arg Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly Ser
210 215 220

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu

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225 230 235 240

Asp Ser Ala Val Tyr Tyr Cys Gln Gln Tyr His Ser Ser Pro Ser Trp
245 250 255

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Thr Thr Thr Pro Ala
260 265 270

Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser
275 280 285

Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr
290 295 300

Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala
305 310 315 320

Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys
325 330 335

Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met
340 345 350

Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe
355 360 365

Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg
370 375 380

Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn
385 390 395 400

Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg
405 410 415

Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro
420 425 430

Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala
435 440 445

Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His
450 455 460

Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp
465 470 475 480

_SL
Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 639
<211> 1470
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 639
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtgc aactcgtgga atctggtgga ggactcgtgc aacccggaag atcgcttaga 120

ctgtcgtgtg ccgccagcgg gttcactttc tcgaactacg cgatgtcctg ggtccgccag 180

gcacccggaa agggactcgg ttgggtgtcc ggcatttccc ggtccggcga aaatacctac 240

tacgccgact ccgtgaaggg ccgcttcacc atctcaaggg acaacagcaa aaacaccctg 300

tacttgcaaa tgaactccct gcgggatgaa gatacagccg tgtactattg cgcccggtcg 360

cctgcccatt actacggcgg aatggacgtc tggggacagg gaaccactgt gactgtcagc 420

agcgcgtcgg gtggcggcgg ctcaggggggt cgggcctccg gggggggagg gtccgacatc 480

gtgctgaccc agtccccggg aaccctgagc ctgagcccgg gagagcgcgc gaccctgtca 540

tgccgggcat cccagagcat tagctcctcc tttctcgcct ggtatcagca gaagcccgga 600

caggccccga ggctgctgat ctacggcgct agcagaaggg ctaccggaat cccagaccgg 660

ttctccggct ccggttccgg gaccgatttc acccttacta tctcgcgcct ggaacctgag 720

gactccgccg tctactactg ccagcagtac cactcatccc cgtcgtggac gttcggacag 780

ggcaccaagc tggagattaa gaccactacc ccagcaccga ggccacccac cccggctcct 840

accatcgcct cccagcctct gtccctgcgt ccggaggcat gtagacccgc agctggtggg 900

gccgtgcata cccggggtct tgacttcgcc tgcgatatct acatttgggc ccctctggct 960

ggtacttgcg gggtcctgct gctttcactc gtgatcactc tttactgtaa gcgcggtcgg 1020

aagaagctgc tgtacatctt taagcaaccc ttcatgaggc ctgtgcagac tactcaagag 1080

gaggacggct gttcatgccg gttcccagag gaggaggaag gcggctgcga actgcgcgtg 1140

aaattcagcc gcagcgcaga tgctccagcc tacaagcagg ggcagaacca gctctacaac 1200

gaactcaatc ttggtcggag agaggagtac gacgtgctgg acaagcggag aggacgggac 1260

ccagaaatgg gcgggaagcc gcgcagaaag aatccccaag agggcctgta caacgagctc 1320

caaaaggata agatggcaga agcctatagc gagattggta tgaaagggga acgcagaaga 1380

ggcaaaggcc acgacggact gtaccaggga ctcagcaccg ccaccaagga cacctatgac 1440

gctcttcaca tgcaggccct gccgcctcgg 1470

<210> 640
<211> 244
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 640
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
20 25 30

Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Gly Ile Ser Trp Asn Ser Gly Ser Ile Gly Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Leu Tyr Tyr Cys
85 90 95

Ser Val His Ser Phe Leu Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly Gly Arg Ala Ser Gly
115 120 125

Gly Gly Gly Ser Asp Ile Val Met Thr Gln Thr Pro Leu Ser Leu Pro
130 135 140

Val Thr Pro Gly Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser
145 150 155 160

Leu Leu His Ser Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys
165 170 175

Pro Gly Gln Ser Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala
180 185 190

Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe

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195 200 205

Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr
210 215 220

Cys Met Gln Ala Leu Gln Thr Pro Tyr Thr Phe Gly Gln Gly Thr Lys
225 230 235 240

Val Glu Ile Lys

<210> 641
<211> 732
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 641
caagtgcaac tcgtcgaatc cggtggaggt ctggtccaac ctggtagaag cctgagactg 60

tcgtgtgcgg ccagcggatt cacctttgat gactatgcta tgcactgggt gcggcaggcc 120

ccaggaaagg gcctggaatg ggtgtcggga attagctgga actccgggtc cattggctac 180

gccgactccg tgaagggccg cttcaccatc tcccgcgaca acgcaaagaa ctccctgtac 240

ttgcaaatga actcgctcag ggctgaggat accgcgctgt actactgctc cgtgcattcc 300

ttcctggcct actggggaca gggaactctg gtcaccgtgt cgagcgcctc cggcggcggg 360

ggctcgggtg gacgggcctc gggcggaggg gggtccgaca tcgtgatgac ccagaccccg 420

ctgagcttgc ccgtgactcc cggagagcct gcatccatct cctgccggtc atcccagtcc 480

cttctccact ccaacggata caactacctc gactggtacc tccagaagcc gggacagagc 540

cctcagcttc tgatctacct ggggtcaaat agagcctcag gagtgccgga tcggttcagc 600

ggatctggtt cgggaactga tttcactctg aagatttccc gcgtggaagc cgaggacgtg 660

ggcgtctact actgtatgca ggcgctgcag acccccctata ccttcggcca agggacgaaa 720

gtggagatca ag 732

<210> 642
<211> 115
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 642
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
20 25 30

Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Gly Ile Ser Trp Asn Ser Gly Ser Ile Gly Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Leu Tyr Tyr Cys
85 90 95

Ser Val His Ser Phe Leu Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser
115

<210> 643
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 643
Asp Ile Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser
20 25 30

Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala
85 90 95

Leu Gln Thr Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 644
<211> 488
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 644
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu
20 25 30

Val Gln Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
35 40 45

Thr Phe Asp Asp Tyr Ala Met His Trp Val Arg Gln Ala Pro Gly Lys
50 55 60

Gly Leu Glu Trp Val Ser Gly Ile Ser Trp Asn Ser Gly Ser Ile Gly
65 70 75 80

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala
85 90 95

Lys Asn Ser Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
100 105 110

Ala Leu Tyr Tyr Cys Ser Val His Ser Phe Leu Ala Tyr Trp Gly Gln
115 120 125

Gly Thr Leu Val Thr Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly
130 135 140

Gly Arg Ala Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln Thr
145 150 155 160

Pro Leu Ser Leu Pro Val Thr Pro Gly Glu Pro Ala Ser Ile Ser Cys
165 170 175

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Arg Ser Ser Gln Ser Leu Leu His Ser Asn Gly Tyr Asn Tyr Leu Asp
            180                 185                 190

Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Gln Leu Leu Ile Tyr Leu
        195                 200                 205

Gly Ser Asn Arg Ala Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly
    210                 215                 220

Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp
225                 230                 235                 240

Val Gly Val Tyr Tyr Cys Met Gln Ala Leu Gln Thr Pro Tyr Thr Phe
                245                 250                 255

Gly Gln Gly Thr Lys Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg
            260                 265                 270

Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg
        275                 280                 285

Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly
    290                 295                 300

Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr
305                 310                 315                 320

Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg
                325                 330                 335

Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro
            340                 345                 350

Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu
        355                 360                 365

Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala
    370                 375                 380

Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu
385                 390                 395                 400

Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly
                405                 410                 415

Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu
            420                 425                 430
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Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser
435 440 445

Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly
450 455 460

Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu
465 470 475 480

His Met Gln Ala Leu Pro Pro Arg
485

<210> 645
<211> 1464
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 645
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtgc aactcgtcga atccggtgga ggtctggtcc aacctggtag aagcctgaga 120

ctgtcgtgtg cggccagcgg attcaccttt gatgactatg ctatgcactg ggtgcggcag 180

gccccaggaa agggcctgga atgggtgtcg ggaattagct ggaactccgg gtccattggc 240

tacgccgact ccgtgaaggg ccgcttcacc atctcccgcg acaacgcaaa gaactccctg 300

tacttgcaaa tgaactcgct cagggctgag gataccgcgc tgtactactg ctccgtgcat 360

tccttcctgg cctactgggg acagggaact ctggtcaccg tgtcgagcgc ctccggcggc 420

gggggctcgg gtggacgggc ctcgggcgga ggggggtccg acatcgtgat gacccagacc 480

ccgctgagct tgcccgtgac tcccggagag cctgcatcca tctcctgccg gtcatcccag 540

tcccttctcc actccaacgg atacaactac ctcgactggt acctccagaa gccgggacag 600

agccctcagc ttctgatcta cctggggtca aatagagcct caggagtgcc ggatcggttc 660

agcggatctg gttcgggaac tgatttcact ctgaagattt cccgcgtgga agccgaggac 720

gtgggcgtct actactgtat gcaggcgctg cagacccccc ataccttcgg ccaagggacg 780

aaagtggaga tcaagaccac taccccagca ccgaggccac ccaccccggc tcctaccatc 840

gcctcccagc ctctgtccct gcgtccggag gcatgtagac ccgcagctgg tggggccgtg 900

catacccggg gtcttgactt cgcctgcgat atctacattt gggcccctct ggctggtact 960

tgcggggtcc tgctgctttc actcgtgatc actctttact gtaagcgcgg tcggaagaag 1020

_SL

ctgctgtaca tctttaagca acccttcatg aggcctgtgc agactactca agaggaggac 1080

ggctgttcat gccggttccc agaggaggag gaaggcggct gcgaactgcg cgtgaaattc 1140

agccgcagcg cagatgctcc agcctacaag caggggcaga accagctcta caacgaactc 1200

aatcttggtc ggagagagga gtacgacgtg ctggacaagc ggagaggacg ggacccagaa 1260

atgggcggga agccgcgcag aaagaatccc caagagggcc tgtacaacga gctccaaaag 1320

gataagatgg cagaagccta tagcgagatt ggtatgaaag gggaacgcag aagaggcaaa 1380

ggccacgacg gactgtacca gggactcagc accgccacca aggacaccta tgacgctctt 1440

cacatgcagg ccctgccgcc tcgg 1464

<210> 646
<211> 243
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 646

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe Ala Leu Ser Asn His
20 25 30

Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr Ala Ala Ser Val Lys
50 55 60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg Asn Thr Leu Tyr Leu
65 70 75 80

Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Ile Tyr Tyr Cys Ser
85 90 95

Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly Gly Arg Ala Ser Gly
115 120 125

Gly Gly Gly Ser Asp Ile Val Met Thr Gln Thr Pro Leu Ser Leu Ser
130 135 140

Val Thr Pro Gly Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser Gln Ser
145 150 155 160

Leu Leu Arg Asn Asp Gly Lys Thr Pro Leu Tyr Trp Tyr Leu Gln Lys
165 170 175

Ala Gly Gln Pro Pro Gln Leu Leu Ile Tyr Glu Val Ser Asn Arg Phe
180 185 190

Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
195 200 205

Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Val Gly Ala Tyr Tyr
210 215 220

Cys Met Gln Asn Ile Gln Phe Pro Ser Phe Gly Gly Gly Thr Lys Leu
225 230 235 240

Glu Ile Lys

<210> 647
<211> 729
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 647
gaagtgcaat tgttggaatc tggaggagga cttgtgcagc ctggaggatc actgagactt 60

tcgtgtgcgg tgtcaggctt cgccctgagc aaccacggca tgagctgggt gcggagagcc 120

ccggggaagg gtctggaatg ggtgtccggg atcgtctact ccggttcaac ttactacgcc 180

gcaagcgtga agggtcgctt caccatttcc cgcgataact cccggaacac cctgtacctc 240

caaatgaact ccctgcggcc cgaggacacc gccatctact actgttccgc gcatggagga 300

gagtccgatg tctggggaca gggcactacc gtgaccgtgt cgagcgcctc ggggggagga 360

ggctccggcg gtcgcgcctc cggggggggt ggcagcgaca ttgtgatgac gcagactcca 420

ctctcgctgt ccgtgacccc gggacagccc gcgtccatct cgtgcaagag ctcccagagc 480

ctgctgagga acgacggaaa gactcctctg tattggtacc tccagaaggc tggacagccc 540

ccgcaactgc tcatctacga agtgtcaaat cgcttctccg gggtgccgga tcggttttcc 600

ggctcgggat cgggcaccga cttcaccctg aaaatctcca gggtcgaggc cgaggacgtg 660

ggagcctact actgcatgca aaacatccag ttcccttcct tcggcggcgg cacaaagctg 720

gagattaag 729

<210> 648
<211> 115
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 648
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe Ala Leu Ser Asn His
20 25 30

Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr Ala Ala Ser Val Lys
50 55 60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg Asn Thr Leu Tyr Leu
65 70 75 80

Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Ile Tyr Tyr Cys Ser
85 90 95

Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser
115

<210> 649
<211> 111
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 649
Asp Ile Val Met Thr Gln Thr Pro Leu Ser Leu Ser Val Thr Pro Gly
1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser Gln Ser Leu Leu Arg Asn

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20 25 30

Asp Gly Lys Thr Pro Leu Tyr Trp Tyr Leu Gln Lys Ala Gly Gln Pro
35 40 45

Pro Gln Leu Leu Ile Tyr Glu Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Ala Tyr Tyr Cys Met Gln Asn
85 90 95

Ile Gln Phe Pro Ser Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 650
<211> 487
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 650
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu
20 25 30

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe
35 40 45

Ala Leu Ser Asn His Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys
50 55 60

Gly Leu Glu Trp Val Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr
65 70 75 80

Ala Ala Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg
85 90 95

Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala
100 105 110

Ile Tyr Tyr Cys Ser Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln

_SL

115 120 125

Gly Thr Thr Val Thr Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly
130 135 140

Gly Arg Ala Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln Thr
145 150 155 160

Pro Leu Ser Leu Ser Val Thr Pro Gly Gln Pro Ala Ser Ile Ser Cys
165 170 175

Lys Ser Ser Gln Ser Leu Leu Arg Asn Asp Gly Lys Thr Pro Leu Tyr
180 185 190

Trp Tyr Leu Gln Lys Ala Gly Gln Pro Pro Gln Leu Leu Ile Tyr Glu
195 200 205

Val Ser Asn Arg Phe Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly
210 215 220

Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp
225 230 235 240

Val Gly Ala Tyr Tyr Cys Met Gln Asn Ile Gln Phe Pro Ser Phe Gly
245 250 255

Gly Gly Thr Lys Leu Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro
260 265 270

Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro
275 280 285

Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu
290 295 300

Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys
305 310 315 320

Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly
325 330 335

Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val
340 345 350

Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu
355 360 365

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                                                _SL
Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp
    370                 375                 380

Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn
385                 390                 395                 400

Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg
                405                 410                 415

Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly
            420                 425                 430

Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu
        435                 440                 445

Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu
    450                 455                 460

Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His
465                 470                 475                 480

Met Gln Ala Leu Pro Pro Arg
                485
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<210> 651
<211> 1461
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 651
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaagtgc aattgttgga atctggagga ggacttgtgc agcctggagg atcactgaga 120

ctttcgtgtg cggtgtcagg cttcgccctg agcaaccacg gcatgagctg ggtgcggaga 180

gccccgggga agggtctgga atgggtgtcc gggatcgtct actccggttc aacttactac 240

gccgcaagcg tgaagggtcg cttcaccatt tcccgcgata actcccggaa caccctgtac 300

ctccaaatga actccctgcg gcccgaggac accgccatct actactgttc cgcgcatgga 360

ggagagtccg atgtctgggg acagggcact accgtgaccg tgtcgagcgc ctcgggggga 420

ggaggctccg gcggtcgcgc ctccgggggg ggtggcagcg acattgtgat gacgcagact 480

ccactctcgc tgtccgtgac cccgggacag cccgcgtcca tctcgtgcaa gagctcccag 540

agcctgctga ggaacgacgg aaagactcct ctgtattggt acctccagaa ggctggacag 600

cccccgcaac tgctcatcta cgaagtgtca aatcgcttct ccggggtgcc ggatcggttt 660

tccggctcgg gatcgggcac cgacttcacc ctgaaaatct ccagggtcga ggccgaggac 720

gtgggagcct actactgcat gcaaaacatc cagttccctt ccttcggcgg cggcacaaag 780

ctggagatta agaccactac cccagcaccg aggccaccca ccccggctcc taccatcgcc 840

tcccagcctc tgtccctgcg tccggaggca tgtagacccg cagctggtgg ggccgtgcat 900

acccggggtc ttgacttcgc ctgcgatatc tacatttggg cccctctggc tggtacttgc 960

ggggtcctgc tgctttcact cgtgatcact ctttactgta agcgcggtcg gaagaagctg 1020

ctgtacatct ttaagcaacc cttcatgagg cctgtgcaga ctactcaaga ggaggacggc 1080

tgttcatgcc ggttcccaga ggaggaggaa ggcggctgcg aactgcgcgt gaaattcagc 1140

cgcagcgcag atgctccagc ctacaagcag gggcagaacc agctctacaa cgaactcaat 1200

cttggtcgga gagaggagta cgacgtgctg gacaagcgga gaggacggga cccagaaatg 1260

ggcgggaagc cgcgcagaaa gaatccccaa gagggcctgt acaacgagct ccaaaaggat 1320

aagatggcag aagcctatag cgagattggt atgaaagggg aacgcagaag aggcaaaggc 1380

cacgacggac tgtaccaggg actcagcacc gccaccaagg acacctatga cgctcttcac 1440

atgcaggccc tgccgcctcg g 1461

<210> 652
<211> 249
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 652
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Arg Lys Thr Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Asp Asn Phe
20 25 30

Gly Ile Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Asn Pro Lys Asn Asn Asn Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Asn Thr Ala Tyr
65 70 75 80

Met Glu Val Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys

_SL
85 90 95

Ala Arg Gly Pro Tyr Tyr Tyr Gln Ser Tyr Met Asp Val Trp Gly Gln
100 105 110

Gly Thr Met Val Thr Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly
115 120 125

Gly Arg Ala Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln Thr
130 135 140

Pro Leu Ser Leu Pro Val Thr Pro Gly Glu Pro Ala Ser Ile Ser Cys
145 150 155 160

Arg Ser Ser Gln Ser Leu Leu His Ser Asn Gly Tyr Asn Tyr Leu Asn
165 170 175

Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Gln Leu Leu Ile Tyr Leu
180 185 190

Gly Ser Lys Arg Ala Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly
195 200 205

Ser Gly Thr Asp Phe Thr Leu His Ile Thr Arg Val Gly Ala Glu Asp
210 215 220

Val Gly Val Tyr Tyr Cys Met Gln Ala Leu Gln Thr Pro Tyr Thr Phe
225 230 235 240

Gly Gln Gly Thr Lys Leu Glu Ile Lys
245

<210> 653
<211> 747
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 653
caagtccaac tcgtccagtc cggcgcagaa gtcagaaaaa ccggtgctag cgtgaaagtg 60

tcctgcaagg cctccggcta cattttcgat aacttcggaa tcaactgggt cagacaggcc 120

ccgggccagg ggctggaatg gatgggatgg atcaacccca agaacaacaa caccaactac 180

gcacagaagt tccagggccg cgtgactatc accgccgatg aatcgaccaa taccgcctac 240

atggaggtgt cctccctgcg gtcggaggac actgccgtgt attactgcgc gaggggccca 300

tactactacc aaagctacat ggacgtctgg ggacagggaa ccatggtgac cgtgtcatcc 360

gcctccggtg gtggaggctc cgggggggcgg gcttcaggag gcggaggaag cgatattgtg 420

atgacccaga ctccgcttag cctgcccgtg actcctggag aaccggcctc catttcctgc 480

cggtcctcgc aatcactcct gcattccaac ggttacaact acctgaattg gtacctccag 540

aagcctggcc agtcgcccca gttgctgatc tatctgggct cgaagcgcgc ctccggggtg 600

cctgaccggt ttagcggatc tgggagcggc acggacttca ctctccacat cacccgcgtg 660

ggagcggagg acgtgggagt gtactactgt atgcaggcgc tgcagactcc gtacacattc 720

ggacagggca ccaagctgga gatcaag 747

<210> 654
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 654

Gln	Val	Gln	Leu	Val	Gln	Ser	Gly	Ala	Glu	Val	Arg	Lys	Thr	Gly	Ala
1				5				10					15		
Ser	Val	Lys	Val	Ser	Cys	Lys	Ala	Ser	Gly	Tyr	Ile	Phe	Asp	Asn	Phe
			20					25					30		
Gly	Ile	Asn	Trp	Val	Arg	Gln	Ala	Pro	Gly	Gln	Gly	Leu	Glu	Trp	Met
		35					40					45			
Gly	Trp	Ile	Asn	Pro	Lys	Asn	Asn	Asn	Thr	Asn	Tyr	Ala	Gln	Lys	Phe
	50					55					60				
Gln	Gly	Arg	Val	Thr	Ile	Thr	Ala	Asp	Glu	Ser	Thr	Asn	Thr	Ala	Tyr
65					70					75					80
Met	Glu	Val	Ser	Ser	Leu	Arg	Ser	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys
				85					90					95	
Ala	Arg	Gly	Pro	Tyr	Tyr	Tyr	Gln	Ser	Tyr	Met	Asp	Val	Trp	Gly	Gln
			100					105					110		
Gly	Thr	Met	Val	Thr	Val	Ser	Ser								
		115					120								

<210> 655
<211> 112

<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 655
Asp Ile Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser
20 25 30

Asn Gly Tyr Asn Tyr Leu Asn Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Leu Gly Ser Lys Arg Ala Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu His Ile
65 70 75 80

Thr Arg Val Gly Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala
85 90 95

Leu Gln Thr Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 656
<211> 493
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 656
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
20 25 30

Arg Lys Thr Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
35 40 45

Ile Phe Asp Asn Phe Gly Ile Asn Trp Val Arg Gln Ala Pro Gly Gln
50 55 60

```
Gly Leu Glu Trp Met Gly Trp Ile Asn Pro Lys Asn Asn Asn Thr Asn
65                  70                  75                  80

Tyr Ala Gln Lys Phe Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser
                85                  90                  95

Thr Asn Thr Ala Tyr Met Glu Val Ser Ser Leu Arg Ser Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Arg Gly Pro Tyr Tyr Tyr Gln Ser Tyr Met
        115                 120                 125

Asp Val Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Ala Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gly Gly Arg Ala Ser Gly Gly Gly Gly Ser Asp Ile
145                 150                 155                 160

Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val Thr Pro Gly Glu Pro
                165                 170                 175

Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser Asn Gly
            180                 185                 190

Tyr Asn Tyr Leu Asn Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Gln
        195                 200                 205

Leu Leu Ile Tyr Leu Gly Ser Lys Arg Ala Ser Gly Val Pro Asp Arg
    210                 215                 220

Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu His Ile Thr Arg
225                 230                 235                 240

Val Gly Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala Leu Gln
                245                 250                 255

Thr Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Thr Thr
            260                 265                 270

Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln
        275                 280                 285

Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala
    290                 295                 300

Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala
305                 310                 315                 320
```

Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr
325 330 335

Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln
340 345 350

Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser
355 360 365

Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys
370 375 380

Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln
385 390 395 400

Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu
405 410 415

Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg
420 425 430

Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met
435 440 445

Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly
450 455 460

Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp
465 470 475 480

Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 657
<211> 1479
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 657
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtcc aactcgtcca gtccggcgca gaagtcagaa aaaccggtgc tagcgtgaaa 120

gtgtcctgca aggcctccgg ctacattttc gataacttcg gaatcaactg ggtcagacag 180

gccccgggcc aggggctgga atggatggga tggatcaacc ccaagaacaa caacaccaac 240

tacgcacaga agttccaggg ccgcgtgact atcaccgccg atgaatcgac caataccgcc 300

tacatggagg tgtcctccct gcggtcggag gacactgccg tgtattactg cgcgaggggc 360

ccatactact accaaagcta catggacgtc tggggacagg gaaccatggt gaccgtgtca 420

tccgcctccg gtggtggagg ctccgggggg cgggcttcag gaggcggagg aagcgatatt 480

gtgatgaccc agactccgct tagcctgccc gtgactcctg gagaaccggc ctccatttcc 540

tgccggtcct cgcaatcact cctgcattcc aacggttaca actacctgaa ttggtacctc 600

cagaagcctg gccagtcgcc ccagttgctg atctatctgg gctcgaagcg cgcctccggg 660

gtgcctgacc ggtttagcgg atctgggagc ggcacggact tcactctcca catcacccgc 720

gtgggagcgg aggacgtggg agtgtactac tgtatgcagg cgctgcagac tccgtacaca 780

ttcggacagg gcaccaagct ggagatcaag accactaccc cagcaccgag gccacccacc 840

ccggctccta ccatcgcctc ccagcctctg tccctgcgtc cggaggcatg tagacccgca 900

gctggtgggg ccgtgcatac ccggggtctt gacttcgcct gcgatatcta catttgggcc 960

cctctggctg gtacttgcgg ggtcctgctg ctttcactcg tgatcactct ttactgtaag 1020

cgcggtcgga agaagctgct gtacatcttt aagcaaccct tcatgaggcc tgtgcagact 1080

actcaagagg aggacggctg ttcatgccgg ttcccagagg aggaggaagg cggctgcgaa 1140

ctgcgcgtga aattcagccg cagcgcagat gctccagcct acaagcaggg gcagaaccag 1200

ctctacaacg aactcaatct tggtcggaga gaggagtacg acgtgctgga caagcggaga 1260

ggacgggacc cagaaatggg cgggaagccg cgcagaaaga atccccaaga gggcctgtac 1320

aacgagctcc aaaaggataa gatggcagaa gcctatagcg agattggtat gaaaggggaa 1380

cgcagaagag gcaaaggcca cgacggactg taccagggac tcagcaccgc caccaaggac 1440

acctatgacg ctcttcacat gcaggccctg ccgcctcgg 1479

<210> 658
<211> 246
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 658
Gln Val Gln Leu Gln Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Asp
20 25 30

```
Ala Met Thr Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Val Ile Ser Gly Ser Gly Gly Thr Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Leu Asp Ser Ser Gly Tyr Tyr Tyr Ala Arg Gly Pro Arg Tyr
            100                 105                 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Gly Gly Gly
        115                 120                 125

Gly Ser Gly Gly Arg Ala Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu
    130                 135                 140

Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr
145                 150                 155                 160

Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr
                165                 170                 175

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Gly Ala Ser
            180                 185                 190

Thr Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly
        195                 200                 205

Thr His Phe Thr Leu Thr Ile Asn Ser Leu Gln Ser Glu Asp Ser Ala
    210                 215                 220

Thr Tyr Tyr Cys Gln Gln Ser Tyr Lys Arg Ala Ser Phe Gly Gln Gly
225                 230                 235                 240

Thr Lys Val Glu Ile Lys
                245
```

<210> 659
<211> 738
<212> DNA
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 659
caagtgcaac ttcaagaatc aggcggagga ctcgtgcagc ccggaggatc attgcggctc 60

tcgtgcgccg cctcgggctt caccttctcg agcgacgcca tgacctgggt ccgccaggcc 120

ccggggaagg ggctggaatg ggtgtctgtg atttccggct ccgggggaac tacgtactac 180

gccgattccg tgaaaggtcg cttcactatc tcccgggaca acagcaagaa cacccttttat 240

ctgcaaatga attccctccg cgccgaggac accgccgtgt actactgcgc caagctggac 300

tcctcgggct actactatgc ccggggtccg agatactggg gacagggaac cctcgtgacc 360

gtgtcctccg cgtccggcgg aggagggtcg ggagggcggg cctccggcgg cggcggttcg 420

gacatccagc tgacccagtc cccatcctca ctgagcgcaa gcgtgggcga cagagtcacc 480

attacatgca gggcgtccca gagcatcagc tcctacctga actggtacca acagaagcct 540

ggaaaggctc ctaagctgtt gatctacggg gcttcgaccc tggcatccgg ggtgcccgcg 600

aggtttagcg gaagcggtag cggcactcac ttcactctga ccattaacag cctccagtcc 660

gaggattcag ccacttacta ctgtcagcag tcctacaagc gggccagctt cggacagggc 720

actaaggtcg agatcaag 738

<210> 660
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 660
Gln Val Gln Leu Gln Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Asp
20 25 30

Ala Met Thr Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Val Ile Ser Gly Ser Gly Gly Thr Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

_SL
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Ala Lys Leu Asp Ser Ser Gly Tyr Tyr Tyr Ala Arg Gly Pro Arg Tyr
            100   105   110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
        115   120

<210> 661
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 661
Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1   5   10   15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr
            20   25   30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35   40   45

Tyr Gly Ala Ser Thr Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr His Phe Thr Leu Thr Ile Asn Ser Leu Gln Ser
65   70   75   80

Glu Asp Ser Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Lys Arg Ala Ser
                85   90   95

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
            100   105

<210> 662
<211> 490
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 662
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu

_SL

1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Gln Glu Ser Gly Gly Gly Leu
20 25 30

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
35 40 45

Thr Phe Ser Ser Asp Ala Met Thr Trp Val Arg Gln Ala Pro Gly Lys
50 55 60

Gly Leu Glu Trp Val Ser Val Ile Ser Gly Ser Gly Gly Thr Thr Tyr
65 70 75 80

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser
85 90 95

Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Ala Lys Leu Asp Ser Ser Gly Tyr Tyr Tyr Ala
115 120 125

Arg Gly Pro Arg Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
130 135 140

Ala Ser Gly Gly Gly Gly Ser Gly Gly Arg Ala Ser Gly Gly Gly Gly
145 150 155 160

Ser Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val
165 170 175

Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser
180 185 190

Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu
195 200 205

Ile Tyr Gly Ala Ser Thr Leu Ala Ser Gly Val Pro Ala Arg Phe Ser
210 215 220

Gly Ser Gly Ser Gly Thr His Phe Thr Leu Thr Ile Asn Ser Leu Gln
225 230 235 240

Ser Glu Asp Ser Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Lys Arg Ala
245 250 255

_SL
Ser Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Thr Thr Thr Pro Ala
260 265 270

Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser
275 280 285

Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr
290 295 300

Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala
305 310 315 320

Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys
325 330 335

Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met
340 345 350

Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe
355 360 365

Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg
370 375 380

Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn
385 390 395 400

Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg
405 410 415

Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro
420 425 430

Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala
435 440 445

Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His
450 455 460

Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp
465 470 475 480

Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 663
<211> 1470
<212> DNA

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 663
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtgc aacttcaaga atcaggcgga ggactcgtgc agcccggagg atcattgcgg 120

ctctcgtgcg ccgcctcggg cttcaccttc tcgagcgacg ccatgacctg ggtccgccag 180

gccccgggga aggggctgga atgggtgtct gtgatttccg gctccggggg aactacgtac 240

tacgccgatt ccgtgaaagg tcgcttcact atctcccggg acaacagcaa gaacaccctt 300

tatctgcaaa tgaattccct ccgcgccgag gacaccgccg tgtactactg cgccaagctg 360

gactcctcgg gctactacta tgcccggggt ccgagatact ggggacaggg aaccctcgtg 420

accgtgtcct ccgcgtccgg cggaggaggg tcgggagggc gggcctccgg cggcggcggt 480

tcggacatcc agctgaccca gtccccatcc tcactgagcg caagcgtggg cgacagagtc 540

accattacat gcagggcgtc ccagagcatc agctcctacc tgaactggta ccaacagaag 600

cctggaaagg ctcctaagct gttgatctac ggggcttcga ccctggcatc cggggtgccc 660

gcgaggttta gcggaagcgg tagcggcact cacttcactc tgaccattaa cagcctccag 720

tccgaggatt cagccactta ctactgtcag cagtcctaca agcgggccag cttcggacag 780

ggcactaagg tcgagatcaa gaccactacc ccagcaccga ggccacccac cccggctcct 840

accatcgcct cccagcctct gtccctgcgt ccggaggcat gtagacccgc agctggtggg 900

gccgtgcata cccggggtct tgacttcgcc tgcgatatct acatttgggc ccctctggct 960

ggtacttgcg gggtcctgct gctttcactc gtgatcactc tttactgtaa gcgcggtcgg 1020

aagaagctgc tgtacatctt taagcaaccc ttcatgaggc ctgtgcagac tactcaagag 1080

gaggacggct gttcatgccg gttcccagag gaggaggaag gcggctgcga actgcgcgtg 1140

aaattcagcc gcagcgcaga tgctccagcc tacaagcagg ggcagaacca gctctacaac 1200

gaactcaatc ttggtcggag agaggagtac gacgtgctgg acaagcggag aggacgggac 1260

ccagaaatgg gcgggaagcc gcgcagaaag aatccccaag agggcctgta caacgagctc 1320

caaaaggata agatggcaga agcctatagc gagattggta tgaaagggga acgcagaaga 1380

ggcaaaggcc acgacggact gtaccaggga ctcagcaccg ccaccaagga cacctatgac 1440

gctcttcaca tgcaggccct gccgcctcgg 1470

<210> 664
<211> 247
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 664

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Ser Asn Tyr
            20                  25                  30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

Gly Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Phe
    50                  55                  60

Gln Gly Arg Val Thr Met Thr Arg Asn Thr Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Gly Pro Tyr Tyr Tyr Tyr Met Asp Val Trp Gly Lys Gly Thr
            100                 105                 110

Met Val Thr Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly Gly Arg
        115                 120                 125

Ala Ser Gly Gly Gly Gly Ser Glu Ile Val Met Thr Gln Ser Pro Leu
    130                 135                 140

Ser Leu Pro Val Thr Pro Gly Glu Pro Ala Ser Ile Ser Cys Arg Ser
145                 150                 155                 160

Ser Gln Ser Leu Leu Tyr Ser Asn Gly Tyr Asn Tyr Val Asp Trp Tyr
                165                 170                 175

Leu Gln Lys Pro Gly Gln Ser Pro Gln Leu Leu Ile Tyr Leu Gly Ser
            180                 185                 190

Asn Arg Ala Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly
        195                 200                 205

Thr Asp Phe Lys Leu Gln Ile Ser Arg Val Glu Ala Glu Asp Val Gly
    210                 215                 220
```

_SL
Ile Tyr Tyr Cys Met Gln Gly Arg Gln Phe Pro Tyr Ser Phe Gly Gln
225 230 235 240

Gly Thr Lys Val Glu Ile Lys
245

<210> 665
<211> 741
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 665
caagtccaac tggtccagag cggtgcagaa gtgaagaagc ccggagcgag cgtgaaagtg 60

tcctgcaagg cttccgggta caccttctcc aactacggca tcacttgggt gcgccaggcc 120

ccgggacagg gcctggaatg gatggggtgg atttccgcgt acaacggcaa tacgaactac 180

gctcagaagt tccagggtag agtgaccatg actaggaaca cctccatttc caccgcctac 240

atggaactgt cctccctgcg gagcgaggac accgccgtgt actattgcgc ccggggacca 300

tactactact acatggatgt ctgggggaag gggactatgg tcaccgtgtc atccgcctcg 360

ggaggcggcg gatcaggagg acgcgcctct ggtggtggag gatcggagat cgtgatgacc 420

cagagccctc tctccttgcc cgtgactcct ggggagcccg catccatttc atgccggagc 480

tcccagtcac ttctctactc caacggctat aactacgtgg attggtacct ccaaaagccg 540

ggccagagcc cgcagctgct gatctacctg ggctcgaaca gggccagcgg agtgcctgac 600

cggttctccg ggtcgggaag cgggaccgac ttcaagctgc aaatctcgag agtggaggcc 660

gaggacgtgg gaatctacta ctgtatgcag ggccgccagt ttccgtactc gttcggacag 720

ggcaccaaag tggaaatcaa g 741

<210> 666
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 666
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Ser Asn Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asn Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Pro Tyr Tyr Tyr Tyr Met Asp Val Trp Gly Lys Gly Thr
100 105 110

Met Val Thr Val Ser Ser
115

<210> 667
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 667
Glu Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu Tyr Ser
20 25 30

Asn Gly Tyr Asn Tyr Val Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Lys Leu Gln Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Ile Tyr Tyr Cys Met Gln Gly
85 90 95

Arg Gln Phe Pro Tyr Ser Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 668
<211> 491
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 668
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
20 25 30

Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
35 40 45

Thr Phe Ser Asn Tyr Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln
50 55 60

Gly Leu Glu Trp Met Gly Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn
65 70 75 80

Tyr Ala Gln Lys Phe Gln Gly Arg Val Thr Met Thr Arg Asn Thr Ser
85 90 95

Ile Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Ala Arg Gly Pro Tyr Tyr Tyr Tyr Met Asp Val
115 120 125

Trp Gly Lys Gly Thr Met Val Thr Val Ser Ser Ala Ser Gly Gly Gly
130 135 140

Gly Ser Gly Gly Arg Ala Ser Gly Gly Gly Gly Ser Glu Ile Val Met
145 150 155 160

Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly Glu Pro Ala Ser
165 170 175

Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu Tyr Ser Asn Gly Tyr Asn
180 185 190

Tyr Val Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Gln Leu Leu
195 200 205

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Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro Asp Arg Phe Ser
    210                 215                 220

Gly Ser Gly Ser Gly Thr Asp Phe Lys Leu Gln Ile Ser Arg Val Glu
225                 230                 235                 240

Ala Glu Asp Val Gly Ile Tyr Tyr Cys Met Gln Gly Arg Gln Phe Pro
                245                 250                 255

Tyr Ser Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Thr Thr Thr Pro
            260                 265                 270

Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu
        275                 280                 285

Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His
    290                 295                 300

Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu
305                 310                 315                 320

Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr
                325                 330                 335

Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe
            340                 345                 350

Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg
        355                 360                 365

Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser
    370                 375                 380

Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr
385                 390                 395                 400

Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys
                405                 410                 415

Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn
            420                 425                 430

Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu
        435                 440                 445

Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly
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_SL
450 455 460

His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr
465 470 475 480

Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 669
<211> 1473
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 669
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtcc aactggtcca gagcggtgca gaagtgaaga agcccggagc gagcgtgaaa 120

gtgtcctgca aggcttccgg gtacaccttc tccaactacg gcatcacttg ggtgcgccag 180

gccccgggac agggcctgga atggatgggg tggatttccg cgtacaacgg caatacgaac 240

tacgctcaga agttccaggg tagagtgacc atgactagga acacctccat ttccaccgcc 300

tacatggaac tgtcctccct gcggagcgag gacaccgccg tgtactattg cgcccgggga 360

ccatactact actacatgga tgtctggggg aaggggacta tggtcaccgt gtcatccgcc 420

tcgggaggcg gcggatcagg aggacgcgcc tctggtggtg gaggatcgga gatcgtgatg 480

acccagagcc ctctctcctt gcccgtgact cctggggagc ccgcatccat ttcatgccgg 540

agctcccagt cacttctcta ctccaacggc tataactacg tggattggta cctccaaaag 600

ccgggccaga gcccgcagct gctgatctac ctgggctcga acagggccag cggagtgcct 660

gaccggttct ccgggtcggg aagcgggacc gacttcaagc tgcaaatctc gagagtggag 720

gccgaggacg tgggaatcta ctactgtatg cagggccgcc agtttccgta ctcgttcgga 780

cagggcacca aagtggaaat caagaccact accccagcac cgaggccacc caccccggct 840

cctaccatcg cctcccagcc tctgtccctg cgtccggagg catgtagacc cgcagctggt 900

ggggccgtgc atacccgggg tcttgacttc gcctgcgata tctacatttg ggcccctctg 960

gctggtactt gcggggtcct gctgctttca ctcgtgatca ctctttactg taagcgcggt 1020

cggaagaagc tgctgtacat ctttaagcaa cccttcatga ggcctgtgca gactactcaa 1080

gaggaggacg gctgttcatg ccggttccca gaggaggagg aaggcggctg cgaactgcgc 1140

gtgaaattca gccgcagcgc agatgctcca gcctacaagc aggggcagaa ccagctctac 1200

aacgaactca atcttggtcg gagagaggag tacgacgtgc tggacaagcg gagaggacgg 1260

gacccagaaa tgggcgggaa gccgcgcaga aagaatcccc aagagggcct gtacaacgag 1320

ctccaaaagg ataagatggc agaagcctat agcgagattg gtatgaaagg ggaacgcaga 1380

agaggcaaag gccacgacgg actgtaccag ggactcagca ccgccaccaa ggacacctat 1440

gacgctcttc acatgcaggc cctgccgcct cgg 1473

<210> 670
<211> 238
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 670
Glu Val Gln Leu Leu Glu Thr Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe Ala Leu Ser Asn His
20 25 30

Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr Ala Ala Ser Val Lys
50 55 60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg Asn Thr Leu Tyr Leu
65 70 75 80

Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Ile Tyr Tyr Cys Ser
85 90 95

Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly Gly Arg Ala Ser Gly
115 120 125

Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser
130 135 140

Val Ser Pro Gly Glu Ser Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser
145 150 155 160

Val Ser Ser Asn Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro
165 170 175

Arg Leu Leu Ile Tyr Gly Ala Ser Thr Arg Ala Ser Gly Ile Pro Asp
180 185 190

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
195 200 205

Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln Tyr Gly
210 215 220

Ser Ser Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
225 230 235

<210> 671
<211> 714
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 671
gaagtgcaat tgctcgaaac tggaggaggt ctggtgcaac ctggaggatc acttcgcctg 60

tcctgcgccg tgtcgggctt tgccctgtcc aaccatggaa tgagctgggt ccgccgcgcg 120

ccggggaagg gcctcgaatg ggtgtccggc atcgtctact ccggctccac ctactacgcc 180

gcgtccgtga agggccggtt cacgatttca cgggacaact cgcggaacac cctgtacctc 240

caaatgaatt cccttcggcc ggaggatact gccatctact actgctccgc ccacggtggc 300

gaatccgacg tctggggcca gggaaccacc gtgaccgtgt ccagcgcgtc cgggggagga 360

ggaagcgggg gtagagcatc gggtggaggc ggatcagaga tcgtgctgac ccagtccccc 420

gccaccttga gcgtgtcacc aggagagtcc gccaccctgt catgccgcgc cagccagtcc 480

gtgtcctcca acctggcttg gtaccagcag aagccggggc aggcccctag actcctgatc 540

tatggggcgt cgacccgggc atctggaatt cccgataggt tcagcggatc gggctcgggc 600

actgacttca ctctgaccat ctcctcgctg caagccgagg acgtggctgt gtactactgt 660

cagcagtacg gaagctccct gactttcggt ggcgggacca aagtcgagat taag 714

<210> 672
<211> 115
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 672
Glu Val Gln Leu Leu Glu Thr Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe Ala Leu Ser Asn His
20 25 30

Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr Ala Ala Ser Val Lys
50 55 60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg Asn Thr Leu Tyr Leu
65 70 75 80

Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Ile Tyr Tyr Cys Ser
85 90 95

Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser
115

<210> 673
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 673
Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly
1 5 10 15

Glu Ser Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Asn
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45

Tyr Gly Ala Ser Thr Arg Ala Ser Gly Ile Pro Asp Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala
65 70 75 80

Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Leu Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 674
<211> 482
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 674
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Val Gln Leu Leu Glu Thr Gly Gly Gly Leu
20 25 30

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe
35 40 45

Ala Leu Ser Asn His Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys
50 55 60

Gly Leu Glu Trp Val Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr
65 70 75 80

Ala Ala Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg
85 90 95

Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala
100 105 110

Ile Tyr Tyr Cys Ser Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln
115 120 125

Gly Thr Thr Val Thr Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly
130 135 140

Gly Arg Ala Ser Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser
145 150 155 160

Pro Ala Thr Leu Ser Val Ser Pro Gly Glu Ser Ala Thr Leu Ser Cys
165 170 175

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Arg Ala Ser Gln Ser Val Ser Ser Asn Leu Ala Trp Tyr Gln Gln Lys
            180                 185                 190

Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Thr Arg Ala
        195                 200                 205

Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
    210                 215                 220

Thr Leu Thr Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr
225                 230                 235                 240

Cys Gln Gln Tyr Gly Ser Ser Leu Thr Phe Gly Gly Gly Thr Lys Val
                245                 250                 255

Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro
            260                 265                 270

Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro
        275                 280                 285

Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp
    290                 295                 300

Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu
305                 310                 315                 320

Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu
                325                 330                 335

Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu
            340                 345                 350

Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys
        355                 360                 365

Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys
    370                 375                 380

Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu
385                 390                 395                 400

Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly
                405                 410                 415

Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu
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_SL
420 425 430

Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly
435 440 445

Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser
450 455 460

Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro
465 470 475 480

Pro Arg

<210> 675
<211> 1446
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 675
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaagtgc aattgctcga aactggagga ggtctggtgc aacctggagg atcacttcgc 120

ctgtcctgcg ccgtgtcggg ctttgccctg tccaaccatg gaatgagctg ggtccgccgc 180

gcgccgggga agggcctcga atgggtgtcc ggcatcgtct actccggctc cacctactac 240

gccgcgtccg tgaagggccg gttcacgatt tcacgggaca actcgcggaa caccctgtac 300

ctccaaatga attcccttcg gccggaggat actgccatct actactgctc cgcccacggt 360

ggcgaatccg acgtctgggg ccagggaacc accgtgaccg tgtccagcgc gtccggggga 420

ggaggaagcg ggggtagagc atcgggtgga ggcggatcag agatcgtgct gacccagtcc 480

cccgccacct tgagcgtgtc accaggagag tccgccaccc tgtcatgccg cgccagccag 540

tccgtgtcct ccaacctggc ttggtaccag cagaagccgg ggcaggcccc tagactcctg 600

atctatgggg cgtcgacccg ggcatctgga attcccgata ggttcagcgg atcgggctcg 660

ggcactgact tcactctgac catctcctcg ctgcaagccg aggacgtggc tgtgtactac 720

tgtcagcagt acggaagctc cctgactttc ggtggcggga ccaaagtcga gattaagacc 780

actaccccag caccgaggcc acccaccccg gctcctacca tcgcctccca gcctctgtcc 840

ctgcgtccgg aggcatgtag acccgcagct ggtggggccg tgcatacccg gggtcttgac 900

ttcgcctgcg atatctacat ttgggcccct ctggctggta cttgcggggt cctgctgctt 960

tcactcgtga tcactcttta ctgtaagcgc ggtcggaaga agctgctgta catctttaag 1020

caacccttca tgaggcctgt gcagactact caagaggagg acggctgttc atgccggttc 1080

ccagaggagg aggaaggcgg ctgcgaactg cgcgtgaaat tcagccgcag cgcagatgct 1140

ccagcctaca agcaggggca gaaccagctc tacaacgaac tcaatcttgg tcggagagag 1200

gagtacgacg tgctggacaa gcggagagga cgggacccag aaatgggcgg gaagccgcgc 1260

agaaagaatc cccaagaggg cctgtacaac gagctccaaa aggataagat ggcagaagcc 1320

tatagcgaga ttggtatgaa aggggaacgc agaagaggca aaggccacga cggactgtac 1380

cagggactca gcaccgccac caaggacacc tatgacgctc ttcacatgca ggccctgccg 1440

cctcgg 1446

<210> 676
<211> 239
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 676
Glu Val Gln Leu Val Glu Thr Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe Ala Leu Ser Asn His
20 25 30

Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr Ala Ala Ser Val Lys
50 55 60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg Asn Thr Leu Tyr Leu
65 70 75 80

Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Ile Tyr Tyr Cys Ser
85 90 95

Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly Gly Arg Ala Ser Gly
115 120 125

Gly Gly Gly Ser Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser
130 135 140

Val Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser
145 150 155 160

Val Ser Ser Lys Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro
165 170 175

Arg Leu Leu Met Tyr Gly Ala Ser Ile Arg Ala Thr Gly Ile Pro Asp
180 185 190

Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser
195 200 205

Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly
210 215 220

Ser Ser Ser Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
225 230 235

<210> 677
<211> 717
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 677
gaagtgcaat tggtggaaac tggaggagga cttgtgcaac ctggaggatc attgagactg 60

agctgcgcag tgtcgggatt cgccctgagc aaccatggaa tgtcctgggt cagaagggcc 120

cctggaaaag gcctcgaatg ggtgtcaggg atcgtgtact ccggttccac ttactacgcc 180

gcctccgtga aggggcgctt cactatctca cgggataact cccgcaatac cctgtacctc 240

caaatgaaca gcctgcggcc ggaggatacc gccatctact actgttccgc ccacggtgga 300

gagtctgacg tctggggcca gggaactacc gtgaccgtgt cctccgcgtc cggcggtgga 360

gggagcggcg gccgcgccag cggcggcgga ggctccgaga tcgtgatgac ccagagcccc 420

gctactctgt cggtgtcgcc cggagaaagg gcgaccctgt cctgccgggc gtcgcagtcc 480

gtgagcagca agctggcttg gtaccagcag aagccgggcc aggcaccacg cctgcttatg 540

tacggtgcct ccattcgggc caccggaatc ccggaccggt tctcggggtc ggggtccggt 600

accgagttca cactgaccat ttcctcgctc gagcccgagg actttgccgt ctattactgc 660

cagcagtacg gctcctcctc atggacgttc ggccagggga ccaaggtcga aatcaag 717

<210> 678

<211> 115
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 678
Glu Val Gln Leu Val Glu Thr Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe Ala Leu Ser Asn His
20 25 30

Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr Ala Ala Ser Val Lys
50 55 60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg Asn Thr Leu Tyr Leu
65 70 75 80

Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Ile Tyr Tyr Cys Ser
85 90 95

Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser
115

<210> 679
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 679
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Lys
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Met
35 40 45

Tyr Gly Ala Ser Ile Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
65   70   75   80

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Ser Trp
                85   90   95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
            100   105

<210> 680
<211> 483
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 680
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1   5   10   15

His Ala Ala Arg Pro Glu Val Gln Leu Val Glu Thr Gly Gly Gly Leu
            20   25   30

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe
        35   40   45

Ala Leu Ser Asn His Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys
    50   55   60

Gly Leu Glu Trp Val Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr
65   70   75   80

Ala Ala Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg
                85   90   95

Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala
            100   105   110

Ile Tyr Tyr Cys Ser Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln
        115   120   125

Gly Thr Thr Val Thr Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly
    130   135   140

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Gly Arg Ala Ser Gly Gly Gly Gly Ser Glu Ile Val Met Thr Gln Ser
145                 150                 155                 160

Pro Ala Thr Leu Ser Val Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
                165                 170                 175

Arg Ala Ser Gln Ser Val Ser Ser Lys Leu Ala Trp Tyr Gln Gln Lys
            180                 185                 190

Pro Gly Gln Ala Pro Arg Leu Leu Met Tyr Gly Ala Ser Ile Arg Ala
        195                 200                 205

Thr Gly Ile Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe
    210                 215                 220

Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr
225                 230                 235                 240

Cys Gln Gln Tyr Gly Ser Ser Ser Trp Thr Phe Gly Gln Gly Thr Lys
                245                 250                 255

Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala
            260                 265                 270

Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg
        275                 280                 285

Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys
    290                 295                 300

Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu
305                 310                 315                 320

Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu
                325                 330                 335

Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln
            340                 345                 350

Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly
        355                 360                 365

Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr
    370                 375                 380

Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg
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                                                _SL
385                 390                 395                 400

Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met
                405                 410                 415

Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu
            420                 425                 430

Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys
        435                 440                 445

Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu
    450                 455                 460

Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu
465                 470                 475                 480

Pro Pro Arg
```

<210> 681
<211> 1449
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 681
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaagtgc aattggtgga aactggagga ggacttgtgc aacctggagg atcattgaga 120

ctgagctgcg cagtgtcggg attcgccctg agcaaccatg gaatgtcctg ggtcagaagg 180

gcccctggaa aaggcctcga atgggtgtca gggatcgtgt actccggttc cacttactac 240

gccgcctccg tgaaggggcg cttcactatc tcacgggata actcccgcaa taccctgtac 300

ctccaaatga acagcctgcg gccggaggat accgccatct actactgttc cgcccacggt 360

ggagagtctg acgtctgggg ccagggaact accgtgaccg tgtcctccgc gtccggcggt 420

ggagggagcg gcggccgcgc cagcggcggc ggaggctccg agatcgtgat gacccagagc 480

cccgctactc tgtcggtgtc gcccggagaa agggcgaccc tgtcctgccg ggcgtcgcag 540

tccgtgagca gcaagctggc ttggtaccag cagaagccgg gccaggcacc acgcctgctt 600

atgtacggtg cctccattcg ggccaccgga atcccggacc ggttctcggg gtcggggtcc 660

ggtaccgagt tcacactgac catttcctcg ctcgagcccg aggactttgc cgtctattac 720

tgccagcagt acggctcctc ctcatggacg ttcggccagg ggaccaaggt cgaaatcaag 780

accactaccc cagcaccgag gccacccacc ccggctccta ccatcgcctc ccagcctctg 840

tccctgcgtc cggaggcatg tagacccgca gctggtgggg ccgtgcatac ccggggtctt 900

gacttcgcct gcgatatcta catttgggcc cctctggctg gtacttgcgg ggtcctgctg 960

ctttcactcg tgatcactct ttactgtaag cgcggtcgga agaagctgct gtacatcttt 1020

aagcaaccct tcatgaggcc tgtgcagact actcaagagg aggacggctg ttcatgccgg 1080

ttcccagagg aggaggaagg cggctgcgaa ctgcgcgtga aattcagccg cagcgcagat 1140

gctccagcct acaagcaggg gcagaaccag ctctacaacg aactcaatct tggtcggaga 1200

gaggagtacg acgtgctgga caagcggaga ggacgggacc cagaaatggg cgggaagccg 1260

cgcagaaaga atccccaaga gggcctgtac aacgagctcc aaaaggataa gatggcagaa 1320

gcctatagcg agattggtat gaaaggggaa cgcagaagag gcaaaggcca cgacggactg 1380

taccagggac tcagcaccgc caccaaggac acctatgacg ctcttcacat gcaggccctg 1440

ccgcctcgg 1449

<210> 682
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 682
Glu Val Gln Leu Val Glu Thr Gly Gly Gly Val Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe Ala Leu Ser Asn His
20 25 30

Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr Ala Ala Ser Val Lys
50 55 60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg Asn Thr Leu Tyr Leu
65 70 75 80

Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Ile Tyr Tyr Cys Ser
85 90 95

Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly Gly Arg Ala Ser Gly
115 120 125

Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser
130 135 140

Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser
145 150 155 160

Val Gly Ser Thr Asn Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala
165 170 175

Pro Arg Leu Leu Ile Tyr Asp Ala Ser Asn Arg Ala Thr Gly Ile Pro
180 185 190

Asp Arg Phe Ser Gly Gly Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile
195 200 205

Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr
210 215 220

Gly Ser Ser Pro Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile
225 230 235 240

Lys

<210> 683
<211> 723
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 683
gaagtgcaat tggtggagac tggaggagga gtggtgcaac ctggaggaag cctgagactg 60

tcatgcgcgg tgtcgggctt cgccctctcc aaccacggaa tgtcctgggt ccgccgggcc 120

cctgggaaag gacttgaatg ggtgtccggc atcgtgtact cgggttccac ctactacgcg 180

gcctcagtga agggccggtt tactattagc cgcgacaact ccagaaacac actgtacctc 240

caaatgaact cgctgcggcc ggaagatacc gctatctact actgctccgc ccatggggga 300

gagtcggacg tctggggaca gggcaccact gtcactgtgt ccagcgcttc cggcggtggt 360

ggaagcgggg gacgggcctc aggaggcggt ggcagcgaga ttgtgctgac ccagtccccc 420

gggaccctga gcctgtcccc gggagaaagg gccaccctct cctgtcgggc atcccagtcc 480

gtggggtcta ctaaccttgc atggtaccag cagaagcccg gccaggcccc tcgcctgctg 540

atctacgacg cgtccaatag agccaccggc atcccggatc gcttcagcgg aggcggatcg 600

ggcaccgact tcaccctcac catttcaagg ctggaaccgg aggacttcgc cgtgtactac 660

tgccagcagt atggttcgtc cccaccctgg acgttcggcc aggggactaa ggtcgagatc 720

aag 723

<210> 684
<211> 115
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 684

Glu	Val	Gln	Leu	Val	Glu	Thr	Gly	Gly	Gly	Val	Val	Gln	Pro	Gly	Gly
1				5				10					15		
Ser	Leu	Arg	Leu	Ser	Cys	Ala	Val	Ser	Gly	Phe	Ala	Leu	Ser	Asn	His
			20					25					30		
Gly	Met	Ser	Trp	Val	Arg	Arg	Ala	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Val
		35					40					45			
Ser	Gly	Ile	Val	Tyr	Ser	Gly	Ser	Thr	Tyr	Tyr	Ala	Ala	Ser	Val	Lys
	50					55					60				
Gly	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asn	Ser	Arg	Asn	Thr	Leu	Tyr	Leu
65					70					75					80
Gln	Met	Asn	Ser	Leu	Arg	Pro	Glu	Asp	Thr	Ala	Ile	Tyr	Tyr	Cys	Ser
				85					90					95	
Ala	His	Gly	Gly	Glu	Ser	Asp	Val	Trp	Gly	Gln	Gly	Thr	Thr	Val	Thr
			100					105					110		
Val	Ser	Ser													
		115													

<210> 685
<211> 109
<212> PRT
<213> Artificial Sequence

<220>
<221> source

_SL
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 685
Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Gly Ser Thr
20 25 30

Asn Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45

Ile Tyr Asp Ala Ser Asn Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
50 55 60

Gly Gly Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65 70 75 80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro
85 90 95

Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 686
<211> 485
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 686
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Val Gln Leu Val Glu Thr Gly Gly Gly Val
20 25 30

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe
35 40 45

Ala Leu Ser Asn His Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys
50 55 60

Gly Leu Glu Trp Val Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr
65 70 75 80

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                                                _SL
Ala Ala Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg
                85                  90                  95

Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala
            100                 105                 110

Ile Tyr Tyr Cys Ser Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln
        115                 120                 125

Gly Thr Thr Val Thr Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly
    130                 135                 140

Gly Arg Ala Ser Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser
145                 150                 155                 160

Pro Gly Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
                165                 170                 175

Arg Ala Ser Gln Ser Val Gly Ser Thr Asn Leu Ala Trp Tyr Gln Gln
            180                 185                 190

Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Asp Ala Ser Asn Arg
        195                 200                 205

Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly Gly Gly Ser Gly Thr Asp
    210                 215                 220

Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr
225                 230                 235                 240

Tyr Cys Gln Gln Tyr Gly Ser Ser Pro Pro Trp Thr Phe Gly Gln Gly
                245                 250                 255

Thr Lys Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr
            260                 265                 270

Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala
        275                 280                 285

Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe
    290                 295                 300

Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val
305                 310                 315                 320

Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys
                325                 330                 335
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Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr
            340                 345                 350

Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu
        355                 360                 365

Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro
    370                 375                 380

Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly
385                 390                 395                 400

Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro
                405                 410                 415

Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr
            420                 425                 430

Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly
        435                 440                 445

Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln
    450                 455                 460

Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln
465                 470                 475                 480

Ala Leu Pro Pro Arg
                485
```

<210> 687
<211> 1455
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 687
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaagtgc aattggtgga gactggagga ggagtggtgc aacctggagg aagcctgaga 120

ctgtcatgcg cggtgtcggg cttcgccctc tccaaccacg gaatgtcctg ggtccgccgg 180

gcccctggga aaggacttga atgggtgtcc ggcatcgtgt actcgggttc cacctactac 240

gcggcctcag tgaagggccg gtttactatt agccgcgaca actccagaaa cacactgtac 300

ctccaaatga actcgctgcg gccggaagat accgctatct actactgctc cgcccatggg 360

ggagagtcgg acgtctgggg acagggcacc actgtcactg tgtccagcgc ttccggcggt 420

ggtggaagcg ggggacgggc ctcaggaggc ggtggcagcg agattgtgct gacccagtcc 480

cccgggaccc tgagcctgtc cccgggagaa agggccaccc tctcctgtcg ggcatcccag 540

tccgtggggt ctactaacct tgcatggtac cagcagaagc ccggccaggc ccctcgcctg 600

ctgatctacg acgcgtccaa tagagccacc ggcatcccgg atcgcttcag cggaggcgga 660

tcgggcaccg acttcaccct caccatttca aggctggaac cggaggactt cgccgtgtac 720

tactgccagc agtatggttc gtccccaccc tggacgttcg gccaggggac taaggtcgag 780

atcaagacca ctaccccagc accgaggcca cccaccccgg ctcctaccat cgcctcccag 840

cctctgtccc tgcgtccgga ggcatgtaga cccgcagctg gtggggccgt gcatacccgg 900

ggtcttgact tcgcctgcga tatctacatt tgggcccctc tggctggtac ttgcggggtc 960

ctgctgcttt cactcgtgat cactctttac tgtaagcgcg gtcggaagaa gctgctgtac 1020

atctttaagc aacccttcat gaggcctgtg cagactactc aagaggagga cggctgttca 1080

tgccggttcc cagaggagga ggaaggcggc tgcgaactgc gcgtgaaatt cagccgcagc 1140

gcagatgctc cagcctacaa gcaggggcag aaccagctct acaacgaact caatcttggt 1200

cggagagagg agtacgacgt gctggacaag cggagaggac gggacccaga aatgggcggg 1260

aagccgcgca gaaagaatcc ccaagagggc ctgtacaacg agctccaaaa ggataagatg 1320

gcagaagcct atagcgagat tggtatgaaa ggggaacgca gaagaggcaa aggccacgac 1380

ggactgtacc agggactcag caccgccacc aaggacacct atgacgctct tcacatgcag 1440

gccctgccgc ctcgg 1455

<210> 688
<211> 239
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 688
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
20 25 30

Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

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                                                _SL
Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Glu Ser Gly Asp Gly Met Asp Val Trp Gly Gln Gly Thr Thr
            100                 105                 110

Val Thr Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly Gly Arg Ala
        115                 120                 125

Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser
    130                 135                 140

Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser
145                 150                 155                 160

Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys
                165                 170                 175

Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val
            180                 185                 190

Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
        195                 200                 205

Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln
    210                 215                 220

Ser Tyr Thr Leu Ala Phe Gly Gln Gly Thr Lys Val Asp Ile Lys
225                 230                 235


<210> 689
<211> 717
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 689
caagtgcaac tcgtggaatc tggtggagga ctcgtgaaac ctggaggatc attgagactg       60

tcatgcgcgg cctcgggatt cacgttctcc gattactaca tgagctggat tcgccaggct      120
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ccggggaagg gactggaatg ggtgtcctac atttcctcat ccggctccac catctactac 180

gcggactccg tgaaggggag attcaccatt agccgcgata acgccaagaa cagcctgtac 240

cttcagatga actccctgcg ggctgaagat actgccgtct actactgcgc aagggagagc 300

ggagatggga tggacgtctg gggacagggt accactgtga ccgtgtcgtc ggcctccggc 360

ggaggggtt cgggtggaag ggccagcggc ggcggaggca gcgacatcca gatgacccag 420

tccccctcat cgctgtccgc ctccgtgggc gaccgcgtca ccatcacatg ccgggcctca 480

cagtcgatct cctcctacct caattggtat cagcagaagc ccggaaaggc ccctaagctt 540

ctgatctacg cagcgtcctc cctgcaatcc ggggtcccat ctcggttctc cggctcgggc 600

agcggtaccg acttcactct gaccatctcg agcctgcagc cggaggactt cgccacttac 660

tactgtcagc aaagctacac cctcgcgttt ggccagggca ccaaagtgga catcaag 717

<210> 690
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 690

Gln	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Gly	Leu	Val	Lys	Pro	Gly	Gly
1				5				10					15		
Ser	Leu	Arg	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Phe	Thr	Phe	Ser	Asp	Tyr
			20					25				30			
Tyr	Met	Ser	Trp	Ile	Arg	Gln	Ala	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Val
		35					40					45			
Ser	Tyr	Ile	Ser	Ser	Ser	Gly	Ser	Thr	Ile	Tyr	Tyr	Ala	Asp	Ser	Val
	50					55					60				
Lys	Gly	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asn	Ala	Lys	Asn	Ser	Leu	Tyr
65					70					75					80
Leu	Gln	Met	Asn	Ser	Leu	Arg	Ala	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys
				85					90					95	
Ala	Arg	Glu	Ser	Gly	Asp	Gly	Met	Asp	Val	Trp	Gly	Gln	Gly	Thr	Thr
			100					105					110		
Val	Thr	Val	Ser	Ser											
		115													

<210> 691
<211> 105
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 691
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Thr Leu Ala Phe
85 90 95

Gly Gln Gly Thr Lys Val Asp Ile Lys
100 105

<210> 692
<211> 483
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 692
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu
20 25 30

Val Lys Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
35 40 45

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                                                _SL
Thr Phe Ser Asp Tyr Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys
    50                  55                  60

Gly Leu Glu Trp Val Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr
65                  70                  75                  80

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala
                85                  90                  95

Lys Asn Ser Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Arg Glu Ser Gly Asp Gly Met Asp Val Trp
        115                 120                 125

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Gly Gly Gly Gly
    130                 135                 140

Ser Gly Gly Arg Ala Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr
145                 150                 155                 160

Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile
                165                 170                 175

Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln
            180                 185                 190

Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser
        195                 200                 205

Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr
    210                 215                 220

Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr
225                 230                 235                 240

Tyr Tyr Cys Gln Gln Ser Tyr Thr Leu Ala Phe Gly Gln Gly Thr Lys
                245                 250                 255

Val Asp Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala
            260                 265                 270

Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg
        275                 280                 285

Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys
    290                 295                 300
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Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu
305                 310                 315                 320

Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu
                325                 330                 335

Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln
            340                 345                 350

Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly
        355                 360                 365

Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr
    370                 375                 380

Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg
385                 390                 395                 400

Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met
                405                 410                 415

Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu
            420                 425                 430

Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys
        435                 440                 445

Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu
    450                 455                 460

Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu
465                 470                 475                 480

Pro Pro Arg
```

<210> 693
<211> 1449
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 693
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtgc aactcgtgga atctggtgga ggactcgtga aacctggagg atcattgaga 120

ctgtcatgcg cggcctcggg attcacgttc tccgattact acatgagctg gattcgccag 180

gctccgggga agggactgga atgggtgtcc tacatttcct catccggctc caccatctac 240

tacgcggact ccgtgaaggg gagattcacc attagccgcg ataacgccaa gaacagcctg 300

taccttcaga tgaactccct gcgggctgaa gatactgccg tctactactg cgcaagggag 360

agcggagatg ggatggacgt ctggggacag ggtaccactg tgaccgtgtc gtcggcctcc 420

ggcggagggg gttcgggtgg aagggccagc ggcggcggag gcagcgacat ccagatgacc 480

cagtccccct catcgctgtc cgcctccgtg ggcgaccgcg tcaccatcac atgccgggcc 540

tcacagtcga tctcctccta cctcaattgg tatcagcaga agcccggaaa ggcccctaag 600

cttctgatct acgcagcgtc ctccctgcaa tccggggtcc catctcggtt ctccggctcg 660

ggcagcggta ccgacttcac tctgaccatc tcgagcctgc agccggagga cttcgccact 720

tactactgtc agcaaagcta caccctcgcg tttggccagg gcaccaaagt ggacatcaag 780

accactaccc cagcaccgag gccacccacc ccggctccta ccatcgcctc ccagcctctg 840

tccctgcgtc cggaggcatg tagacccgca gctggtgggg ccgtgcatac ccggggtctt 900

gacttcgcct gcgatatcta catttgggcc cctctggctg gtacttgcgg ggtcctgctg 960

ctttcactcg tgatcactct ttactgtaag cgcggtcgga agaagctgct gtacatcttt 1020

aagcaaccct tcatgaggcc tgtgcagact actcaagagg aggacggctg ttcatgccgg 1080

ttcccagagg aggaggaagg cggctgcgaa ctgcgcgtga aattcagccg cagcgcagat 1140

gctccagcct acaagcaggg gcagaaccag ctctacaacg aactcaatct tggtcggaga 1200

gaggagtacg acgtgctgga caagcggaga ggacgggacc cagaaatggg cgggaagccg 1260

cgcagaaaga atccccaaga gggcctgtac aacgagctcc aaaaggataa gatggcagaa 1320

gcctatagcg agattggtat gaaaggggaa cgcagaagag gcaaaggcca cgacggactg 1380

taccagggac tcagcaccgc caccaaggac acctatgacg ctcttcacat gcaggccctg 1440

ccgcctcgg 1449

<210> 694
<211> 246
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 694
Gln Val Gln Leu Val Gln Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

_SL
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
20 25 30

Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Tyr Ile Ser Ser Ser Gly Asn Thr Ile Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Thr Met Val Arg Glu Asp Tyr Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly Gly Arg Ala
115 120 125

Ser Gly Gly Gly Gly Ser Asp Ile Val Leu Thr Gln Ser Pro Leu Ser
130 135 140

Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser
145 150 155 160

Glu Ser Leu Val His Asn Ser Gly Lys Thr Tyr Leu Asn Trp Phe His
165 170 175

Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr Glu Val Ser Asn
180 185 190

Arg Asp Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr
195 200 205

Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Val Gly Val
210 215 220

Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Gly Thr Phe Gly Gln Gly
225 230 235 240

Thr Lys Leu Glu Ile Lys
245

<210> 695
<211> 738
<212> DNA

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 695
caagtgcaac tggtgcaaag cggaggagga ttggtcaaac ccggaggaag cctgagactg 60

tcatgcgcgg cctctggatt caccttctcc gattactaca tgtcatggat cagacaggcc 120

ccggggaagg gcctcgaatg ggtgtcctac atctcgtcct ccgggaacac catctactac 180

gccgacagcg tgaagggccg ctttaccatt tcccgcgaca acgcaaagaa ctcgctgtac 240

cttcagatga attccctgcg ggctgaagat accgcggtgt actattgcgc ccggtccact 300

atggtccggg aggactactg gggacagggc acactcgtga ccgtgtccag cgcgagcggg 360

ggtggaggca gcggtggacg cgcctccggc ggcggcggtt cagacatcgt gctgactcag 420

tcgcccctgt cgctgccggt caccctgggc caaccggcct caattagctg caagtcctcg 480

gagagcctgg tgcacaactc aggaaagact tacctgaact ggttccatca gcggcctgga 540

cagtccccac ggaggctcat ctatgaagtg tccaacaggg attcgggggt gcccgaccgc 600

ttcactggct ccgggtccgg caccgacttc accttgaaaa tctccagagt ggaagccgag 660

gacgtgggcg tgtactactg tatgcagggt acccactggc ctggaacctt tggacaagga 720

actaagctcg agattaag 738

<210> 696
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 696
Gln Val Gln Leu Val Gln Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
20 25 30

Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Tyr Ile Ser Ser Ser Gly Asn Thr Ile Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr

_SL
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Thr Met Val Arg Glu Asp Tyr Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ser
115

<210> 697
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 697
Asp Ile Val Leu Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Leu Gly
1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser Glu Ser Leu Val His Asn
20 25 30

Ser Gly Lys Thr Tyr Leu Asn Trp Phe His Gln Arg Pro Gly Gln Ser
35 40 45

Pro Arg Arg Leu Ile Tyr Glu Val Ser Asn Arg Asp Ser Gly Val Pro
50 55 60

Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Gly
85 90 95

Thr His Trp Pro Gly Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 698
<211> 490
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 698
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Gly Gly Leu
20 25 30

Val Lys Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
35 40 45

Thr Phe Ser Asp Tyr Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys
50 55 60

Gly Leu Glu Trp Val Ser Tyr Ile Ser Ser Ser Gly Asn Thr Ile Tyr
65 70 75 80

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala
85 90 95

Lys Asn Ser Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Ala Arg Ser Thr Met Val Arg Glu Asp Tyr Trp
115 120 125

Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Gly Gly Gly Gly
130 135 140

Ser Gly Gly Arg Ala Ser Gly Gly Gly Gly Ser Asp Ile Val Leu Thr
145 150 155 160

Gln Ser Pro Leu Ser Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile
165 170 175

Ser Cys Lys Ser Ser Glu Ser Leu Val His Asn Ser Gly Lys Thr Tyr
180 185 190

Leu Asn Trp Phe His Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile
195 200 205

Tyr Glu Val Ser Asn Arg Asp Ser Gly Val Pro Asp Arg Phe Thr Gly
210 215 220

Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala
225 230 235 240

Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Gly

_SL

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                245                 250                 255

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Thr Thr Thr Pro Ala
            260                 265                 270

Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser
        275                 280                 285

Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr
    290                 295                 300

Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala
305                 310                 315                 320

Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys
                325                 330                 335

Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met
            340                 345                 350

Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe
        355                 360                 365

Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg
    370                 375                 380

Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn
385                 390                 395                 400

Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg
                405                 410                 415

Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro
            420                 425                 430

Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala
        435                 440                 445

Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His
    450                 455                 460

Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp
465                 470                 475                 480

Ala Leu His Met Gln Ala Leu Pro Pro Arg
                485                 490
```

<210> 699
<211> 1470
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 699
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtgc aactggtgca aagcggagga ggattggtca aacccggagg aagcctgaga 120

ctgtcatgcg cggcctctgg attcaccttc tccgattact acatgtcatg gatcagacag 180

gccccgggga agggcctcga atgggtgtcc tacatctcgt cctccgggaa caccatctac 240

tacgccgaca gcgtgaaggg ccgctttacc atttcccgcg acaacgcaaa gaactcgctg 300

taccttcaga tgaattccct gcgggctgaa gataccgcgg tgtactattg cgcccggtcc 360

actatggtcc gggaggacta ctggggacag ggcacactcg tgaccgtgtc cagcgcgagc 420

gggggtggag gcagcggtgg acgcgcctcc ggcggcggcg gttcagacat cgtgctgact 480

cagtcgcccc tgtcgctgcc ggtcaccctg ggccaaccgg cctcaattag ctgcaagtcc 540

tcggagagcc tggtgcacaa ctcaggaaag acttacctga actggttcca tcagcggcct 600

ggacagtccc cacggaggct catctatgaa gtgtccaaca gggattcggg ggtgcccgac 660

cgcttcactg gctccgggtc cggcaccgac ttcaccttga aaatctccag agtggaagcc 720

gaggacgtgg gcgtgtacta ctgtatgcag ggtacccact ggcctggaac ctttggacaa 780

ggaactaagc tcgagattaa gaccactacc ccagcaccga ggccacccac cccggctcct 840

accatcgcct cccagcctct gtccctgcgt ccggaggcat gtagacccgc agctggtggg 900

gccgtgcata cccggggtct tgacttcgcc tgcgatatct acatttgggc ccctctggct 960

ggtacttgcg gggtcctgct gctttcactc gtgatcactc tttactgtaa gcgcggtcgg 1020

aagaagctgc tgtacatctt taagcaaccc ttcatgaggc ctgtgcagac tactcaagag 1080

gaggacggct gttcatgccg gttcccagag gaggaggaag gcggctgcga actgcgcgtg 1140

aaattcagcc gcagcgcaga tgctccagcc tacaagcagg ggcagaacca gctctacaac 1200

gaactcaatc ttggtcggag agaggagtac gacgtgctgg acaagcggag aggacgggac 1260

ccagaaatgg gcgggaagcc gcgcagaaag aatccccaag agggcctgta caacgagctc 1320

caaaaggata agatggcaga agcctatagc gagattggta tgaaagggga acgcagaaga 1380

ggcaaaggcc acgacggact gtaccaggga ctcagcaccg ccaccaagga cacctatgac 1440

gctcttcaca tgcaggccct gccgcctcgg 1470

<210> 700

<211> 239
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 700

```
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe Ala Leu Ser Asn His
            20                  25                  30

Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr Ala Ala Ser Val Lys
    50                  55                  60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg Asn Thr Leu Tyr Leu
65                  70                  75                  80

Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Ile Tyr Tyr Cys Ser
                85                  90                  95

Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln Gly Thr Thr Val Thr
            100                 105                 110

Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly Gly Arg Ala Ser Gly
        115                 120                 125

Gly Gly Gly Ser Asp Ile Arg Leu Thr Gln Ser Pro Ser Pro Leu Ser
    130                 135                 140

Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Gln Ala Ser Glu Asp
145                 150                 155                 160

Ile Asn Lys Phe Leu Asn Trp Tyr His Gln Thr Pro Gly Lys Ala Pro
                165                 170                 175

Lys Leu Leu Ile Tyr Asp Ala Ser Thr Leu Gln Thr Gly Val Pro Ser
            180                 185                 190

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asn
        195                 200                 205

Ser Leu Gln Pro Glu Asp Ile Gly Thr Tyr Tyr Cys Gln Gln Tyr Glu
```

_SL
210 215 220

Ser Leu Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
225 230 235

<210> 701
<211> 717
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 701
caagtgcaac tcgtggaatc tggtggagga ctcgtgcaac ccggtggaag ccttaggctg 60

tcgtgcgccg tcagcgggtt tgctctgagc aaccatggaa tgtcctgggt ccgccgggca 120

ccgggaaaag ggctggaatg ggtgtccggc atcgtgtaca gcgggtcaac ctattacgcc 180

gcgtccgtga agggcagatt cactatctca agagacaaca gccggaacac cctgtacttg 240

caaatgaatt ccctgcgccc cgaggacacc gccatctact actgctccgc ccacggagga 300

gagtcggacg tgtggggcca gggaacgact gtgactgtgt ccagcgcatc aggaggggt 360

ggttcgggcg gccgggcctc ggggggagga ggttccgaca ttcggctgac ccagtccccg 420

tccccactgt cggcctccgt cggcgaccgc gtgaccatca cttgtcaggc gtccgaggac 480

attaacaagt tcctgaactg gtaccaccag acccctggaa aggcccccaa gctgctgatc 540

tacgatgcct cgacccttca aactggagtg cctagccggt tctccgggtc cggctccggc 600

actgatttca ctctgaccat caactcattg cagccggaag atatcgggac ctactattgc 660

cagcagtacg aatccctccc gctcacattc ggcgggggaa ccaaggtcga gattaag 717

<210> 702
<211> 115
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 702
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe Ala Leu Ser Asn His
20 25 30

Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys Gly Leu Glu Trp Val

_SL
35 40 45

Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr Ala Ala Ser Val Lys
50 55 60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg Asn Thr Leu Tyr Leu
65 70 75 80

Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Ile Tyr Tyr Cys Ser
85 90 95

Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser
115

<210> 703
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 703
Asp Ile Arg Leu Thr Gln Ser Pro Ser Pro Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Gln Ala Ser Glu Asp Ile Asn Lys Phe
20 25 30

Leu Asn Trp Tyr His Gln Thr Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Asp Ala Ser Thr Leu Gln Thr Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asn Ser Leu Gln Pro
65 70 75 80

Glu Asp Ile Gly Thr Tyr Tyr Cys Gln Gln Tyr Glu Ser Leu Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 704

<211> 483
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 704

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15

His Ala Ala Arg Pro Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu
            20                  25                  30

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe
        35                  40                  45

Ala Leu Ser Asn His Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys
    50                  55                  60

Gly Leu Glu Trp Val Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr
65                  70                  75                  80

Ala Ala Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg
                85                  90                  95

Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala
            100                 105                 110

Ile Tyr Tyr Cys Ser Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln
        115                 120                 125

Gly Thr Thr Val Thr Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly
    130                 135                 140

Gly Arg Ala Ser Gly Gly Gly Gly Ser Asp Ile Arg Leu Thr Gln Ser
145                 150                 155                 160

Pro Ser Pro Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
                165                 170                 175

Gln Ala Ser Glu Asp Ile Asn Lys Phe Leu Asn Trp Tyr His Gln Thr
            180                 185                 190

Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Thr Leu Gln
        195                 200                 205

Thr Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
```

_SL

210 215 220

Thr Leu Thr Ile Asn Ser Leu Gln Pro Glu Asp Ile Gly Thr Tyr Tyr
225 230 235 240

Cys Gln Gln Tyr Glu Ser Leu Pro Leu Thr Phe Gly Gly Gly Thr Lys
245 250 255

Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala
260 265 270

Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg
275 280 285

Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys
290 295 300

Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu
305 310 315 320

Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu
325 330 335

Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln
340 345 350

Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly
355 360 365

Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr
370 375 380

Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg
385 390 395 400

Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met
405 410 415

Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu
420 425 430

Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys
435 440 445

Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu
450 455 460

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                                                _SL
Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu
465                 470                 475                 480


Pro Pro Arg



<210> 705
<211> 1449
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 705
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg       60

ccccaagtgc aactcgtgga atctggtgga ggactcgtgc aacccggtgg aagccttagg      120

ctgtcgtgcg ccgtcagcgg gtttgctctg agcaaccatg gaatgtcctg ggtccgccgg      180

gcaccgggaa aagggctgga atgggtgtcc ggcatcgtgt acagcgggtc aacctattac      240

gccgcgtccg tgaagggcag attcactatc tcaagagaca acagccggaa caccctgtac      300

ttgcaaatga attccctgcg ccccgaggac accgccatct actactgctc cgcccacgga      360

ggagagtcgg acgtgtgggg ccagggaacg actgtgactg tgtccagcgc atcaggaggg      420

ggtggttcgg gcggccgggc ctcgggggga ggaggttccg acattcggct gacccagtcc      480

ccgtccccac tgtcggcctc cgtcggcgac cgcgtgacca tcacttgtca ggcgtccgag      540

gacattaaca agttcctgaa ctggtaccac cagacccctg gaaaggcccc caagctgctg      600

atctacgatg cctcgaccct tcaaactgga gtgcctagcc ggttctccgg gtccggctcc      660

ggcactgatt tcactctgac catcaactca ttgcagccgg aagatatcgg gacctactat      720

tgccagcagt acgaatccct cccgctcaca ttcggcgggg gaaccaaggt cgagattaag      780

accactaccc cagcaccgag gccacccacc ccggctccta ccatcgcctc ccagcctctg      840

tccctgcgtc cggaggcatg tagacccgca gctggtgggg ccgtgcatac ccggggtctt      900

gacttcgcct gcgatatcta catttgggcc cctctggctg gtacttgcgg ggtcctgctg      960

ctttcactcg tgatcactct ttactgtaag cgcggtcgga agaagctgct gtacatcttt     1020

aagcaaccct tcatgaggcc tgtgcagact actcaagagg aggacggctg ttcatgccgg     1080

ttcccagagg aggaggaagg cggctgcgaa ctgcgcgtga aattcagccg cagcgcagat     1140

gctccagcct acaagcaggg gcagaaccag ctctacaacg aactcaatct tggtcggaga     1200

gaggagtacg acgtgctgga caagcggaga ggacgggacc cagaaatggg cgggaagccg     1260

cgcagaaaga atccccaaga gggcctgtac aacgagctcc aaaaggataa gatggcagaa     1320
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gcctatagcg agattggtat gaaaggggaa cgcagaagag gcaaaggcca cgacggactg 1380

taccagggac tcagcaccgc caccaaggac acctatgacg ctcttcacat gcaggccctg 1440

ccgcctcgg 1449

<210> 706
<211> 240
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 706

Glu Val Gln Leu Val Glu Thr Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe Ala Leu Ser Asn His
20 25 30

Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr Ala Ala Ser Val Lys
50 55 60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg Asn Thr Leu Tyr Leu
65 70 75 80

Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Ile Tyr Tyr Cys Ser
85 90 95

Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly Gly Arg Ala Ser Gly
115 120 125

Gly Gly Gly Ser Glu Thr Thr Leu Thr Gln Ser Pro Ala Thr Leu Ser
130 135 140

Val Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser
145 150 155 160

Val Gly Ser Asn Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Gly Pro
165 170 175

Arg Leu Leu Ile Tyr Gly Ala Ser Thr Arg Ala Thr Gly Ile Pro Ala

_SL
180 185 190

Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser
195 200 205

Ser Leu Gln Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Asn
210 215 220

Asp Trp Leu Pro Val Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
225 230 235 240

<210> 707
<211> 720
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 707
gaagtgcaat tggtggaaac tggaggagga cttgtgcaac ctggaggatc attgcggctc 60

tcatgcgctg tctccggctt cgccctgtca aatcacggga tgtcgtgggt cagacgggcc 120

ccgggaaagg gtctggaatg ggtgtcgggg attgtgtaca gcggctccac ctactacgcc 180

gcttcggtca agggccgctt cactatttca cgggacaaca gccgcaacac cctctatctg 240

caaatgaact ctctccgccc ggaggatacc gccatctact actgctccgc acacggcggc 300

gaatccgacg tgtggggaca gggaaccact gtcaccgtgt cgtccgcatc cggtggcgga 360

ggatcgggtg gccgggcctc cgggggcggc ggcagcgaga ctaccctgac ccagtcccct 420

gccactctgt ccgtgagccc gggagagaga gccaccctta gctgccgggc cagccagagc 480

gtgggctcca acctggcctg gtaccagcag aagccaggac agggtcccag gctgctgatc 540

tacggagcct ccactcgcgc gaccggcatc cccgcgaggt tctccgggtc gggttccggg 600

accgagttca ccctgaccat ctcctccctc caaccggagg acttcgcggt gtactactgt 660

cagcagtaca acgattggct gcccgtgaca tttggacagg ggacgaaggt ggaaatcaaa 720

<210> 708
<211> 115
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 708
Glu Val Gln Leu Val Glu Thr Gly Gly Gly Leu Val Gln Pro Gly Gly

_SL
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe Ala Leu Ser Asn His
20 25 30

Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr Ala Ala Ser Val Lys
50 55 60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg Asn Thr Leu Tyr Leu
65 70 75 80

Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Ile Tyr Tyr Cys Ser
85 90 95

Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser
115

<210> 709
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 709
Glu Thr Thr Leu Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Gly Ser Asn
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Gly Pro Arg Leu Leu Ile
35 40 45

Tyr Gly Ala Ser Thr Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Asn Asp Trp Leu Pro

_SL
85 90 95

Val Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 710
<211> 484
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 710
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Val Gln Leu Val Glu Thr Gly Gly Gly Leu
20 25 30

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe
35 40 45

Ala Leu Ser Asn His Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys
50 55 60

Gly Leu Glu Trp Val Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr
65 70 75 80

Ala Ala Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg
85 90 95

Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala
100 105 110

Ile Tyr Tyr Cys Ser Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln
115 120 125

Gly Thr Thr Val Thr Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly
130 135 140

Gly Arg Ala Ser Gly Gly Gly Gly Ser Glu Thr Thr Leu Thr Gln Ser
145 150 155 160

Pro Ala Thr Leu Ser Val Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
165 170 175

Arg Ala Ser Gln Ser Val Gly Ser Asn Leu Ala Trp Tyr Gln Gln Lys

_SL

```
            180                 185                 190

Pro Gly Gln Gly Pro Arg Leu Leu Ile Tyr Gly Ala Ser Thr Arg Ala
        195                 200                 205

Thr Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe
    210                 215                 220

Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Val Tyr Tyr
225                 230                 235                 240

Cys Gln Gln Tyr Asn Asp Trp Leu Pro Val Thr Phe Gly Gln Gly Thr
                245                 250                 255

Lys Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro
            260                 265                 270

Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys
        275                 280                 285

Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala
    290                 295                 300

Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu
305                 310                 315                 320

Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys
                325                 330                 335

Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr
            340                 345                 350

Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly
        355                 360                 365

Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala
    370                 375                 380

Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg
385                 390                 395                 400

Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu
                405                 410                 415

Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn
            420                 425                 430
```

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                                                _SL
Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met
        435                 440                 445

Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly
    450                 455                 460

Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala
465                 470                 475                 480

Leu Pro Pro Arg
```

<210> 711
<211> 1452
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 711

```
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg       60

cccgaagtgc aattggtgga aactggagga ggacttgtgc aacctggagg atcattgcgg      120

ctctcatgcg ctgtctccgg cttcgccctg tcaaatcacg ggatgtcgtg ggtcagacgg      180

gccccgggaa agggtctgga atgggtgtcg gggattgtgt acagcggctc cacctactac      240

gccgcttcgg tcaagggccg cttcactatt tcacgggaca acagccgcaa caccctctat      300

ctgcaaatga actctctccg cccggaggat accgccatct actactgctc cgcacacggc      360

ggcgaatccg acgtgtgggg acagggaacc actgtcaccg tgtcgtccgc atccggtggc      420

ggaggatcgg gtggccgggc ctccgggggc ggcggcagcg agactaccct gacccagtcc      480

cctgccactc tgtccgtgag cccgggagag agagccaccc ttagctgccg ggccagccag      540

agcgtgggct ccaacctggc ctggtaccag cagaagccag gacagggtcc caggctgctg      600

atctacggag cctccactcg cgcgaccggc atccccgcga ggttctccgg gtcgggttcc      660

gggaccgagt tcaccctgac catctcctcc ctccaaccgg aggacttcgc ggtgtactac      720

tgtcagcagt acaacgattg gctgcccgtg acatttggac aggggacgaa ggtggaaatc      780

aaaaccacta ccccagcacc gaggccaccc accccggctc ctaccatcgc ctcccagcct      840

ctgtccctgc gtccggaggc atgtagaccc gcagctggtg gggccgtgca tacccggggt      900

cttgacttcg cctgcgatat ctacatttgg gcccctctgg ctggtacttg cggggtcctg      960

ctgctttcac tcgtgatcac tctttactgt aagcgcggtc ggaagaagct gctgtacatc     1020

tttaagcaac ccttcatgag gcctgtgcag actactcaag aggaggacgg ctgttcatgc     1080
```

cggttcccag aggaggagga aggcggctgc gaactgcgcg tgaaattcag ccgcagcgca 1140

gatgctccag cctacaagca ggggcagaac cagctctaca acgaactcaa tcttggtcgg 1200

agagaggagt acgacgtgct ggacaagcgg agaggacggg acccagaaat gggcgggaag 1260

ccgcgcagaa agaatcccca agagggcctg tacaacgagc tccaaaagga taagatggca 1320

gaagcctata gcgagattgg tatgaaaggg gaacgcagaa gaggcaaagg ccacgacgga 1380

ctgtaccagg gactcagcac cgccaccaag gacacctatg acgctcttca catgcaggcc 1440

ctgccgcctc gg 1452

<210> 712
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 712
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe Ala Leu Ser Asn His
20 25 30

Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr Ala Ala Ser Val Lys
50 55 60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg Asn Thr Leu Tyr Leu
65 70 75 80

Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Ile Tyr Tyr Cys Ser
85 90 95

Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly Gly Arg Ala Ser Gly
115 120 125

Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser
130 135 140

Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser

```
                                                _SL
145                 150                 155                 160

Ile Gly Ser Ser Ser Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala
                165                 170                 175

Pro Arg Leu Leu Met Tyr Gly Ala Ser Ser Arg Ala Ser Gly Ile Pro
            180                 185                 190

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile
        195                 200                 205

Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr
    210                 215                 220

Ala Gly Ser Pro Pro Phe Thr Phe Gly Gln Gly Thr Lys Val Glu Ile
225                 230                 235                 240

Lys
```

<210> 713
<211> 723
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 713
```
gaagtgcaat tggtggaatc tggtggagga cttgtgcaac ctggaggatc actgagactg       60

tcatgcgcgg tgtccggttt tgccctgagc aatcatggga tgtcgtgggt ccggcgcgcc      120

cccggaaagg gtctggaatg ggtgtcgggt atcgtctact ccgggagcac ttactacgcc      180

gcgagcgtga agggccgctt caccatttcc cgcgataact cccgcaacac cctgtacttg      240

caaatgaact cgctccggcc tgaggacact gccatctact actgctccgc acacggagga      300

gaatccgacg tgtggggcca gggaactacc gtgaccgtca gcagcgcctc cggcggcggg      360

ggctcaggcg gacgggctag cggcggcggt ggctccgaga tcgtgctgac ccagtcgcct      420

ggcactctct cgctgagccc cggggaaagg gcaaccctgt cctgtcgggc cagccagtcc      480

attggatcat cctccctcgc ctggtatcag cagaaaccgg gacaggctcc gcggctgctt      540

atgtatgggg ccagctcaag agcctccggc attcccgacc ggttctccgg gtccggttcc      600

ggcaccgatt tcaccctgac tatctcgagg ctggagccag aggacttcgc cgtgtactac      660

tgccagcagt acgcggggtc cccgccgttc acgttcggac agggaaccaa ggtcgagatc      720

aag                                                                    723
```

<210> 714
<211> 115
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 714
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe Ala Leu Ser Asn His
20 25 30

Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr Ala Ala Ser Val Lys
50 55 60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg Asn Thr Leu Tyr Leu
65 70 75 80

Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Ile Tyr Tyr Cys Ser
85 90 95

Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser
115

<210> 715
<211> 109
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 715
Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Ile Gly Ser Ser
20 25 30

```
Ser Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
        35                  40                  45

Met Tyr Gly Ala Ser Ser Arg Ala Ser Gly Ile Pro Asp Arg Phe Ser
    50                  55                  60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65                  70                  75                  80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Ala Gly Ser Pro
                85                  90                  95

Pro Phe Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
            100                 105


<210> 716
<211> 485
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 716
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15

His Ala Ala Arg Pro Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
            20                  25                  30

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe
        35                  40                  45

Ala Leu Ser Asn His Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys
    50                  55                  60

Gly Leu Glu Trp Val Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr
65                  70                  75                  80

Ala Ala Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg
                85                  90                  95

Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala
            100                 105                 110

Ile Tyr Tyr Cys Ser Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln
        115                 120                 125
```

```
Gly Thr Thr Val Thr Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly
    130                 135                 140

Gly Arg Ala Ser Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser
145                 150                 155                 160

Pro Gly Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
                165                 170                 175

Arg Ala Ser Gln Ser Ile Gly Ser Ser Ser Leu Ala Trp Tyr Gln Gln
            180                 185                 190

Lys Pro Gly Gln Ala Pro Arg Leu Leu Met Tyr Gly Ala Ser Ser Arg
        195                 200                 205

Ala Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
    210                 215                 220

Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr
225                 230                 235                 240

Tyr Cys Gln Gln Tyr Ala Gly Ser Pro Pro Phe Thr Phe Gly Gln Gly
                245                 250                 255

Thr Lys Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr
            260                 265                 270

Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala
        275                 280                 285

Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe
    290                 295                 300

Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val
305                 310                 315                 320

Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys
                325                 330                 335

Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr
            340                 345                 350

Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu
        355                 360                 365

Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro
    370                 375                 380
```

Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly
385 390 395 400

Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro
405 410 415

Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr
420 425 430

Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly
435 440 445

Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln
450 455 460

Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln
465 470 475 480

Ala Leu Pro Pro Arg
485

<210> 717
<211> 1455
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 717
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaagtgc aattggtgga atctggtgga ggacttgtgc aacctggagg atcactgaga 120

ctgtcatgcg cggtgtccgg ttttgccctg agcaatcatg ggatgtcgtg ggtccggcgc 180

gcccccggaa agggtctgga atgggtgtcg ggtatcgtct actccgggag cacttactac 240

gccgcgagcg tgaagggccg cttcaccatt tcccgcgata actcccgcaa caccctgtac 300

ttgcaaatga actcgctccg gcctgaggac actgccatct actactgctc cgcacacgga 360

ggagaatccg acgtgtgggg ccagggaact accgtgaccg tcagcagcgc ctccggcggc 420

gggggctcag gcggacgggc tagcggcggc ggtggctccg agatcgtgct gacccagtcg 480

cctggcactc tctcgctgag ccccggggaa agggcaaccc tgtcctgtcg ggccagccag 540

tccattggat catcctccct cgcctggtat cagcagaaac cgggacaggc tccgcggctg 600

cttatgtatg gggccagctc aagagcctcc ggcattcccg accggttctc cgggtccggt 660

tccggcaccg atttcaccct gactatctcg aggctggagc cagaggactt cgccgtgtac 720

tactgccagc agtacgcggg gtccccgccg ttcacgttcg gacagggaac caaggtcgag 780

atcaagacca ctaccccagc accgaggcca cccaccccgg ctcctaccat cgcctcccag 840

cctctgtccc tgcgtccgga ggcatgtaga cccgcagctg gtggggccgt gcatacccgg 900

ggtcttgact tcgcctgcga tatctacatt tgggcccctc tggctggtac ttgcggggtc 960

ctgctgcttt cactcgtgat cactctttac tgtaagcgcg gtcggaagaa gctgctgtac 1020

atctttaagc aacccttcat gaggcctgtg cagactactc aagaggagga cggctgttca 1080

tgccggttcc cagaggagga ggaaggcggc tgcgaactgc gcgtgaaatt cagccgcagc 1140

gcagatgctc cagcctacaa gcaggggcag aaccagctct acaacgaact caatcttggt 1200

cggagagagg agtacgacgt gctggacaag cggagaggac gggacccaga aatgggcggg 1260

aagccgcgca gaaagaatcc ccaagagggc ctgtacaacg agctccaaaa ggataagatg 1320

gcagaagcct atagcgagat tggtatgaaa ggggaacgca gaagaggcaa aggccacgac 1380

ggactgtacc agggactcag caccgccacc aaggacacct atgacgctct tcacatgcag 1440

gccctgccgc ctcgg 1455

<210> 718
<211> 243
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 718

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Ser
20 25 30

Tyr Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45

Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Ser Ala Tyr Tyr Asn Pro Ser
50 55 60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80

Ser Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95

Cys Ala Arg His Trp Gln Glu Trp Pro Asp Ala Phe Asp Ile Trp Gly
100 105 110

Gln Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
115 120 125

Gly Gly Ser Gly Gly Gly Gly Ser Glu Thr Thr Leu Thr Gln Ser Pro
130 135 140

Ala Phe Met Ser Ala Thr Pro Gly Asp Lys Val Ile Ile Ser Cys Lys
145 150 155 160

Ala Ser Gln Asp Ile Asp Asp Ala Met Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Glu Ala Pro Leu Phe Ile Ile Gln Ser Ala Thr Ser Pro Val Pro
180 185 190

Gly Ile Pro Pro Arg Phe Ser Gly Ser Gly Phe Gly Thr Asp Phe Ser
195 200 205

Leu Thr Ile Asn Asn Ile Glu Ser Glu Asp Ala Ala Tyr Tyr Phe Cys
210 215 220

Leu Gln His Asp Asn Phe Pro Leu Thr Phe Gly Gln Gly Thr Lys Leu
225 230 235 240

Glu Ile Lys

<210> 719
<211> 729
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 719
caagtgcagc ttcaggaaag cggaccgggc ctggtcaagc catccgaaac tctctccctg 60

acttgcactg tgtctggcgg ttccatctca tcgtcgtact actactgggg ctggattagg 120

cagccgcccg gaaagggact ggagtggatc ggaagcatct actattccgg ctcggcgtac 180

tacaacccta gcctcaagtc gagagtgacc atctccgtgg atacctccaa gaaccagttt 240

tccctgcgcc tgagctccgt gaccgccgct gacaccgccg tgtactactg tgctcggcat 300

tggcaggaat ggcccgatgc cttcgacatt tggggccagg gcactatggt cactgtgtca 360

tccgggggtg gaggcagcgg gggaggaggg tccgggggggg gaggttcaga gacaaccttg 420

acccagtcac ccgcattcat gtccgccact ccgggagaca aggtcatcat ctcgtgcaaa 480

gcgtcccagg atatcgacga tgccatgaat tggtaccagc agaagcctgg cgaagcgccg 540

ctgttcatta tccaatccgc aacctcgccc gtgcctggaa tcccaccgcg gttcagcggc 600

agcggtttcg gaaccgactt ttccctgacc attaacaaca ttgagtccga ggacgccgcc 660

tactacttct gcctgcaaca cgacaacttc cctctcacgt tcggccaggg aaccaagctg 720

gaaatcaag 729

<210> 720
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 720
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Ser
20 25 30

Tyr Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45

Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Ser Ala Tyr Tyr Asn Pro Ser
50 55 60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80

Ser Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95

Cys Ala Arg His Trp Gln Glu Trp Pro Asp Ala Phe Asp Ile Trp Gly
100 105 110

Gln Gly Thr Met Val Thr Val Ser Ser
115 120

<210> 721
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 721
Glu Thr Thr Leu Thr Gln Ser Pro Ala Phe Met Ser Ala Thr Pro Gly
1 5 10 15

Asp Lys Val Ile Ile Ser Cys Lys Ala Ser Gln Asp Ile Asp Asp Ala
20 25 30

Met Asn Trp Tyr Gln Gln Lys Pro Gly Glu Ala Pro Leu Phe Ile Ile
35 40 45

Gln Ser Ala Thr Ser Pro Val Pro Gly Ile Pro Pro Arg Phe Ser Gly
50 55 60

Ser Gly Phe Gly Thr Asp Phe Ser Leu Thr Ile Asn Asn Ile Glu Ser
65 70 75 80

Glu Asp Ala Ala Tyr Tyr Phe Cys Leu Gln His Asp Asn Phe Pro Leu
85 90 95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 722
<211> 487
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 722
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu
20 25 30

Val Lys Pro Ser Glu Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly
35 40 45

Ser Ile Ser Ser Ser Tyr Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro
50 55 60

Gly Lys Gly Leu Glu Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Ser Ala

```
                                                _SL
65                  70                  75                  80

Tyr Tyr Asn Pro Ser Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr
                85                  90                  95

Ser Lys Asn Gln Phe Ser Leu Arg Leu Ser Ser Val Thr Ala Ala Asp
            100                 105                 110

Thr Ala Val Tyr Tyr Cys Ala Arg His Trp Gln Glu Trp Pro Asp Ala
        115                 120                 125

Phe Asp Ile Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Gly Gly
    130                 135                 140

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Thr Thr
145                 150                 155                 160

Leu Thr Gln Ser Pro Ala Phe Met Ser Ala Thr Pro Gly Asp Lys Val
                165                 170                 175

Ile Ile Ser Cys Lys Ala Ser Gln Asp Ile Asp Asp Ala Met Asn Trp
            180                 185                 190

Tyr Gln Gln Lys Pro Gly Glu Ala Pro Leu Phe Ile Ile Gln Ser Ala
        195                 200                 205

Thr Ser Pro Val Pro Gly Ile Pro Pro Arg Phe Ser Gly Ser Gly Phe
    210                 215                 220

Gly Thr Asp Phe Ser Leu Thr Ile Asn Asn Ile Glu Ser Glu Asp Ala
225                 230                 235                 240

Ala Tyr Tyr Phe Cys Leu Gln His Asp Asn Phe Pro Leu Thr Phe Gly
                245                 250                 255

Gln Gly Thr Lys Leu Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro
            260                 265                 270

Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro
        275                 280                 285

Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu
    290                 295                 300

Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys
305                 310                 315                 320
```

_SL
Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly
325 330 335

Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val
340 345 350

Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu
355 360 365

Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp
370 375 380

Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn
385 390 395 400

Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg
405 410 415

Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly
420 425 430

Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu
435 440 445

Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu
450 455 460

Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His
465 470 475 480

Met Gln Ala Leu Pro Pro Arg
485

<210> 723
<211> 1461
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 723
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtgc agcttcagga aagcggaccg ggcctggtca agccatccga aactctctcc 120

ctgacttgca ctgtgtctgg cggttccatc tcatcgtcgt actactactg gggctggatt 180

aggcagccgc ccggaaaggg actggagtgg atcggaagca tctactattc cggctcggcg 240

tactacaacc ctagcctcaa gtcgagagtg accatctccg tggatacctc caagaaccag 300

ttttccctgc gcctgagctc cgtgaccgcc gctgacaccg ccgtgtacta ctgtgctcgg 360

cattggcagg aatggcccga tgccttcgac atttggggcc agggcactat ggtcactgtg 420

tcatccgggg gtggaggcag cgggggagga gggtccgggg ggggaggttc agagacaacc 480

ttgacccagt cacccgcatt catgtccgcc actccgggag acaaggtcat catctcgtgc 540

aaagcgtccc aggatatcga cgatgccatg aattggtacc agcagaagcc tggcgaagcg 600

ccgctgttca ttatccaatc cgcaacctcg cccgtgcctg gaatcccacc gcggttcagc 660

ggcagcggtt tcggaaccga cttttccctg accattaaca acattgagtc cgaggacgcc 720

gcctactact tctgcctgca acacgacaac ttccctctca cgttcggcca gggaaccaag 780

ctggaaatca agaccactac cccagcaccg aggccaccca ccccggctcc taccatcgcc 840

tcccagcctc tgtccctgcg tccggaggca tgtagacccg cagctggtgg ggccgtgcat 900

acccggggtc ttgacttcgc ctgcgatatc tacatttggg cccctctggc tggtacttgc 960

ggggtcctgc tgctttcact cgtgatcact ctttactgta agcgcggtcg gaagaagctg 1020

ctgtacatct ttaagcaacc cttcatgagg cctgtgcaga ctactcaaga ggaggacggc 1080

tgttcatgcc ggttcccaga ggaggaggaa ggcggctgcg aactgcgcgt gaaattcagc 1140

cgcagcgcag atgctccagc ctacaagcag gggcagaacc agctctacaa cgaactcaat 1200

cttggtcgga gagaggagta cgacgtgctg gacaagcgga gaggacggga cccagaaatg 1260

ggcgggaagc cgcgcagaaa gaatccccaa gagggcctgt acaacgagct ccaaaaggat 1320

aagatggcag aagcctatag cgagattggt atgaaagggg aacgcagaag aggcaaaggc 1380

cacgacggac tgtaccaggg actcagcacc gccaccaagg acacctatga cgctcttcac 1440

atgcaggccc tgccgcctcg g 1461

<210> 724
<211> 244
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 724
Val Asn Leu Arg Glu Ser Gly Pro Ala Leu Val Lys Pro Thr Gln Thr
1 5 10 15

Leu Thr Leu Thr Cys Thr Phe Ser Gly Phe Ser Leu Arg Thr Ser Gly
20 25 30

Met Cys Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Ala Leu Glu Trp

_SL
35 40 45

Leu Ala Arg Ile Asp Trp Asp Glu Asp Lys Phe Tyr Ser Thr Ser Leu
50 55 60

Lys Thr Arg Leu Thr Ile Ser Lys Asp Thr Ser Asp Asn Gln Val Val
65 70 75 80

Leu Arg Met Thr Asn Met Asp Pro Ala Asp Thr Ala Thr Tyr Tyr Cys
85 90 95

Ala Arg Ser Gly Ala Gly Gly Thr Ser Ala Thr Ala Phe Asp Ile Trp
100 105 110

Gly Pro Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
115 120 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser
130 135 140

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
145 150 155 160

Arg Ala Ser Gln Asp Ile Tyr Asn Asn Leu Ala Trp Phe Gln Leu Lys
165 170 175

Pro Gly Ser Ala Pro Arg Ser Leu Met Tyr Ala Ala Asn Lys Ser Gln
180 185 190

Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Ala Ser Gly Thr Asp Phe
195 200 205

Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr
210 215 220

Cys Gln His Tyr Tyr Arg Phe Pro Tyr Ser Phe Gly Gln Gly Thr Lys
225 230 235 240

Leu Glu Ile Lys

<210> 725
<211> 735
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

polynucleotide"

<400> 725
caagtcaatc tgcgcgaatc cggccccgcc ttggtcaagc ctacccagac cctcactctg 60

acctgtactt tctccggctt ctccctgcgg acttccggga tgtgcgtgtc ctggatcaga 120

cagcctccgg gaaaggccct ggagtggctc gctcgcattg actgggatga ggacaagttc 180

tactccacct cactcaagac caggctgacc atcagcaaag atacctctga caaccaagtg 240

gtgctccgca tgaccaacat ggacccagcc gacactgcca cttactactg cgcgaggagc 300

ggagcgggcg gaacctccgc caccgccttc gatatttggg gcccgggtac catggtcacc 360

gtgtcaagcg gaggaggggg gtccgggggc ggcggttccg ggggaggcgg atcggacatt 420

cagatgactc agtcaccatc gtccctgagc gctagcgtgg gcgacagagt gacaatcact 480

tgccgggcat cccaggacat ctataacaac cttgcgtggt tccagctgaa gcctggttcc 540

gcaccgcggt cacttatgta cgccgccaac aagagccagt cgggagtgcc gtcccggttt 600

tccggttcgg cctcgggaac tgacttcacc ctgacgatct ccagcctgca acccgaggat 660

ttcgccacct actactgcca gcactactac cgctttccct actcgttcgg acagggaacc 720

aagctggaaa tcaag 735

<210> 726
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 726
Gln Val Asn Leu Arg Glu Ser Gly Pro Ala Leu Val Lys Pro Thr Gln
1 5 10 15

Thr Leu Thr Leu Thr Cys Thr Phe Ser Gly Phe Ser Leu Arg Thr Ser
20 25 30

Gly Met Cys Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Ala Leu Glu
35 40 45

Trp Leu Ala Arg Ile Asp Trp Asp Glu Asp Lys Phe Tyr Ser Thr Ser
50 55 60

Leu Lys Thr Arg Leu Thr Ile Ser Lys Asp Thr Ser Asp Asn Gln Val
65 70 75 80

Val Leu Arg Met Thr Asn Met Asp Pro Ala Asp Thr Ala Thr Tyr Tyr
85 90 95

Cys Ala Arg Ser Gly Ala Gly Gly Thr Ser Ala Thr Ala Phe Asp Ile
100 105 110

Trp Gly Pro Gly Thr Met Val Thr Val Ser Ser
115 120

<210> 727
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 727
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Tyr Asn Asn
20 25 30

Leu Ala Trp Phe Gln Leu Lys Pro Gly Ser Ala Pro Arg Ser Leu Met
35 40 45

Tyr Ala Ala Asn Lys Ser Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Ala Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln His Tyr Tyr Arg Phe Pro Tyr
85 90 95

Ser Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 728
<211> 489
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 728
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

```
His Ala Ala Arg Pro Gln Val Asn Leu Arg Glu Ser Gly Pro Ala Leu
            20                  25                  30

Val Lys Pro Thr Gln Thr Leu Thr Leu Thr Cys Thr Phe Ser Gly Phe
        35                  40                  45

Ser Leu Arg Thr Ser Gly Met Cys Val Ser Trp Ile Arg Gln Pro Pro
    50                  55                  60

Gly Lys Ala Leu Glu Trp Leu Ala Arg Ile Asp Trp Asp Glu Asp Lys
65                  70                  75                  80

Phe Tyr Ser Thr Ser Leu Lys Thr Arg Leu Thr Ile Ser Lys Asp Thr
                85                  90                  95

Ser Asp Asn Gln Val Val Leu Arg Met Thr Asn Met Asp Pro Ala Asp
            100                 105                 110

Thr Ala Thr Tyr Tyr Cys Ala Arg Ser Gly Ala Gly Gly Thr Ser Ala
        115                 120                 125

Thr Ala Phe Asp Ile Trp Gly Pro Gly Thr Met Val Thr Val Ser Ser
    130                 135                 140

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp
145                 150                 155                 160

Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp
                165                 170                 175

Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Tyr Asn Asn Leu
            180                 185                 190

Ala Trp Phe Gln Leu Lys Pro Gly Ser Ala Pro Arg Ser Leu Met Tyr
        195                 200                 205

Ala Ala Asn Lys Ser Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
    210                 215                 220

Ala Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
225                 230                 235                 240

Asp Phe Ala Thr Tyr Tyr Cys Gln His Tyr Tyr Arg Phe Pro Tyr Ser
                245                 250                 255

Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Thr Thr Thr Pro Ala Pro
            260                 265                 270
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Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu
        275                 280                 285

Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg
    290                 295                 300

Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly
305                 310                 315                 320

Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys
                325                 330                 335

Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg
            340                 345                 350

Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro
        355                 360                 365

Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser
    370                 375                 380

Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu
385                 390                 395                 400

Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg
                405                 410                 415

Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln
            420                 425                 430

Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr
        435                 440                 445

Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp
    450                 455                 460

Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala
465                 470                 475                 480

Leu His Met Gln Ala Leu Pro Pro Arg
                485
```

<210> 729
<211> 1467
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 729
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtca atctgcgcga atccggcccc gccttggtca agcctaccca gaccctcact 120

ctgacctgta ctttctccgg cttctccctg cggacttccg ggatgtgcgt gtcctggatc 180

agacagcctc cgggaaaggc cctggagtgg ctcgctcgca ttgactggga tgaggacaag 240

ttctactcca cctcactcaa gaccaggctg accatcagca aagatacctc tgacaaccaa 300

gtggtgctcc gcatgaccaa catggaccca gccgacactg ccacttacta ctgcgcgagg 360

agcggagcgg gcggaacctc cgccaccgcc ttcgatattt ggggcccggg taccatggtc 420

accgtgtcaa gcggaggagg ggggtccggg ggcggcggtt ccgggggagg cggatcggac 480

attcagatga ctcagtcacc atcgtccctg agcgctagcg tgggcgacag agtgacaatc 540

acttgccggg catcccagga catctataac aaccttgcgt ggttccagct gaagcctggt 600

tccgcaccgc ggtcacttat gtacgccgcc aacaagagcc agtcgggagt gccgtcccgg 660

ttttccggtt cggcctcggg aactgacttc accctgacga tctccagcct gcaacccgag 720

gatttcgcca cctactactg ccagcactac taccgctttc cctactcgtt cggacaggga 780

accaagctgg aaatcaagac cactacccca gcaccgaggc cacccacccc ggctcctacc 840

atcgcctccc agcctctgtc cctgcgtccg gaggcatgta gacccgcagc tggtggggcc 900

gtgcataccc ggggtcttga cttcgcctgc gatatctaca tttgggcccc tctggctggt 960

acttgcgggg tcctgctgct ttcactcgtg atcactcttt actgtaagcg cggtcggaag 1020

aagctgctgt acatctttaa gcaacccttc atgaggcctg tgcagactac tcaagaggag 1080

gacggctgtt catgccggtt cccagaggag gaggaaggcg gctgcgaact gcgcgtgaaa 1140

ttcagccgca gcgcagatgc tccagcctac aagcaggggc agaaccagct ctacaacgaa 1200

ctcaatcttg gtcggagaga ggagtacgac gtgctggaca agcggagagg acgggaccca 1260

gaaatgggcg ggaagccgcg cagaaagaat ccccaagagg gcctgtacaa cgagctccaa 1320

aaggataaga tggcagaagc ctatagcgag attggtatga aaggggaacg cagaagaggc 1380

aaaggccacg acggactgta ccagggactc agcaccgcca ccaaggacac ctatgacgct 1440

cttcacatgc aggccctgcc gcctcgg 1467

<210> 730
<211> 246
<212> PRT
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 730
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ser Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ser Ile Ser Ser Ser Ser Ser Tyr Ile Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Thr Ile Ala Ala Val Tyr Ala Phe Asp Ile Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
115 120 125

Ser Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Leu Ser
130 135 140

Leu Pro Val Thr Pro Glu Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser
145 150 155 160

Gln Ser Leu Leu His Ser Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu
165 170 175

Gln Lys Pro Gly Gln Ser Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn
180 185 190

Arg Ala Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr
195 200 205

Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Val Gly Val
210 215 220

Tyr Tyr Cys Met Gln Ala Leu Gln Thr Pro Tyr Thr Phe Gly Gln Gly
225 230 235 240

Thr Lys Leu Glu Ile Lys
245

<210> 731
<211> 738
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 731
gaagtgcagc ttgtcgaatc cgggggggga ctggtcaagc cgggcggatc actgagactg 60

tcctgcgccg cgagcggctt cacgttctcc tcctactcca tgaactgggt ccgccaagcc 120

cccgggaagg gactggaatg ggtgtcctct atctcctcgt cgtcgtccta catctactac 180

gccgactccg tgaagggaag attcaccatt tcccgcgaca acgcaaagaa ctcactgtac 240

ttgcaaatga actcactccg ggccgaagat actgctgtgt actattgcgc caagactatt 300

gccgccgtct acgctttcga catctggggc cagggaacca ccgtgactgt gtcgtccggt 360

ggtggtggct cgggcggagg aggaagcggc ggcggggggt ccgagattgt gctgacccag 420

tcgccactga gcctccctgt gacccccgag gaacccgcca gcatcagctg ccggtccagc 480

cagtccctgc tccactccaa cggatacaat tacctcgatt ggtaccttca gaagcctgga 540

caaagcccgc agctgctcat ctacttggga tcaaaccgcg cgtcaggagt gcctgaccgg 600

ttctccggct cgggcagcgg taccgatttc accctgaaaa tctccagggt ggaggcagag 660

gacgtgggag tgtattactg tatgcaggcg ctgcagactc cgtacacatt tgggcagggc 720

accaagctgg agatcaag 738

<210> 732
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 732
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

```
                                                _SL
Ser Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Ser Ile Ser Ser Ser Ser Ser Tyr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Thr Ile Ala Ala Val Tyr Ala Phe Asp Ile Trp Gly Gln Gly
            100                 105                 110

Thr Thr Val Thr Val Ser Ser
        115


<210> 733
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 733
Glu Ile Val Leu Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Glu
1               5                   10                  15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser
            20                  25                  30

Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
        35                  40                  45

Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro
    50                  55                  60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65                  70                  75                  80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala
                85                  90                  95

Leu Gln Thr Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100                 105                 110
```

<210> 734
<211> 490
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 734

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Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15

His Ala Ala Arg Pro Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
            20                  25                  30

Val Lys Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
        35                  40                  45

Thr Phe Ser Ser Tyr Ser Met Asn Trp Val Arg Gln Ala Pro Gly Lys
    50                  55                  60

Gly Leu Glu Trp Val Ser Ser Ile Ser Ser Ser Ser Ser Tyr Ile Tyr
65                  70                  75                  80

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala
                85                  90                  95

Lys Asn Ser Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Lys Thr Ile Ala Ala Val Tyr Ala Phe Asp
        115                 120                 125

Ile Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly
    130                 135                 140

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Leu Thr
145                 150                 155                 160

Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Glu Glu Pro Ala Ser Ile
                165                 170                 175

Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser Asn Gly Tyr Asn Tyr
            180                 185                 190

Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Gln Leu Leu Ile
        195                 200                 205
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                                                _SL
Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro Asp Arg Phe Ser Gly
    210                 215                 220

Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala
225                 230                 235                 240

Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala Leu Gln Thr Pro Tyr
                245                 250                 255

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Thr Thr Thr Pro Ala
            260                 265                 270

Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser
        275                 280                 285

Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr
    290                 295                 300

Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala
305                 310                 315                 320

Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys
                325                 330                 335

Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met
            340                 345                 350

Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe
        355                 360                 365

Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg
    370                 375                 380

Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn
385                 390                 395                 400

Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg
                405                 410                 415

Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro
            420                 425                 430

Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala
        435                 440                 445

Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His
    450                 455                 460
```

Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp
465 470 475 480

Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 735
<211> 1470
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 735
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaagtgc agcttgtcga atccgggggg ggactggtca agccgggcgg atcactgaga 120

ctgtcctgcg ccgcgagcgg cttcacgttc tcctcctact ccatgaactg ggtccgccaa 180

gcccccggga agggactgga atgggtgtcc tctatctcct cgtcgtcgtc ctacatctac 240

tacgccgact ccgtgaaggg aagattcacc atttcccgcg acaacgcaaa gaactcactg 300

tacttgcaaa tgaactcact ccgggccgaa gatactgctg tgtactattg cgccaagact 360

attgccgccg tctacgcttt cgacatctgg ggccagggaa ccaccgtgac tgtgtcgtcc 420

ggtggtggtg gctcgggcgg aggaggaagc ggcggcgggg ggtccgagat tgtgctgacc 480

cagtcgccac tgagcctccc tgtgaccccc gaggaacccg ccagcatcag ctgccggtcc 540

agccagtccc tgctccactc caacggatac aattacctcg attggtacct tcagaagcct 600

ggacaaagcc cgcagctgct catctacttg ggatcaaacc gcgcgtcagg agtgcctgac 660

cggttctccg gctcgggcag cggtaccgat ttcaccctga aaatctccag ggtggaggca 720

gaggacgtgg gagtgtatta ctgtatgcag gcgctgcaga ctccgtacac atttgggcag 780

ggcaccaagc tggagatcaa gaccactacc ccagcaccga ggccacccac cccggctcct 840

accatcgcct cccagcctct gtccctgcgt ccggaggcat gtagacccgc agctggtggg 900

gccgtgcata cccggggtct tgacttcgcc tgcgatatct acatttgggc ccctctggct 960

ggtacttgcg gggtcctgct gctttcactc gtgatcactc tttactgtaa gcgcggtcgg 1020

aagaagctgc tgtacatctt taagcaaccc ttcatgaggc ctgtgcagac tactcaagag 1080

gaggacggct gttcatgccg gttcccagag gaggaggaag gcggctgcga actgcgcgtg 1140

aaattcagcc gcagcgcaga tgctccagcc tacaagcagg ggcagaacca gctctacaac 1200

gaactcaatc ttggtcggag agaggagtac gacgtgctgg acaagcggag aggacgggac 1260

ccagaaatgg gcgggaagcc gcgcagaaag aatccccaag agggcctgta caacgagctc 1320

caaaaggata agatggcaga agcctatagc gagattggta tgaaagggga acgcagaaga 1380

ggcaaaggcc acgacggact gtaccaggga ctcagcaccg ccaccaagga cacctatgac 1440

gctcttcaca tgcaggccct gccgcctcgg 1470

<210> 736
<211> 240
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 736
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
20 25 30

Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Leu Arg Gly Ala Phe Asp Ile Trp Gly Gln Gly Thr Met
100 105 110

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
115 120 125

Gly Gly Gly Ser Ser Tyr Val Leu Thr Gln Ser Pro Ser Val Ser Ala
130 135 140

Ala Pro Gly Tyr Thr Ala Thr Ile Ser Cys Gly Gly Asn Asn Ile Gly
145 150 155 160

Thr Lys Ser Val His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu
165 170 175

_SL
Leu Val Ile Arg Asp Asp Ser Val Arg Pro Ser Lys Ile Pro Gly Arg
            180   185   190

Phe Ser Gly Ser Asn Ser Gly Asn Met Ala Thr Leu Thr Ile Ser Gly
        195   200   205

Val Gln Ala Gly Asp Glu Ala Asp Phe Tyr Cys Gln Val Trp Asp Ser
    210   215   220

Asp Ser Glu His Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
225   230   235   240

<210> 737
<211> 720
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 737
gaagtccagc tcgtggagtc cggcggaggc cttgtgaagc ctggaggttc gctgagactg 60

tcctgcgccg cctccggctt caccttctcc gactactaca tgtcctggat cagacaggcc 120

ccgggaaagg gcctggaatg ggtgtcctac atctcgtcat cgggcagcac tatctactac 180

gcggactcag tgaaggggcg gttcaccatt tcccgggata acgcgaagaa ctcgctgtat 240

ctgcaaatga actcactgag ggccgaggac accgccgtgt actactgcgc ccgcgatctc 300

cgcggggcat ttgacatctg gggacaggga accatggtca cagtgtccag cggaggggga 360

ggatcgggtg gcggaggttc cgggggtgga ggctcctcct acgtgctgac tcagagccca 420

agcgtcagcg ctgcgcccgg ttacacggca accatctcct gtggcggaaa caacattggg 480

accaagtctg tgcactggta tcagcagaag ccgggccaag ctcccctgtt ggtgatccgc 540

gatgactccg tgcggcctag caaaattccg ggacggttct ccggctccaa cagcggcaat 600

atggccactc tcaccatctc gggagtgcag gccggagatg aagccgactt ctactgccaa 660

gtctgggact cagactccga gcatgtggtg ttcgggggcg gaaccaagct gactgtgctc 720

<210> 738
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 738

_SL
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
20 25 30

Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Leu Arg Gly Ala Phe Asp Ile Trp Gly Gln Gly Thr Met
100 105 110

Val Thr Val Ser Ser
115

<210> 739
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 739
Ser Tyr Val Leu Thr Gln Ser Pro Ser Val Ser Ala Ala Pro Gly Tyr
1 5 10 15

Thr Ala Thr Ile Ser Cys Gly Gly Asn Asn Ile Gly Thr Lys Ser Val
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Leu Val Ile Arg
35 40 45

Asp Asp Ser Val Arg Pro Ser Lys Ile Pro Gly Arg Phe Ser Gly Ser
50 55 60

Asn Ser Gly Asn Met Ala Thr Leu Thr Ile Ser Gly Val Gln Ala Gly
65 70 75 80

_SL
Asp Glu Ala Asp Phe Tyr Cys Gln Val Trp Asp Ser Asp Ser Glu His
85 90 95

Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 740
<211> 484
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 740
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
20 25 30

Val Lys Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
35 40 45

Thr Phe Ser Asp Tyr Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys
50 55 60

Gly Leu Glu Trp Val Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr
65 70 75 80

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala
85 90 95

Lys Asn Ser Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Ala Arg Asp Leu Arg Gly Ala Phe Asp Ile Trp
115 120 125

Gly Gln Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
130 135 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Ser Tyr Val Leu Thr Gln Ser
145 150 155 160

Pro Ser Val Ser Ala Ala Pro Gly Tyr Thr Ala Thr Ile Ser Cys Gly
165 170 175

_SL

Gly Asn Asn Ile Gly Thr Lys Ser Val His Trp Tyr Gln Gln Lys Pro
180 185 190

Gly Gln Ala Pro Leu Leu Val Ile Arg Asp Asp Ser Val Arg Pro Ser
195 200 205

Lys Ile Pro Gly Arg Phe Ser Gly Ser Asn Ser Gly Asn Met Ala Thr
210 215 220

Leu Thr Ile Ser Gly Val Gln Ala Gly Asp Glu Ala Asp Phe Tyr Cys
225 230 235 240

Gln Val Trp Asp Ser Asp Ser Glu His Val Val Phe Gly Gly Gly Thr
245 250 255

Lys Leu Thr Val Leu Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro
260 265 270

Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys
275 280 285

Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala
290 295 300

Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu
305 310 315 320

Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys
325 330 335

Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr
340 345 350

Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly
355 360 365

Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala
370 375 380

Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg
385 390 395 400

Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu
405 410 415

Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn
420 425 430

Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met
435 440 445

Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly
450 455 460

Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala
465 470 475 480

Leu Pro Pro Arg

<210> 741
<211> 1452
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 741
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaagtcc agctcgtgga gtccggcgga ggccttgtga agcctggagg ttcgctgaga 120

ctgtcctgcg ccgcctccgg cttcaccttc tccgactact acatgtcctg gatcagacag 180

gccccgggaa agggcctgga atgggtgtcc tacatctcgt catcgggcag cactatctac 240

tacgcggact cagtgaaggg gcggttcacc atttcccggg ataacgcgaa gaactcgctg 300

tatctgcaaa tgaactcact gagggccgag gacaccgccg tgtactactg cgcccgcgat 360

ctccgcgggg catttgacat ctggggacag ggaaccatgg tcacagtgtc cagcggaggg 420

ggaggatcgg gtggcggagg ttccgggggt ggaggctcct cctacgtgct gactcagagc 480

ccaagcgtca gcgctgcgcc cggttacacg gcaaccatct cctgtggcgg aaacaacatt 540

gggaccaagt ctgtgcactg gtatcagcag aagccgggcc aagctcccct gttggtgatc 600

cgcgatgact ccgtgcggcc tagcaaaatt ccgggacggt tctccggctc caacagcggc 660

aatatggcca ctctcaccat ctcgggagtg caggccggag atgaagccga cttctactgc 720

caagtctggg actcagactc cgagcatgtg gtgttcgggg gcggaaccaa gctgactgtg 780

ctcaccacta ccccagcacc gaggccaccc accccggctc ctaccatcgc ctcccagcct 840

ctgtccctgc gtccggaggc atgtagaccc gcagctggtg gggccgtgca tacccggggt 900

cttgacttcg cctgcgatat ctacatttgg gcccctctgg ctggtacttg cggggtcctg 960

ctgctttcac tcgtgatcac tctttactgt aagcgcggtc ggaagaagct gctgtacatc 1020

tttaagcaac ccttcatgag gcctgtgcag actactcaag aggaggacgg ctgttcatgc 1080

cggttcccag aggaggagga aggcggctgc gaactgcgcg tgaaattcag ccgcagcgca 1140

gatgctccag cctacaagca ggggcagaac cagctctaca acgaactcaa tcttggtcgg 1200

agagaggagt acgacgtgct ggacaagcgg agaggacggg acccagaaat gggcgggaag 1260

ccgcgcagaa agaatcccca agagggcctg tacaacgagc tccaaaagga taagatggca 1320

gaagcctata gcgagattgg tatgaaaggg gaacgcagaa gaggcaaagg ccacgacgga 1380

ctgtaccagg gactcagcac cgccaccaag gacacctatg acgctcttca catgcaggcc 1440

ctgccgcctc gg 1452

<210> 742
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 742
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Pro Ser Gly Tyr Thr Val Thr Ser His
20 25 30

Tyr Ile His Trp Val Arg Arg Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Met Ile Asn Pro Ser Gly Gly Val Thr Ala Tyr Ser Gln Thr Leu
50 55 60

Gln Gly Arg Val Thr Met Thr Ser Asp Thr Ser Ser Ser Thr Val Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Met Tyr Tyr Cys
85 90 95

Ala Arg Glu Gly Ser Gly Ser Gly Trp Tyr Phe Asp Phe Trp Gly Arg
100 105 110

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Ser Tyr Val Leu Thr Gln Pro Pro Ser
130 135 140

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                                                _SL
Val Ser Val Ser Pro Gly Gln Thr Ala Ser Ile Thr Cys Ser Gly Asp
145                 150                 155                 160

Gly Leu Ser Lys Lys Tyr Val Ser Trp Tyr Gln Gln Lys Ala Gly Gln
                165                 170                 175

Ser Pro Val Val Leu Ile Ser Arg Asp Lys Glu Arg Pro Ser Gly Ile
            180                 185                 190

Pro Asp Arg Phe Ser Gly Ser Asn Ser Ala Asp Thr Ala Thr Leu Thr
        195                 200                 205

Ile Ser Gly Thr Gln Ala Met Asp Glu Ala Asp Tyr Tyr Cys Gln Ala
    210                 215                 220

Trp Asp Asp Thr Thr Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val
225                 230                 235                 240

Leu
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<210> 743
<211> 723
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 743
caagtgcagc tggtgcagag cggggccgaa gtcaagaagc cgggagcctc cgtgaaagtg 60

tcctgcaagc cttcgggata caccgtgacc tcccactaca ttcattgggt ccgccgcgcc 120

cccggccaag gactcgagtg gatgggcatg atcaacccta gcggcggagt gaccgcgtac 180

agccagacgc tgcagggacg cgtgactatg acctcggata cctcctcctc caccgtctat 240

atggaactgt ccagcctgcg gtccgaggat accgccatgt actactgcgc ccgggaagga 300

tcaggctccg ggtggtattt cgacttctgg ggaagaggca ccctcgtgac tgtgtcatct 360

gggggagggg gttccggtgg tggcggatcg ggaggaggcg gttcatccta cgtgctgacc 420

cagccaccct ccgtgtccgt gagccccggc cagactgcat cgattacatg tagcggcgac 480

ggcctctcca agaaatacgt gtcgtggtac cagcagaagg ccggacagag cccggtggtg 540

ctgatctcaa gagataagga gcggcctagc ggaatcccgg acaggttctc gggttccaac 600

tccgcggaca ctgctactct gaccatctcg gggacccagg ctatggacga agccgattac 660

tactgccaag cctgggacga cactactgtc gtgtttggag ggggcaccaa gttgaccgtc 720

<210> 744
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 744
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Pro Ser Gly Tyr Thr Val Thr Ser His
20 25 30

Tyr Ile His Trp Val Arg Arg Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Met Ile Asn Pro Ser Gly Gly Val Thr Ala Tyr Ser Gln Thr Leu
50 55 60

Gln Gly Arg Val Thr Met Thr Ser Asp Thr Ser Ser Ser Thr Val Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Met Tyr Tyr Cys
85 90 95

Ala Arg Glu Gly Ser Gly Ser Gly Trp Tyr Phe Asp Phe Trp Gly Arg
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 745
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 745
Ser Tyr Val Leu Thr Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln
1 5 10 15

Thr Ala Ser Ile Thr Cys Ser Gly Asp Gly Leu Ser Lys Lys Tyr Val
20 25 30

Ser Trp Tyr Gln Gln Lys Ala Gly Gln Ser Pro Val Val Leu Ile Ser
        35   40   45

Arg Asp Lys Glu Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser
    50   55   60

Asn Ser Ala Asp Thr Ala Thr Leu Thr Ile Ser Gly Thr Gln Ala Met
65   70   75   80

Asp Glu Ala Asp Tyr Tyr Cys Gln Ala Trp Asp Asp Thr Thr Val Val
                85   90   95

Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
            100   105

<210> 746
<211> 485
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 746
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1   5   10   15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
            20   25   30

Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Pro Ser Gly Tyr
        35   40   45

Thr Val Thr Ser His Tyr Ile His Trp Val Arg Arg Ala Pro Gly Gln
    50   55   60

Gly Leu Glu Trp Met Gly Met Ile Asn Pro Ser Gly Gly Val Thr Ala
65   70   75   80

Tyr Ser Gln Thr Leu Gln Gly Arg Val Thr Met Thr Ser Asp Thr Ser
                85   90   95

Ser Ser Thr Val Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
            100   105   110

Ala Met Tyr Tyr Cys Ala Arg Glu Gly Ser Gly Ser Gly Trp Tyr Phe
        115   120   125

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Asp Phe Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
    130                 135                 140

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ser Tyr Val Leu
145                 150                 155                 160

Thr Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln Thr Ala Ser Ile
                165                 170                 175

Thr Cys Ser Gly Asp Gly Leu Ser Lys Lys Tyr Val Ser Trp Tyr Gln
            180                 185                 190

Gln Lys Ala Gly Gln Ser Pro Val Val Leu Ile Ser Arg Asp Lys Glu
        195                 200                 205

Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser Asn Ser Ala Asp
    210                 215                 220

Thr Ala Thr Leu Thr Ile Ser Gly Thr Gln Ala Met Asp Glu Ala Asp
225                 230                 235                 240

Tyr Tyr Cys Gln Ala Trp Asp Asp Thr Thr Val Val Phe Gly Gly Gly
                245                 250                 255

Thr Lys Leu Thr Val Leu Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr
            260                 265                 270

Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala
        275                 280                 285

Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe
    290                 295                 300

Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val
305                 310                 315                 320

Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys
                325                 330                 335

Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr
            340                 345                 350

Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu
        355                 360                 365

Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro
```

_SL
370 375 380

Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly
385 390 395 400

Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro
405 410 415

Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr
420 425 430

Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly
435 440 445

Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln
450 455 460

Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln
465 470 475 480

Ala Leu Pro Pro Arg
485

<210> 747
<211> 1455
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 747
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtgc agctggtgca gagcggggcc gaagtcaaga agccgggagc ctccgtgaaa 120

gtgtcctgca agccttcggg atacaccgtg acctcccact acattcattg ggtccgccgc 180

gcccccggcc aaggactcga gtggatgggc atgatcaacc ctagcggcgg agtgaccgcg 240

tacagccaga cgctgcaggg acgcgtgact atgacctcgg atacctcctc ctccaccgtc 300

tatatggaac tgtccagcct gcggtccgag gataccgcca tgtactactg cgcccgggaa 360

ggatcaggct ccgggtggta tttcgacttc tggggaagag gcaccctcgt gactgtgtca 420

tctgggggag ggggttccgg tggtggcgga tcgggaggag gcggttcatc ctacgtgctg 480

acccagccac cctccgtgtc cgtgagcccc ggccagactg catcgattac atgtagcggc 540

gacggcctct ccaagaaata cgtgtcgtgg taccagcaga aggccggaca gagcccggtg 600

gtgctgatct caagagataa ggagcggcct agcggaatcc cggacaggtt ctcgggttcc 660

aactccgcgg acactgctac tctgaccatc tcggggaccc aggctatgga cgaagccgat 720

tactactgcc aagcctggga cgacactact gtcgtgtttg gaggggcac caagttgacc 780

gtccttacca ctaccccagc accgaggcca cccaccccgg ctcctaccat cgcctcccag 840

cctctgtccc tgcgtccgga ggcatgtaga cccgcagctg gtggggccgt gcatacccgg 900

ggtcttgact tcgcctgcga tatctacatt tgggcccctc tggctggtac ttgcggggtc 960

ctgctgcttt cactcgtgat cactctttac tgtaagcgcg gtcggaagaa gctgctgtac 1020

atctttaagc aacccttcat gaggcctgtg cagactactc aagaggagga cggctgttca 1080

tgccggttcc cagaggagga ggaaggcggc tgcgaactgc gcgtgaaatt cagccgcagc 1140

gcagatgctc cagcctacaa gcaggggcag aaccagctct acaacgaact caatcttggt 1200

cggagagagg agtacgacgt gctggacaag cggagaggac gggacccaga aatgggcggg 1260

aagccgcgca gaaagaatcc ccaagagggc ctgtacaacg agctccaaaa ggataagatg 1320

gcagaagcct atagcgagat tggtatgaaa ggggaacgca gaagaggcaa aggccacgac 1380

ggactgtacc agggactcag caccgccacc aaggacacct atgacgctct tcacatgcag 1440

gccctgccgc ctcgg 1455

<210> 748
<211> 245
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 748
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
20 25 30

Gly Tyr Tyr Trp Ser Trp Ile Arg Gln His Pro Gly Lys Gly Leu Glu
35 40 45

Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
50 55 60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95

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Cys Ala Arg Ala Gly Ile Ala Ala Arg Leu Arg Gly Ala Phe Asp Ile
            100                 105                 110

Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln
    130                 135                 140

Ser Pro Ser Ser Val Ser Ala Ser Val Gly Asp Arg Val Ile Ile Thr
145                 150                 155                 160

Cys Arg Ala Ser Gln Gly Ile Arg Asn Trp Leu Ala Trp Tyr Gln Gln
                165                 170                 175

Lys Pro Gly Lys Ala Pro Asn Leu Leu Ile Tyr Ala Ala Ser Asn Leu
            180                 185                 190

Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Ala Asp
        195                 200                 205

Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Val Ala Thr Tyr
    210                 215                 220

Tyr Cys Gln Lys Tyr Asn Ser Ala Pro Phe Thr Phe Gly Pro Gly Thr
225                 230                 235                 240

Lys Val Asp Ile Lys
                245
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<210> 749
<211> 735
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 749

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caagtgcagc ttcaggagag cggcccggga ctcgtgaagc cgtcccagac cctgtccctg       60

acttgcaccg tgtcgggagg aagcatctcg agcggaggct actattggtc gtggattcgg      120

cagcaccctg gaaagggcct ggaatggatc ggctacatct actactccgg ctcgacctac      180

tacaacccat cgctgaagtc cagagtgaca atctcagtgg acacgtccaa gaatcagttc      240

agcctgaagc tctcttccgt gactgcggcc gacaccgccg tgtactactg cgcacgcgct      300
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ggaattgccg cccggctgag gggtgccttc gacatttggg gacagggcac catggtcacc 360

gtgtcctccg gcggcggagg ttccgggggt ggaggctcag gaggaggggg gtccgacatc 420

gtcatgactc agtcgccctc aagcgtcagc gcgtccgtcg gggacagagt gatcatcacc 480

tgtcgggcgt cccagggaat tcgcaactgg ctggcctggt atcagcagaa gcccggaaag 540

gcccccaacc tgttgatcta cgccgcctca aacctccaat ccggggtgcc gagccgcttc 600

agcggctccg gttcgggtgc cgatttcact ctgaccatct cctccctgca acctgaagat 660

gtggctacct actactgcca aaagtacaac tccgcacctt ttactttcgg accggggacc 720

aaagtggaca ttaag 735

<210> 750
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 750

Gln	Val	Gln	Leu	Gln	Glu	Ser	Gly	Pro	Gly	Leu	Val	Lys	Pro	Ser	Gln
1				5				10					15		
Thr	Leu	Ser	Leu	Thr	Cys	Thr	Val	Ser	Gly	Gly	Ser	Ile	Ser	Ser	Gly
			20					25					30		
Gly	Tyr	Tyr	Trp	Ser	Trp	Ile	Arg	Gln	His	Pro	Gly	Lys	Gly	Leu	Glu
		35					40					45			
Trp	Ile	Gly	Tyr	Ile	Tyr	Tyr	Ser	Gly	Ser	Thr	Tyr	Tyr	Asn	Pro	Ser
	50					55					60				
Leu	Lys	Ser	Arg	Val	Thr	Ile	Ser	Val	Asp	Thr	Ser	Lys	Asn	Gln	Phe
65					70					75					80
Ser	Leu	Lys	Leu	Ser	Ser	Val	Thr	Ala	Ala	Asp	Thr	Ala	Val	Tyr	Tyr
				85					90					95	
Cys	Ala	Arg	Ala	Gly	Ile	Ala	Ala	Arg	Leu	Arg	Gly	Ala	Phe	Asp	Ile
			100					105					110		
Trp	Gly	Gln	Gly	Thr	Met	Val	Thr	Val	Ser	Ser					
		115					120								

<210> 751
<211> 107
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 751
Asp Ile Val Met Thr Gln Ser Pro Ser Ser Val Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Ile Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Trp
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Asn Leu Leu Ile
35 40 45

Tyr Ala Ala Ser Asn Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Ala Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Val Ala Thr Tyr Tyr Cys Gln Lys Tyr Asn Ser Ala Pro Phe
85 90 95

Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys
100 105

<210> 752
<211> 489
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 752
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu
20 25 30

Val Lys Pro Ser Gln Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly
35 40 45

Ser Ile Ser Ser Gly Gly Tyr Tyr Trp Ser Trp Ile Arg Gln His Pro
50 55 60

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                                                _SL
Gly Lys Gly Leu Glu Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr
65                  70                  75                  80

Tyr Tyr Asn Pro Ser Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr
                85                  90                  95

Ser Lys Asn Gln Phe Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp
            100                 105                 110

Thr Ala Val Tyr Tyr Cys Ala Arg Ala Gly Ile Ala Ala Arg Leu Arg
        115                 120                 125

Gly Ala Phe Asp Ile Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
    130                 135                 140

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp
145                 150                 155                 160

Ile Val Met Thr Gln Ser Pro Ser Ser Val Ser Ala Ser Val Gly Asp
                165                 170                 175

Arg Val Ile Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Trp Leu
            180                 185                 190

Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Asn Leu Leu Ile Tyr
        195                 200                 205

Ala Ala Ser Asn Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
    210                 215                 220

Gly Ser Gly Ala Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
225                 230                 235                 240

Asp Val Ala Thr Tyr Tyr Cys Gln Lys Tyr Asn Ser Ala Pro Phe Thr
                245                 250                 255

Phe Gly Pro Gly Thr Lys Val Asp Ile Lys Thr Thr Thr Pro Ala Pro
            260                 265                 270

Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu
        275                 280                 285

Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg
    290                 295                 300

Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly
305                 310                 315                 320
```

Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys
325 330 335

Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg
340 345 350

Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro
355 360 365

Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser
370 375 380

Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu
385 390 395 400

Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg
405 410 415

Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln
420 425 430

Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr
435 440 445

Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp
450 455 460

Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala
465 470 475 480

Leu His Met Gln Ala Leu Pro Pro Arg
485

<210> 753
<211> 1467
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 753
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtgc agcttcagga gagcggcccg ggactcgtga agccgtccca gaccctgtcc 120

ctgacttgca ccgtgtcggg aggaagcatc tcgagcggag gctactattg gtcgtggatt 180

cggcagcacc ctggaaaggg cctggaatgg atcggctaca tctactactc cggctcgacc 240

tactacaacc catcgctgaa gtccagagtg acaatctcag tggacacgtc caagaatcag 300

ttcagcctga agctctcttc cgtgactgcg gccgacaccg ccgtgtacta ctgcgcacgc 360

gctggaattg ccgcccggct gaggggtgcc ttcgacattt ggggacaggg caccatggtc 420

accgtgtcct ccggcggcgg aggttccggg ggtggaggct caggaggagg ggggtccgac 480

atcgtcatga ctcagtcgcc ctcaagcgtc agcgcgtccg tcggggacag agtgatcatc 540

acctgtcggg cgtcccaggg aattcgcaac tggctggcct ggtatcagca gaagcccgga 600

aaggccccca acctgttgat ctacgccgcc tcaaacctcc aatccggggt gccgagccgc 660

ttcagcggct ccggttcggg tgccgatttc actctgacca tctcctccct gcaacctgaa 720

gatgtggcta cctactactg ccaaaagtac aactccgcac cttttacttt cggaccgggg 780

accaaagtgg acattaagac cactacccca gcaccgaggc cacccacccc ggctcctacc 840

atcgcctccc agcctctgtc cctgcgtccg gaggcatgta gacccgcagc tggtggggcc 900

gtgcataccc ggggtcttga cttcgcctgc gatatctaca tttgggcccc tctggctggt 960

acttgcgggg tcctgctgct ttcactcgtg atcactcttt actgtaagcg cggtcggaag 1020

aagctgctgt acatctttaa gcaacccttc atgaggcctg tgcagactac tcaagaggag 1080

gacggctgtt catgccggtt cccagaggag gaggaaggcg gctgcgaact gcgcgtgaaa 1140

ttcagccgca gcgcagatgc tccagcctac aagcaggggc agaaccagct ctacaacgaa 1200

ctcaatcttg gtcggagaga ggagtacgac gtgctggaca agcggagagg acgggaccca 1260

gaaatgggcg ggaagccgcg cagaaagaat ccccaagagg gcctgtacaa cgagctccaa 1320

aaggataaga tggcagaagc ctatagcgag attggtatga aaggggaacg cagaagaggc 1380

aaaggccacg acggactgta ccagggactc agcaccgcca ccaaggacac ctatgacgct 1440

cttcacatgc aggccctgcc gcctcgg 1467

<210> 754
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 754
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Thr Phe Ser Ser Tyr
20 25 30

_SL
Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35   40   45

Gly Gly Ile Ile Pro Ile Phe Gly Thr Ala Asn Tyr Ala Gln Lys Phe
    50   55   60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ala Tyr
65   70   75   80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Ala Arg Arg Gly Gly Tyr Gln Leu Leu Arg Trp Asp Val Gly Leu Leu
            100   105   110

Arg Ser Ala Phe Asp Ile Trp Gly Gln Gly Thr Met Val Thr Val Ser
        115   120   125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
    130   135   140

Ser Tyr Val Leu Thr Gln Pro Pro Ser Val Ser Val Ala Pro Gly Gln
145   150   155   160

Thr Ala Arg Ile Thr Cys Gly Gly Asn Asn Ile Gly Ser Lys Ser Val
                165   170   175

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Leu Tyr
            180   185   190

Gly Lys Asn Asn Arg Pro Ser Gly Val Pro Asp Arg Phe Ser Gly Ser
        195   200   205

Arg Ser Gly Thr Thr Ala Ser Leu Thr Ile Thr Gly Ala Gln Ala Glu
    210   215   220

Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Arg Asp Ser Ser Gly Asp His
225   230   235   240

Leu Arg Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu
                245   250

<210> 755
<211> 759
<212> DNA
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 755
caagtgcagc tggtccagtc gggcgccgag gtcaagaagc ccgggagctc tgtgaaagtg 60

tcctgcaagg cctccggggg cacctttagc tcctacgcca tctcctgggt ccgccaagca 120

ccgggtcaag gcctggagtg gatgggggga attatcccta tcttcggcac tgccaactac 180

gcccagaagt tccagggacg cgtgaccatt accgcggacg aatccacctc caccgcttat 240

atggagctgt ccagcttgcg ctcggaagat accgccgtgt actactgcgc ccggaggggt 300

ggataccagc tgctgagatg ggacgtgggc ctcctgcggt cggcgttcga catctggggc 360

cagggcacta tggtcactgt gtccagcgga ggaggcggat cgggaggcgg cggatcaggg 420

ggaggcggtt ccagctacgt gcttactcaa ccccccttcgg tgtccgtggc cccgggacag 480

accgccagaa tcacttgcgg aggaaacaac attgggtcca agagcgtgca ttggtaccag 540

cagaagccag gacaggcccc tgtgctggtg ctctacggga agaacaatcg gcccagcgga 600

gtgccggaca ggttctcggg ttcacgctcc ggtacaaccg cttcactgac tatcaccggg 660

gcccaggcag aggatgaagc ggactactac tgttcctccc gggattcatc cggcgaccac 720

ctccgggtgt tcggaaccgg aacgaaggtc accgtgctg 759

<210> 756
<211> 129
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 756
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Thr Phe Ser Ser Tyr
20 25 30

Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Gly Ile Ile Pro Ile Phe Gly Thr Ala Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys

_SL
85 90 95

Ala Arg Arg Gly Gly Tyr Gln Leu Leu Arg Trp Asp Val Gly Leu Leu
100 105 110

Arg Ser Ala Phe Asp Ile Trp Gly Gln Gly Thr Met Val Thr Val Ser
115 120 125

Ser

<210> 757
<211> 109
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 757
Ser Tyr Val Leu Thr Gln Pro Pro Ser Val Ser Val Ala Pro Gly Gln
1 5 10 15

Thr Ala Arg Ile Thr Cys Gly Gly Asn Asn Ile Gly Ser Lys Ser Val
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Leu Tyr
35 40 45

Gly Lys Asn Asn Arg Pro Ser Gly Val Pro Asp Arg Phe Ser Gly Ser
50 55 60

Arg Ser Gly Thr Thr Ala Ser Leu Thr Ile Thr Gly Ala Gln Ala Glu
65 70 75 80

Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Arg Asp Ser Ser Gly Asp His
85 90 95

Leu Arg Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu
100 105

<210> 758
<211> 497
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 758
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
20 25 30

Lys Lys Pro Gly Ser Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly
35 40 45

Thr Phe Ser Ser Tyr Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln
50 55 60

Gly Leu Glu Trp Met Gly Gly Ile Ile Pro Ile Phe Gly Thr Ala Asn
65 70 75 80

Tyr Ala Gln Lys Phe Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser
85 90 95

Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Ala Arg Arg Gly Gly Tyr Gln Leu Leu Arg Trp
115 120 125

Asp Val Gly Leu Leu Arg Ser Ala Phe Asp Ile Trp Gly Gln Gly Thr
130 135 140

Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
145 150 155 160

Gly Gly Gly Gly Ser Ser Tyr Val Leu Thr Gln Pro Pro Ser Val Ser
165 170 175

Val Ala Pro Gly Gln Thr Ala Arg Ile Thr Cys Gly Gly Asn Asn Ile
180 185 190

Gly Ser Lys Ser Val His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro
195 200 205

Val Leu Val Leu Tyr Gly Lys Asn Asn Arg Pro Ser Gly Val Pro Asp
210 215 220

Arg Phe Ser Gly Ser Arg Ser Gly Thr Thr Ala Ser Leu Thr Ile Thr
225 230 235 240

Gly Ala Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Arg Asp

_SL

245 250 255

Ser Ser Gly Asp His Leu Arg Val Phe Gly Thr Gly Thr Lys Val Thr
260 265 270

Val Leu Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr
275 280 285

Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala
290 295 300

Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile
305 310 315 320

Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser
325 330 335

Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr
340 345 350

Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu
355 360 365

Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu
370 375 380

Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln
385 390 395 400

Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu
405 410 415

Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly
420 425 430

Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln
435 440 445

Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu
450 455 460

Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr
465 470 475 480

Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro
485 490 495

Arg

<210> 759
<211> 1491
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 759
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtgc agctggtcca gtcgggcgcc gaggtcaaga agcccgggag ctctgtgaaa 120

gtgtcctgca aggcctccgg gggcaccttt agctcctacg ccatctcctg ggtccgccaa 180

gcaccgggtc aaggcctgga gtggatgggg ggaattatcc ctatcttcgg cactgccaac 240

tacgcccaga agttccaggg acgcgtgacc attaccgcgg acgaatccac ctccaccgct 300

tatatggagc tgtccagctt gcgctcggaa gataccgccg tgtactactg cgcccggagg 360

ggtggatacc agctgctgag atgggacgtg ggcctcctgc ggtcggcgtt cgacatctgg 420

ggccagggca ctatggtcac tgtgtccagc ggaggaggcg gatcgggagg cggcggatca 480

gggggaggcg gttccagcta cgtgcttact caacccccct cggtgtccgt ggccccggga 540

cagaccgcca gaatcacttg cggaggaaac aacattgggt ccaagagcgt gcattggtac 600

cagcagaagc caggacaggc ccctgtgctg gtgctctacg ggaagaacaa tcggcccagc 660

ggagtgccgg acaggttctc gggttcacgc tccggtacaa ccgcttcact gactatcacc 720

ggggcccagg cagaggatga agcggactac tactgttcct cccgggattc atccggcgac 780

cacctccggg tgttcggaac cggaacgaag gtcaccgtgc tgaccactac cccagcaccg 840

aggccaccca ccccggctcc taccatcgcc tcccagcctc tgtccctgcg tccggaggca 900

tgtagacccg cagctggtgg ggccgtgcat acccggggtc ttgacttcgc ctgcgatatc 960

tacatttggg cccctctggc tggtacttgc ggggtcctgc tgctttcact cgtgatcact 1020

ctttactgta agcgcggtcg gaagaagctg ctgtacatct ttaagcaacc cttcatgagg 1080

cctgtgcaga ctactcaaga ggaggacggc tgttcatgcc ggttcccaga ggaggaggaa 1140

ggcggctgcg aactgcgcgt gaaattcagc cgcagcgcag atgctccagc ctacaagcag 1200

gggcagaacc agctctacaa cgaactcaat cttggtcgga gagaggagta cgacgtgctg 1260

gacaagcgga gaggacggga cccagaaatg ggcgggaagc cgcgcagaaa gaatccccaa 1320

gagggcctgt acaacgagct ccaaaaggat aagatggcag aagcctatag cgagattggt 1380

atgaaagggg aacgcagaag aggcaaaggc cacgacggac tgtaccaggg actcagcacc 1440

gccaccaagg acacctatga cgctcttcac atgcaggccc tgccgcctcg g 1491

<210> 760
<211> 248
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 760
Glu Val Gln Leu Gln Gln Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Ala Ile Ser Gly Asp Ser Val Ser Ser Asn
20 25 30

Ser Ala Ala Trp Asn Trp Ile Arg Gln Ser Pro Ser Arg Gly Leu Glu
35 40 45

Trp Leu Gly Arg Thr Tyr Tyr Arg Ser Lys Trp Tyr Ser Phe Tyr Ala
50 55 60

Ile Ser Leu Lys Ser Arg Ile Ile Ile Asn Pro Asp Thr Ser Lys Asn
65 70 75 80

Gln Phe Ser Leu Gln Leu Lys Ser Val Thr Pro Glu Asp Thr Ala Val
85 90 95

Tyr Tyr Cys Ala Arg Ser Ser Pro Glu Gly Leu Phe Leu Tyr Trp Phe
100 105 110

Asp Pro Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Asp
115 120 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ser Ser Glu Leu
130 135 140

Thr Gln Asp Pro Ala Val Ser Val Ala Leu Gly Gln Thr Ile Arg Ile
145 150 155 160

Thr Cys Gln Gly Asp Ser Leu Gly Asn Tyr Tyr Ala Thr Trp Tyr Gln
165 170 175

Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Tyr Gly Thr Asn Asn
180 185 190

Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser Ala Ser Ser Ser Gly Asn

_SL
195 200 205

Thr Ala Ser Leu Thr Ile Thr Gly Ala Gln Ala Glu Asp Glu Ala Asp
210 215 220

Tyr Tyr Cys Asn Ser Arg Asp Ser Ser Gly His His Leu Leu Phe Gly
225 230 235 240

Thr Gly Thr Lys Val Thr Val Leu
245

<210> 761
<211> 744
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 761
gaagtgcagc tccaacagtc aggaccgggg ctcgtgaagc catcccagac cctgtccctg 60

acttgtgcca tctcgggaga tagcgtgtca tcgaactccg ccgcctggaa ctggattcgg 120

cagagcccgt cccgcggact ggagtggctt ggaaggacct actaccggtc caagtggtac 180

tctttctacg cgatctcgct gaagtcccgc attatcatta accctgatac ctccaagaat 240

cagttctccc tccaactgaa atccgtcacc cccgaggaca cagcagtgta ttactgcgca 300

cggagcagcc ccgaaggact gttcctgtat tggtttgacc cctggggcca ggggactctt 360

gtgaccgtgt cgagcggcgg agatgggtcc ggtggcggtg gttcgggggg cggcggatca 420

tcatccgaac tgacccagga cccggctgtg tccgtggcgc tgggacaaac catccgcatt 480

acgtgccagg gagactccct gggcaactac tacgccactt ggtaccagca gaagccgggc 540

caagcccctg tgttggtcat ctacgggacc aacaacagac cttccggcat ccccgaccgg 600

ttcagcgctt cgtcctccgg caacactgcc agcctgacca tcactggagc gcaggccgaa 660

gatgaggccg actactactg caacagcaga gactcctcgg gtcatcacct cttgttcgga 720

actggaacca aggtcaccgt gctg 744

<210> 762
<211> 125
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 762
Glu Val Gln Leu Gln Gln Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Ala Ile Ser Gly Asp Ser Val Ser Ser Asn
20 25 30

Ser Ala Ala Trp Asn Trp Ile Arg Gln Ser Pro Ser Arg Gly Leu Glu
35 40 45

Trp Leu Gly Arg Thr Tyr Tyr Arg Ser Lys Trp Tyr Ser Phe Tyr Ala
50 55 60

Ile Ser Leu Lys Ser Arg Ile Ile Ile Asn Pro Asp Thr Ser Lys Asn
65 70 75 80

Gln Phe Ser Leu Gln Leu Lys Ser Val Thr Pro Glu Asp Thr Ala Val
85 90 95

Tyr Tyr Cys Ala Arg Ser Ser Pro Glu Gly Leu Phe Leu Tyr Trp Phe
100 105 110

Asp Pro Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 763
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 763
Ser Ser Glu Leu Thr Gln Asp Pro Ala Val Ser Val Ala Leu Gly Gln
1 5 10 15

Thr Ile Arg Ile Thr Cys Gln Gly Asp Ser Leu Gly Asn Tyr Tyr Ala
20 25 30

Thr Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Tyr
35 40 45

Gly Thr Asn Asn Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser Ala Ser
50 55 60

Ser Ser Gly Asn Thr Ala Ser Leu Thr Ile Thr Gly Ala Gln Ala Glu
65 70 75 80

```
Asp Glu Ala Asp Tyr Tyr Cys Asn Ser Arg Asp Ser Ser Gly His His
                85                  90                  95

Leu Leu Phe Gly Thr Gly Thr Lys Val Thr Val Leu
            100                 105
```

<210> 764
<211> 492
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 764

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15

His Ala Ala Arg Pro Glu Val Gln Leu Gln Gln Ser Gly Pro Gly Leu
            20                  25                  30

Val Lys Pro Ser Gln Thr Leu Ser Leu Thr Cys Ala Ile Ser Gly Asp
        35                  40                  45

Ser Val Ser Ser Asn Ser Ala Ala Trp Asn Trp Ile Arg Gln Ser Pro
    50                  55                  60

Ser Arg Gly Leu Glu Trp Leu Gly Arg Thr Tyr Tyr Arg Ser Lys Trp
65                  70                  75                  80

Tyr Ser Phe Tyr Ala Ile Ser Leu Lys Ser Arg Ile Ile Ile Asn Pro
                85                  90                  95

Asp Thr Ser Lys Asn Gln Phe Ser Leu Gln Leu Lys Ser Val Thr Pro
            100                 105                 110

Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Ser Pro Glu Gly Leu
        115                 120                 125

Phe Leu Tyr Trp Phe Asp Pro Trp Gly Gln Gly Thr Leu Val Thr Val
    130                 135                 140

Ser Ser Gly Gly Asp Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
145                 150                 155                 160

Ser Ser Ser Glu Leu Thr Gln Asp Pro Ala Val Ser Val Ala Leu Gly
                165                 170                 175
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Gln Thr Ile Arg Ile Thr Cys Gln Gly Asp Ser Leu Gly Asn Tyr Tyr
            180                 185                 190

Ala Thr Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile
        195                 200                 205

Tyr Gly Thr Asn Asn Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser Ala
    210                 215                 220

Ser Ser Ser Gly Asn Thr Ala Ser Leu Thr Ile Thr Gly Ala Gln Ala
225                 230                 235                 240

Glu Asp Glu Ala Asp Tyr Tyr Cys Asn Ser Arg Asp Ser Ser Gly His
                245                 250                 255

His Leu Leu Phe Gly Thr Gly Thr Lys Val Thr Val Leu Thr Thr Thr
            260                 265                 270

Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro
        275                 280                 285

Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val
    290                 295                 300

His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro
305                 310                 315                 320

Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu
                325                 330                 335

Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro
            340                 345                 350

Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys
        355                 360                 365

Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe
    370                 375                 380

Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu
385                 390                 395                 400

Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp
                405                 410                 415

Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys
            420                 425                 430
```

Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala
435 440 445

Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys
450 455 460

Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr
465 470 475 480

Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 765
<211> 1476
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 765
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaagtgc agctccaaca gtcaggaccg gggctcgtga agccatccca gaccctgtcc 120

ctgacttgtg ccatctcggg agatagcgtg tcatcgaact ccgccgcctg gaactggatt 180

cggcagagcc cgtcccgcgg actggagtgg cttggaagga cctactaccg gtccaagtgg 240

tactctttct acgcgatctc gctgaagtcc cgcattatca ttaaccctga tacctccaag 300

aatcagttct ccctccaact gaaatccgtc acccccgagg acacagcagt gtattactgc 360

gcacggagca gccccgaagg actgttcctg tattggtttg acccctgggg ccaggggact 420

cttgtgaccg tgtcgagcgg cggagatggg tccggtggcg gtggttcggg gggcggcgga 480

tcatcatccg aactgaccca ggacccggct gtgtccgtgg cgctgggaca aaccatccgc 540

attacgtgcc agggagactc cctgggcaac tactacgcca cttggtacca gcagaagccg 600

ggccaagccc ctgtgttggt catctacggg accaacaaca gaccttccgg catccccgac 660

cggttcagcg cttcgtcctc cggcaacact gccagcctga ccatcactgg agcgcaggcc 720

gaagatgagg ccgactacta ctgcaacagc agagactcct cgggtcatca cctcttgttc 780

ggaactggaa ccaaggtcac cgtgctgacc actaccccag caccgaggcc acccaccccg 840

gctcctacca tcgcctccca gcctctgtcc ctgcgtccgg aggcatgtag acccgcagct 900

ggtggggccg tgcatacccg gggtcttgac ttcgcctgcg atatctacat ttgggccct 960

ctggctggta cttgcggggt cctgctgctt tcactcgtga tcactcttta ctgtaagcgc 1020

_SL

ggtcggaaga agctgctgta catctttaag caacccttca tgaggcctgt gcagactact 1080

caagaggagg acggctgttc atgccggttc ccagaggagg aggaaggcgg ctgcgaactg 1140

cgcgtgaaat tcagccgcag cgcagatgct ccagcctaca agcaggggca gaaccagctc 1200

tacaacgaac tcaatcttgg tcggagagag gagtacgacg tgctggacaa gcggagagga 1260

cgggacccag aaatgggcgg gaagccgcgc agaaagaatc cccaagaggg cctgtacaac 1320

gagctccaaa aggataagat ggcagaagcc tatagcgaga ttggtatgaa aggggaacgc 1380

agaagaggca aaggccacga cggactgtac cagggactca gcaccgccac caaggacacc 1440

tatgacgctc ttcacatgca ggccctgccg cctcgg 1476

<210> 766
<211> 246
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 766

```
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                  10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Val Glu Gly Ser Gly Ser Leu Asp Tyr Trp Gly Gln Gly Thr
            100                 105                 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125

Gly Gly Gly Gly Ser Glu Ile Val Met Thr Gln Ser Pro Gly Thr Leu
    130                 135                 140
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Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln
145 150 155 160

Ser Val Ser Ser Ala Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
165 170 175

Pro Pro Arg Leu Leu Ile Ser Gly Ala Ser Thr Arg Ala Thr Gly Ile
180 185 190

Pro Asp Arg Phe Gly Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
195 200 205

Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln His
210 215 220

Tyr Gly Ser Ser Phe Asn Gly Ser Ser Leu Phe Thr Phe Gly Gln Gly
225 230 235 240

Thr Arg Leu Glu Ile Lys
245

<210> 767
<211> 738
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 767
gaagtgcagc tcgtggagtc aggaggcggc ctggtccagc cgggagggtc ccttagactg 60

tcatgcgccg caagcggatt cactttctcc tcctatgcca tgagctgggt ccgccaagcc 120

cccggaaagg gactggaatg ggtgtccgcc atctcggggt ctggaggctc aacttactac 180

gctgactccg tgaagggacg gttcaccatt agccgcgaca actccaagaa caccctctac 240

ctccaaatga actccctgcg ggccgaggat accgccgtct actactgcgc caaagtggaa 300

ggttcaggat cgctggacta ctggggacag ggtactctcg tgaccgtgtc atcgggcgga 360

ggaggttccg gcggtggcgg ctccggcggc ggagggtcgg agatcgtgat gacccagagc 420

cctggtactc tgagcctttc gccgggagaa agggccaccc tgtcctgccg cgcttcccaa 480

tccgtgtcct ccgcgtactt ggcgtggtac cagcagaagc cgggacagcc ccctcggctg 540

ctgatcagcg gggccagcac ccgggcaacc ggaatcccag acagattcgg gggttccggc 600

agcggcacag atttcaccct gactatttcg aggttggagc ccgaggactt tgcggtgtat 660

tactgtcagc actacgggtc gtcctttaat ggctccagcc tgttcacgtt cggacagggg 720

acccgcctgg aaatcaag 738

<210> 768
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 768
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Val Glu Gly Ser Gly Ser Leu Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser
115

<210> 769
<211> 113
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 769
Glu Ile Val Met Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ala

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20 25 30

Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Arg Leu Leu
35 40 45

Ile Ser Gly Ala Ser Thr Arg Ala Thr Gly Ile Pro Asp Arg Phe Gly
50 55 60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65 70 75 80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln His Tyr Gly Ser Ser Phe
85 90 95

Asn Gly Ser Ser Leu Phe Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile
100 105 110

Lys

<210> 770
<211> 490
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 770
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
20 25 30

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
35 40 45

Thr Phe Ser Ser Tyr Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys
50 55 60

Gly Leu Glu Trp Val Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr
65 70 75 80

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser
85 90 95

Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr

_SL

100 105 110

Ala Val Tyr Tyr Cys Ala Lys Val Glu Gly Ser Gly Ser Leu Asp Tyr
115 120 125

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser
130 135 140

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Met Thr Gln
145 150 155 160

Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser
165 170 175

Cys Arg Ala Ser Gln Ser Val Ser Ser Ala Tyr Leu Ala Trp Tyr Gln
180 185 190

Gln Lys Pro Gly Gln Pro Pro Arg Leu Leu Ile Ser Gly Ala Ser Thr
195 200 205

Arg Ala Thr Gly Ile Pro Asp Arg Phe Gly Gly Ser Gly Ser Gly Thr
210 215 220

Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val
225 230 235 240

Tyr Tyr Cys Gln His Tyr Gly Ser Ser Phe Asn Gly Ser Ser Leu Phe
245 250 255

Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys Thr Thr Thr Pro Ala
260 265 270

Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser
275 280 285

Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr
290 295 300

Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala
305 310 315 320

Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys
325 330 335

Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met
340 345 350

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                                                _SL
Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe
        355                 360                 365

Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg
    370                 375                 380

Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn
385                 390                 395                 400

Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg
                405                 410                 415

Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro
            420                 425                 430

Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala
        435                 440                 445

Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His
    450                 455                 460

Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp
465                 470                 475                 480

Ala Leu His Met Gln Ala Leu Pro Pro Arg
                485                 490
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<210> 771
<211> 1470
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 771
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaagtgc agctcgtgga gtcaggaggc ggcctggtcc agccgggagg gtcccttaga 120

ctgtcatgcg ccgcaagcgg attcactttc tcctcctatg ccatgagctg ggtccgccaa 180

gcccccggaa agggactgga atgggtgtcc gccatctcgg ggtctggagg ctcaacttac 240

tacgctgact ccgtgaaggg acggttcacc attagccgcg acaactccaa gaacaccctc 300

tacctccaaa tgaactccct gcgggccgag gataccgccg tctactactg cgccaaagtg 360

gaaggttcag gatcgctgga ctactgggga cagggtactc tcgtgaccgt gtcatcgggc 420

ggaggaggtt ccggcggtgg cggctccggc ggcggagggt cggagatcgt gatgacccag 480

agccctggta ctctgagcct ttcgccggga gaaagggcca ccctgtcctg ccgcgcttcc 540

caatccgtgt cctccgcgta cttggcgtgg taccagcaga agccgggaca gccccctcgg 600

ctgctgatca gcggggccag cacccgggca accggaatcc cagacagatt cgggggttcc 660

ggcagcggca cagatttcac cctgactatt tcgaggttgg agcccgagga ctttgcggtg 720

tattactgtc agcactacgg gtcgtccttt aatggctcca gcctgttcac gttcggacag 780

gggacccgcc tggaaatcaa gaccactacc ccagcaccga ggccacccac cccggctcct 840

accatcgcct cccagcctct gtccctgcgt ccggaggcat gtagacccgc agctggtggg 900

gccgtgcata cccggggtct tgacttcgcc tgcgatatct acatttgggc ccctctggct 960

ggtacttgcg gggtcctgct gctttcactc gtgatcactc tttactgtaa gcgcggtcgg 1020

aagaagctgc tgtacatctt taagcaaccc ttcatgaggc ctgtgcagac tactcaagag 1080

gaggacggct gttcatgccg gttcccagag gaggaggaag gcggctgcga actgcgcgtg 1140

aaattcagcc gcagcgcaga tgctccagcc tacaagcagg ggcagaacca gctctacaac 1200

gaactcaatc ttggtcggag agaggagtac gacgtgctgg acaagcggag aggacgggac 1260

ccagaaatgg gcgggaagcc gcgcagaaag aatccccaag agggcctgta caacgagctc 1320

caaaaggata agatggcaga agcctatagc gagattggta tgaaagggga acgcagaaga 1380

ggcaaaggcc acgacggact gtaccaggga ctcagcaccg ccaccaagga cacctatgac 1440

gctcttcaca tgcaggccct gccgcctcgg 1470

<210> 772
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 772
Glu Val Gln Leu Val Glu Thr Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Ile Thr Phe Ser Arg Tyr
20 25 30

Pro Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Gly Ile Ser Asp Ser Gly Val Ser Thr Tyr Tyr Ala Asp Ser Ala
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Phe

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65 70 75 80

Leu Gln Met Ser Ser Leu Arg Asp Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Val Thr Arg Ala Gly Ser Glu Ala Ser Asp Ile Trp Gly Gln Gly Thr
100 105 110

Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu
130 135 140

Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln
145 150 155 160

Ser Val Ser Asn Ser Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala
165 170 175

Pro Arg Leu Leu Ile Tyr Asp Ala Ser Ser Arg Ala Thr Gly Ile Pro
180 185 190

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile
195 200 205

Ser Arg Leu Glu Pro Glu Asp Phe Ala Ile Tyr Tyr Cys Gln Gln Phe
210 215 220

Gly Thr Ser Ser Gly Leu Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile
225 230 235 240

Lys

<210> 773
<211> 723
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 773
gaagtgcaac tggtggaaac cggtggcggc ctggtgcagc ctggaggatc attgaggctg 60

tcatgcgcgg ccagcggtat taccttctcc cggtacccca tgtcctgggt cagacaggcc 120

ccggggaaag ggcttgaatg ggtgtccggg atctcggact ccggtgtcag cacttactac 180

gccgactccg ccaagggacg cttcaccatt tcccgggaca actcgaagaa caccctgttc 240

ctccaaatga gctccctccg ggacgaggat actgcagtgt actactgcgt gacccgcgcc 300

gggtccgagg cgtctgacat ttggggacag ggcactatgg tcaccgtgtc gtccggcgga 360

gggggctcgg gaggcggtgg cagcggagga ggagggtccg agatcgtgct gacccaatcc 420

ccggccaccc tctcgctgag ccctggagaa agggcaacct tgtcctgtcg cgcgagccag 480

tccgtgagca actccctggc ctggtaccag cagaagcccg gacaggctcc gagacttctg 540

atctacgacg cttcgagccg ggccactgga atccccgacc gcttttcggg gtccggctca 600

ggaaccgatt tcaccctgac aatctcacgg ctggagccag aggatttcgc catctattac 660

tgccagcagt tcggtacttc ctccggcctg actttcggag gcggcacgaa gctcgaaatc 720

aag 723

<210> 774
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 774

Glu	Val	Gln	Leu	Val	Glu	Thr	Gly	Gly	Gly	Leu	Val	Gln	Pro	Gly	Gly
1				5				10					15		
Ser	Leu	Arg	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Ile	Thr	Phe	Ser	Arg	Tyr
			20					25				30			
Pro	Met	Ser	Trp	Val	Arg	Gln	Ala	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Val
		35					40					45			
Ser	Gly	Ile	Ser	Asp	Ser	Gly	Val	Ser	Thr	Tyr	Tyr	Ala	Asp	Ser	Ala
	50					55					60				
Lys	Gly	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asn	Ser	Lys	Asn	Thr	Leu	Phe
65					70					75					80
Leu	Gln	Met	Ser	Ser	Leu	Arg	Asp	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys
				85					90					95	
Val	Thr	Arg	Ala	Gly	Ser	Glu	Ala	Ser	Asp	Ile	Trp	Gly	Gln	Gly	Thr
			100					105					110		
Met	Val	Thr	Val	Ser	Ser										
		115													

<210> 775
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 775
Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Asn Ser
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45

Tyr Asp Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro
65 70 75 80

Glu Asp Phe Ala Ile Tyr Tyr Cys Gln Gln Phe Gly Thr Ser Ser Gly
85 90 95

Leu Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 776
<211> 485
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 776
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Val Gln Leu Val Glu Thr Gly Gly Gly Leu
20 25 30

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Ile
35 40 45

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Thr Phe Ser Arg Tyr Pro Met Ser Trp Val Arg Gln Ala Pro Gly Lys
    50                  55                  60

Gly Leu Glu Trp Val Ser Gly Ile Ser Asp Ser Gly Val Ser Thr Tyr
65                  70                  75                  80

Tyr Ala Asp Ser Ala Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser
                85                  90                  95

Lys Asn Thr Leu Phe Leu Gln Met Ser Ser Leu Arg Asp Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Val Thr Arg Ala Gly Ser Glu Ala Ser Asp Ile
        115                 120                 125

Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser
    130                 135                 140

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln
145                 150                 155                 160

Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser
                165                 170                 175

Cys Arg Ala Ser Gln Ser Val Ser Asn Ser Leu Ala Trp Tyr Gln Gln
            180                 185                 190

Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Asp Ala Ser Ser Arg
        195                 200                 205

Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
    210                 215                 220

Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Ile Tyr
225                 230                 235                 240

Tyr Cys Gln Gln Phe Gly Thr Ser Ser Gly Leu Thr Phe Gly Gly Gly
                245                 250                 255

Thr Lys Leu Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr
            260                 265                 270

Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala
        275                 280                 285

Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe
    290                 295                 300
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Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val
305 310 315 320

Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys
325 330 335

Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr
340 345 350

Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu
355 360 365

Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro
370 375 380

Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly
385 390 395 400

Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro
405 410 415

Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr
420 425 430

Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly
435 440 445

Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln
450 455 460

Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln
465 470 475 480

Ala Leu Pro Pro Arg
485

<210> 777
<211> 1455
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 777
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaagtgc aactggtgga aaccggtggc ggcctggtgc agcctggagg atcattgagg 120

ctgtcatgcg cggccagcgg tattaccttc tcccggtacc ccatgtcctg ggtcagacag 180

gccccgggga aagggcttga atgggtgtcc gggatctcgg actccggtgt cagcacttac 240

tacgccgact ccgccaaggg acgcttcacc atttcccggg acaactcgaa gaacaccctg 300

ttcctccaaa tgagctccct ccgggacgag gatactgcag tgtactactg cgtgacccgc 360

gccgggtccg aggcgtctga catttgggga cagggcacta tggtcaccgt gtcgtccggc 420

ggaggggct cgggaggcgg tggcagcgga ggaggagggt ccgagatcgt gctgacccaa 480

tccccggcca ccctctcgct gagccctgga gaaagggcaa ccttgtcctg tcgcgcgagc 540

cagtccgtga gcaactccct ggcctggtac cagcagaagc ccggacaggc tccgagactt 600

ctgatctacg acgcttcgag ccgggccact ggaatccccg accgcttttc ggggtccggc 660

tcaggaaccg atttcaccct gacaatctca cggctggagc cagaggattt cgccatctat 720

tactgccagc agttcggtac ttcctccggc ctgactttcg gaggcggcac gaagctcgaa 780

atcaagacca ctaccccagc accgaggcca cccaccccgg ctcctaccat cgcctcccag 840

cctctgtccc tgcgtccgga ggcatgtaga cccgcagctg gtggggccgt gcatacccgg 900

ggtcttgact tcgcctgcga tatctacatt tgggcccctc tggctggtac ttgcggggtc 960

ctgctgcttt cactcgtgat cactctttac tgtaagcgcg gtcggaagaa gctgctgtac 1020

atctttaagc aacccttcat gaggcctgtg cagactactc aagaggagga cggctgttca 1080

tgccggttcc cagaggagga ggaaggcggc tgcgaactgc gcgtgaaatt cagccgcagc 1140

gcagatgctc cagcctacaa gcaggggcag aaccagctct acaacgaact caatcttggt 1200

cggagagagg agtacgacgt gctggacaag cggagaggac gggacccaga aatgggcggg 1260

aagccgcgca gaaagaatcc ccaagagggc ctgtacaacg agctccaaaa ggataagatg 1320

gcagaagcct atagcgagat tggtatgaaa ggggaacgca gaagaggcaa aggccacgac 1380

ggactgtacc agggactcag caccgccacc aaggacacct atgacgctct tcacatgcag 1440

gccctgccgc ctcgg 1455

<210> 778
<211> 248
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 778
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

```
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Ile Tyr Tyr Cys
                85                  90                  95

Ala Arg Ala Thr Tyr Lys Arg Glu Leu Arg Tyr Tyr Tyr Gly Met Asp
            100                 105                 110

Val Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly
        115                 120                 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Met Thr
    130                 135                 140

Gln Ser Pro Gly Thr Val Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu
145                 150                 155                 160

Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser Phe Leu Ala Trp Tyr
                165                 170                 175

Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser
            180                 185                 190

Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly
        195                 200                 205

Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu Asp Ser Ala
    210                 215                 220

Val Tyr Tyr Cys Gln Gln Tyr His Ser Ser Pro Ser Trp Thr Phe Gly
225                 230                 235                 240

Gln Gly Thr Arg Leu Glu Ile Lys
                245
```

<210> 779
<211> 744

<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 779
caagtgcagc tcgtggaatc gggtggcgga ctggtgcagc cgggggctc acttagactg 60

tcctgcgcgg ccagcggatt cactttctcc tcctacgcca tgtcctgggt cagacaggcc 120

cctggaaagg gcctggaatg ggtgtccgca atcagcggca gcggcggctc gacctattac 180

gcggattcag tgaagggcag attcaccatt tcccgggaca acgccaagaa ctccttgtac 240

cttcaaatga actccctccg cgcggaagat accgcaatct actactgcgc tcgggccact 300

tacaagaggg aactgcgcta ctactacggg atggacgtct ggggccaggg aaccatggtc 360

accgtgtcca gcggaggagg aggatcggga ggaggcggta gcgggggtgg agggtcggag 420

atcgtgatga cccagtcccc cggcactgtg tcgctgtccc ccggcgaacg ggccaccctg 480

tcatgtcggg ccagccagtc agtgtcgtca agcttcctcg cctggtacca gcagaaaccg 540

ggacaagctc cccgcctgct gatctacgga gccagcagcc gggccaccgg tattcctgac 600

cggttctccg gttcggggtc cgggaccgac tttactctga ctatctctcg cctcgagcca 660

gaggactccg ccgtgtatta ctgccagcag taccactcct ccccgtcctg gacgttcgga 720

cagggcacaa ggctggagat taag 744

<210> 780
<211> 124
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 780
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

_SL
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Ile Tyr Tyr Cys
85 90 95

Ala Arg Ala Thr Tyr Lys Arg Glu Leu Arg Tyr Tyr Tyr Gly Met Asp
100 105 110

Val Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
115 120

<210> 781
<211> 109
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 781
Glu Ile Val Met Thr Gln Ser Pro Gly Thr Val Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser
20 25 30

Phe Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45

Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
50 55 60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65 70 75 80

Pro Glu Asp Ser Ala Val Tyr Tyr Cys Gln Gln Tyr His Ser Ser Pro
85 90 95

Ser Trp Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys
100 105

<210> 782
<211> 492
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

polypeptide"

<400> 782

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15

His Ala Ala Arg Pro Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu
            20                  25                  30

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
        35                  40                  45

Thr Phe Ser Ser Tyr Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys
    50                  55                  60

Gly Leu Glu Trp Val Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr
65                  70                  75                  80

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala
                85                  90                  95

Lys Asn Ser Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
            100                 105                 110

Ala Ile Tyr Tyr Cys Ala Arg Ala Thr Tyr Lys Arg Glu Leu Arg Tyr
        115                 120                 125

Tyr Tyr Gly Met Asp Val Trp Gly Gln Gly Thr Met Val Thr Val Ser
    130                 135                 140

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
145                 150                 155                 160

Glu Ile Val Met Thr Gln Ser Pro Gly Thr Val Ser Leu Ser Pro Gly
                165                 170                 175

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser
            180                 185                 190

Phe Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
        195                 200                 205

Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
    210                 215                 220

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
225                 230                 235                 240
```

```
                                                  _SL
Pro Glu Asp Ser Ala Val Tyr Tyr Cys Gln Gln Tyr His Ser Ser Pro
                245                 250                 255

Ser Trp Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys Thr Thr Thr
            260                 265                 270

Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro
        275                 280                 285

Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val
    290                 295                 300

His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro
305                 310                 315                 320

Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu
                325                 330                 335

Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro
            340                 345                 350

Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys
        355                 360                 365

Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe
    370                 375                 380

Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu
385                 390                 395                 400

Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp
                405                 410                 415

Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys
            420                 425                 430

Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala
        435                 440                 445

Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys
    450                 455                 460

Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr
465                 470                 475                 480

Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
                485                 490
```

<210> 783
<211> 1476
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 783
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtgc agctcgtgga atcgggtggc ggactggtgc agccgggggg ctcacttaga 120

ctgtcctgcg cggccagcgg attcactttc tcctcctacg ccatgtcctg ggtcagacag 180

gcccctggaa agggcctgga atgggtgtcc gcaatcagcg gcagcggcgg ctcgacctat 240

tacgcggatt cagtgaaggg cagattcacc atttcccggg acaacgccaa gaactccttg 300

taccttcaaa tgaactccct ccgcgcggaa gataccgcaa tctactactg cgctcgggcc 360

acttacaaga gggaactgcg ctactactac gggatggacg tctggggcca gggaaccatg 420

gtcaccgtgt ccagcggagg aggaggatcg ggaggaggcg gtagcggggg tggagggtcg 480

gagatcgtga tgacccagtc ccccggcact gtgtcgctgt cccccggcga acgggccacc 540

ctgtcatgtc gggccagcca gtcagtgtcg tcaagcttcc tcgcctggta ccagcagaaa 600

ccgggacaag ctccccgcct gctgatctac ggagccagca gccgggccac cggtattcct 660

gaccggttct ccggttcggg gtccgggacc gactttactc tgactatctc tcgcctcgag 720

ccagaggact ccgccgtgta ttactgccag cagtaccact cctccccgtc ctggacgttc 780

ggacagggca caaggctgga gattaagacc actaccccag caccgaggcc acccaccccg 840

gctcctacca tcgcctccca gcctctgtcc ctgcgtccgg aggcatgtag acccgcagct 900

ggtggggccg tgcatacccg gggtcttgac ttcgcctgcg atatctacat ttgggccccc 960

ctggctggta cttgcggggt cctgctgctt tcactcgtga tcactcttta ctgtaagcgc 1020

ggtcggaaga agctgctgta catctttaag caacccttca tgaggcctgt gcagactact 1080

caagaggagg acggctgttc atgccggttc ccagaggagg aggaaggcgg ctgcgaactg 1140

cgcgtgaaat tcagccgcag cgcagatgct ccagcctaca agcaggggca gaaccagctc 1200

tacaacgaac tcaatcttgg tcggagagag gagtacgacg tgctggacaa gcggagagga 1260

cgggacccag aaatgggcgg gaagccgcgc agaaagaatc cccaagaggg cctgtacaac 1320

gagctccaaa aggataagat ggcagaagcc tatagcgaga ttggtatgaa aggggaacgc 1380

agaagaggca aaggccacga cggactgtac cagggactca gcaccgccac caaggacacc 1440

tatgacgctc ttcacatgca ggccctgccg cctcgg 1476

<210> 784
<211> 248
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 784

```
Glu Val Gln Leu Val Glu Thr Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Thr Leu Lys Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ala Thr Tyr Lys Arg Glu Leu Arg Tyr Tyr Tyr Gly Met Asp
            100                 105                 110

Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly
        115                 120                 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Leu Thr
    130                 135                 140

Gln Ser Pro Ser Thr Leu Ser Leu Ser Pro Gly Glu Ser Ala Thr Leu
145                 150                 155                 160

Ser Cys Arg Ala Ser Gln Ser Val Ser Thr Thr Phe Leu Ala Trp Tyr
                165                 170                 175

Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Gly Ser Ser
            180                 185                 190

Asn Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly
        195                 200                 205
```

_SL
Thr Asp Phe Thr Leu Thr Ile Arg Arg Leu Glu Pro Glu Asp Phe Ala
210 215 220

Val Tyr Tyr Cys Gln Gln Tyr His Ser Ser Pro Ser Trp Thr Phe Gly
225 230 235 240

Gln Gly Thr Lys Val Glu Ile Lys
245

<210> 785
<211> 744
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 785
gaggtgcagc ttgtggaaac cggtggcgga ctggtgcagc ccggaggaag cctcaggctg 60

tcctgcgccg cgtccggctt caccttctcc tcgtacgcca tgtcctgggt ccgccaggcc 120

cccggaaagg gcctggaatg ggtgtccgcc atctctggaa gcggaggttc cacgtactac 180

gcggacagcg tcaagggaag gttcacaatc tcccgcgata attcgaagaa cactctgtac 240

cttcaaatga acaccctgaa ggccgaggac actgctgtgt actactgcgc acgggccacc 300

tacaagagag agctccggta ctactacgga atggacgtct ggggccaggg aactactgtg 360

accgtgtcct cgggaggggg tggctccggg gggggcggct ccggcggagg cggttccgag 420

attgtgctga cccagtcacc ttcaactctg tcgctgtccc cgggagagag cgctactctg 480

agctgccggg ccagccagtc cgtgtccacc accttcctcg cctggtatca gcagaagccg 540

gggcaggcac cacggctctt gatctacggg tcaagcaaca gagcgaccgg aattcctgac 600

cgcttctcgg ggagcggttc aggcaccgac ttcaccctga ctatccggcg cctggaaccc 660

gaagatttcg ccgtgtatta ctgtcaacag taccactcct cgccgtcctg gacctttggc 720

caaggaacca aagtggaaat caag 744

<210> 786
<211> 124
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 786
Glu Val Gln Leu Val Glu Thr Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

```
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Thr Leu Lys Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ala Thr Tyr Lys Arg Glu Leu Arg Tyr Tyr Tyr Gly Met Asp
            100                 105                 110

Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120


<210> 787
<211> 109
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 787
Glu Ile Val Leu Thr Gln Ser Pro Ser Thr Leu Ser Leu Ser Pro Gly
1               5                   10                  15

Glu Ser Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Thr Thr
            20                  25                  30

Phe Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
        35                  40                  45

Ile Tyr Gly Ser Ser Asn Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
    50                  55                  60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Arg Arg Leu Glu
65                  70                  75                  80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr His Ser Ser Pro
                85                  90                  95
```

Ser Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 788
<211> 492
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 788
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Val Gln Leu Val Glu Thr Gly Gly Gly Leu
20 25 30

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
35 40 45

Thr Phe Ser Ser Tyr Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys
50 55 60

Gly Leu Glu Trp Val Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr
65 70 75 80

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser
85 90 95

Lys Asn Thr Leu Tyr Leu Gln Met Asn Thr Leu Lys Ala Glu Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Ala Arg Ala Thr Tyr Lys Arg Glu Leu Arg Tyr
115 120 125

Tyr Tyr Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser
130 135 140

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
145 150 155 160

Glu Ile Val Leu Thr Gln Ser Pro Ser Thr Leu Ser Leu Ser Pro Gly
165 170 175

Glu Ser Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Thr Thr
180 185 190

```
Phe Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
        195                 200                 205

Ile Tyr Gly Ser Ser Asn Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
    210                 215                 220

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Arg Arg Leu Glu
225                 230                 235                 240

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr His Ser Ser Pro
                245                 250                 255

Ser Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Thr Thr Thr
            260                 265                 270

Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro
        275                 280                 285

Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val
    290                 295                 300

His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro
305                 310                 315                 320

Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu
                325                 330                 335

Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro
            340                 345                 350

Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys
        355                 360                 365

Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe
    370                 375                 380

Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu
385                 390                 395                 400

Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp
                405                 410                 415

Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys
            420                 425                 430

Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala
```

_SL

435 440 445

Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys
450 455 460

Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr
465 470 475 480

Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 789
<211> 1476
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 789
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaggtgc agcttgtgga aaccggtggc ggactggtgc agcccggagg aagcctcagg 120

ctgtcctgcg ccgcgtccgg cttcaccttc tcctcgtacg ccatgtcctg ggtccgccag 180

gcccccggaa agggcctgga atgggtgtcc gccatctctg gaagcggagg ttccacgtac 240

tacgcggaca gcgtcaaggg aaggttcaca atctcccgcg ataattcgaa gaacactctg 300

taccttcaaa tgaacaccct gaaggccgag gacactgctg tgtactactg cgcacgggcc 360

acctacaaga gagagctccg gtactactac ggaatggacg tctggggcca gggaactact 420

gtgaccgtgt cctcgggagg gggtggctcc gggggggggcg gctccggcgg aggcggttcc 480

gagattgtgc tgacccagtc accttcaact ctgtcgctgt ccccgggaga gagcgctact 540

ctgagctgcc gggccagcca gtccgtgtcc accaccttcc tcgcctggta tcagcagaag 600

ccggggcagg caccacggct cttgatctac gggtcaagca acagagcgac cggaattcct 660

gaccgcttct cggggagcgg ttcaggcacc gacttcaccc tgactatccg gcgcctggaa 720

cccgaagatt tcgccgtgta ttactgtcaa cagtaccact cctcgccgtc ctggaccttt 780

ggccaaggaa ccaaagtgga aatcaagacc actaccccag caccgaggcc acccaccccg 840

gctcctacca tcgcctccca gcctctgtcc ctgcgtccgg aggcatgtag acccgcagct 900

ggtggggccg tgcatacccg gggtcttgac ttcgcctgcg atatctacat ttgggccccct 960

ctggctggta cttgcggggt cctgctgctt tcactcgtga tcactcttta ctgtaagcgc 1020

ggtcggaaga agctgctgta catctttaag caacccttca tgaggcctgt gcagactact 1080

caagaggagg acggctgttc atgccggttc ccagaggagg aggaaggcgg ctgcgaactg 1140

cgcgtgaaat tcagccgcag cgcagatgct ccagcctaca agcaggggca gaaccagctc 1200

tacaacgaac tcaatcttgg tcggagagag gagtacgacg tgctggacaa gcggagagga 1260

cgggacccag aaatgggcgg gaagccgcgc agaaagaatc cccaagaggg cctgtacaac 1320

gagctccaaa aggataagat ggcagaagcc tatagcgaga ttggtatgaa aggggaacgc 1380

agaagaggca aaggccacga cggactgtac cagggactca gcaccgccac caaggacacc 1440

tatgacgctc ttcacatgca ggccctgccg cctcgg 1476

<210> 790
<211> 239
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 790
Glu Val Gln Leu Val Glu Thr Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
20 25 30

Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Gly Ile Ser Trp Asn Ser Gly Ser Ile Gly Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Asp Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Val Gly Lys Ala Val Pro Asp Val Trp Gly Gln Gly Thr Thr
100 105 110

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
115 120 125

Gly Gly Gly Ser Asp Ile Val Met Thr Gln Thr Pro Ser Ser Leu Ser
130 135 140

Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser
145 150 155 160

Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro
165 170 175

Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser
180 185 190

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
195 200 205

Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr
210 215 220

Ser Thr Pro Tyr Ser Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys
225 230 235

<210> 791
<211> 717
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 791
gaagtgcagc tcgtggaaac tggaggtgga ctcgtgcagc ctggacggtc gctgcggctg 60

agctgcgctg catccggctt caccttcgac gattatgcca tgcactgggt cagacaggcg 120

ccagggaagg gacttgagtg ggtgtccggt atcagctgga atagcggctc aatcggatac 180

gcggactccg tgaagggaag gttcaccatt tcccgcgaca acgccaagaa ctccctgtac 240

ttgcaaatga acagcctccg ggatgaggac actgccgtgt actactgcgc ccgcgtcgga 300

aaagctgtgc ccgacgtctg gggccaggga accactgtga ccgtgtccag cggcgggggt 360

ggatcgggcg gtggagggtc cggtggaggg ggctcagata ttgtgatgac ccagaccccc 420

tcgtccctgt ccgcctcggt cggcgaccgc gtgactatca catgtagagc ctcgcagagc 480

atctccagct acctgaactg gtatcagcag aagccgggga aggccccgaa gctcctgatc 540

tacgcggcat catcactgca atcgggagtg ccgagccggt tttccgggtc cggctccggc 600

accgacttca cgctgaccat ttcttccctg caacccgagg acttcgccac ttactactgc 660

cagcagtcct actccacccc ttactccttc ggccaaggaa ccaggctgga aatcaag 717

<210> 792
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 792
Glu Val Gln Leu Val Glu Thr Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
20 25 30

Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Gly Ile Ser Trp Asn Ser Gly Ser Ile Gly Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Asp Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Val Gly Lys Ala Val Pro Asp Val Trp Gly Gln Gly Thr Thr
100 105 110

Val Thr Val Ser Ser
115

<210> 793
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 793
Asp Ile Val Met Thr Gln Thr Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

```
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80


Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Tyr
                85                  90                  95


Ser Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys
            100                 105


<210> 794
<211> 483
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 794
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15


His Ala Ala Arg Pro Glu Val Gln Leu Val Glu Thr Gly Gly Gly Leu
            20                  25                  30


Val Gln Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
        35                  40                  45


Thr Phe Asp Asp Tyr Ala Met His Trp Val Arg Gln Ala Pro Gly Lys
    50                  55                  60


Gly Leu Glu Trp Val Ser Gly Ile Ser Trp Asn Ser Gly Ser Ile Gly
65                  70                  75                  80


Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala
                85                  90                  95


Lys Asn Ser Leu Tyr Leu Gln Met Asn Ser Leu Arg Asp Glu Asp Thr
            100                 105                 110


Ala Val Tyr Tyr Cys Ala Arg Val Gly Lys Ala Val Pro Asp Val Trp
        115                 120                 125


Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
    130                 135                 140


Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln Thr
145                 150                 155                 160
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```
Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
                165                 170                 175

Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys
            180                 185                 190

Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln
        195                 200                 205

Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
    210                 215                 220

Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr
225                 230                 235                 240

Cys Gln Gln Ser Tyr Ser Thr Pro Tyr Ser Phe Gly Gln Gly Thr Arg
                245                 250                 255

Leu Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala
            260                 265                 270

Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg
        275                 280                 285

Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys
    290                 295                 300

Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu
305                 310                 315                 320

Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu
                325                 330                 335

Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln
            340                 345                 350

Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly
        355                 360                 365

Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr
    370                 375                 380

Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg
385                 390                 395                 400

Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met
```

_SL
405 410 415

Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu
420 425 430

Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys
435 440 445

Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu
450 455 460

Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu
465 470 475 480

Pro Pro Arg

<210> 795
<211> 1449
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 795
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaagtgc agctcgtgga aactggaggt ggactcgtgc agcctggacg gtcgctgcgg 120

ctgagctgcg ctgcatccgg cttcaccttc gacgattatg ccatgcactg ggtcagacag 180

gcgccaggga agggacttga gtgggtgtcc ggtatcagct ggaatagcgg ctcaatcgga 240

tacgcggact ccgtgaaggg aaggttcacc atttcccgcg acaacgccaa gaactccctg 300

tacttgcaaa tgaacagcct ccgggatgag gacactgccg tgtactactg cgcccgcgtc 360

ggaaaagctg tgcccgacgt ctggggccag ggaaccactg tgaccgtgtc cagcggcggg 420

ggtggatcgg gcggtggagg gtccggtgga gggggctcag atattgtgat gacccagacc 480

ccctcgtccc tgtccgcctc ggtcggcgac cgcgtgacta tcacatgtag agcctcgcag 540

agcatctcca gctacctgaa ctggtatcag cagaagccgg ggaaggcccc gaagctcctg 600

atctacgcgg catcatcact gcaatcggga gtgccgagcc ggttttccgg gtccggctcc 660

ggcaccgact tcacgctgac catttcttcc ctgcaacccg aggacttcgc cacttactac 720

tgccagcagt cctactccac cccttactcc ttcggccaag gaaccaggct ggaaatcaag 780

accactaccc cagcaccgag gccacccacc ccggctccta ccatcgcctc ccagcctctg 840

tccctgcgtc cggaggcatg tagacccgca gctggtgggg ccgtgcatac ccggggtctt 900

gacttcgcct gcgatatcta catttgggcc cctctggctg gtacttgcgg ggtcctgctg 960

ctttcactcg tgatcactct ttactgtaag cgcggtcgga agaagctgct gtacatcttt 1020

aagcaaccct tcatgaggcc tgtgcagact actcaagagg aggacggctg ttcatgccgg 1080

ttcccagagg aggaggaagg cggctgcgaa ctgcgcgtga aattcagccg cagcgcagat 1140

gctccagcct acaagcaggg gcagaaccag ctctacaacg aactcaatct tggtcggaga 1200

gaggagtacg acgtgctgga caagcggaga ggacgggacc cagaaatggg cgggaagccg 1260

cgcagaaaga atccccaaga gggcctgtac aacgagctcc aaaaggataa gatggcagaa 1320

gcctatagcg agattggtat gaaaggggaa cgcagaagag gcaaaggcca cgacggactg 1380

taccagggac tcagcaccgc caccaaggac acctatgacg ctcttcacat gcaggccctg 1440

ccgcctcgg 1449

<210> 796
<211> 246
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 796

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Thr Ala Ser Gly Phe Thr Phe Asp Asp Tyr
20 25 30

Ala Met His Trp Val Arg Gln Arg Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Ser Ile Asn Trp Lys Gly Asn Ser Leu Ala Tyr Gly Asp Ser Val
50 55 60

Lys Gly Arg Phe Ala Ile Ser Arg Asp Asn Ala Lys Asn Thr Val Phe
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Thr Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Ser His Gln Gly Val Ala Tyr Tyr Asn Tyr Ala Met Asp Val Trp
100 105 110

Gly Arg Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
115 120 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser
130 135 140

Pro Gly Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
145 150 155 160

Arg Ala Thr Gln Ser Ile Gly Ser Ser Phe Leu Ala Trp Tyr Gln Gln
165 170 175

Arg Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Gln Arg
180 185 190

Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly Arg Gly Ser Gly Thr Asp
195 200 205

Phe Thr Leu Thr Ile Ser Arg Val Glu Pro Glu Asp Ser Ala Val Tyr
210 215 220

Tyr Cys Gln His Tyr Glu Ser Ser Pro Ser Trp Thr Phe Gly Gln Gly
225 230 235 240

Thr Lys Val Glu Ile Lys
245

<210> 797
<211> 738
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 797
gaagtgcagc tcgtggagag cgggggagga ttggtgcagc ccggaaggtc cctgcggctc 60

tcctgcactg cgtctggctt caccttcgac gactacgcga tgcactgggt cagacagcgc 120

ccgggaaagg gcctggaatg ggtcgcctca atcaactgga agggaaactc cctggcctat 180

ggcgacagcg tgaagggccg cttcgccatt tcgcgcgaca acgccaagaa caccgtgttt 240

ctgcaaatga attccctgcg gaccgaggat accgctgtgt actactgcgc cagccaccag 300

ggcgtggcat actataacta cgccatggac gtgtggggaa gagggacgct cgtcaccgtg 360

tcctccgggg gcggtggatc gggtggagga ggaagcggtg gcgggggcag cgaaatcgtg 420

ctgactcaga gcccgggaac tctttcactg tccccgggag aacgggccac tctctcgtgc 480

cgggccaccc agtccatcgg ctcctccttc cttgcctggt accagcagag gccaggacag 540

gcgccccgcc tgctgatcta cggtgcttcc caacgcgcca ctggcattcc tgaccggttc 600

agcggcagag ggtcgggaac cgatttcaca ctgaccattt cccgggtgga gcccgaagat 660

tcggcagtct actactgtca gcattacgag tcctcccctt catggacctt cggtcaaggg 720

accaaagtgg agatcaag 738

<210> 798
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 798

Glu	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Gly	Leu	Val	Gln	Pro	Gly	Arg
1				5				10					15		
Ser	Leu	Arg	Leu	Ser	Cys	Thr	Ala	Ser	Gly	Phe	Thr	Phe	Asp	Asp	Tyr
			20					25					30		
Ala	Met	His	Trp	Val	Arg	Gln	Arg	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Val
		35					40					45			
Ala	Ser	Ile	Asn	Trp	Lys	Gly	Asn	Ser	Leu	Ala	Tyr	Gly	Asp	Ser	Val
	50					55					60				
Lys	Gly	Arg	Phe	Ala	Ile	Ser	Arg	Asp	Asn	Ala	Lys	Asn	Thr	Val	Phe
65					70					75					80
Leu	Gln	Met	Asn	Ser	Leu	Arg	Thr	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys
				85					90					95	
Ala	Ser	His	Gln	Gly	Val	Ala	Tyr	Tyr	Asn	Tyr	Ala	Met	Asp	Val	Trp
			100					105					110		
Gly	Arg	Gly	Thr	Leu	Val	Thr	Val	Ser	Ser						
		115					120								

<210> 799
<211> 109
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 799

_SL
Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Thr Gln Ser Ile Gly Ser Ser
20 25 30

Phe Leu Ala Trp Tyr Gln Gln Arg Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45

Ile Tyr Gly Ala Ser Gln Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
50 55 60

Gly Arg Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Val Glu
65 70 75 80

Pro Glu Asp Ser Ala Val Tyr Tyr Cys Gln His Tyr Glu Ser Ser Pro
85 90 95

Ser Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 800
<211> 490
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 800
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
20 25 30

Val Gln Pro Gly Arg Ser Leu Arg Leu Ser Cys Thr Ala Ser Gly Phe
35 40 45

Thr Phe Asp Asp Tyr Ala Met His Trp Val Arg Gln Arg Pro Gly Lys
50 55 60

Gly Leu Glu Trp Val Ala Ser Ile Asn Trp Lys Gly Asn Ser Leu Ala
65 70 75 80

Tyr Gly Asp Ser Val Lys Gly Arg Phe Ala Ile Ser Arg Asp Asn Ala
85 90 95

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                                                    _SL
Lys Asn Thr Val Phe Leu Gln Met Asn Ser Leu Arg Thr Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Ser His Gln Gly Val Ala Tyr Tyr Asn Tyr
        115                 120                 125

Ala Met Asp Val Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile
145                 150                 155                 160

Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly Glu Arg
                165                 170                 175

Ala Thr Leu Ser Cys Arg Ala Thr Gln Ser Ile Gly Ser Ser Phe Leu
            180                 185                 190

Ala Trp Tyr Gln Gln Arg Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr
        195                 200                 205

Gly Ala Ser Gln Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly Arg
    210                 215                 220

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Val Glu Pro Glu
225                 230                 235                 240

Asp Ser Ala Val Tyr Tyr Cys Gln His Tyr Glu Ser Ser Pro Ser Trp
                245                 250                 255

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Thr Thr Thr Pro Ala
            260                 265                 270

Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser
        275                 280                 285

Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr
    290                 295                 300

Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala
305                 310                 315                 320

Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys
                325                 330                 335

Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met
            340                 345                 350
```

```
Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe
        355                 360                 365

Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg
    370                 375                 380

Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn
385                 390                 395                 400

Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg
                405                 410                 415

Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro
            420                 425                 430

Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala
        435                 440                 445

Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His
    450                 455                 460

Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp
465                 470                 475                 480

Ala Leu His Met Gln Ala Leu Pro Pro Arg
                485                 490
```

<210> 801
<211> 1470
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 801

```
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg       60

cccgaagtgc agctcgtgga gagcggggga ggattggtgc agcccggaag gtccctgcgg      120

ctctcctgca ctgcgtctgg cttcaccttc gacgactacg cgatgcactg ggtcagacag      180

cgcccgggaa agggcctgga atgggtcgcc tcaatcaact ggaagggaaa ctccctggcc      240

tatggcgaca gcgtgaaggg ccgcttcgcc atttcgcgcg acaacgccaa gaacaccgtg      300

tttctgcaaa tgaattccct gcggaccgag gataccgctg tgtactactg cgccagccac      360

cagggcgtgg catactataa ctacgccatg gacgtgtggg gaagagggac gctcgtcacc      420

gtgtcctccg ggggcggtgg atcgggtgga ggaggaagcg gtggcggggg cagcgaaatc      480
```

gtgctgactc agagcccggg aactctttca ctgtccccgg gagaacgggc cactctctcg 540

tgccgggcca cccagtccat cggctcctcc ttccttgcct ggtaccagca gaggccagga 600

caggcgcccc gcctgctgat ctacggtgct tcccaacgcg ccactggcat tcctgaccgg 660

ttcagcggca gagggtcggg aaccgatttc acactgacca tttcccgggt ggagcccgaa 720

gattcggcag tctactactg tcagcattac gagtcctccc cttcatggac cttcggtcaa 780

gggaccaaag tggagatcaa gaccactacc ccagcaccga ggccacccac cccggctcct 840

accatcgcct cccagcctct gtccctgcgt ccggaggcat gtagacccgc agctggtggg 900

gccgtgcata cccggggtct tgacttcgcc tgcgatatct acatttgggc ccctctggct 960

ggtacttgcg gggtcctgct gctttcactc gtgatcactc tttactgtaa gcgcggtcgg 1020

aagaagctgc tgtacatctt taagcaaccc ttcatgaggc ctgtgcagac tactcaagag 1080

gaggacggct gttcatgccg gttcccagag gaggaggaag gcggctgcga actgcgcgtg 1140

aaattcagcc gcagcgcaga tgctccagcc tacaagcagg ggcagaacca gctctacaac 1200

gaactcaatc ttggtcggag agaggagtac gacgtgctgg acaagcggag aggacgggac 1260

ccagaaatgg gcgggaagcc gcgcagaaag aatccccaag agggcctgta caacgagctc 1320

caaaaggata agatggcaga agcctatagc gagattggta tgaaaggggа acgcagaaga 1380

ggcaaaggcc acgacggact gtaccaggga ctcagcaccg ccaccaagga cacctatgac 1440

gctcttcaca tgcaggccct gccgcctcgg 1470

<210> 802
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 802
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

```
                                                _SL
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Val Val Arg Asp Gly Met Asp Val Trp Gly Gln Gly Thr Thr
            100                 105                 110

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser
    130                 135                 140

Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser
145                 150                 155                 160

Val Ser Ser Ser Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala
                165                 170                 175

Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro
            180                 185                 190

Asp Arg Phe Ser Gly Asn Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile
        195                 200                 205

Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr
    210                 215                 220

Gly Ser Pro Pro Arg Phe Thr Phe Gly Pro Gly Thr Lys Val Asp Ile
225                 230                 235                 240

Lys
```

<210> 803
<211> 723
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 803
gaggtgcagt tggtcgaaag cgggggcggg cttgtgcagc ctggcggatc actgcggctg 60

tcctgcgcgg catcaggctt cacgttttct tcctacgcca tgtcctgggt gcgccaggcc 120

cctggaaagg gactggaatg ggtgtccgcg atttcggggt ccggcgggag cacctactac 180

gccgattccg tgaagggccg cttcactatc tcgcgggaca actccaagaa caccctctac 240

ctccaaatga atagcctgcg ggccgaggat accgccgtct actattgcgc taaggtcgtg 300

cgcgacggaa tggacgtgtg gggacagggt accaccgtga cagtgtcctc gggggggaggc 360

ggtagcggcg gaggaggaag cggtggtgga ggttccgaga ttgtgctgac tcaatcaccc 420

gcgaccctga gcctgtcccc cggcgaaagg gccactctgt cctgtcgggc cagccaatca 480

gtctcctcct cgtacctggc ctggtaccag cagaagccag gacaggctcc gagactcctt 540

atctatggcg catcctcccg cgccaccgga atcccggata ggttctcggg aaacggatcg 600

gggaccgact tcactctcac catctcccgg ctggaaccgg aggacttcgc cgtgtactac 660

tgccagcagt acggcagccc gcctagattc actttcggcc ccggcaccaa agtggacatc 720

aag 723

<210> 804
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 804

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Val Val Arg Asp Gly Met Asp Val Trp Gly Gln Gly Thr Thr
100 105 110

Val Thr Val Ser Ser

115

<210> 805
<211> 109
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 805
Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser
20 25 30

Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45

Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
50 55 60

Gly Asn Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65 70 75 80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Pro Pro
85 90 95

Arg Phe Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys
100 105

<210> 806
<211> 485
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 806
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
20 25 30

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
35 40 45

```
Thr Phe Ser Ser Tyr Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys
    50                  55                  60

Gly Leu Glu Trp Val Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr
65                  70                  75                  80

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser
                85                  90                  95

Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Lys Val Val Arg Asp Gly Met Asp Val Trp
        115                 120                 125

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser
145                 150                 155                 160

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
                165                 170                 175

Arg Ala Ser Gln Ser Val Ser Ser Ser Tyr Leu Ala Trp Tyr Gln Gln
            180                 185                 190

Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg
        195                 200                 205

Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly Asn Gly Ser Gly Thr Asp
    210                 215                 220

Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr
225                 230                 235                 240

Tyr Cys Gln Gln Tyr Gly Ser Pro Pro Arg Phe Thr Phe Gly Pro Gly
                245                 250                 255

Thr Lys Val Asp Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr
            260                 265                 270

Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala
        275                 280                 285

Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe
```

_SL
290 295 300

Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val
305 310 315 320

Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys
325 330 335

Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr
340 345 350

Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu
355 360 365

Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro
370 375 380

Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly
385 390 395 400

Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro
405 410 415

Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr
420 425 430

Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly
435 440 445

Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln
450 455 460

Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln
465 470 475 480

Ala Leu Pro Pro Arg
485

<210> 807
<211> 1455
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 807
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaggtgc agttggtcga aagcgggggc gggcttgtgc agcctggcgg atcactgcgg 120

ctgtcctgcg cggcatcagg cttcacgttt tcttcctacg ccatgtcctg ggtgcgccag 180

gcccctggaa agggactgga atgggtgtcc gcgatttcgg ggtccggcgg gagcacctac 240

tacgccgatt ccgtgaaggg ccgcttcact atctcgcggg acaactccaa gaacaccctc 300

tacctccaaa tgaatagcct gcgggccgag gataccgccg tctactattg cgctaaggtc 360

gtgcgcgacg gaatggacgt gtggggacag ggtaccaccg tgacagtgtc ctcgggggga 420

ggcggtagcg gcggaggagg aagcggtggt ggaggttccg agattgtgct gactcaatca 480

cccgcgaccc tgagcctgtc ccccggcgaa agggccactc tgtcctgtcg ggccagccaa 540

tcagtctcct cctcgtacct ggcctggtac cagcagaagc caggacaggc tccgagactc 600

cttatctatg gcgcatcctc ccgcgccacc ggaatcccgg ataggttctc gggaaacgga 660

tcggggaccg acttcactct caccatctcc cggctggaac cggaggactt cgccgtgtac 720

tactgccagc agtacggcag cccgcctaga ttcactttcg gccccggcac caaagtggac 780

atcaagacca ctaccccagc accgaggcca cccaccccgg ctcctaccat cgcctcccag 840

cctctgtccc tgcgtccgga ggcatgtaga cccgcagctg gtggggccgt gcatacccgg 900

ggtcttgact tcgcctgcga tatctacatt tgggcccctc tggctggtac ttgcggggtc 960

ctgctgcttt cactcgtgat cactctttac tgtaagcgcg gtcggaagaa gctgctgtac 1020

atctttaagc aacccttcat gaggcctgtg cagactactc aagaggagga cggctgttca 1080

tgccggttcc cagaggagga ggaaggcggc tgcgaactgc gcgtgaaatt cagccgcagc 1140

gcagatgctc cagcctacaa gcaggggcag aaccagctct acaacgaact caatcttggt 1200

cggagagagg agtacgacgt gctggacaag cggagaggac gggacccaga aatgggcggg 1260

aagccgcgca gaaagaatcc ccaagagggc ctgtacaacg agctccaaaa ggataagatg 1320

gcagaagcct atagcgagat tggtatgaaa ggggaacgca gaagaggcaa aggccacgac 1380

ggactgtacc agggactcag caccgccacc aaggacacct atgacgctct tcacatgcag 1440

gccctgccgc ctcgg 1455

<210> 808
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 808
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

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Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Ile Pro Gln Thr Gly Thr Phe Asp Tyr Trp Gly Gln Gly Thr
            100                 105                 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125

Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu
    130                 135                 140

Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln
145                 150                 155                 160

Ser Val Ser Ser Ser Tyr Leu Ala Trp Tyr Gln Gln Arg Pro Gly Gln
                165                 170                 175

Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile
            180                 185                 190

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
        195                 200                 205

Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln His
    210                 215                 220

Tyr Gly Ser Ser Pro Ser Trp Thr Phe Gly Gln Gly Thr Arg Leu Glu
225                 230                 235                 240

Ile Lys
```

<210> 809

<211> 726
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 809
gaagtgcagc tgctggagtc cggcggtgga ttggtgcaac cgggggggatc gctcagactg 60

tcctgtgcgg cgtcaggctt caccttctcg agctacgcca tgtcatgggt cagacaggcc 120

cctggaaagg gtctggaatg ggtgtccgcc atttccggga gcgggggatc tacatactac 180

gccgatagcg tgaagggccg cttcaccatt tcccgggaca actccaagaa cactctctat 240

ctgcaaatga actccctccg cgctgaggac actgccgtgt actactgcgc caaaatccct 300

cagaccggca ccttcgacta ctggggacag gggactctgg tcaccgtcag cagcggtggc 360

ggaggttcgg ggggaggagg aagcggcggc ggagggtccg agattgtgct gacccagtca 420

cccggcactt tgtccctgtc gcctggagaa agggccaccc tttcctgccg ggcatcccaa 480

tccgtgtcct cctcgtacct ggcctggtac cagcagaggc ccggacaggc cccacggctt 540

ctgatctacg gagcaagcag ccgcgcgacc ggtatcccgg accggttttc gggctcgggc 600

tcaggaactg acttcaccct caccatctcc cgcctggaac ccgaagattt cgctgtgtat 660

tactgccagc actacggcag ctccccgtcc tggacgttcg gccagggaac tcggctggag 720

atcaag 726

<210> 810
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 810
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

```
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Lys Ile Pro Gln Thr Gly Thr Phe Asp Tyr Trp Gly Gln Gly Thr
            100                 105                 110


Leu Val Thr Val Ser Ser
        115


<210> 811
<211> 109
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 811
Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1               5                   10                  15


Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser
            20                  25                  30


Tyr Leu Ala Trp Tyr Gln Gln Arg Pro Gly Gln Ala Pro Arg Leu Leu
        35                  40                  45


Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
    50                  55                  60


Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65                  70                  75                  80


Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln His Tyr Gly Ser Ser Pro
                85                  90                  95


Ser Trp Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys
            100                 105


<210> 812
<211> 486
<212> PRT
<213> Artificial Sequence

<220>
<221> source
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_SL
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 812

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Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15

His Ala Ala Arg Pro Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu
            20                  25                  30

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
        35                  40                  45

Thr Phe Ser Ser Tyr Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys
    50                  55                  60

Gly Leu Glu Trp Val Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr
65                  70                  75                  80

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser
                85                  90                  95

Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Lys Ile Pro Gln Thr Gly Thr Phe Asp Tyr
        115                 120                 125

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser
    130                 135                 140

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln
145                 150                 155                 160

Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser
                165                 170                 175

Cys Arg Ala Ser Gln Ser Val Ser Ser Ser Tyr Leu Ala Trp Tyr Gln
            180                 185                 190

Gln Arg Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser
        195                 200                 205

Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr
    210                 215                 220

Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val
225                 230                 235                 240
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Tyr Tyr Cys Gln His Tyr Gly Ser Ser Pro Ser Trp Thr Phe Gly Gln
                245                 250                 255

Gly Thr Arg Leu Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro
            260                 265                 270

Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu
        275                 280                 285

Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
    290                 295                 300

Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly
305                 310                 315                 320

Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg
                325                 330                 335

Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln
            340                 345                 350

Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu
        355                 360                 365

Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
    370                 375                 380

Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
385                 390                 395                 400

Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
                405                 410                 415

Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
            420                 425                 430

Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
        435                 440                 445

Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
    450                 455                 460

Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
465                 470                 475                 480

Gln Ala Leu Pro Pro Arg
                485
```

<210> 813
<211> 1458
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 813
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaagtgc agctgctgga gtccggcggt ggattggtgc aaccgggggg atcgctcaga 120

ctgtcctgtg cggcgtcagg cttcaccttc tcgagctacg ccatgtcatg ggtcagacag 180

gcccctggaa agggtctgga atgggtgtcc gccatttccg ggagcggggg atctacatac 240

tacgccgata gcgtgaaggg ccgcttcacc atttcccggg acaactccaa gaacactctc 300

tatctgcaaa tgaactccct ccgcgctgag gacactgccg tgtactactg cgccaaaatc 360

cctcagaccg gcaccttcga ctactgggga caggggactc tggtcaccgt cagcagcggt 420

ggcggaggtt cgggggggagg aggaagcggc ggcggagggt ccgagattgt gctgacccag 480

tcacccggca ctttgtccct gtcgcctgga gaaagggcca ccctttcctg ccgggcatcc 540

caatccgtgt cctcctcgta cctggcctgg taccagcaga ggcccggaca ggccccacgg 600

cttctgatct acggagcaag cagccgcgcg accggtatcc cggaccggtt ttcgggctcg 660

ggctcaggaa ctgacttcac cctcaccatc tcccgcctgg aacccgaaga tttcgctgtg 720

tattactgcc agcactacgg cagctccccg tcctggacgt tcggccaggg aactcggctg 780

gagatcaaga ccactacccc agcaccgagg ccacccaccc cggctcctac catcgcctcc 840

cagcctctgt ccctgcgtcc ggaggcatgt agacccgcag ctggtggggc cgtgcatacc 900

cggggtcttg acttcgcctg cgatatctac atttgggccc ctctggctgg tacttgcggg 960

gtcctgctgc tttcactcgt gatcactctt tactgtaagc gcggtcggaa gaagctgctg 1020

tacatcttta agcaaccctt catgaggcct gtgcagacta ctcaagagga ggacggctgt 1080

tcatgccggt tcccagagga ggaggaaggc ggctgcgaac tgcgcgtgaa attcagccgc 1140

agcgcagatg ctccagccta caagcagggg cagaaccagc tctacaacga actcaatctt 1200

ggtcggagag aggagtacga cgtgctggac aagcggagag gacgggaccc agaaatgggc 1260

gggaagccgc gcagaaagaa tccccaagag ggcctgtaca acgagctcca aaaggataag 1320

atggcagaag cctatagcga gattggtatg aaaggggaac gcagaagagg caaaggccac 1380

gacggactgt accagggact cagcaccgcc accaaggaca cctatgacgc tcttcacatg 1440

caggccctgc cgcctcgg 1458

<210> 814
<211> 248
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 814
Glu Val Gln Leu Val Glu Thr Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Met Ser Arg Glu Asn Asp Lys Asn Ser Val Phe
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Val Glu Asp Thr Gly Val Tyr Tyr Cys
85 90 95

Ala Arg Ala Asn Tyr Lys Arg Glu Leu Arg Tyr Tyr Tyr Gly Met Asp
100 105 110

Val Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly
115 120 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Met Thr
130 135 140

Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly Glu Ser Ala Thr Leu
145 150 155 160

Ser Cys Arg Ala Ser Gln Arg Val Ala Ser Asn Tyr Leu Ala Trp Tyr
165 170 175

Gln His Lys Pro Gly Gln Ala Pro Ser Leu Leu Ile Ser Gly Ala Ser
180 185 190

Ser Arg Ala Thr Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly
195 200 205

Thr Asp Phe Thr Leu Ala Ile Ser Arg Leu Glu Pro Glu Asp Ser Ala
210 215 220

Val Tyr Tyr Cys Gln His Tyr Asp Ser Ser Pro Ser Trp Thr Phe Gly
225 230 235 240

Gln Gly Thr Lys Val Glu Ile Lys
245

<210> 815
<211> 744
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 815
gaagtgcaac tggtggaaac cggtggagga ctcgtgcagc ctggcggcag cctccggctg 60

agctgcgccg cttcgggatt caccttttcc tcctacgcga tgtcttgggt cagacaggcc 120

cccggaaagg ggctggaatg ggtgtcagcc atctccggct ccggcggatc aacgtactac 180

gccgactccg tgaaaggccg gttcaccatg tcgcgcgaga atgacaagaa ctccgtgttc 240

ctgcaaatga actccctgag ggtggaggac accggagtgt actattgtgc gcgcgccaac 300

tacaagagag agctgcggta ctactacgga atggacgtct ggggacaggg aactatggtg 360

accgtgtcat ccggtggagg gggaagcggc ggtggaggca gcgggggcgg gggttcagaa 420

attgtcatga cccagtcccc gggaactctt tccctctccc ccggggaatc cgcgactttg 480

tcctgccggg ccagccagcg cgtggcctcg aactacctcg catggtacca gcataagcca 540

ggccaagccc cttccctgct gatttccggg gctagcagcc gcgccactgg cgtgccggat 600

aggttctcgg gaagcggctc gggtaccgat ttcaccctgg caatctcgcg gctggaaccg 660

gaggattcgg ccgtgtacta ctgccagcac tatgactcat ccccctcctg gacattcgga 720

cagggcacca aggtcgagat caag 744

<210> 816
<211> 124
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 816
Glu Val Gln Leu Val Glu Thr Gly Gly Gly Leu Val Gln Pro Gly Gly

_SL
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Met Ser Arg Glu Asn Asp Lys Asn Ser Val Phe
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Val Glu Asp Thr Gly Val Tyr Tyr Cys
85 90 95

Ala Arg Ala Asn Tyr Lys Arg Glu Leu Arg Tyr Tyr Tyr Gly Met Asp
100 105 110

Val Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
115 120

<210> 817
<211> 109
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 817
Glu Ile Val Met Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Ser Ala Thr Leu Ser Cys Arg Ala Ser Gln Arg Val Ala Ser Asn
20 25 30

Tyr Leu Ala Trp Tyr Gln His Lys Pro Gly Gln Ala Pro Ser Leu Leu
35 40 45

Ile Ser Gly Ala Ser Ser Arg Ala Thr Gly Val Pro Asp Arg Phe Ser
50 55 60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Ala Ile Ser Arg Leu Glu
65 70 75 80

Pro Glu Asp Ser Ala Val Tyr Tyr Cys Gln His Tyr Asp Ser Ser Pro

_SL
85 90 95

Ser Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 818
<211> 492
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 818
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Val Gln Leu Val Glu Thr Gly Gly Gly Leu
20 25 30

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
35 40 45

Thr Phe Ser Ser Tyr Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys
50 55 60

Gly Leu Glu Trp Val Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr
65 70 75 80

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Met Ser Arg Glu Asn Asp
85 90 95

Lys Asn Ser Val Phe Leu Gln Met Asn Ser Leu Arg Val Glu Asp Thr
100 105 110

Gly Val Tyr Tyr Cys Ala Arg Ala Asn Tyr Lys Arg Glu Leu Arg Tyr
115 120 125

Tyr Tyr Gly Met Asp Val Trp Gly Gln Gly Thr Met Val Thr Val Ser
130 135 140

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
145 150 155 160

Glu Ile Val Met Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
165 170 175

Glu Ser Ala Thr Leu Ser Cys Arg Ala Ser Gln Arg Val Ala Ser Asn

_SL

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            180                 185                 190

Tyr Leu Ala Trp Tyr Gln His Lys Pro Gly Gln Ala Pro Ser Leu Leu
        195                 200                 205

Ile Ser Gly Ala Ser Ser Arg Ala Thr Gly Val Pro Asp Arg Phe Ser
    210                 215                 220

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Ala Ile Ser Arg Leu Glu
225                 230                 235                 240

Pro Glu Asp Ser Ala Val Tyr Tyr Cys Gln His Tyr Asp Ser Ser Pro
                245                 250                 255

Ser Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Thr Thr Thr
            260                 265                 270

Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro
        275                 280                 285

Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val
    290                 295                 300

His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro
305                 310                 315                 320

Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu
                325                 330                 335

Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro
            340                 345                 350

Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys
        355                 360                 365

Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe
    370                 375                 380

Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu
385                 390                 395                 400

Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp
                405                 410                 415

Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys
            420                 425                 430
```

_SL
Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala
435 440 445

Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys
450 455 460

Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr
465 470 475 480

Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 819
<211> 1476
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 819
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaagtgc aactggtgga aaccggtgga ggactcgtgc agcctggcgg cagcctccgg 120

ctgagctgcg ccgcttcggg attcaccttt tcctcctacg cgatgtcttg ggtcagacag 180

gcccccggaa aggggctgga atgggtgtca gccatctccg gctccggcgg atcaacgtac 240

tacgccgact ccgtgaaagg ccggttcacc atgtcgcgcg agaatgacaa gaactccgtg 300

ttcctgcaaa tgaactccct gagggtggag gacaccggag tgtactattg tgcgcgcgcc 360

aactacaaga gagagctgcg gtactactac ggaatggacg tctggggaca gggaactatg 420

gtgaccgtgt catccggtgg agggggaagc ggcggtggag gcagcggggg cgggggttca 480

gaaattgtca tgacccagtc cccgggaact ctttccctct cccccgggga atccgcgact 540

ttgtcctgcc gggccagcca gcgcgtggcc tcgaactacc tcgcatggta ccagcataag 600

ccaggccaag ccccttccct gctgatttcc ggggctagca gccgcgccac tggcgtgccg 660

gataggttct cgggaagcgg ctcgggtacc gatttcaccc tggcaatctc gcggctggaa 720

ccggaggatt cggccgtgta ctactgccag cactatgact catccccctc ctggacattc 780

ggacagggca ccaaggtcga gatcaagacc actaccccag caccgaggcc acccaccccg 840

gctcctacca tcgcctccca gcctctgtcc ctgcgtccgg aggcatgtag acccgcagct 900

ggtggggccg tgcatacccg gggtcttgac ttcgcctgcg atatctacat ttgggccccc 960

ctggctggta cttgcggggt cctgctgctt tcactcgtga tcactcttta ctgtaagcgc 1020

ggtcggaaga agctgctgta catctttaag caacccttca tgaggcctgt gcagactact 1080

caagaggagg acggctgttc atgccggttc ccagaggagg aggaaggcgg ctgcgaactg 1140

cgcgtgaaat tcagccgcag cgcagatgct ccagcctaca agcaggggca gaaccagctc 1200

tacaacgaac tcaatcttgg tcggagagag gagtacgacg tgctggacaa gcggagagga 1260

cgggacccag aaatgggcgg gaagccgcgc agaaagaatc cccaagaggg cctgtacaac 1320

gagctccaaa aggataagat ggcagaagcc tatagcgaga ttggtatgaa aggggaacgc 1380

agaaggaggca aaggccacga cggactgtac cagggactca gcaccgccac caaggacacc 1440

tatgacgctc ttcacatgca ggccctgccg cctcgg 1476

<210> 820
<211> 244
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 820
Glu Val Gln Leu Leu Glu Thr Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ser Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Ala Leu Val Gly Ala Thr Gly Ala Phe Asp Ile Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly
130 135 140

Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala

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                                                _SL
145                 150                 155                 160

Ser Gln Ser Leu Ser Ser Asn Phe Leu Ala Trp Tyr Gln Gln Lys Pro
                165                 170                 175

Gly Gln Ala Pro Gly Leu Leu Ile Tyr Gly Ala Ser Asn Trp Ala Thr
            180                 185                 190

Gly Thr Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
        195                 200                 205

Leu Thr Ile Thr Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys
    210                 215                 220

Gln Tyr Tyr Gly Thr Ser Pro Met Tyr Thr Phe Gly Gln Gly Thr Lys
225                 230                 235                 240

Val Glu Ile Lys
```

<210> 821
<211> 732
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 821

```
gaagtgcagc tgctcgaaac cggtggaggg ctggtgcagc cagggggctc cctgaggctt       60

tcatgcgccg ctagcggatt ctccttctcc tcttacgcca tgtcgtgggt ccgccaagcc      120

cctggaaaag gcctggaatg ggtgtccgcg atttccggga gcggaggttc gacctattac      180

gccgactccg tgaagggccg ctttaccatc tcccgggata actccaagaa cactctgtac      240

ctccaaatga actcgctgag agccgaggac accgccgtgt attactgcgc gaaggcgctg      300

gtcggcgcga ctggggcatt cgacatctgg ggacagggaa ctcttgtgac cgtgtcgagc      360

ggaggcggcg gctccggcgg aggagggagc gggggcggtg gttccgaaat cgtgttgact      420

cagtccccgg gaaccctgag cttgtcaccc ggggagcggg ccactctctc ctgtcgcgcc      480

tcccaatcgc tctcatccaa tttcctggcc tggtaccagc agaagcccgg acaggccccg      540

ggcctgctca tctacggcgc ttcaaactgg gcaacgggaa cccctgatcg gttcagcgga      600

agcggatcgg gtactgactt taccctgacc atcaccagac tggaaccgga ggacttcgcc      660

gtgtactact gccagtacta cggcacctcc cccatgtaca cattcggaca gggtaccaag      720

gtcgagatta ag                                                          732
```

<210> 822
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 822
Glu Val Gln Leu Leu Glu Thr Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ser Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Ala Leu Val Gly Ala Thr Gly Ala Phe Asp Ile Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 823
<211> 109
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 823
Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Leu Ser Ser Asn
20 25 30

Phe Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Gly Leu Leu
35 40 45

Ile Tyr Gly Ala Ser Asn Trp Ala Thr Gly Thr Pro Asp Arg Phe Ser
50 55 60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Thr Arg Leu Glu
65 70 75 80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Tyr Tyr Gly Thr Ser Pro
85 90 95

Met Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 824
<211> 488
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 824
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Val Gln Leu Leu Glu Thr Gly Gly Gly Leu
20 25 30

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
35 40 45

Ser Phe Ser Ser Tyr Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys
50 55 60

Gly Leu Glu Trp Val Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr
65 70 75 80

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser
85 90 95

Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Ala Lys Ala Leu Val Gly Ala Thr Gly Ala Phe
115 120 125

```
Asp Ile Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
    130                 135                 140

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Leu
145                 150                 155                 160

Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr
                165                 170                 175

Leu Ser Cys Arg Ala Ser Gln Ser Leu Ser Ser Asn Phe Leu Ala Trp
            180                 185                 190

Tyr Gln Gln Lys Pro Gly Gln Ala Pro Gly Leu Leu Ile Tyr Gly Ala
        195                 200                 205

Ser Asn Trp Ala Thr Gly Thr Pro Asp Arg Phe Ser Gly Ser Gly Ser
    210                 215                 220

Gly Thr Asp Phe Thr Leu Thr Ile Thr Arg Leu Glu Pro Glu Asp Phe
225                 230                 235                 240

Ala Val Tyr Tyr Cys Gln Tyr Tyr Gly Thr Ser Pro Met Tyr Thr Phe
                245                 250                 255

Gly Gln Gly Thr Lys Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg
            260                 265                 270

Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg
        275                 280                 285

Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly
    290                 295                 300

Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr
305                 310                 315                 320

Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg
                325                 330                 335

Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro
            340                 345                 350

Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu
        355                 360                 365

Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala
    370                 375                 380
```

Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu
385 390 395 400

Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly
405 410 415

Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu
420 425 430

Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser
435 440 445

Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly
450 455 460

Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu
465 470 475 480

His Met Gln Ala Leu Pro Pro Arg
485

<210> 825
<211> 1464
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 825
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaagtgc agctgctcga aaccggtgga gggctggtgc agccaggggg ctccctgagg 120

ctttcatgcg ccgctagcgg attctccttc tcctcttacg ccatgtcgtg ggtccgccaa 180

gcccctggaa aaggcctgga atgggtgtcc gcgatttccg ggagcggagg ttcgacctat 240

tacgccgact ccgtgaaggg ccgctttacc atctcccggg ataactccaa gaacactctg 300

tacctccaaa tgaactcgct gagagccgag gacaccgccg tgtattactg cgcgaaggcg 360

ctggtcggcg cgactggggc attcgacatc tggggacagg gaactcttgt gaccgtgtcg 420

agcggaggcg gcggctccgg cggaggaggg agcgggggcg gtggttccga aatcgtgttg 480

actcagtccc cgggaaccct gagcttgtca cccggggagc gggccactct ctcctgtcgc 540

gcctcccaat cgctctcatc caatttcctg gcctggtacc agcagaagcc cggacaggcc 600

ccgggcctgc tcatctacgg cgcttcaaac tgggcaacgg gaacccctga tcggttcagc 660

_SL

ggaagcggat cgggtactga ctttaccctg accatcacca gactggaacc ggaggacttc 720

gccgtgtact actgccagta ctacggcacc tcccccatgt acacattcgg acagggtacc 780

aaggtcgaga ttaagaccac taccccagca ccgaggccac ccaccccggc tcctaccatc 840

gcctcccagc ctctgtccct gcgtccggag gcatgtagac ccgcagctgg tggggccgtg 900

catacccggg gtcttgactt cgcctgcgat atctacattt gggcccctct ggctggtact 960

tgcggggtcc tgctgctttc actcgtgatc actctttact gtaagcgcgg tcggaagaag 1020

ctgctgtaca tctttaagca acccttcatg aggcctgtgc agactactca agaggaggac 1080

ggctgttcat gccggttccc agaggaggag gaaggcggct gcgaactgcg cgtgaaattc 1140

agccgcagcg cagatgctcc agcctacaag caggggcaga accagctcta caacgaactc 1200

aatcttggtc ggagagagga gtacgacgtg ctggacaagc ggagaggacg ggacccagaa 1260

atgggcggga agccgcgcag aaagaatccc caagagggcc tgtacaacga gctccaaaag 1320

gataagatgg cagaagccta tagcgagatt ggtatgaaag gggaacgcag aagaggcaaa 1380

ggccacgacg gactgtacca gggactcagc accgccacca aggacaccta tgacgctctt 1440

cacatgcagg ccctgccgcc tcgg 1464

<210> 826
<211> 244
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 826
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

```
Val Leu Trp Phe Gly Glu Gly Phe Asp Pro Trp Gly Gln Gly Thr Leu
            100                 105                 110

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Asp Ile Val Leu Thr Gln Ser Pro Leu Ser Leu Pro
    130                 135                 140

Val Thr Pro Gly Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser
145                 150                 155                 160

Leu Leu His Ser Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys
                165                 170                 175

Pro Gly Gln Ser Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala
            180                 185                 190

Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
        195                 200                 205

Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr
    210                 215                 220

Cys Met Gln Ala Leu Gln Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys
225                 230                 235                 240

Val Asp Ile Lys
```

<210> 827
<211> 733
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 827

```
gaagtgcagc tgcttgagag cggtggaggt ctggtgcagc ccgggggatc actgcgcctg       60

tcctgtgccg cgtccggttt cactttctcc tcgtacgcca tgtcgtgggt cagacaggca      120

ccgggaaagg gactggaatg ggtgtcagcc atttcgggtt cgggggcag cacctactac       180

gctgactccg tgaagggccg gttcaccatt tcccgcgaca actccaagaa caccttgtac      240

ctccaaatga actccctgcg ggccgaagat accgccgtgt attactgcgt gctgtggttc      300

ggagagggat tcgacccgtg gggacaagga acactcgtga ctgtgtcatc cggcggaggc      360
```

ggcagcggtg gcggcggttc cggcggcggc ggatctgaca tcgtgttgac ccagtcccct 420

ctgagcctgc cggtcactcc tggcgaacca gccagcatct cctgccggtc gagccagtcc 480

ctcctgcact ccaatgggta caactacctc gattggtatc tgcaaaagcc gggccagagc 540

ccccagctgc tgatctacct tgggtcaaac cgcgcttccg gggtgcctga tagattctcc 600

gggtccggga gcggaaccga ctttaccctg aaaatctcga gggtggaggc cgaggacgtc 660

ggagtgtact actgcatgca ggcgctccag actcccctga ccttcggagg aggaacgaag 720

gtcgacatca aga 733

<210> 828
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 828
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Val Leu Trp Phe Gly Glu Gly Phe Asp Pro Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ser
115

<210> 829
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 829
Asp Ile Val Leu Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser
20 25 30

Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala
85 90 95

Leu Gln Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Asp Ile Lys
100 105 110

<210> 830
<211> 488
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 830
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu
20 25 30

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
35 40 45

Thr Phe Ser Ser Tyr Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys
50 55 60

Gly Leu Glu Trp Val Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr

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65 70 75 80

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser
85 90 95

Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Val Leu Trp Phe Gly Glu Gly Phe Asp Pro Trp
115 120 125

Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
130 135 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Leu Thr Gln Ser
145 150 155 160

Pro Leu Ser Leu Pro Val Thr Pro Gly Glu Pro Ala Ser Ile Ser Cys
165 170 175

Arg Ser Ser Gln Ser Leu Leu His Ser Asn Gly Tyr Asn Tyr Leu Asp
180 185 190

Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Gln Leu Leu Ile Tyr Leu
195 200 205

Gly Ser Asn Arg Ala Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly
210 215 220

Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp
225 230 235 240

Val Gly Val Tyr Tyr Cys Met Gln Ala Leu Gln Thr Pro Leu Thr Phe
245 250 255

Gly Gly Gly Thr Lys Val Asp Ile Lys Thr Thr Thr Pro Ala Pro Arg
260 265 270

Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg
275 280 285

Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly
290 295 300

Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr
305 310 315 320

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                                                _SL
Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg
                325                 330                 335

Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro
            340                 345                 350

Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu
        355                 360                 365

Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala
    370                 375                 380

Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu
385                 390                 395                 400

Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly
                405                 410                 415

Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu
            420                 425                 430

Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser
        435                 440                 445

Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly
    450                 455                 460

Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu
465                 470                 475                 480

His Met Gln Ala Leu Pro Pro Arg
                485
```

<210> 831
<211> 1464
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 831
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaagtgc agctgcttga gagcggtgga ggtctggtgc agcccggggg atcactgcgc 120

ctgtcctgtg ccgcgtccgg tttcactttc tcctcgtacg ccatgtcgtg ggtcagacag 180

gcaccgggaa agggactgga atgggtgtca gccatttcgg gttcgggggg cagcacctac 240

tacgctgact ccgtgaaggg ccggttcacc atttcccgcg acaactccaa gaacaccttg 300

tacctccaaa tgaactccct gcgggccgaa gataccgccg tgtattactg cgtgctgtgg 360

ttcggagagg gattcgaccc gtggggacaa ggaacactcg tgactgtgtc atccggcgga 420

ggcggcagcg gtggcggcgg ttccggcggc ggcggatctg acatcgtgtt gacccagtcc 480

cctctgagcc tgccggtcac tcctggcgaa ccagccagca tctcctgccg gtcgagccag 540

tccctcctgc actccaatgg gtacaactac ctcgattggt atctgcaaaa gccgggccag 600

agcccccagc tgctgatcta ccttgggtca aaccgcgctt ccggggtgcc tgatagattc 660

tccgggtccg ggagcggaac cgactttacc ctgaaaatct cgagggtgga ggccgaggac 720

gtcggagtgt actactgcat gcaggcgctc cagactcccc tgaccttcgg aggaggaacg 780

aaggtcgaca tcaagaccac taccccagca ccgaggccac ccaccccggc tcctaccatc 840

gcctcccagc ctctgtccct gcgtccggag gcatgtagac ccgcagctgg tggggccgtg 900

catacccggg gtcttgactt cgcctgcgat atctacattt gggcccctct ggctggtact 960

tgcggggtcc tgctgctttc actcgtgatc actctttact gtaagcgcgg tcggaagaag 1020

ctgctgtaca tctttaagca acccttcatg aggcctgtgc agactactca agaggaggac 1080

ggctgttcat gccggttccc agaggaggag gaaggcggct gcgaactgcg cgtgaaattc 1140

agccgcagcg cagatgctcc agcctacaag caggggcaga accagctcta caacgaactc 1200

aatcttggtc ggagagagga gtacgacgtg ctggacaagc ggagaggacg ggacccagaa 1260

atgggcggga agccgcgcag aaagaatccc caagagggcc tgtacaacga gctccaaaag 1320

gataagatgg cagaagccta tagcgagatt ggtatgaaag gggaacgcag aagaggcaaa 1380

ggccacgacg gactgtacca gggactcagc accgccacca aggacaccta tgacgctctt 1440

cacatgcagg ccctgccgcc tcgg 1464

<210> 832
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 832
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val

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35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Val Gly Tyr Asp Ser Ser Gly Tyr Tyr Arg Asp Tyr Tyr Gly
100 105 110

Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly
115 120 125

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val
130 135 140

Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala
145 150 155 160

Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser Tyr Leu Ala
165 170 175

Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Gly
180 185 190

Thr Ser Ser Arg Ala Thr Gly Ile Ser Asp Arg Phe Ser Gly Ser Gly
195 200 205

Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu Asp
210 215 220

Phe Ala Val Tyr Tyr Cys Gln His Tyr Gly Asn Ser Pro Pro Lys Phe
225 230 235 240

Thr Phe Gly Pro Gly Thr Lys Leu Glu Ile Lys
245 250

<210> 833
<211> 753
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

polynucleotide"

<400> 833
caagtgcagc tcgtggagtc aggcggagga ctggtgcagc ccgggggctc cctgagactt 60

tcctgcgcgg catcgggttt taccttctcc tcctatgcta tgtcctgggt gcgccaggcc 120

ccgggaaagg gactggaatg ggtgtccgca atcagcggta gcgggggctc aacatactac 180

gccgactccg tcaagggtcg cttcactatt tcccgggaca actccaagaa taccctgtac 240

ctccaaatga acagcctcag ggccgaggat actgccgtgt actactgcgc caaagtcgga 300

tacgatagct ccggttacta ccgggactac tacggaatgg acgtgtgggg acagggcacc 360

accgtgaccg tgtcaagcgg cggaggcggt tcaggagggg gaggctccgg cggtggaggg 420

tccgaaatcg tcctgactca gtcgcctggc actctgtcgt tgtccccggg ggagcgcgct 480

accctgtcgt gtcgggcgtc gcagtccgtg tcgagctcct acctcgcgtg gtaccagcag 540

aagcccggac aggcccctag acttctgatc tacggcactt cttcacgcgc caccgggatc 600

agcgacaggt tcagcggctc cggctccggg accgacttca ccctgaccat tagccggctg 660

gagcctgaag atttcgccgt gtattactgc caacactacg gaaactcgcc gccaaagttc 720

acgttcggac ccggaaccaa gctggaaatc aag 753

<210> 834
<211> 126
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 834
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Val Gly Tyr Asp Ser Ser Gly Tyr Tyr Arg Asp Tyr Tyr Gly
100 105 110

Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120 125

<210> 835
<211> 110
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 835
Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser
20 25 30

Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45

Ile Tyr Gly Thr Ser Ser Arg Ala Thr Gly Ile Ser Asp Arg Phe Ser
50 55 60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65 70 75 80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln His Tyr Gly Asn Ser Pro
85 90 95

Pro Lys Phe Thr Phe Gly Pro Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 836
<211> 495
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 836
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

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His Ala Ala Arg Pro Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu
            20                  25                  30

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
        35                  40                  45

Thr Phe Ser Ser Tyr Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys
    50                  55                  60

Gly Leu Glu Trp Val Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr
65                  70                  75                  80

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser
                85                  90                  95

Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Lys Val Gly Tyr Asp Ser Ser Gly Tyr Tyr
        115                 120                 125

Arg Asp Tyr Tyr Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr
    130                 135                 140

Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
145                 150                 155                 160

Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser
                165                 170                 175

Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser
            180                 185                 190

Ser Ser Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg
        195                 200                 205

Leu Leu Ile Tyr Gly Thr Ser Ser Arg Ala Thr Gly Ile Ser Asp Arg
    210                 215                 220

Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg
225                 230                 235                 240

Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln His Tyr Gly Asn
                245                 250                 255

Ser Pro Pro Lys Phe Thr Phe Gly Pro Gly Thr Lys Leu Glu Ile Lys
            260                 265                 270
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Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala
        275                 280                 285

Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly
    290                 295                 300

Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile
305                 310                 315                 320

Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val
                325                 330                 335

Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe
            340                 345                 350

Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly
        355                 360                 365

Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg
    370                 375                 380

Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln
385                 390                 395                 400

Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp
                405                 410                 415

Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro
            420                 425                 430

Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp
        435                 440                 445

Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg
    450                 455                 460

Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr
465                 470                 475                 480

Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
                485                 490                 495
```

<210> 837
<211> 1485
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 837
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtgc agctcgtgga gtcaggcgga ggactggtgc agcccggggg ctccctgaga 120

ctttcctgcg cggcatcggg ttttaccttc tcctcctatg ctatgtcctg ggtgcgccag 180

gccccgggaa agggactgga atgggtgtcc gcaatcagcg gtagcggggg ctcaacatac 240

tacgccgact ccgtcaaggg tcgcttcact atttcccggg acaactccaa gaataccctg 300

tacctccaaa tgaacagcct cagggccgag gatactgccg tgtactactg cgccaaagtc 360

ggatacgata gctccggtta ctaccgggac tactacggaa tggacgtgtg gggacagggc 420

accaccgtga ccgtgtcaag cggcggaggc ggttcaggag ggggaggctc cggcggtgga 480

gggtccgaaa tcgtcctgac tcagtcgcct ggcactctgt cgttgtcccc gggggagcgc 540

gctaccctgt cgtgtcgggc gtcgcagtcc gtgtcgagct cctacctcgc gtggtaccag 600

cagaagcccg gacaggcccc tagacttctg atctacggca cttcttcacg cgccaccggg 660

atcagcgaca ggttcagcgg ctccggctcc gggaccgact tcaccctgac cattagccgg 720

ctggagcctg aagatttcgc cgtgtattac tgccaacact acggaaactc gccgccaaag 780

ttcacgttcg gacccggaac caagctggaa atcaagacca ctaccccagc accgaggcca 840

cccaccccgg ctcctaccat cgcctcccag cctctgtccc tgcgtccgga ggcatgtaga 900

cccgcagctg gtggggccgt gcatacccgg ggtcttgact tcgcctgcga tatctacatt 960

tgggcccctc tggctggtac ttgcggggtc ctgctgcttt cactcgtgat cactctttac 1020

tgtaagcgcg gtcggaagaa gctgctgtac atctttaagc aacccttcat gaggcctgtg 1080

cagactactc aagaggagga cggctgttca tgccggttcc cagaggagga ggaaggcggc 1140

tgcgaactgc gcgtgaaatt cagccgcagc gcagatgctc cagcctacaa gcaggggcag 1200

aaccagctct acaacgaact caatcttggt cggagagagg agtacgacgt gctggacaag 1260

cggagaggac gggacccaga aatgggcggg aagccgcgca gaaagaatcc ccaagagggc 1320

ctgtacaacg agctccaaaa ggataagatg gcagaagcct atagcgagat tggtatgaaa 1380

ggggaacgca gaagaggcaa aggccacgac ggactgtacc agggactcag caccgccacc 1440

aaggacacct atgacgctct tcacatgcag gccctgccgc ctcgg 1485

<210> 838
<211> 246
<212> PRT
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 838
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Met Gly Trp Ser Ser Gly Tyr Leu Gly Ala Phe Asp Ile Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
115 120 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser
130 135 140

Pro Gly Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
145 150 155 160

Arg Ala Ser Gln Ser Val Ala Ser Ser Phe Leu Ala Trp Tyr Gln Gln
165 170 175

Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Gly Arg
180 185 190

Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
195 200 205

Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr
210 215 220

Tyr Cys Gln His Tyr Gly Gly Ser Pro Arg Leu Thr Phe Gly Gly Gly
225 230 235 240

Thr Lys Val Asp Ile Lys
245

<210> 839
<211> 739
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 839
gaagtccaac tggtggagtc cgggggaggg ctcgtgcagc ccggaggcag ccttcggctg 60

tcgtgcgccg cctccgggtt cacgttctca tcctacgcga tgtcgtgggt cagacaggca 120

ccaggaaagg gactggaatg ggtgtccgcc attagcggct ccggcggtag cacctactat 180

gccgactcag tgaagggaag gttcactatc tcccgcgaca acagcaagaa caccctgtac 240

ctccaaatga actctctgcg ggccgaggat accgcggtgt actattgcgc caagatgggt 300

tggtccagcg gatacttggg agccttcgac atttggggac agggcactac tgtgaccgtg 360

tcctccgggg gtggcggatc gggaggcggc ggctcgggtg gaggggttc cgaaatcgtg 420

ttgacccagt caccgggaac cctctcgctg tccccgggag aacgggctac actgtcatgt 480

agagcgtccc agtccgtggc ttcctcgttc ctggcctggt accagcagaa gccgggacag 540

gcaccccgcc tgctcatcta cggagccagc ggccgggcga ccggcatccc tgaccgcttc 600

tccggttccg gctcgggcac cgactttact ctgaccatta gcaggcttga gcccgaggat 660

tttgccgtgt actactgcca acactacggg gggagccctc gcctgacctt cggaggcgga 720

actaaggtcg atatcaaaa 739

<210> 840
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 840
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

_SL
Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
    50   55   60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65   70   75   80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Ala Lys Met Gly Trp Ser Ser Gly Tyr Leu Gly Ala Phe Asp Ile Trp
            100   105   110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115   120

<210> 841
<211> 109
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 841
Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1   5   10   15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ala Ser Ser
            20   25   30

Phe Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
        35   40   45

Ile Tyr Gly Ala Ser Gly Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
    50   55   60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65   70   75   80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln His Tyr Gly Gly Ser Pro
                85   90   95

Arg Leu Thr Phe Gly Gly Gly Thr Lys Val Asp Ile Lys
            100   105

<210> 842
<211> 490
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 842

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15

His Ala Ala Arg Pro Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
            20                  25                  30

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
        35                  40                  45

Thr Phe Ser Ser Tyr Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys
    50                  55                  60

Gly Leu Glu Trp Val Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr
65                  70                  75                  80

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser
                85                  90                  95

Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Lys Met Gly Trp Ser Ser Gly Tyr Leu Gly
        115                 120                 125

Ala Phe Asp Ile Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile
145                 150                 155                 160

Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly Glu Arg
                165                 170                 175

Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ala Ser Ser Phe Leu
            180                 185                 190

Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr
        195                 200                 205
```

_SL
Gly Ala Ser Gly Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly Ser
    210   215   220

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu
225   230   235   240

Asp Phe Ala Val Tyr Tyr Cys Gln His Tyr Gly Gly Ser Pro Arg Leu
                245   250   255

Thr Phe Gly Gly Gly Thr Lys Val Asp Ile Lys Thr Thr Thr Pro Ala
            260   265   270

Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser
        275   280   285

Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr
    290   295   300

Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala
305   310   315   320

Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys
                325   330   335

Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met
            340   345   350

Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe
        355   360   365

Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg
    370   375   380

Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn
385   390   395   400

Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg
                405   410   415

Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro
            420   425   430

Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala
        435   440   445

Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His
    450   455   460

Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp
465 470 475 480

Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 843
<211> 1470
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 843
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaagtcc aactggtgga gtccggggga gggctcgtgc agcccggagg cagccttcgg 120

ctgtcgtgcg ccgcctccgg gttcacgttc tcatcctacg cgatgtcgtg ggtcagacag 180

gcaccaggaa agggactgga atgggtgtcc gccattagcg gctccggcgg tagcacctac 240

tatgccgact cagtgaaggg aaggttcact atctcccgcg acaacagcaa gaacaccctg 300

tacctccaaa tgaactctct gcgggccgag gataccgcgg tgtactattg cgccaagatg 360

ggttggtcca gcggatactt gggagccttc gacatttggg gacagggcac tactgtgacc 420

gtgtcctccg ggggtggcgg atcgggaggc ggcggctcgg gtggaggggg ttccgaaatc 480

gtgttgaccc agtcaccggg aaccctctcg ctgtccccgg gagaacgggc tacactgtca 540

tgtagagcgt cccagtccgt ggcttcctcg ttcctggcct ggtaccagca gaagccggga 600

caggcacccc gcctgctcat ctacggagcc agcggccggg cgaccggcat ccctgaccgc 660

ttctccggtt ccggctcggg caccgacttt actctgacca ttagcaggct tgagcccgag 720

gattttgccg tgtactactg ccaacactac ggggggagcc ctcgcctgac cttcggaggc 780

ggaactaagg tcgatatcaa aaccactacc ccagcaccga ggccacccac cccggctcct 840

accatcgcct cccagcctct gtccctgcgt ccggaggcat gtagacccgc agctggtggg 900

gccgtgcata cccggggtct tgacttcgcc tgcgatatct acatttgggc ccctctggct 960

ggtacttgcg gggtcctgct gctttcactc gtgatcactc tttactgtaa gcgcggtcgg 1020

aagaagctgc tgtacatctt taagcaaccc ttcatgaggc ctgtgcagac tactcaagag 1080

gaggacggct gttcatgccg gttcccagag gaggaggaag gcggctgcga actgcgcgtg 1140

aaattcagcc gcagcgcaga tgctccagcc tacaagcagg ggcagaacca gctctacaac 1200

gaactcaatc ttggtcggag agaggagtac gacgtgctgg acaagcggag aggacgggac 1260

ccagaaatgg gcgggaagcc gcgcagaaag aatccccaag agggcctgta caacgagctc 1320

caaaaggata agatggcaga agcctatagc gagattggta tgaaagggga acgcagaaga 1380

ggcaaaggcc acgacggact gtaccaggga ctcagcaccg ccaccaagga cacctatgac 1440

gctcttcaca tgcaggccct gccgcctcgg 1470

<210> 844
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 844
Gln Ile Gln Leu Val Gln Ser Gly Pro Asp Leu Lys Lys Pro Gly Glu
1 5 10 15

Thr Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Phe
20 25 30

Gly Met Asn Trp Val Lys Gln Ala Pro Gly Lys Gly Phe Lys Trp Met
35 40 45

Ala Trp Ile Asn Thr Tyr Thr Gly Glu Ser Tyr Phe Ala Asp Asp Phe
50 55 60

Lys Gly Arg Phe Ala Phe Ser Val Glu Thr Ser Ala Thr Thr Ala Tyr
65 70 75 80

Leu Gln Ile Asn Asn Leu Lys Thr Glu Asp Thr Ala Thr Tyr Phe Cys
85 90 95

Ala Arg Gly Glu Ile Tyr Tyr Gly Tyr Asp Gly Gly Phe Ala Tyr Trp
100 105 110

Gly Gln Gly Thr Leu Val Thr Val Ser Ala
115 120

<210> 845
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 845
Asp Val Val Met Thr Gln Ser His Arg Phe Met Ser Thr Ser Val Gly

_SL
1 5 10 15

Asp Arg Val Ser Ile Thr Cys Arg Ala Ser Gln Asp Val Asn Thr Ala
20 25 30

Val Ser Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile
35 40 45

Phe Ser Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp Arg Phe Thr Gly
50 55 60

Ser Gly Ser Gly Ala Asp Phe Thr Leu Thr Ile Ser Ser Val Gln Ala
65 70 75 80

Glu Asp Leu Ala Val Tyr Tyr Cys Gln Gln His Tyr Ser Thr Pro Trp
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Asp Ile Lys
100 105

<210> 846
<211> 244
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 846
Gln Ile Gln Leu Val Gln Ser Gly Pro Asp Leu Lys Lys Pro Gly Glu
1 5 10 15

Thr Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Phe
20 25 30

Gly Met Asn Trp Val Lys Gln Ala Pro Gly Lys Gly Phe Lys Trp Met
35 40 45

Ala Trp Ile Asn Thr Tyr Thr Gly Glu Ser Tyr Phe Ala Asp Asp Phe
50 55 60

Lys Gly Arg Phe Ala Phe Ser Val Glu Thr Ser Ala Thr Thr Ala Tyr
65 70 75 80

Leu Gln Ile Asn Asn Leu Lys Thr Glu Asp Thr Ala Thr Tyr Phe Cys
85 90 95

Ala Arg Gly Glu Ile Tyr Tyr Gly Tyr Asp Gly Gly Phe Ala Tyr Trp

_SL
100 105 110

Gly Gln Gly Thr Leu Val Thr Val Ser Ala Gly Gly Gly Gly Ser Gly
115 120 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln Ser
130 135 140

His Arg Phe Met Ser Thr Ser Val Gly Asp Arg Val Ser Ile Thr Cys
145 150 155 160

Arg Ala Ser Gln Asp Val Asn Thr Ala Val Ser Trp Tyr Gln Gln Lys
165 170 175

Pro Gly Gln Ser Pro Lys Leu Leu Ile Phe Ser Ala Ser Tyr Arg Tyr
180 185 190

Thr Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Ala Asp Phe
195 200 205

Thr Leu Thr Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr
210 215 220

Cys Gln Gln His Tyr Ser Thr Pro Trp Thr Phe Gly Gly Gly Thr Lys
225 230 235 240

Leu Asp Ile Lys

<210> 847
<211> 467
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 847
Gln Ile Gln Leu Val Gln Ser Gly Pro Asp Leu Lys Lys Pro Gly Glu
1 5 10 15

Thr Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Phe
20 25 30

Gly Met Asn Trp Val Lys Gln Ala Pro Gly Lys Gly Phe Lys Trp Met
35 40 45

Ala Trp Ile Asn Thr Tyr Thr Gly Glu Ser Tyr Phe Ala Asp Asp Phe

_SL

50 55 60

Lys Gly Arg Phe Ala Phe Ser Val Glu Thr Ser Ala Thr Thr Ala Tyr
65 70 75 80

Leu Gln Ile Asn Asn Leu Lys Thr Glu Asp Thr Ala Thr Tyr Phe Cys
85 90 95

Ala Arg Gly Glu Ile Tyr Tyr Gly Tyr Asp Gly Gly Phe Ala Tyr Trp
100 105 110

Gly Gln Gly Thr Leu Val Thr Val Ser Ala Gly Gly Gly Gly Ser Gly
115 120 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln Ser
130 135 140

His Arg Phe Met Ser Thr Ser Val Gly Asp Arg Val Ser Ile Thr Cys
145 150 155 160

Arg Ala Ser Gln Asp Val Asn Thr Ala Val Ser Trp Tyr Gln Gln Lys
165 170 175

Pro Gly Gln Ser Pro Lys Leu Leu Ile Phe Ser Ala Ser Tyr Arg Tyr
180 185 190

Thr Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Ala Asp Phe
195 200 205

Thr Leu Thr Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr
210 215 220

Cys Gln Gln His Tyr Ser Thr Pro Trp Thr Phe Gly Gly Gly Thr Lys
225 230 235 240

Leu Asp Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala
245 250 255

Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg
260 265 270

Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys
275 280 285

Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu
290 295 300

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                                                _SL
Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu
305                 310                 315                 320


Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln
                325                 330                 335


Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly
            340                 345                 350


Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr
        355                 360                 365


Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg
    370                 375                 380


Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met
385                 390                 395                 400


Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu
                405                 410                 415


Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys
            420                 425                 430


Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu
        435                 440                 445


Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu
    450                 455                 460


Pro Pro Arg
465


<210> 848
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 848
Gln Ile Gln Leu Val Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu
1               5                   10                  15


Thr Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
            20                  25                  30
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                                                _SL
Ser Ile Asn Trp Val Lys Arg Ala Pro Gly Lys Gly Leu Lys Trp Met
        35                  40                  45

Gly Trp Ile Asn Thr Glu Thr Arg Glu Pro Ala Tyr Ala Tyr Asp Phe
    50                  55                  60

Arg Gly Arg Phe Ala Phe Ser Leu Glu Thr Ser Ala Ser Thr Ala Tyr
65                  70                  75                  80

Leu Gln Ile Asn Asn Leu Lys Tyr Glu Asp Thr Ala Thr Tyr Phe Cys
                85                  90                  95

Ala Leu Asp Tyr Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser
            100                 105                 110

Val Thr Val Ser Ser
        115


<210> 849
<211> 111
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 849
Asp Ile Val Leu Thr Gln Ser Pro Ala Ser Leu Ala Met Ser Leu Gly
1               5                   10                  15

Lys Arg Ala Thr Ile Ser Cys Arg Ala Ser Glu Ser Val Ser Val Ile
            20                  25                  30

Gly Ala His Leu Ile His Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
        35                  40                  45

Lys Leu Leu Ile Tyr Leu Ala Ser Asn Leu Glu Thr Gly Val Pro Ala
    50                  55                  60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asp
65                  70                  75                  80

Pro Val Glu Glu Asp Asp Val Ala Ile Tyr Ser Cys Leu Gln Ser Arg
                85                  90                  95

Ile Phe Pro Arg Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
            100                 105                 110
```

<210> 850
<211> 249
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 850

```
Gln Ile Gln Leu Val Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu
1               5                   10                  15

Thr Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
            20                  25                  30

Ser Ile Asn Trp Val Lys Arg Ala Pro Gly Lys Gly Leu Lys Trp Met
        35                  40                  45

Gly Trp Ile Asn Thr Glu Thr Arg Glu Pro Ala Tyr Ala Tyr Asp Phe
    50                  55                  60

Arg Gly Arg Phe Ala Phe Ser Leu Glu Thr Ser Ala Ser Thr Ala Tyr
65                  70                  75                  80

Leu Gln Ile Asn Asn Leu Lys Tyr Glu Asp Thr Ala Thr Tyr Phe Cys
                85                  90                  95

Ala Leu Asp Tyr Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser
            100                 105                 110

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Gln Ile Gln Leu Val Gln Ser Gly Pro Glu Leu Lys
    130                 135                 140

Lys Pro Gly Glu Thr Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr
145                 150                 155                 160

Phe Thr Asp Tyr Ser Ile Asn Trp Val Lys Arg Ala Pro Gly Lys Gly
                165                 170                 175

Leu Lys Trp Met Gly Trp Ile Asn Thr Glu Thr Arg Glu Pro Ala Tyr
            180                 185                 190

Ala Tyr Asp Phe Arg Gly Arg Phe Ala Phe Ser Leu Glu Thr Ser Ala
        195                 200                 205
```

_SL
Ser Thr Ala Tyr Leu Gln Ile Asn Asn Leu Lys Tyr Glu Asp Thr Ala
    210   215   220

Thr Tyr Phe Cys Ala Leu Asp Tyr Ser Tyr Ala Met Asp Tyr Trp Gly
225   230   235   240

Gln Gly Thr Ser Val Thr Val Ser Ser
                245

<210> 851
<211> 472
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 851
Gln Ile Gln Leu Val Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu
1   5   10   15

Thr Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
            20   25   30

Ser Ile Asn Trp Val Lys Arg Ala Pro Gly Lys Gly Leu Lys Trp Met
        35   40   45

Gly Trp Ile Asn Thr Glu Thr Arg Glu Pro Ala Tyr Ala Tyr Asp Phe
    50   55   60

Arg Gly Arg Phe Ala Phe Ser Leu Glu Thr Ser Ala Ser Thr Ala Tyr
65   70   75   80

Leu Gln Ile Asn Asn Leu Lys Tyr Glu Asp Thr Ala Thr Tyr Phe Cys
                85   90   95

Ala Leu Asp Tyr Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser
            100   105   110

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
        115   120   125

Gly Gly Gly Ser Gln Ile Gln Leu Val Gln Ser Gly Pro Glu Leu Lys
    130   135   140

Lys Pro Gly Glu Thr Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr
145   150   155   160

_SL

```
Phe Thr Asp Tyr Ser Ile Asn Trp Val Lys Arg Ala Pro Gly Lys Gly
                165                 170                 175

Leu Lys Trp Met Gly Trp Ile Asn Thr Glu Thr Arg Glu Pro Ala Tyr
            180                 185                 190

Ala Tyr Asp Phe Arg Gly Arg Phe Ala Phe Ser Leu Glu Thr Ser Ala
        195                 200                 205

Ser Thr Ala Tyr Leu Gln Ile Asn Asn Leu Lys Tyr Glu Asp Thr Ala
    210                 215                 220

Thr Tyr Phe Cys Ala Leu Asp Tyr Ser Tyr Ala Met Asp Tyr Trp Gly
225                 230                 235                 240

Gln Gly Thr Ser Val Thr Val Ser Ser Thr Thr Thr Pro Ala Pro Arg
                245                 250                 255

Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg
            260                 265                 270

Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly
        275                 280                 285

Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr
    290                 295                 300

Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg
305                 310                 315                 320

Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro
                325                 330                 335

Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu
            340                 345                 350

Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala
        355                 360                 365

Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu
    370                 375                 380

Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly
385                 390                 395                 400

Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu
                405                 410                 415
```

```
Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser
            420                 425                 430

Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly
        435                 440                 445

Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu
    450                 455                 460

His Met Gln Ala Leu Pro Pro Arg
465                 470
```

<210> 852
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 852

```
Gln Ile Gln Leu Val Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu
1               5                   10                  15

Thr Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Arg His Tyr
            20                  25                  30

Ser Met Asn Trp Val Lys Gln Ala Pro Gly Lys Gly Leu Lys Trp Met
        35                  40                  45

Gly Arg Ile Asn Thr Glu Ser Gly Val Pro Ile Tyr Ala Asp Asp Phe
    50                  55                  60

Lys Gly Arg Phe Ala Phe Ser Val Glu Thr Ser Ala Ser Thr Ala Tyr
65                  70                  75                  80

Leu Val Ile Asn Asn Leu Lys Asp Glu Asp Thr Ala Ser Tyr Phe Cys
                85                  90                  95

Ser Asn Asp Tyr Leu Tyr Ser Leu Asp Phe Trp Gly Gln Gly Thr Ala
            100                 105                 110

Leu Thr Val Ser Ser
        115
```

<210> 853
<211> 111
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 853
Asp Ile Val Leu Thr Gln Ser Pro Pro Ser Leu Ala Met Ser Leu Gly
1 5 10 15

Lys Arg Ala Thr Ile Ser Cys Arg Ala Ser Glu Ser Val Thr Ile Leu
20 25 30

Gly Ser His Leu Ile Tyr Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
35 40 45

Thr Leu Leu Ile Gln Leu Ala Ser Asn Val Gln Thr Gly Val Pro Ala
50 55 60

Arg Phe Ser Gly Ser Gly Ser Arg Thr Asp Phe Thr Leu Thr Ile Asp
65 70 75 80

Pro Val Glu Glu Asp Asp Val Ala Val Tyr Tyr Cys Leu Gln Ser Arg
85 90 95

Thr Ile Pro Arg Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 854
<211> 243
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 854
Gln Ile Gln Leu Val Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu
1 5 10 15

Thr Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Arg His Tyr
20 25 30

Ser Met Asn Trp Val Lys Gln Ala Pro Gly Lys Gly Leu Lys Trp Met
35 40 45

Gly Arg Ile Asn Thr Glu Ser Gly Val Pro Ile Tyr Ala Asp Asp Phe
50 55 60

```
                                                _SL
Lys Gly Arg Phe Ala Phe Ser Val Glu Thr Ser Ala Ser Thr Ala Tyr
65                  70                  75                  80


Leu Val Ile Asn Asn Leu Lys Asp Glu Asp Thr Ala Ser Tyr Phe Cys
                85                  90                  95


Ser Asn Asp Tyr Leu Tyr Ser Leu Asp Phe Trp Gly Gln Gly Thr Ala
            100                 105                 110


Leu Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125


Gly Gly Gly Ser Asp Ile Val Leu Thr Gln Ser Pro Pro Ser Leu Ala
    130                 135                 140


Met Ser Leu Gly Lys Arg Ala Thr Ile Ser Cys Arg Ala Ser Glu Ser
145                 150                 155                 160


Val Thr Ile Leu Gly Ser His Leu Ile Tyr Trp Tyr Gln Gln Lys Pro
                165                 170                 175


Gly Gln Pro Pro Thr Leu Leu Ile Gln Leu Ala Ser Asn Val Gln Thr
            180                 185                 190


Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Arg Thr Asp Phe Thr
        195                 200                 205


Leu Thr Ile Asp Pro Val Glu Glu Asp Asp Val Ala Val Tyr Tyr Cys
    210                 215                 220


Leu Gln Ser Arg Thr Ile Pro Arg Thr Phe Gly Gly Gly Thr Lys Leu
225                 230                 235                 240


Glu Ile Lys
```

<210> 855
<211> 466
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 855

```
Gln Ile Gln Leu Val Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu
1               5                   10                  15
```

_SL
Thr Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Arg His Tyr
            20   25   30

Ser Met Asn Trp Val Lys Gln Ala Pro Gly Lys Gly Leu Lys Trp Met
        35   40   45

Gly Arg Ile Asn Thr Glu Ser Gly Val Pro Ile Tyr Ala Asp Asp Phe
    50   55   60

Lys Gly Arg Phe Ala Phe Ser Val Glu Thr Ser Ala Ser Thr Ala Tyr
65   70   75   80

Leu Val Ile Asn Asn Leu Lys Asp Glu Asp Thr Ala Ser Tyr Phe Cys
                85   90   95

Ser Asn Asp Tyr Leu Tyr Ser Leu Asp Phe Trp Gly Gln Gly Thr Ala
            100   105   110

Leu Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
        115   120   125

Gly Gly Gly Ser Asp Ile Val Leu Thr Gln Ser Pro Pro Ser Leu Ala
    130   135   140

Met Ser Leu Gly Lys Arg Ala Thr Ile Ser Cys Arg Ala Ser Glu Ser
145   150   155   160

Val Thr Ile Leu Gly Ser His Leu Ile Tyr Trp Tyr Gln Gln Lys Pro
                165   170   175

Gly Gln Pro Pro Thr Leu Leu Ile Gln Leu Ala Ser Asn Val Gln Thr
            180   185   190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Arg Thr Asp Phe Thr
        195   200   205

Leu Thr Ile Asp Pro Val Glu Glu Asp Asp Val Ala Val Tyr Tyr Cys
    210   215   220

Leu Gln Ser Arg Thr Ile Pro Arg Thr Phe Gly Gly Gly Thr Lys Leu
225   230   235   240

Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro
                245   250   255

Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro
            260   265   270

```
Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp
        275                 280                 285

Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu
    290                 295                 300

Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu
305                 310                 315                 320

Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu
                325                 330                 335

Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys
            340                 345                 350

Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys
        355                 360                 365

Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu
    370                 375                 380

Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly
385                 390                 395                 400

Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu
                405                 410                 415

Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly
            420                 425                 430

Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser
        435                 440                 445

Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro
    450                 455                 460

Pro Arg
465
```

<210> 856
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 856
Gln Ile Gln Leu Val Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu
1 5 10 15

Thr Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr His Tyr
20 25 30

Ser Met Asn Trp Val Lys Gln Ala Pro Gly Lys Gly Leu Lys Trp Met
35 40 45

Gly Arg Ile Asn Thr Glu Thr Gly Glu Pro Leu Tyr Ala Asp Asp Phe
50 55 60

Lys Gly Arg Phe Ala Phe Ser Leu Glu Thr Ser Ala Ser Thr Ala Tyr
65 70 75 80

Leu Val Ile Asn Asn Leu Lys Asn Glu Asp Thr Ala Thr Phe Phe Cys
85 90 95

Ser Asn Asp Tyr Leu Tyr Ser Cys Asp Tyr Trp Gly Gln Gly Thr Thr
100 105 110

Leu Thr Val Ser Ser
115

<210> 857
<211> 111
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 857
Asp Ile Val Leu Thr Gln Ser Pro Pro Ser Leu Ala Met Ser Leu Gly
1 5 10 15

Lys Arg Ala Thr Ile Ser Cys Arg Ala Ser Glu Ser Val Thr Ile Leu
20 25 30

Gly Ser His Leu Ile Tyr Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
35 40 45

Thr Leu Leu Ile Gln Leu Ala Ser Asn Val Gln Thr Gly Val Pro Ala
50 55 60

Arg Phe Ser Gly Ser Gly Ser Arg Thr Asp Phe Thr Leu Thr Ile Asp
65 70 75 80

Pro Val Glu Glu Asp Asp Val Ala Val Tyr Tyr Cys Leu Gln Ser Arg
85 90 95

Thr Ile Pro Arg Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 858
<211> 243
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 858
Gln Ile Gln Leu Val Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu
1 5 10 15

Thr Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr His Tyr
20 25 30

Ser Met Asn Trp Val Lys Gln Ala Pro Gly Lys Gly Leu Lys Trp Met
35 40 45

Gly Arg Ile Asn Thr Glu Thr Gly Glu Pro Leu Tyr Ala Asp Asp Phe
50 55 60

Lys Gly Arg Phe Ala Phe Ser Leu Glu Thr Ser Ala Ser Thr Ala Tyr
65 70 75 80

Leu Val Ile Asn Asn Leu Lys Asn Glu Asp Thr Ala Thr Phe Phe Cys
85 90 95

Ser Asn Asp Tyr Leu Tyr Ser Cys Asp Tyr Trp Gly Gln Gly Thr Thr
100 105 110

Leu Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
115 120 125

Gly Gly Gly Ser Asp Ile Val Leu Thr Gln Ser Pro Pro Ser Leu Ala
130 135 140

Met Ser Leu Gly Lys Arg Ala Thr Ile Ser Cys Arg Ala Ser Glu Ser
145 150 155 160

Val Thr Ile Leu Gly Ser His Leu Ile Tyr Trp Tyr Gln Gln Lys Pro
165 170 175

```
Gly Gln Pro Pro Thr Leu Leu Ile Gln Leu Ala Ser Asn Val Gln Thr
            180                 185                 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Arg Thr Asp Phe Thr
        195                 200                 205

Leu Thr Ile Asp Pro Val Glu Glu Asp Asp Val Ala Val Tyr Tyr Cys
    210                 215                 220

Leu Gln Ser Arg Thr Ile Pro Arg Thr Phe Gly Gly Gly Thr Lys Leu
225                 230                 235                 240

Glu Ile Lys
```

<210> 859
<211> 466
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 859

```
Gln Ile Gln Leu Val Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu
1               5                   10                  15

Thr Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr His Tyr
            20                  25                  30

Ser Met Asn Trp Val Lys Gln Ala Pro Gly Lys Gly Leu Lys Trp Met
        35                  40                  45

Gly Arg Ile Asn Thr Glu Thr Gly Glu Pro Leu Tyr Ala Asp Asp Phe
    50                  55                  60

Lys Gly Arg Phe Ala Phe Ser Leu Glu Thr Ser Ala Ser Thr Ala Tyr
65                  70                  75                  80

Leu Val Ile Asn Asn Leu Lys Asn Glu Asp Thr Ala Thr Phe Phe Cys
                85                  90                  95

Ser Asn Asp Tyr Leu Tyr Ser Cys Asp Tyr Trp Gly Gln Gly Thr Thr
            100                 105                 110

Leu Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125
```

```
Gly Gly Gly Ser Asp Ile Val Leu Thr Gln Ser Pro Pro Ser Leu Ala
    130                 135                 140

Met Ser Leu Gly Lys Arg Ala Thr Ile Ser Cys Arg Ala Ser Glu Ser
145                 150                 155                 160

Val Thr Ile Leu Gly Ser His Leu Ile Tyr Trp Tyr Gln Gln Lys Pro
                165                 170                 175

Gly Gln Pro Pro Thr Leu Leu Ile Gln Leu Ala Ser Asn Val Gln Thr
            180                 185                 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Arg Thr Asp Phe Thr
        195                 200                 205

Leu Thr Ile Asp Pro Val Glu Glu Asp Asp Val Ala Val Tyr Tyr Cys
    210                 215                 220

Leu Gln Ser Arg Thr Ile Pro Arg Thr Phe Gly Gly Gly Thr Lys Leu
225                 230                 235                 240

Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro
                245                 250                 255

Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro
            260                 265                 270

Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp
        275                 280                 285

Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu
    290                 295                 300

Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu
305                 310                 315                 320

Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu
                325                 330                 335

Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys
            340                 345                 350

Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys
        355                 360                 365

Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu
    370                 375                 380
```

Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly
385 390 395 400

Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu
405 410 415

Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly
420 425 430

Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser
435 440 445

Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro
450 455 460

Pro Arg
465

<210> 860
<211> 246
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 860
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Glu Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Pro Ala Asn Thr Phe Ser Asp His
20 25 30

Val Met His Trp Val Arg Gln Ala Pro Gly Gln Arg Phe Glu Trp Met
35 40 45

Gly Tyr Ile His Ala Ala Asn Gly Gly Thr His Tyr Ser Gln Lys Phe
50 55 60

Gln Asp Arg Val Thr Ile Thr Arg Asp Thr Ser Ala Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Tyr Asn Ser Asp Ala Phe Asp Ile Trp Gly Gln Gly
100 105 110

```
Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
        115                 120                 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr
    130                 135                 140

Gln Ser Pro Ser Ser Val Ser Ala Ser Val Gly Asp Arg Val Thr Ile
145                 150                 155                 160

Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Trp Leu Ala Trp Tyr Gln
                165                 170                 175

Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser
            180                 185                 190

Leu Gln Ser Gly Val Pro Ser Arg Phe Asn Gly Ser Gly Ser Gly Thr
        195                 200                 205

Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr
    210                 215                 220

Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly
225                 230                 235                 240

Thr Lys Val Glu Ile Lys
                245
```

<210> 861
<211> 738
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 861
caagtgcaac tcgtccagtc cggtgcagaa gtcaaggaac ccggagcctc cgtgaaagtg 60

tcctgcaaag ctcctgccaa cactttctcg gaccacgtga tgcactgggt gcgccaggcg 120

ccgggccagc gcttcgaatg gatgggatac attcatgccg ccaatggcgg tacccactac 180

tcccaaaagt tccaggatag agtcaccatc acccgggaca ccagcgccaa caccgtgtat 240

atggatctgt ccagcctgag gtccgaggat accgccgtgt actactgcgc ccggggcgga 300

tacaactcag acgcgttcga catttgggga cagggtacta tggtcaccgt gtcatccggg 360

ggcggtggca gcgggggcgg aggctctggc ggaggcggat caggggggagg agggtccgac 420

atcgtgatga cccagtcccc gtcatcggtg tccgcgtccg tgggagacag agtgaccatc 480

acgtgtcgcg ccagccagga catctcctcg tggttggcat ggtaccagca gaagcctgga 540

aaggccccga agctgctcat ctacgccgcc tcctcccttc aatcgggagt gccctcgcgg 600

ttcaacggaa gcggaagcgg gacagatttt accctgacta ttagctcgct gcagcccgag 660

gacttcgcta cttactactg ccaacagagc tactccaccc cactgacttt cggcggggt 720

accaaggtcg agatcaag 738

<210> 862
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 862
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Glu Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Pro Ala Asn Thr Phe Ser Asp His
20 25 30

Val Met His Trp Val Arg Gln Ala Pro Gly Gln Arg Phe Glu Trp Met
35 40 45

Gly Tyr Ile His Ala Ala Asn Gly Gly Thr His Tyr Ser Gln Lys Phe
50 55 60

Gln Asp Arg Val Thr Ile Thr Arg Asp Thr Ser Ala Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Tyr Asn Ser Asp Ala Phe Asp Ile Trp Gly Gln Gly
100 105 110

Thr Met Val Thr Val Ser Ser
115

<210> 863
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source

_SL
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 863
Asp Ile Val Met Thr Gln Ser Pro Ser Ser Val Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Trp
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Asn Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 864
<211> 490
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 864
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
20 25 30

Lys Glu Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Pro Ala Asn
35 40 45

Thr Phe Ser Asp His Val Met His Trp Val Arg Gln Ala Pro Gly Gln
50 55 60

Arg Phe Glu Trp Met Gly Tyr Ile His Ala Ala Asn Gly Gly Thr His
65 70 75 80

```
                                                _SL
Tyr Ser Gln Lys Phe Gln Asp Arg Val Thr Ile Thr Arg Asp Thr Ser
                85                  90                  95

Ala Asn Thr Val Tyr Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Arg Gly Gly Tyr Asn Ser Asp Ala Phe Asp
        115                 120                 125

Ile Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly
    130                 135                 140

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
145                 150                 155                 160

Asp Ile Val Met Thr Gln Ser Pro Ser Ser Val Ser Ala Ser Val Gly
                165                 170                 175

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Trp
            180                 185                 190

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        195                 200                 205

Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Asn Gly
    210                 215                 220

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
225                 230                 235                 240

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu
                245                 250                 255

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Thr Thr Thr Pro Ala
            260                 265                 270

Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser
        275                 280                 285

Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr
    290                 295                 300

Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala
305                 310                 315                 320

Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys
                325                 330                 335
```

Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met
340 345 350

Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe
355 360 365

Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg
370 375 380

Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn
385 390 395 400

Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg
405 410 415

Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro
420 425 430

Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala
435 440 445

Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His
450 455 460

Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp
465 470 475 480

Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 865
<211> 1470
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 865
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtgc aactcgtcca gtccggtgca gaagtcaagg aacccggagc ctccgtgaaa 120

gtgtcctgca aagctcctgc caacactttc tcggaccacg tgatgcactg ggtgcgccag 180

gcgccgggcc agcgcttcga atggatggga tacattcatg ccgccaatgg cggtacccac 240

tactcccaaa agttccagga tagagtcacc atcacccggg acaccagcgc caacaccgtg 300

tatatggatc tgtccagcct gaggtccgag gataccgccg tgtactactg cgcccggggc 360

ggatacaact cagacgcgtt cgacatttgg ggacagggta ctatggtcac cgtgtcatcc 420

gggggcggtg gcagcggggg cggaggctct ggcggaggcg gatcaggggg aggagggtcc 480

gacatcgtga tgacccagtc cccgtcatcg gtgtccgcgt ccgtgggaga cagagtgacc 540

atcacgtgtc gcgccagcca ggacatctcc tcgtggttgg catggtacca gcagaagcct 600

ggaaaggccc cgaagctgct catctacgcc gcctcctccc ttcaatcggg agtgccctcg 660

cggttcaacg gaagcggaag cgggacagat tttaccctga ctattagctc gctgcagccc 720

gaggacttcg ctacttacta ctgccaacag agctactcca ccccactgac tttcggcggg 780

ggtaccaagg tcgagatcaa gaccactacc ccagcaccga ggccacccac cccggctcct 840

accatcgcct cccagcctct gtccctgcgt ccggaggcat gtagacccgc agctggtggg 900

gccgtgcata cccggggtct tgacttcgcc tgcgatatct acatttgggc ccctctggct 960

ggtacttgcg gggtcctgct gctttcactc gtgatcactc tttactgtaa gcgcggtcgg 1020

aagaagctgc tgtacatctt taagcaaccc ttcatgaggc ctgtgcagac tactcaagag 1080

gaggacggct gttcatgccg gttcccagag gaggaggaag gcggctgcga actgcgcgtg 1140

aaattcagcc gcagcgcaga tgctccagcc tacaagcagg ggcagaacca gctctacaac 1200

gaactcaatc ttggtcggag agaggagtac gacgtgctgg acaagcggag aggacgggac 1260

ccagaaatgg gcgggaagcc gcgcagaaag aatccccaag agggcctgta caacgagctc 1320

caaaaggata agatggcaga agcctatagc gagattggta tgaaagggga acgcagaaga 1380

ggcaaaggcc acgacggact gtaccaggga ctcagcaccg ccaccaagga cacctatgac 1440

gctcttcaca tgcaggccct gccgcctcgg 1470

<210> 866
<211> 249
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 866
Gln Val Gln Leu Gln Glu Ser Gly Ala Gly Leu Leu Lys Pro Ser Glu
1 5 10 15

Thr Leu Ser Leu Thr Cys Ala Val Tyr Gly Gly Ser Phe Ser Gly Tyr
20 25 30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

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                                                _SL
Gly Glu Ile Asn His Ser Gly Ser Thr Asn Tyr Asn Pro Ser Leu Lys
    50                  55                  60

Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu
65                  70                  75                  80

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
                85                  90                  95

Arg Gly Ser Gly Leu Val Val Tyr Ala Ile Arg Val Gly Ser Gly Trp
            100                 105                 110

Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly
        115                 120                 125

Gly Gly Ser Gly Gly Gly Asp Ser Gly Gly Gly Gly Ser Asp Ile Gln
    130                 135                 140

Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
145                 150                 155                 160

Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp
                165                 170                 175

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Met Tyr Ala Ala
            180                 185                 190

Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser
        195                 200                 205

Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe
    210                 215                 220

Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Pro Trp Thr Phe
225                 230                 235                 240

Gly Gln Gly Thr Lys Val Asp Ile Lys
                245
```

<210> 867
<211> 747
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 867

caagtgcaac ttcaagaatc aggcgcagga cttctcaagc catccgaaac actctccctc 60

acttgcgcgg tgtacggggg aagcttctcg ggatactact ggtcctggat taggcagcct 120

cccggcaaag gcctggaatg ggtcggggag atcaaccact ccggttcaac caactacaac 180

ccgtcgctga agtcccgcgt gaccatttcc gtggacacct ctaagaatca gttcagcctg 240

aagctctcgt ccgtgaccgc ggcggacacc gccgtctact actgcgctcg gggatcagga 300

ctggtggtgt acgccatccg cgtgggctcg ggctggttcg attactgggg ccagggaacc 360

ctggtcactg tgtcgtccgg cggaggaggt tcgggggggcg gagacagcgg tggagggggt 420

agcgacatcc agatgaccca gtccccgtcc tcgctgtccg cctccgtggg agatagagtg 480

accatcacct gtcgggcatc ccagagcatt tccagctacc tgaactggta tcagcagaag 540

cccggaaagg cccctaagct gttgatgtac gccgccagca gcttgcagtc gggcgtgccg 600

agccggtttt ccggttccgg ctccgggact gacttcaccc tgactatctc atccctgcaa 660

cccgaggact tcgccactta ttactgccag cagtcctact caacccctcc ctggacgttc 720

ggacagggca ccaaggtcga tatcaag 747

<210> 868
<211> 126
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 868

Gln Val Gln Leu Gln Glu Ser Gly Ala Gly Leu Leu Lys Pro Ser Glu
1 5 10 15

Thr Leu Ser Leu Thr Cys Ala Val Tyr Gly Gly Ser Phe Ser Gly Tyr
20 25 30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Gly Glu Ile Asn His Ser Gly Ser Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60

Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu
65 70 75 80

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Arg Gly Ser Gly Leu Val Val Tyr Ala Ile Arg Val Gly Ser Gly Trp

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100 105 110

Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 869
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 869
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Met
35 40 45

Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Pro
85 90 95

Trp Thr Phe Gly Gln Gly Thr Lys Val Asp Ile Lys
100 105

<210> 870
<211> 493
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 870
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Gln Glu Ser Gly Ala Gly Leu
20 25 30

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Leu Lys Pro Ser Glu Thr Leu Ser Leu Thr Cys Ala Val Tyr Gly Gly
        35                  40                  45

Ser Phe Ser Gly Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys
    50                  55                  60

Gly Leu Glu Trp Val Gly Glu Ile Asn His Ser Gly Ser Thr Asn Tyr
65                  70                  75                  80

Asn Pro Ser Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys
                85                  90                  95

Asn Gln Phe Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala
            100                 105                 110

Val Tyr Tyr Cys Ala Arg Gly Ser Gly Leu Val Val Tyr Ala Ile Arg
        115                 120                 125

Val Gly Ser Gly Trp Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr
    130                 135                 140

Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Asp Ser Gly Gly Gly
145                 150                 155                 160

Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser
                165                 170                 175

Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser
            180                 185                 190

Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu
        195                 200                 205

Leu Met Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe
    210                 215                 220

Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu
225                 230                 235                 240

Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr
                245                 250                 255

Pro Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Asp Ile Lys Thr Thr
            260                 265                 270

Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln
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_SL

275 280 285

Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala
290 295 300

Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala
305 310 315 320

Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr
325 330 335

Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln
340 345 350

Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser
355 360 365

Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys
370 375 380

Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln
385 390 395 400

Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu
405 410 415

Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg
420 425 430

Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met
435 440 445

Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly
450 455 460

Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp
465 470 475 480

Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 871
<211> 1479
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

polynucleotide"

<400> 871
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtgc aacttcaaga atcaggcgca ggacttctca agccatccga aacactctcc 120

ctcacttgcg cggtgtacgg gggaagcttc tcgggatact actggtcctg gattaggcag 180

cctcccggca aaggcctgga atgggtcggg gagatcaacc actccggttc aaccaactac 240

aacccgtcgc tgaagtcccg cgtgaccatt tccgtggaca cctctaagaa tcagttcagc 300

ctgaagctct cgtccgtgac cgcggcggac accgccgtct actactgcgc tcggggatca 360

ggactggtgg tgtacgccat ccgcgtgggc tcgggctggt tcgattactg gggccaggga 420

accctggtca ctgtgtcgtc cggcggagga ggttcggggg gcggagacag cggtggaggg 480

ggtagcgaca tccagatgac ccagtccccg tcctcgctgt ccgcctccgt gggagataga 540

gtgaccatca cctgtcgggc atcccagagc atttccagct acctgaactg gtatcagcag 600

aagcccggaa aggcccctaa gctgttgatg tacgccgcca gcagcttgca gtcgggcgtg 660

ccgagccggt tttccggttc cggctccggg actgacttca ccctgactat ctcatccctg 720

caacccgagg acttcgccac ttattactgc cagcagtcct actcaacccc tccctggacg 780

ttcggacagg gcaccaaggt cgatatcaag accactaccc cagcaccgag gccacccacc 840

ccggctccta ccatcgcctc ccagcctctg tccctgcgtc cggaggcatg tagacccgca 900

gctggtgggg ccgtgcatac ccggggtctt gacttcgcct gcgatatcta catttgggcc 960

cctctggctg gtacttgcgg ggtcctgctg ctttcactcg tgatcactct ttactgtaag 1020

cgcggtcgga agaagctgct gtacatcttt aagcaaccct tcatgaggcc tgtgcagact 1080

actcaagagg aggacggctg ttcatgccgg ttcccagagg aggaggaagg cggctgcgaa 1140

ctgcgcgtga aattcagccg cagcgcagat gctccagcct acaagcaggg gcagaaccag 1200

ctctacaacg aactcaatct tggtcggaga gaggagtacg acgtgctgga caagcggaga 1260

ggacgggacc cagaaatggg cgggaagccg cgcagaaaga atccccaaga gggcctgtac 1320

aacgagctcc aaaaggataa gatggcagaa gcctatagcg agattggtat gaaaggggaa 1380

cgcagaagag gcaaaggcca cgacggactg taccagggac tcagcaccgc caccaaggac 1440

acctatgacg ctcttcacat gcaggccctg ccgcctcgg 1479

<210> 872
<211> 248
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 872
Gln Val Gln Leu Val Gln Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ser Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Tyr Ile Ser Ser Ser Ser Ser Thr Ile Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Leu Ser Val Arg Ala Ile Asp Ala Phe Asp Ile Trp Gly
100 105 110

Gln Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
115 120 125

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val
130 135 140

Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
145 150 155 160

Thr Ile Thr Cys Gln Ala Ser Gln Asp Ile Ser Asn Tyr Leu Asn Trp
165 170 175

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala
180 185 190

Ser Asn Leu Glu Thr Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser
195 200 205

Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe
210 215 220

Ala Thr Tyr Tyr Cys Gln Gln Ala Tyr Ser Thr Pro Phe Thr Phe Gly
225 230 235 240

Pro Gly Thr Lys Val Glu Ile Lys

<210> 873
<211> 744
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 873
caagtgcaac ttgttcaatc cggtggaggt cttgtgcagc ccggaggatc actcagactg 60

tcgtgcgccg cctctgggtt cactttctcc tcatactcga tgaactgggt gcgccaggcg 120

ccgggaaagg gcctggaatg ggtgtcatac atctcctcct catcctccac catctactac 180

gccgattccg tgaagggccg cttcactatt tcccgggaca acgcgaaaaa ctcgctctat 240

ctgcaaatga actccctgcg cgccgaggac accgccgtgt actactgcgc ccgggacctg 300

agcgtgcggg ctattgatgc gttcgacatc tggggacagg gcaccatggt cacagtgtcc 360

agcggaggcg gcggcagcgg tggaggagga tcaggggggag gaggttcggg gggcggtggc 420

tccgatatcg tgctgaccca gagcccgtcg agcctctccg cctccgtcgg cgacagagtg 480

accatcacgt gtcaggcatc ccaggacatt agcaactacc tgaattggta ccagcagaag 540

cctggaaagg cacccaagtt gctgatctac gacgcctcca acctggaaac cggagtgcca 600

tccaggttct cgggcagcgg ctcgggaacc gacttcactt ttactatctc ctccctgcaa 660

cccgaggatt tcgcgaccta ctactgccag caggcctaca gcaccccttt caccttcggg 720

ccgggaacta aggtcgaaat caag 744

<210> 874
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 874
Gln Val Gln Leu Val Gln Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ser Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Tyr Ile Ser Ser Ser Ser Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50   55   60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65   70   75   80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Ala Arg Asp Leu Ser Val Arg Ala Ile Asp Ala Phe Asp Ile Trp Gly
            100   105   110

Gln Gly Thr Met Val Thr Val Ser Ser
        115   120

<210> 875
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 875
Asp Ile Val Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1   5   10   15

Asp Arg Val Thr Ile Thr Cys Gln Ala Ser Gln Asp Ile Ser Asn Tyr
            20   25   30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35   40   45

Tyr Asp Ala Ser Asn Leu Glu Thr Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65   70   75   80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ala Tyr Ser Thr Pro Phe
                85   90   95

Thr Phe Gly Pro Gly Thr Lys Val Glu Ile Lys
            100   105

<210> 876
<211> 492
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 876

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Gly Gly Leu
            20                  25                  30

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
        35                  40                  45

Thr Phe Ser Ser Tyr Ser Met Asn Trp Val Arg Gln Ala Pro Gly Lys
    50                  55                  60

Gly Leu Glu Trp Val Ser Tyr Ile Ser Ser Ser Ser Ser Thr Ile Tyr
65                  70                  75                  80

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala
                85                  90                  95

Lys Asn Ser Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Arg Asp Leu Ser Val Arg Ala Ile Asp Ala
        115                 120                 125

Phe Asp Ile Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Gly Gly
    130                 135                 140

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
145                 150                 155                 160

Gly Ser Asp Ile Val Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser
                165                 170                 175

Val Gly Asp Arg Val Thr Ile Thr Cys Gln Ala Ser Gln Asp Ile Ser
            180                 185                 190

Asn Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu
        195                 200                 205

Leu Ile Tyr Asp Ala Ser Asn Leu Glu Thr Gly Val Pro Ser Arg Phe
    210                 215                 220
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Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu
225                 230                 235                 240

Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ala Tyr Ser Thr
                245                 250                 255

Pro Phe Thr Phe Gly Pro Gly Thr Lys Val Glu Ile Lys Thr Thr Thr
            260                 265                 270

Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro
        275                 280                 285

Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val
    290                 295                 300

His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro
305                 310                 315                 320

Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu
                325                 330                 335

Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro
            340                 345                 350

Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys
        355                 360                 365

Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe
    370                 375                 380

Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu
385                 390                 395                 400

Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp
                405                 410                 415

Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys
            420                 425                 430

Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala
        435                 440                 445

Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys
    450                 455                 460

Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr
465                 470                 475                 480
```

Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 877
<211> 1476
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 877
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtgc aacttgttca atccggtgga ggtcttgtgc agcccggagg atcactcaga 120

ctgtcgtgcg ccgcctctgg gttcactttc tcctcatact cgatgaactg ggtgcgccag 180

gcgccgggaa agggcctgga atgggtgtca tacatctcct cctcatcctc caccatctac 240

tacgccgatt ccgtgaaggg ccgcttcact atttcccggg acaacgcgaa aaactcgctc 300

tatctgcaaa tgaactccct gcgcgccgag gacaccgccg tgtactactg cgcccgggac 360

ctgagcgtgc gggctattga tgcgttcgac atctggggac agggcaccat ggtcacagtg 420

tccagcggag gcggcggcag cggtggagga ggatcagggg gaggaggttc gggggcggt 480

ggctccgata tcgtgctgac ccagagcccg tcgagcctct ccgcctccgt cggcgacaga 540

gtgaccatca cgtgtcaggc atcccaggac attagcaact acctgaattg gtaccagcag 600

aagcctggaa aggcacccaa gttgctgatc tacgacgcct ccaacctgga aaccggagtg 660

ccatccaggt tctcgggcag cggctcggga accgacttca cttttactat ctcctccctg 720

caacccgagg atttcgcgac ctactactgc cagcaggcct acagcacccc tttcaccttc 780

gggccgggaa ctaaggtcga aatcaagacc actaccccag caccgaggcc acccaccccg 840

gctcctacca tcgcctccca gcctctgtcc ctgcgtccgg aggcatgtag acccgcagct 900

ggtggggccg tgcatacccg gggtcttgac ttcgcctgcg atatctacat ttgggccct 960

ctggctggta cttgcggggt cctgctgctt tcactcgtga tcactcttta ctgtaagcgc 1020

ggtcggaaga agctgctgta catctttaag caacccttca tgaggcctgt gcagactact 1080

caagaggagg acggctgttc atgccggttc ccagaggagg aggaaggcgg ctgcgaactg 1140

cgcgtgaaat tcagccgcag cgcagatgct ccagcctaca agcaggggca gaaccagctc 1200

tacaacgaac tcaatcttgg tcggagagag gagtacgacg tgctggacaa gcggagagga 1260

cgggacccag aaatgggcgg gaagccgcgc agaaagaatc cccaagaggg cctgtacaac 1320

gagctccaaa aggataagat ggcagaagcc tatagcgaga ttggtatgaa aggggaacgc 1380

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agaagaggca aaggccacga cggactgtac cagggactca gcaccgccac caaggacacc 1440

tatgacgctc ttcacatgca ggccctgccg cctcgg 1476

<210> 878
<211> 246
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 878
Glu Val Gln Leu Val Gln Ser Gly Gly Gly Val Val Arg Ser Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Ser Tyr
20 25 30

Gly Leu His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Leu Ile Glu Tyr Asp Gly Ser Asn Lys Tyr Tyr Gly Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Lys Ser Lys Ser Thr Leu Tyr
65 70 75 80

Leu Gln Met Asp Asn Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Glu Gly Asn Glu Asp Leu Ala Phe Asp Ile Trp Gly Gln Gly
100 105 110

Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
115 120 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Leu Thr
130 135 140

Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile
145 150 155 160

Thr Cys Gln Ala Ser Gln Phe Ile Lys Lys Asn Leu Asn Trp Tyr Gln
165 170 175

His Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser
180 185 190

Leu Gln Thr Gly Val Pro Ser Arg Phe Ser Gly Asn Arg Ser Gly Thr
195 200 205

Thr Phe Ser Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Val Ala Thr
210 215 220

Tyr Tyr Cys Gln Gln His Asp Asn Leu Pro Leu Thr Phe Gly Gly Gly
225 230 235 240

Thr Lys Val Glu Ile Lys
245

<210> 879
<211> 738
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 879
gaagtgcaat tggtgcaatc aggaggagga gtggtcagat ctggaagaag cctgagactg 60

tcatgcgcgg cttcgggctt taccttcaac tcctacggcc tccactgggt gcgccaggcc 120

cccggaaaag gcctcgaatg ggtcgcactg attgagtacg acgggtccaa caagtactac 180

ggagatagcg tgaagggccg cttcaccatc tcacgggaca agtccaagtc caccctgtat 240

ctgcaaatgg acaacctgag ggccgaggat actgccgtgt actactgcgc ccgcgaagga 300

aacgaagatc tggccttcga tatttggggc cagggtactc ttgtgaccgt gtcgagcgga 360

ggcggaggct ccggtggagg aggatcgggg ggtggtggtt ccggcggcgg ggggagcgaa 420

atcgtgctga cccagtcgcc ttcctccctc tccgcttccg tgggggaccg ggtcactatt 480

acgtgtcagg cgtcccaatt catcaagaag aatctgaact ggtaccagca caagccggga 540

aaggccccca aactgctcat ctacgacgcc agctcgctgc agactggcgt gccttcccgg 600

ttttccggga accggtcggg aaccaccttc tcattcacca tcagcagcct ccagccggag 660

gacgtggcga cctactactg ccagcagcat gacaaccttc cactgacttt cggcgggggc 720

accaaggtcg agattaag 738

<210> 880
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

polypeptide"

<400> 880
Glu Val Gln Leu Val Gln Ser Gly Gly Gly Val Val Arg Ser Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Ser Tyr
20 25 30

Gly Leu His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Leu Ile Glu Tyr Asp Gly Ser Asn Lys Tyr Tyr Gly Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Lys Ser Lys Ser Thr Leu Tyr
65 70 75 80

Leu Gln Met Asp Asn Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Glu Gly Asn Glu Asp Leu Ala Phe Asp Ile Trp Gly Gln Gly
100 105 110

Thr Leu Val Thr Val Ser Ser
115

<210> 881
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 881
Glu Ile Val Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Gln Ala Ser Gln Phe Ile Lys Lys Asn
20 25 30

Leu Asn Trp Tyr Gln His Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Asp Ala Ser Ser Leu Gln Thr Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Asn Arg Ser Gly Thr Thr Phe Ser Phe Thr Ile Ser Ser Leu Gln Pro

_SL
65 70 75 80

Glu Asp Val Ala Thr Tyr Tyr Cys Gln Gln His Asp Asn Leu Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 882
<211> 490
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 882
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Val Gln Leu Val Gln Ser Gly Gly Gly Val
20 25 30

Val Arg Ser Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
35 40 45

Thr Phe Asn Ser Tyr Gly Leu His Trp Val Arg Gln Ala Pro Gly Lys
50 55 60

Gly Leu Glu Trp Val Ala Leu Ile Glu Tyr Asp Gly Ser Asn Lys Tyr
65 70 75 80

Tyr Gly Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Lys Ser
85 90 95

Lys Ser Thr Leu Tyr Leu Gln Met Asp Asn Leu Arg Ala Glu Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Ala Arg Glu Gly Asn Glu Asp Leu Ala Phe Asp
115 120 125

Ile Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly
130 135 140

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
145 150 155 160

Glu Ile Val Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly

_SL

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                165                 170                 175

Asp Arg Val Thr Ile Thr Cys Gln Ala Ser Gln Phe Ile Lys Lys Asn
            180                 185                 190

Leu Asn Trp Tyr Gln His Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        195                 200                 205

Tyr Asp Ala Ser Ser Leu Gln Thr Gly Val Pro Ser Arg Phe Ser Gly
    210                 215                 220

Asn Arg Ser Gly Thr Thr Phe Ser Phe Thr Ile Ser Ser Leu Gln Pro
225                 230                 235                 240

Glu Asp Val Ala Thr Tyr Tyr Cys Gln Gln His Asp Asn Leu Pro Leu
                245                 250                 255

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Thr Thr Thr Pro Ala
            260                 265                 270

Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser
        275                 280                 285

Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr
    290                 295                 300

Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala
305                 310                 315                 320

Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys
                325                 330                 335

Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met
            340                 345                 350

Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe
        355                 360                 365

Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg
    370                 375                 380

Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn
385                 390                 395                 400

Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg
                405                 410                 415
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                                                _SL
Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro
            420                 425                 430

Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala
        435                 440                 445

Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His
    450                 455                 460

Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp
465                 470                 475                 480

Ala Leu His Met Gln Ala Leu Pro Pro Arg
                485                 490
```

<210> 883
<211> 1470
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 883

```
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg       60

cccgaagtgc aattggtgca atcaggagga ggagtggtca gatctggaag aagcctgaga      120

ctgtcatgcg cggcttcggg ctttaccttc aactcctacg gcctccactg ggtgcgccag      180

gcccccggaa aaggcctcga atgggtcgca ctgattgagt acgacgggtc caacaagtac      240

tacggagata gcgtgaaggg ccgcttcacc atctcacggg acaagtccaa gtccaccctg      300

tatctgcaaa tggacaacct gagggccgag gatactgccg tgtactactg cgcccgcgaa      360

ggaaacgaag atctggcctt cgatatttgg ggccagggta ctcttgtgac cgtgtcgagc      420

ggaggcggag gctccggtgg aggaggatcg gggggtggtg gttccggcgg cgggggggagc      480

gaaatcgtgc tgacccagtc gccttcctcc ctctccgctt ccgtgggggga ccgggtcact      540

attacgtgtc aggcgtccca attcatcaag aagaatctga actggtacca gcacaagccg      600

ggaaaggccc ccaaactgct catctacgac gccagctcgc tgcagactgg cgtgccttcc      660

cggttttccg ggaaccggtc gggaaccacc ttctcattca ccatcagcag cctccagccg      720

gaggacgtgg cgacctacta ctgccagcag catgacaacc ttccactgac tttcggcggg      780

ggcaccaagg tcgagattaa gaccactacc ccagcaccga ggccacccac cccggctcct      840

accatcgcct cccagcctct gtccctgcgt ccggaggcat gtagacccgc agctggtggg      900

gccgtgcata cccggggtct tgacttcgcc tgcgatatct acatttgggc ccctctggct      960
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ggtacttgcg gggtcctgct gctttcactc gtgatcactc tttactgtaa gcgcggtcgg 1020

aagaagctgc tgtacatctt taagcaaccc ttcatgaggc ctgtgcagac tactcaagag 1080

gaggacggct gttcatgccg gttcccagag gaggaggaag gcggctgcga actgcgcgtg 1140

aaattcagcc gcagcgcaga tgctccagcc tacaagcagg ggcagaacca gctctacaac 1200

gaactcaatc ttggtcggag agaggagtac gacgtgctgg acaagcggag aggacgggac 1260

ccagaaatgg gcgggaagcc gcgcagaaag aatccccaag agggcctgta caacgagctc 1320

caaaaggata agatggcaga agcctatagc gagattggta tgaaagggga acgcagaaga 1380

ggcaaaggcc acgacggact gtaccaggga ctcagcaccg ccaccaagga cacctatgac 1440

gctcttcaca tgcaggccct gccgcctcgg 1470

<210> 884
<211> 255
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 884

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Val Ser Ser Asn
20 25 30

Tyr Met Thr Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Val Ile Tyr Ser Gly Gly Ala Thr Tyr Tyr Gly Asp Ser Val Lys
50 55 60

Gly Arg Phe Thr Val Ser Arg Asp Asn Ser Lys Asn Thr Val Tyr Leu
65 70 75 80

Gln Met Asn Arg Leu Thr Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Arg Asp Arg Leu Tyr Cys Gly Asn Asn Cys Tyr Leu Tyr Tyr Tyr Tyr
100 105 110

Gly Met Asp Val Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly
115 120 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly

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130 135 140

Gly Gly Ser Asp Ile Gln Val Thr Gln Ser Pro Ser Ser Leu Ser Ala
145 150 155 160

Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile
165 170 175

Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys
180 185 190

Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg
195 200 205

Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser
210 215 220

Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser
225 230 235 240

Thr Pro Pro Leu Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
245 250 255

<210> 885
<211> 765
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 885
caagtgcaac tcgtggaatc aggcggagga ctcgtgcaac ccggaggttc ccttagactg 60

tcatgtgccg cttccgggtt caatgtgtcc agcaactaca tgacctgggt cagacaggcg 120

ccgggaaagg gacttgaatg ggtgtccgtg atctactccg gtggagcaac atactacgga 180

gactccgtga aaggccgctt taccgtgtcc cgcgataact cgaagaacac cgtgtacttg 240

cagatgaaca ggctgactgc cgaggacacc gccgtgtatt attgcgcccg ggacaggctg 300

tactgtggaa acaactgcta cctgtactac tactacggga tggacgtgtg gggacagggc 360

actctcgtca ctgtgtcatc cgggggggc ggtagcggtg gcggagggtc cggcggagga 420

ggctcagggg gaggcggaag cgatatccag gtcacccagt ctccctcctc gctgtccgcc 480

tccgtgggcg accgcgtcac cattacttgc cgggcgtcgc agtcgatcag ctcctacctg 540

aactggtacc agcagaagcc tggaaaggcc ccgaagctgc tgatctacgc ggcctcgtcc 600

ctgcaaagcg gcgtcccgtc gcggttcagc ggttccggtt cgggaaccga cttcaccctg 660

actatttcct ccctgcaacc cgaggatttc gccacttact actgccagca gtcctactcc 720

accccacctc tgaccttcgg ccaaggaacc aaggtcgaaa tcaag 765

<210> 886
<211> 127
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 886
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Val Ser Ser Asn
20 25 30

Tyr Met Thr Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Val Ile Tyr Ser Gly Gly Ala Thr Tyr Tyr Gly Asp Ser Val Lys
50 55 60

Gly Arg Phe Thr Val Ser Arg Asp Asn Ser Lys Asn Thr Val Tyr Leu
65 70 75 80

Gln Met Asn Arg Leu Thr Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Arg Asp Arg Leu Tyr Cys Gly Asn Asn Cys Tyr Leu Tyr Tyr Tyr Tyr
100 105 110

Gly Met Asp Val Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 887
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 887
Asp Ile Gln Val Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr
            20   25   30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35   40   45

Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Pro
                85   90   95

Leu Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
            100   105

<210> 888
<211> 499
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 888
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1   5   10   15

His Ala Ala Arg Pro Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu
            20   25   30

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
        35   40   45

Asn Val Ser Ser Asn Tyr Met Thr Trp Val Arg Gln Ala Pro Gly Lys
    50   55   60

Gly Leu Glu Trp Val Ser Val Ile Tyr Ser Gly Gly Ala Thr Tyr Tyr
65   70   75   80

Gly Asp Ser Val Lys Gly Arg Phe Thr Val Ser Arg Asp Asn Ser Lys
                85   90   95

Asn Thr Val Tyr Leu Gln Met Asn Arg Leu Thr Ala Glu Asp Thr Ala
            100   105   110

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Val Tyr Tyr Cys Ala Arg Asp Arg Leu Tyr Cys Gly Asn Asn Cys Tyr
        115                 120                 125

Leu Tyr Tyr Tyr Tyr Gly Met Asp Val Trp Gly Gln Gly Thr Leu Val
    130                 135                 140

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
145                 150                 155                 160

Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Val Thr Gln Ser Pro
                165                 170                 175

Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
            180                 185                 190

Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro
        195                 200                 205

Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser
    210                 215                 220

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
225                 230                 235                 240

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
                245                 250                 255

Gln Gln Ser Tyr Ser Thr Pro Pro Leu Thr Phe Gly Gln Gly Thr Lys
            260                 265                 270

Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala
        275                 280                 285

Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg
    290                 295                 300

Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys
305                 310                 315                 320

Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu
                325                 330                 335

Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu
            340                 345                 350

Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln
        355                 360                 365
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Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly
370 375 380

Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr
385 390 395 400

Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg
405 410 415

Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met
420 425 430

Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu
435 440 445

Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys
450 455 460

Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu
465 470 475 480

Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu
485 490 495

Pro Pro Arg

<210> 889
<211> 1497
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 889
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtgc aactcgtgga atcaggcgga ggactcgtgc aacccggagg ttcccttaga 120

ctgtcatgtg ccgcttccgg gttcaatgtg tccagcaact acatgacctg ggtcagacag 180

gcgccgggaa agggacttga atgggtgtcc gtgatctact ccggtggagc aacatactac 240

ggagactccg tgaaaggccg ctttaccgtg tcccgcgata actcgaagaa caccgtgtac 300

ttgcagatga acaggctgac tgccgaggac accgccgtgt attattgcgc ccgggacagg 360

ctgtactgtg gaaacaactg ctacctgtac tactactacg ggatggacgt gtggggacag 420

ggcactctcg tcactgtgtc atccgggggg ggcggtagcg gtggcggagg gtccggcgga 480

ggaggctcag ggggaggcgg aagcgatatc caggtcaccc agtctccctc ctcgctgtcc 540

gcctccgtgg gcgaccgcgt caccattact tgccgggcgt cgcagtcgat cagctcctac 600

ctgaactggt accagcagaa gcctggaaag gccccgaagc tgctgatcta cgcggcctcg 660

tccctgcaaa gcggcgtccc gtcgcggttc agcggttccg gttcgggaac cgacttcacc 720

ctgactattt cctccctgca acccgaggat ttcgccactt actactgcca gcagtcctac 780

tccaccccac ctctgacctt cggccaagga accaaggtcg aaatcaagac cactacccca 840

gcaccgaggc cacccacccc ggctcctacc atcgcctccc agcctctgtc cctgcgtccg 900

gaggcatgta gacccgcagc tggtggggcc gtgcataccc ggggtcttga cttcgcctgc 960

gatatctaca tttgggcccc tctggctggt acttgcgggg tcctgctgct ttcactcgtg 1020

atcactcttt actgtaagcg cggtcggaag aagctgctgt acatctttaa gcaacccttc 1080

atgaggcctg tgcagactac tcaagaggag gacggctgtt catgccggtt cccagaggag 1140

gaggaaggcg gctgcgaact gcgcgtgaaa ttcagccgca gcgcagatgc tccagcctac 1200

aagcaggggc agaaccagct ctacaacgaa ctcaatcttg gtcggagaga ggagtacgac 1260

gtgctggaca agcggagagg acgggaccca gaaatgggcg ggaagccgcg cagaaagaat 1320

ccccaagagg gcctgtacaa cgagctccaa aaggataaga tggcagaagc ctatagcgag 1380

attggtatga aaggggaacg cagaagaggc aaaggccacg acggactgta ccagggactc 1440

agcaccgcca ccaaggacac ctatgacgct cttcacatgc aggccctgcc gcctcgg 1497

<210> 890
<211> 247
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 890

Glu Val Gln Leu Gln Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Thr Phe Ser Ser Tyr
20 25 30

Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Gly Ile Ile Pro Ile Phe Gly Thr Ala Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Leu Glu Met Ala Thr Ile Met Gly Gly Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Gln Ser Ala Leu Thr Gln Pro Ala Ser
130 135 140

Val Ser Gly Ser Pro Gly Gln Ser Ile Thr Ile Ser Cys Thr Gly Thr
145 150 155 160

Ser Ser Asp Val Gly Gly Tyr Asn Tyr Val Ser Trp Tyr Gln Gln His
165 170 175

Pro Gly Lys Ala Pro Lys Leu Met Ile Tyr Asp Val Ser Asn Arg Pro
180 185 190

Ser Gly Val Ser Asn Arg Phe Ser Gly Ser Lys Ser Gly Asn Thr Ala
195 200 205

Ser Leu Thr Ile Ser Gly Leu Gln Ala Glu Asp Glu Ala Asp Tyr Tyr
210 215 220

Cys Ser Ser Tyr Thr Ser Ser Ser Thr Leu Asp Val Val Phe Gly Gly
225 230 235 240

Gly Thr Lys Leu Thr Val Leu
245

<210> 891
<211> 741
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 891
gaagtgcaac tccaacagtc aggcgcagaa gtcaagaagc ccggatcgtc agtgaaagtg 60

tcctgcaaag cctccggcgg aaccttcagc tcctacgcaa tcagctgggt gcggcaggcg 120

cccggacagg gactggagtg gatgggcggt atcattccga tctttggcac cgccaattac 180

gcccagaagt tccagggacg cgtcacaatc accgccgacg aatcgacttc caccgcctac 240

atggagctgt cgtccttgag gagcgaagat accgccgtgt actactgcgc tcgggatctg 300

gagatggcca ctatcatggg gggttactgg ggccagggga ccctggtcac tgtgtcctcg 360

ggaggagggg gatcaggcgg cggcggttcc gggggaggag gaagccagtc cgcgctgact 420

cagccagctt ccgtgtctgg ttcgccggga cagtccatca ctattagctg taccggcacc 480

agcagcgacg tgggcggcta caactatgtg tcatggtacc agcagcaccc ggggaaggcg 540

cctaagctga tgatctacga cgtgtccaac cgccctagcg gagtgtccaa cagattctcc 600

ggttcgaagt cagggaacac tgcctccctc acgattagcg ggctgcaagc cgaggatgaa 660

gccgactact actgctcctc ctatacctcc tcctcgaccc tggacgtggt gttcggagga 720

ggcaccaagc tcaccgtcct t 741

<210> 892
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 892
Glu Val Gln Leu Gln Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Thr Phe Ser Ser Tyr
20 25 30

Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Gly Ile Ile Pro Ile Phe Gly Thr Ala Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Leu Glu Met Ala Thr Ile Met Gly Gly Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
        115   120

<210> 893
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 893
Gln Ser Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1   5   10   15

Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr
            20   25   30

Asn Tyr Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
        35   40   45

Met Ile Tyr Asp Val Ser Asn Arg Pro Ser Gly Val Ser Asn Arg Phe
    50   55   60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65   70   75   80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Ser Ser
                85   90   95

Ser Thr Leu Asp Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
            100   105   110

<210> 894
<211> 491
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 894
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1   5   10   15

His Ala Ala Arg Pro Glu Val Gln Leu Gln Gln Ser Gly Ala Glu Val
            20   25   30

Lys Lys Pro Gly Ser Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly

_SL

35 40 45

Thr Phe Ser Ser Tyr Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln
50 55 60

Gly Leu Glu Trp Met Gly Gly Ile Ile Pro Ile Phe Gly Thr Ala Asn
65 70 75 80

Tyr Ala Gln Lys Phe Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser
85 90 95

Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Ala Arg Asp Leu Glu Met Ala Thr Ile Met Gly
115 120 125

Gly Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
130 135 140

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Ser Ala Leu
145 150 155 160

Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln Ser Ile Thr Ile
165 170 175

Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr Asn Tyr Val Ser
180 185 190

Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu Met Ile Tyr Asp
195 200 205

Val Ser Asn Arg Pro Ser Gly Val Ser Asn Arg Phe Ser Gly Ser Lys
210 215 220

Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu Gln Ala Glu Asp
225 230 235 240

Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Ser Ser Ser Thr Leu Asp
245 250 255

Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Thr Thr Thr Pro
260 265 270

Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu
275 280 285

_SL
Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His
290 295 300

Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu
305 310 315 320

Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr
325 330 335

Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe
340 345 350

Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg
355 360 365

Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser
370 375 380

Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr
385 390 395 400

Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys
405 410 415

Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn
420 425 430

Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu
435 440 445

Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly
450 455 460

His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr
465 470 475 480

Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 895
<211> 1473
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 895

atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaagtgc aactccaaca gtcaggcgca gaagtcaaga agcccggatc gtcagtgaaa 120

gtgtcctgca aagcctccgg cggaaccttc agctcctacg caatcagctg ggtgcggcag 180

gcgcccggac agggactgga gtggatgggc ggtatcattc cgatctttgg caccgccaat 240

tacgcccaga agttccaggg acgcgtcaca atcaccgccg acgaatcgac ttccaccgcc 300

tacatggagc tgtcgtcctt gaggagcgaa gataccgccg tgtactactg cgctcgggat 360

ctggagatgg ccactatcat ggggggttac tggggccagg ggaccctggt cactgtgtcc 420

tcgggaggag ggggatcagg cggcggcggt tccgggggag gaggaagcca gtccgcgctg 480

actcagccag cttccgtgtc tggttcgccg ggacagtcca tcactattag ctgtaccggc 540

accagcagcg acgtgggcgg ctacaactat gtgtcatggt accagcagca cccggggaag 600

gcgcctaagc tgatgatcta cgacgtgtcc aaccgcccta gcggagtgtc caacagattc 660

tccggttcga agtcagggaa cactgcctcc ctcacgatta gcgggctgca agccgaggat 720

gaagccgact actactgctc ctcctatacc tcctcctcga ccctggacgt ggtgttcgga 780

ggaggcacca agctcaccgt ccttaccact accccagcac cgaggccacc caccccggct 840

cctaccatcg cctcccagcc tctgtccctg cgtccggagg catgtagacc cgcagctggt 900

ggggccgtgc atacccgggg tcttgacttc gcctgcgata tctacatttg ggcccctctg 960

gctggtactt gcggggtcct gctgctttca ctcgtgatca ctctttactg taagcgcggt 1020

cggaagaagc tgctgtacat ctttaagcaa cccttcatga ggcctgtgca gactactcaa 1080

gaggaggacg gctgttcatg ccggttccca gaggaggagg aaggcggctg cgaactgcgc 1140

gtgaaattca gccgcagcgc agatgctcca gcctacaagc aggggcagaa ccagctctac 1200

aacgaactca atcttggtcg gagagaggag tacgacgtgc tggacaagcg gagaggacgg 1260

gacccagaaa tgggcgggaa gccgcgcaga aagaatcccc aagagggcct gtacaacgag 1320

ctccaaaagg ataagatggc agaagcctat agcgagattg gtatgaaagg ggaacgcaga 1380

agaggcaaag gccacgacgg actgtaccag ggactcagca ccgccaccaa ggacacctat 1440

gacgctcttc acatgcaggc cctgccgcct cgg 1473

<210> 896
<211> 245
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 896
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Gly

```
                                                _SL
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
            20                  25                  30

Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Leu Ile Ser Gly Asp Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Val Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Val Phe Asp Ser Tyr Tyr Met Asp Val Trp Gly Lys Gly Thr
            100                 105                 110

Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125

Gly Ser Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Leu Ser Leu
    130                 135                 140

Pro Val Thr Pro Gly Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln
145                 150                 155                 160

Ser Leu Val Tyr Thr Asp Gly Asn Thr Tyr Leu Asn Trp Phe Gln Gln
                165                 170                 175

Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr Lys Val Ser Asn Arg
            180                 185                 190

Asp Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Asp Thr Asp
        195                 200                 205

Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Val Gly Ile Tyr
    210                 215                 220

Tyr Cys Met Gln Gly Thr His Trp Ser Phe Thr Phe Gly Gln Gly Thr
225                 230                 235                 240

Arg Leu Glu Ile Lys
                245
```

<210> 897
<211> 735
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 897
gaagtgcaat tggtggaaag cggaggagga gtggtgcaac ctggaggaag cctgagactg 60

tcatgtgccg cctcgggatt cactttcgat gactacgcaa tgcactgggt ccgccaggcc 120

cccggaaagg gtctggaatg ggtgtccctc atctccggcg atgggggttc cacttactat 180

gcggattctg tgaagggccg cttcacaatc tcccgggaca attccaagaa cactctgtac 240

cttcaaatga actccctgag ggtggaggac accgctgtgt actactgcgc gagagtgttt 300

gactcgtact atatggacgt ctggggaaag ggcaccaccg tgaccgtgtc cagcggtggc 360

ggtggatcgg ggggcggcgg ctccgggagc ggaggttccg agattgtgct gactcagtcg 420

ccgttgtcac tgcctgtcac ccccgggcag ccggcctcca tttcatgccg gtccagccag 480

tccctggtct acaccgatgg gaacacttac ctcaactggt tccagcagcg cccaggacag 540

tccccgcgga ggctgatcta caaagtgtca aaccgggact ccggcgtccc cgatcggttc 600

tcgggaagcg gcagcgacac cgacttcacg ctgaagattt cccgcgtgga agccgaggac 660

gtgggcatct actactgtat gcagggcacc cactggtcgt ttaccttcgg acaaggaact 720

aggctcgaga tcaag 735

<210> 898
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 898
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
20 25 30

Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Leu Ile Ser Gly Asp Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Val Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Val Phe Asp Ser Tyr Tyr Met Asp Val Trp Gly Lys Gly Thr
100 105 110

Thr Val Thr Val Ser Ser
115

<210> 899
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 899
Glu Ile Val Leu Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val Tyr Thr
20 25 30

Asp Gly Asn Thr Tyr Leu Asn Trp Phe Gln Gln Arg Pro Gly Gln Ser
35 40 45

Pro Arg Arg Leu Ile Tyr Lys Val Ser Asn Arg Asp Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Asp Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Ile Tyr Tyr Cys Met Gln Gly
85 90 95

Thr His Trp Ser Phe Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys
100 105 110

<210> 900
<211> 489
<212> PRT
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 900
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Val Gln Leu Val Glu Ser Gly Gly Gly Val
20 25 30

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
35 40 45

Thr Phe Asp Asp Tyr Ala Met His Trp Val Arg Gln Ala Pro Gly Lys
50 55 60

Gly Leu Glu Trp Val Ser Leu Ile Ser Gly Asp Gly Gly Ser Thr Tyr
65 70 75 80

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser
85 90 95

Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Val Glu Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Ala Arg Val Phe Asp Ser Tyr Tyr Met Asp Val
115 120 125

Trp Gly Lys Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
130 135 140

Gly Gly Gly Gly Ser Gly Ser Gly Gly Ser Glu Ile Val Leu Thr Gln
145 150 155 160

Ser Pro Leu Ser Leu Pro Val Thr Pro Gly Gln Pro Ala Ser Ile Ser
165 170 175

Cys Arg Ser Ser Gln Ser Leu Val Tyr Thr Asp Gly Asn Thr Tyr Leu
180 185 190

Asn Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
195 200 205

Lys Val Ser Asn Arg Asp Ser Gly Val Pro Asp Arg Phe Ser Gly Ser
210 215 220

Gly Ser Asp Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
225 230 235 240

```
Asp Val Gly Ile Tyr Tyr Cys Met Gln Gly Thr His Trp Ser Phe Thr
                245                 250                 255

Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys Thr Thr Thr Pro Ala Pro
            260                 265                 270

Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu
        275                 280                 285

Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg
    290                 295                 300

Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly
305                 310                 315                 320

Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys
                325                 330                 335

Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg
            340                 345                 350

Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro
        355                 360                 365

Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser
    370                 375                 380

Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu
385                 390                 395                 400

Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg
                405                 410                 415

Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln
            420                 425                 430

Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr
        435                 440                 445

Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp
    450                 455                 460

Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala
465                 470                 475                 480

Leu His Met Gln Ala Leu Pro Pro Arg
```

<210> 901
<211> 1467
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 901
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaagtgc aattggtgga aagcggagga ggagtggtgc aacctggagg aagcctgaga 120

ctgtcatgtg ccgcctcggg attcactttc gatgactacg caatgcactg ggtccgccag 180

gcccccggaa agggtctgga atgggtgtcc ctcatctccg gcgatggggg ttccacttac 240

tatgcggatt ctgtgaaggg ccgcttcaca atctcccggg acaattccaa gaacactctg 300

taccttcaaa tgaactccct gagggtggag gacaccgctg tgtactactg cgcgagagtg 360

tttgactcgt actatatgga cgtctgggga aagggcacca ccgtgaccgt gtccagcggt 420

ggcggtggat cgggggcgg cggctccggg agcggaggtt ccgagattgt gctgactcag 480

tcgccgttgt cactgcctgt cacccccggg cagccggcct ccatttcatg ccggtccagc 540

cagtccctgg tctacaccga tgggaacact tacctcaact ggttccagca gcgcccagga 600

cagtccccgc ggaggctgat ctacaaagtg tcaaaccggg actccggcgt ccccgatcgg 660

ttctcgggaa gcggcagcga caccgacttc acgctgaaga tttcccgcgt ggaagccgag 720

gacgtgggca tctactactg tatgcagggc acccactggt cgtttacctt cggacaagga 780

actaggctcg agatcaagac cactacccca gcaccgaggc cacccacccc ggctcctacc 840

atcgcctccc agcctctgtc cctgcgtccg gaggcatgta gacccgcagc tggtggggcc 900

gtgcataccc ggggtcttga cttcgcctgc gatatctaca tttgggcccc tctggctggt 960

acttgcgggg tcctgctgct ttcactcgtg atcactcttt actgtaagcg cggtcggaag 1020

aagctgctgt acatctttaa gcaacccttc atgaggcctg tgcagactac tcaagaggag 1080

gacggctgtt catgccggtt cccagaggag gaggaaggcg gctgcgaact gcgcgtgaaa 1140

ttcagccgca gcgcagatgc tccagcctac aagcaggggc agaaccagct ctacaacgaa 1200

ctcaatcttg gtcggagaga ggagtacgac gtgctggaca agcggagagg acgggaccca 1260

gaaatgggcg ggaagccgcg cagaaagaat ccccaagagg gcctgtacaa cgagctccaa 1320

aaggataaga tggcagaagc ctatagcgag attggtatga aaggggaacg cagaagaggc 1380

aaaggccacg acggactgta ccagggactc agcaccgcca ccaaggacac ctatgacgct 1440

cttcacatgc aggccctgcc gcctcgg 1467

<210> 902
<211> 247
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 902
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Ser
20 25 30

Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45

Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
50 55 60

Leu Lys Ser Arg Val Ser Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80

Ser Leu Lys Leu Lys Tyr Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95

Cys Ala Thr Pro Gly Thr Tyr Tyr Asp Phe Leu Ser Gly Tyr Tyr Pro
100 105 110

Phe Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Met
130 135 140

Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr
145 150 155 160

Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Tyr Leu Ala Trp Tyr
165 170 175

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser
180 185 190

Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
195 200 205

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
210 215 220

Thr Tyr Tyr Cys Gln Gln Leu Asn Ser Tyr Pro Tyr Thr Phe Gly Gln
225 230 235 240

Gly Thr Lys Leu Glu Ile Lys
245

<210> 903
<211> 741
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 903
caagtgcagc ttcaagaaag cggtccagga ctcgtcaagc catcagaaac tctttccctc 60

acttgtaccg tgtcgggagg cagcatctcc tcgagctcct actactgggg ttggattaga 120

cagcccccgg gaaaggggtt ggagtggatc ggttccatct actactccgg gtcgacctac 180

tacaaccctt ccctgaaatc tcgggtgtcc atctccgtcg acacctccaa gaaccagttc 240

agcctgaagc tgaaatatgt gaccgcggcc gatactgccg tgtactattg cgccaccccg 300

ggaacctact acgacttcct ctcggggtac tacccgtttt actggggaca ggggactctc 360

gtgaccgtgt cctcgggcgg cggaggttca ggcggtggcg gatcgggggg aggaggctca 420

gacattgtga tgacccagag cccgtccagc ctgagcgcct ccgtgggcga tagggtcacg 480

attacttgcc gggcgtccca gggaatctca agctacctgg cctggtacca acagaagccc 540

ggaaaggcac ccaagttgct gatctatgcc gctagcactc tgcagtccgg ggtgccttcc 600

cgcttctccg gctccggctc gggcaccgac ttcaccctga ccatttcctc actgcaaccc 660

gaggacttcg ccacttacta ctgccagcag ctgaactcct acccttacac attcggacag 720

ggaaccaagc tggaaatcaa g 741

<210> 904
<211> 125
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 904

_SL
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Ser
20 25 30

Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45

Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
50 55 60

Leu Lys Ser Arg Val Ser Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80

Ser Leu Lys Leu Lys Tyr Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95

Cys Ala Thr Pro Gly Thr Tyr Tyr Asp Phe Leu Ser Gly Tyr Tyr Pro
100 105 110

Phe Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 905
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 905
Asp Ile Val Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Tyr
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ala Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

                                                _SL
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Leu Asn Ser Tyr Pro Tyr
                85   90   95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100   105

<210> 906
<211> 491
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 906
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1   5   10   15

His Ala Ala Arg Pro Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu
            20   25   30

Val Lys Pro Ser Glu Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly
        35   40   45

Ser Ile Ser Ser Ser Ser Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro
    50   55   60

Gly Lys Gly Leu Glu Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Ser Thr
65   70   75   80

Tyr Tyr Asn Pro Ser Leu Lys Ser Arg Val Ser Ile Ser Val Asp Thr
                85   90   95

Ser Lys Asn Gln Phe Ser Leu Lys Leu Lys Tyr Val Thr Ala Ala Asp
            100   105   110

Thr Ala Val Tyr Tyr Cys Ala Thr Pro Gly Thr Tyr Tyr Asp Phe Leu
        115   120   125

Ser Gly Tyr Tyr Pro Phe Tyr Trp Gly Gln Gly Thr Leu Val Thr Val
    130   135   140

Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
145   150   155   160

Ser Asp Ile Val Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val
                165   170   175

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                                                _SL
Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser
            180                 185                 190

Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu
        195                 200                 205

Ile Tyr Ala Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser
    210                 215                 220

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln
225                 230                 235                 240

Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Leu Asn Ser Tyr Pro
                245                 250                 255

Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Thr Thr Thr Pro
            260                 265                 270

Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu
        275                 280                 285

Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His
    290                 295                 300

Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu
305                 310                 315                 320

Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr
                325                 330                 335

Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe
            340                 345                 350

Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg
        355                 360                 365

Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser
    370                 375                 380

Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr
385                 390                 395                 400

Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys
                405                 410                 415

Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn
            420                 425                 430
```

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Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu
        435                 440                 445

Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly
    450                 455                 460

His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr
465                 470                 475                 480

Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
                485                 490
```

<210> 907
<211> 1473
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 907

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atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg       60

ccccaagtgc agcttcaaga aagcggtcca ggactcgtca agccatcaga aactctttcc      120

ctcacttgta ccgtgtcggg aggcagcatc tcctcgagct cctactactg gggttggatt      180

agacagcccc cgggaaaggg gttggagtgg atcggttcca tctactactc cgggtcgacc      240

tactacaacc cttccctgaa atctcgggtg tccatctccg tcgacacctc caagaaccag      300

ttcagcctga agctgaaata tgtgaccgcg gccgatactg ccgtgtacta ttgcgccacc      360

ccgggaacct actacgactt cctctcgggg tactacccgt tttactgggg acaggggact      420

ctcgtgaccg tgtcctcggg cggcggaggt tcaggcggtg gcggatcggg gggaggaggc      480

tcagacattg tgatgaccca gagcccgtcc agcctgagcg cctccgtggg cgatagggtc      540

acgattactt gccgggcgtc ccagggaatc tcaagctacc tggcctggta ccaacagaag      600

cccggaaagg cacccaagtt gctgatctat gccgctagca ctctgcagtc cggggtgcct      660

tcccgcttct ccggctccgg ctcgggcacc gacttcaccc tgaccatttc ctcactgcaa      720

cccgaggact tcgccactta ctactgccag cagctgaact cctaccctta cacattcgga      780

cagggaacca agctggaaat caagaccact accccagcac cgaggccacc caccccggct      840

cctaccatcg cctcccagcc tctgtccctg cgtccggagg catgtagacc cgcagctggt      900

ggggccgtgc atacccgggg tcttgacttc gcctgcgata tctacatttg ggcccctctg      960

gctggtactt gcggggtcct gctgctttca ctcgtgatca ctctttactg taagcgcggt     1020

cggaagaagc tgctgtacat ctttaagcaa cccttcatga ggcctgtgca gactactcaa     1080
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gaggaggacg gctgttcatg ccggttccca gaggaggagg aaggcggctg cgaactgcgc 1140

gtgaaattca gccgcagcgc agatgctcca gcctacaagc aggggcagaa ccagctctac 1200

aacgaactca atcttggtcg gagagaggag tacgacgtgc tggacaagcg gagaggacgg 1260

gacccagaaa tgggcgggaa gccgcgcaga aagaatcccc aagagggcct gtacaacgag 1320

ctccaaaagg ataagatggc agaagcctat agcgagattg gtatgaaagg ggaacgcaga 1380

agaggcaaag gccacgacgg actgtaccag ggactcagca ccgccaccaa ggacacctat 1440

gacgctcttc acatgcaggc cctgccgcct cgg 1473

<210> 908
<211> 239
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 908

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Trp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Asn Ile Asn Glu Asp Gly Ser Ala Lys Phe Tyr Val Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Phe Cys
85 90 95

Ala Arg Asp Leu Arg Ser Gly Arg Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
115 120 125

Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu
130 135 140

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                                                _SL
Ser Pro Gly Gly Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Ile
145                 150                 155                 160


Ser Gly Ser Phe Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro
                165                 170                 175


Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp
            180                 185                 190


Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
        195                 200                 205


Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly
    210                 215                 220


Ser Ser Pro Pro Thr Phe Gly Leu Gly Thr Lys Leu Glu Ile Lys
225                 230                 235


<210> 909
<211> 717
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 909
caagtgcaac tcgtggaatc tggtggagga ctcgtgcaac ccggaggatc attgcgactc       60

tcgtgtgcgg catccggctt tacctttca tcctactgga tgtcctgggt cagacaggcc      120

cccgggaagg gactggaatg ggtcgcgaac atcaacgagg acggctcggc caagttctac      180

gtggactccg tgaagggccg cttcacgatc tcacgggata acgccaagaa ttccctgtat      240

ctgcaaatga acagcctgag ggccgaggac actgcggtgt acttctgcgc acgcgacctg      300

aggtccggga gatactgggg acagggcacc ctcgtgaccg tgtcgagcgg aggaggggg      360

tcgggcggcg gcggttccgg tggcggcggt agcgaaattg tgttgaccca gtcccctgga      420

accctgagcc tgtcacctgg aggacgcgcc accctgtcct gccgggccag ccagagcatc      480

tcagggtcct tcctggcttg gtaccagcag aagccgggac aggctccgag acttctgatc      540

tacggcgcct cctcgcgggc gaccggaatc ccggatcggt tctccggctc gggaagcgga      600

actgacttca ctcttaccat ttcccgcctg gagccggaag atttcgccgt gtactactgc      660

cagcagtacg ggtcatcccc tccaaccttc ggcctgggaa ctaagctgga aatcaaa          717


<210> 910
<211> 116
<212> PRT
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<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 910
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Trp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Asn Ile Asn Glu Asp Gly Ser Ala Lys Phe Tyr Val Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Phe Cys
85 90 95

Ala Arg Asp Leu Arg Ser Gly Arg Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

Thr Val Ser Ser
115

<210> 911
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 911
Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Gly Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Ile Ser Gly Ser
20 25 30

Phe Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45

_SL
Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
    50   55   60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65   70   75   80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro
                85   90   95

Pro Thr Phe Gly Leu Gly Thr Lys Leu Glu Ile Lys
            100   105

<210> 912
<211> 483
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 912
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1   5   10   15

His Ala Ala Arg Pro Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu
            20   25   30

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
        35   40   45

Thr Phe Ser Ser Tyr Trp Met Ser Trp Val Arg Gln Ala Pro Gly Lys
    50   55   60

Gly Leu Glu Trp Val Ala Asn Ile Asn Glu Asp Gly Ser Ala Lys Phe
65   70   75   80

Tyr Val Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala
                85   90   95

Lys Asn Ser Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
            100   105   110

Ala Val Tyr Phe Cys Ala Arg Asp Leu Arg Ser Gly Arg Tyr Trp Gly
        115   120   125

Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
    130   135   140

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                                                    _SL
Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro
145                 150                 155                 160

Gly Thr Leu Ser Leu Ser Pro Gly Gly Arg Ala Thr Leu Ser Cys Arg
                165                 170                 175

Ala Ser Gln Ser Ile Ser Gly Ser Phe Leu Ala Trp Tyr Gln Gln Lys
            180                 185                 190

Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala
        195                 200                 205

Thr Gly Ile Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
    210                 215                 220

Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr
225                 230                 235                 240

Cys Gln Gln Tyr Gly Ser Ser Pro Pro Thr Phe Gly Leu Gly Thr Lys
                245                 250                 255

Leu Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala
            260                 265                 270

Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg
        275                 280                 285

Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys
    290                 295                 300

Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu
305                 310                 315                 320

Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu
                325                 330                 335

Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln
            340                 345                 350

Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly
        355                 360                 365

Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr
    370                 375                 380

Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg
385                 390                 395                 400
```

Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met
405 410 415

Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu
420 425 430

Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys
435 440 445

Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu
450 455 460

Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu
465 470 475 480

Pro Pro Arg

<210> 913
<211> 1449
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 913
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtgc aactcgtgga atctggtgga ggactcgtgc aacccggagg atcattgcga 120

ctctcgtgtg cggcatccgg ctttaccttt tcatcctact ggatgtcctg ggtcagacag 180

gcccccggga agggactgga atgggtcgcg aacatcaacg aggacggctc ggccaagttc 240

tacgtggact ccgtgaaggg ccgcttcacg atctcacggg ataacgccaa gaattccctg 300

tatctgcaaa tgaacagcct gagggccgag gacactgcgg tgtacttctg cgcacgcgac 360

ctgaggtccg ggagatactg gggacagggc accctcgtga ccgtgtcgag cggaggaggg 420

gggtcgggcg gcggcggttc cggtggcggc ggtagcgaaa ttgtgttgac ccagtcccct 480

ggaaccctga gcctgtcacc tggaggacgc gccaccctgt cctgccgggc cagccagagc 540

atctcagggt ccttcctggc ttggtaccag cagaagccgg gacaggctcc gagacttctg 600

atctacggcg cctcctcgcg ggcgaccgga atcccggatc ggttctccgg ctcgggaagc 660

ggaactgact tcactcttac catttcccgc ctggagccgg aagatttcgc cgtgtactac 720

tgccagcagt acgggtcatc ccctccaacc ttcggcctgg gaactaagct ggaaatcaaa 780

accactaccc cagcaccgag gccacccacc ccggctccta ccatcgcctc ccagcctctg 840

tccctgcgtc cggaggcatg tagacccgca gctggtgggg ccgtgcatac ccggggtctt 900

gacttcgcct gcgatatcta catttgggcc cctctggctg gtacttgcgg ggtcctgctg 960

ctttcactcg tgatcactct ttactgtaag cgcggtcgga agaagctgct gtacatcttt 1020

aagcaaccct tcatgaggcc tgtgcagact actcaagagg aggacggctg ttcatgccgg 1080

ttcccagagg aggaggaagg cggctgcgaa ctgcgcgtga aattcagccg cagcgcagat 1140

gctccagcct acaagcaggg gcagaaccag ctctacaacg aactcaatct tggtcggaga 1200

gaggagtacg acgtgctgga caagcggaga ggacgggacc cagaaatggg cgggaagccg 1260

cgcagaaaga atccccaaga gggcctgtac aacgagctcc aaaaggataa gatggcagaa 1320

gcctatagcg agattggtat gaaaggggaa cgcagaagag gcaaaggcca cgacggactg 1380

taccagggac tcagcaccgc caccaaggac acctatgacg ctcttcacat gcaggccctg 1440

ccgcctcgg 1449

<210> 914
<211> 245
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 914

Glu Val Gln Leu Gln Gln Ser Gly Pro Gly Leu Val Arg Pro Ser Glu
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Pro Val Arg Ser Gly
20 25 30

Ser His Tyr Trp Asn Trp Ile Arg Gln Pro Pro Gly Arg Gly Leu Glu
35 40 45

Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Asn Tyr Asn Pro Ser
50 55 60

Leu Glu Asn Arg Val Thr Ile Ser Ile Asp Thr Ser Asn Asn His Phe
65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Leu Tyr Phe
85 90 95

Cys Ala Arg Gly Thr Ala Thr Phe Asp Trp Asn Phe Pro Phe Asp Ser
100 105 110

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                                                _SL
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser
        115                 120                 125

Gly Gly Gly Gly Ser Gly Ser Gly Gly Ser Asp Ile Gln Met Thr Gln
    130                 135                 140

Ser Pro Ser Ser Leu Ser Ala Ser Ile Gly Asp Arg Val Thr Ile Thr
145                 150                 155                 160

Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln
                165                 170                 175

Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu
            180                 185                 190

Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
        195                 200                 205

Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr
    210                 215                 220

Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Trp Thr Phe Gly Gln Gly Thr
225                 230                 235                 240

Lys Leu Glu Ile Lys
                245
```

<210> 915
<211> 735
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 915
gaagtgcaac tccaacaatc cggtccagga ctcgtcagac cctccgaaac tctctcgctt 60

acatgcactg tgtccggcgg ccctgtgcgg tccggctctc attactggaa ctggattcgc 120

cagcccccgg gacgcggact ggagtggatc ggctacatct attactcggg gtcgactaac 180

tacaacccga gcctggaaaa tagagtgacc atctcaatcg acacgtccaa caaccacttc 240

tcgctgaagt tgtcctccgt gactgccgcc gatactgccc tgtacttctg tgctcgcgga 300

accgccacct tcgactggaa cttccctttt gactcatggg gccaggggac ccttgtgacc 360

gtgtccagcg gaggaggagg ctccggtggt ggcgggagcg gtagcggcgg aagcgacatc 420

cagatgaccc agtcaccgtc ctcgctgtcc gcatccattg gggatcgggt cactattact 480

tgccgggcgt cccagtccat ctcgtcctac ctgaactggt atcagcagaa gccagggaaa 540

gcccccaagc tgctgatcta cgcggccagc agcctgcagt caggagtgcc ttcaaggttt 600

agcggcagcg gatcgggaac cgacttcacc ctgaccattt cctccctcca acccgaggat 660

ttcgccacct actactgcca gcagtcctac tccaccccgt ggaccttcgg acagggaacc 720

aagctggaga tcaag 735

<210> 916
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 916

Glu	Val	Gln	Leu	Gln	Gln	Ser	Gly	Pro	Gly	Leu	Val	Arg	Pro	Ser	Glu
1				5				10					15		
Thr	Leu	Ser	Leu	Thr	Cys	Thr	Val	Ser	Gly	Gly	Pro	Val	Arg	Ser	Gly
			20					25					30		
Ser	His	Tyr	Trp	Asn	Trp	Ile	Arg	Gln	Pro	Pro	Gly	Arg	Gly	Leu	Glu
		35					40					45			
Trp	Ile	Gly	Tyr	Ile	Tyr	Tyr	Ser	Gly	Ser	Thr	Asn	Tyr	Asn	Pro	Ser
	50					55					60				
Leu	Glu	Asn	Arg	Val	Thr	Ile	Ser	Ile	Asp	Thr	Ser	Asn	Asn	His	Phe
65					70					75					80
Ser	Leu	Lys	Leu	Ser	Ser	Val	Thr	Ala	Ala	Asp	Thr	Ala	Leu	Tyr	Phe
				85					90					95	
Cys	Ala	Arg	Gly	Thr	Ala	Thr	Phe	Asp	Trp	Asn	Phe	Pro	Phe	Asp	Ser
			100					105					110		
Trp	Gly	Gln	Gly	Thr	Leu	Val	Thr	Val	Ser	Ser					
		115					120								

<210> 917
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 917
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Ile Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Trp
85 90 95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 918
<211> 489
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 918
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Val Gln Leu Gln Gln Ser Gly Pro Gly Leu
20 25 30

Val Arg Pro Ser Glu Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly
35 40 45

Pro Val Arg Ser Gly Ser His Tyr Trp Asn Trp Ile Arg Gln Pro Pro
50 55 60

Gly Arg Gly Leu Glu Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr
65 70 75 80

Asn Tyr Asn Pro Ser Leu Glu Asn Arg Val Thr Ile Ser Ile Asp Thr
85 90 95

```
Ser Asn Asn His Phe Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp
            100                 105                 110

Thr Ala Leu Tyr Phe Cys Ala Arg Gly Thr Ala Thr Phe Asp Trp Asn
        115                 120                 125

Phe Pro Phe Asp Ser Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
    130                 135                 140

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Ser Gly Gly Ser Asp
145                 150                 155                 160

Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Ile Gly Asp
                165                 170                 175

Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu
            180                 185                 190

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
        195                 200                 205

Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
    210                 215                 220

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
225                 230                 235                 240

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Trp Thr
                245                 250                 255

Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Thr Thr Thr Pro Ala Pro
            260                 265                 270

Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu
        275                 280                 285

Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg
    290                 295                 300

Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly
305                 310                 315                 320

Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys
                325                 330                 335

Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg
```

_SL
340 345 350

Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro
355 360 365

Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser
370 375 380

Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu
385 390 395 400

Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg
405 410 415

Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln
420 425 430

Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr
435 440 445

Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp
450 455 460

Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala
465 470 475 480

Leu His Met Gln Ala Leu Pro Pro Arg
485

<210> 919
<211> 1467
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 919
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaagtgc aactccaaca atccggtcca ggactcgtca gaccctccga aactctctcg 120

cttacatgca ctgtgtccgg cggccctgtg cggtccggct ctcattactg gaactggatt 180

cgccagcccc cgggacgcgg actggagtgg atcggctaca tctattactc ggggtcgact 240

aactacaacc cgagcctgga aaatagagtg accatctcaa tcgacacgtc caacaaccac 300

ttctcgctga agttgtcctc cgtgactgcc gccgatactg ccctgtactt ctgtgctcgc 360

ggaaccgcca ccttcgactg gaacttccct tttgactcat ggggccaggg gacccttgtg 420

accgtgtcca gcggaggagg aggctccggt ggtggcggga gcggtagcgg cggaagcgac 480

atccagatga cccagtcacc gtcctcgctg tccgcatcca ttggggatcg ggtcactatt 540

acttgccggg cgtcccagtc catctcgtcc tacctgaact ggtatcagca gaagccaggg 600

aaagccccca agctgctgat ctacgcggcc agcagcctgc agtcaggagt gccttcaagg 660

tttagcggca gcggatcggg aaccgacttc accctgacca tttcctccct ccaacccgag 720

gatttcgcca cctactactg ccagcagtcc tactccaccc cgtggacctt cggacaggga 780

accaagctgg agatcaagac cactacccca gcaccgaggc cacccacccc ggctcctacc 840

atcgcctccc agcctctgtc cctgcgtccg gaggcatgta gacccgcagc tggtggggcc 900

gtgcataccc ggggtcttga cttcgcctgc gatatctaca tttgggcccc tctggctggt 960

acttgcgggg tcctgctgct ttcactcgtg atcactcttt actgtaagcg cggtcggaag 1020

aagctgctgt acatctttaa gcaacccttc atgaggcctg tgcagactac tcaagaggag 1080

gacggctgtt catgccggtt cccagaggag gaggaaggcg gctgcgaact gcgcgtgaaa 1140

ttcagccgca gcgcagatgc tccagcctac aagcaggggc agaaccagct ctacaacgaa 1200

ctcaatcttg gtcggagaga ggagtacgac gtgctggaca agcggagagg acgggaccca 1260

gaaatgggcg ggaagccgcg cagaaagaat ccccaagagg gcctgtacaa cgagctccaa 1320

aaggataaga tggcagaagc ctatagcgag attggtatga aaggggaacg cagaagaggc 1380

aaaggccacg acggactgta ccagggactc agcaccgcca ccaaggacac ctatgacgct 1440

cttcacatgc aggccctgcc gcctcgg 1467

<210> 920
<211> 255
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 920
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ser Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ser Ile Ser Ser Ser Ser Ser Tyr Ile Tyr Tyr Ala Asp Ser Val
50 55 60

```
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Asp Pro Ser Ser Ser Gly Ser Tyr Tyr Met Glu Asp Ser Tyr
            100                 105                 110

Tyr Tyr Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser
        115                 120                 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
    130                 135                 140

Asn Phe Met Leu Thr Gln Pro His Ser Val Ser Glu Ser Pro Gly Lys
145                 150                 155                 160

Thr Val Thr Ile Ser Cys Thr Gly Ser Ser Gly Ser Ile Ala Ser Asn
                165                 170                 175

Tyr Val Gln Trp Tyr Gln Gln Arg Pro Gly Ser Ala Pro Thr Thr Val
            180                 185                 190

Ile Tyr Glu Asp Asn Gln Arg Pro Ser Gly Val Pro Asp Arg Phe Ser
        195                 200                 205

Gly Ser Ile Asp Ser Ser Ser Asn Ser Ala Ser Leu Thr Ile Ser Gly
    210                 215                 220

Leu Lys Thr Glu Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Tyr Asp Ser
225                 230                 235                 240

Ser Asn Gln Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
                245                 250                 255
```

<210> 921
<211> 765
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 921
gaagtgcaat tggtggaatc tggaggagga cttgtgaaac ctggtggaag cctgagactt 60

tcctgtgcgg cctcgggatt cactttctcc tcctactcca tgaactgggt cagacaggcc 120

cctgggaagg gactggaatg ggtgtcatcc atctcctcct catcgtcgta catctactac 180

gccgatagcg tgaaggggcg gttcaccatt tcccgggaca acgctaagaa cagcctctat 240

ctgcaaatga attccctccg cgccgaggac actgccgtgt actactgcgc gagggacccc 300

tcatcaagcg gcagctacta catggaggac tcgtattact acggaatgga cgtctggggc 360

cagggaacca ctgtgacggt gtcctccggt ggagggggct ccgggggcgg gggatctggc 420

ggaggaggct ccaacttcat gctgacccag ccgcactccg tgtccgaaag ccccggaaag 480

accgtgacaa tttcctgcac cgggtcctcc ggctcgatcg catcaaacta cgtgcagtgg 540

taccagcagc gcccgggcag cgcccccacc actgtcatct acgaggataa ccagcggccg 600

tcgggtgtcc cagaccggtt ttccggttcg atcgatagca gcagcaacag cgcctccctg 660

accatttccg gcctcaagac cgaggatgag gctgactact actgccagtc gtatgactcc 720

tcgaaccaag tggtgttcgg tggcggcacc aagctgactg tgctg 765

<210> 922
<211> 129
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 922
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ser Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ser Ile Ser Ser Ser Ser Ser Tyr Ile Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Pro Ser Ser Ser Gly Ser Tyr Tyr Met Glu Asp Ser Tyr
100 105 110

Tyr Tyr Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser
115 120 125

Ser

<210> 923
<211> 111
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 923
Asn Phe Met Leu Thr Gln Pro His Ser Val Ser Glu Ser Pro Gly Lys
1 5 10 15

Thr Val Thr Ile Ser Cys Thr Gly Ser Ser Gly Ser Ile Ala Ser Asn
20 25 30

Tyr Val Gln Trp Tyr Gln Gln Arg Pro Gly Ser Ala Pro Thr Thr Val
35 40 45

Ile Tyr Glu Asp Asn Gln Arg Pro Ser Gly Val Pro Asp Arg Phe Ser
50 55 60

Gly Ser Ile Asp Ser Ser Ser Asn Ser Ala Ser Leu Thr Ile Ser Gly
65 70 75 80

Leu Lys Thr Glu Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Tyr Asp Ser
85 90 95

Ser Asn Gln Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105 110

<210> 924
<211> 499
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 924
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

```
                                                _SL
His Ala Ala Arg Pro Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
            20                  25                  30

Val Lys Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
        35                  40                  45

Thr Phe Ser Ser Tyr Ser Met Asn Trp Val Arg Gln Ala Pro Gly Lys
    50                  55                  60

Gly Leu Glu Trp Val Ser Ser Ile Ser Ser Ser Ser Ser Tyr Ile Tyr
65                  70                  75                  80

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala
                85                  90                  95

Lys Asn Ser Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Arg Asp Pro Ser Ser Ser Gly Ser Tyr Tyr
        115                 120                 125

Met Glu Asp Ser Tyr Tyr Tyr Gly Met Asp Val Trp Gly Gln Gly Thr
    130                 135                 140

Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
145                 150                 155                 160

Gly Gly Gly Gly Ser Asn Phe Met Leu Thr Gln Pro His Ser Val Ser
                165                 170                 175

Glu Ser Pro Gly Lys Thr Val Thr Ile Ser Cys Thr Gly Ser Ser Gly
            180                 185                 190

Ser Ile Ala Ser Asn Tyr Val Gln Trp Tyr Gln Gln Arg Pro Gly Ser
        195                 200                 205

Ala Pro Thr Thr Val Ile Tyr Glu Asp Asn Gln Arg Pro Ser Gly Val
    210                 215                 220

Pro Asp Arg Phe Ser Gly Ser Ile Asp Ser Ser Ser Asn Ser Ala Ser
225                 230                 235                 240

Leu Thr Ile Ser Gly Leu Lys Thr Glu Asp Glu Ala Asp Tyr Tyr Cys
                245                 250                 255

Gln Ser Tyr Asp Ser Ser Asn Gln Val Val Phe Gly Gly Gly Thr Lys
            260                 265                 270
```

```
Leu Thr Val Leu Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala
        275                 280                 285

Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg
    290                 295                 300

Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys
305                 310                 315                 320

Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu
                325                 330                 335

Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu
            340                 345                 350

Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln
        355                 360                 365

Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly
    370                 375                 380

Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr
385                 390                 395                 400

Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg
                405                 410                 415

Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met
            420                 425                 430

Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu
        435                 440                 445

Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys
    450                 455                 460

Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu
465                 470                 475                 480

Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu
                485                 490                 495

Pro Pro Arg
```

<210> 925
<211> 1497

<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 925
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaagtgc aattggtgga atctggagga ggacttgtga aacctggtgg aagcctgaga 120

ctttcctgtg cggcctcggg attcactttc tcctcctact ccatgaactg ggtcagacag 180

gcccctggga agggactgga atgggtgtca tccatctcct cctcatcgtc gtacatctac 240

tacgccgata gcgtgaaggg gcggttcacc atttcccggg acaacgctaa gaacagcctc 300

tatctgcaaa tgaattccct ccgcgccgag gacactgccg tgtactactg cgcgagggac 360

ccctcatcaa gcggcagcta ctacatggag gactcgtatt actacggaat ggacgtctgg 420

ggccagggaa ccactgtgac ggtgtcctcc ggtggagggg gctccggggg cgggggatct 480

ggcggaggag gctccaactt catgctgacc cagccgcact ccgtgtccga aagccccgga 540

aagaccgtga caatttcctg caccgggtcc tccggctcga tcgcatcaaa ctacgtgcag 600

tggtaccagc agcgcccggg cagcgccccc accactgtca tctacgagga taaccagcgg 660

ccgtcgggtg tcccagaccg gttttccggt tcgatcgata gcagcagcaa cagcgcctcc 720

ctgaccattt ccggcctcaa gaccgaggat gaggctgact actactgcca gtcgtatgac 780

tcctcgaacc aagtggtgtt cggtggcggc accaagctga ctgtgctgac cactacccca 840

gcaccgaggc cacccacccc ggctcctacc atcgcctccc agcctctgtc cctgcgtccg 900

gaggcatgta gacccgcagc tggtggggcc gtgcataccc ggggtcttga cttcgcctgc 960

gatatctaca tttgggcccc tctggctggt acttgcgggg tcctgctgct ttcactcgtg 1020

atcactcttt actgtaagcg cggtcggaag aagctgctgt acatctttaa gcaacccttc 1080

atgaggcctg tgcagactac tcaagaggag gacggctgtt catgccggtt cccagaggag 1140

gaggaaggcg gctgcgaact gcgcgtgaaa ttcagccgca gcgcagatgc tccagcctac 1200

aagcaggggc agaaccagct ctacaacgaa ctcaatcttg gtcggagaga ggagtacgac 1260

gtgctggaca agcggagagg acgggaccca gaaatgggcg ggaagccgcg cagaaagaat 1320

ccccaagagg gcctgtacaa cgagctccaa aaggataaga tggcagaagc ctatagcgag 1380

attggtatga aaggggaacg cagaagaggc aaaggccacg acggactgta ccagggactc 1440

agcaccgcca ccaaggacac ctatgacgct cttcacatgc aggccctgcc gcctcgg 1497

<210> 926
<211> 239
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 926

```
Gln Val Asn Leu Arg Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                  10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30

Glu Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Glu Ala Leu Gly Ser Ser Trp Glu Trp Gly Gln Gly Thr Thr
            100                 105                 110

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser
    130                 135                 140

Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Gln Ala Ser Gln Asp
145                 150                 155                 160

Ile Ser Asn Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro
                165                 170                 175

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Glu Thr Gly Val Pro Ser
            180                 185                 190

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser
        195                 200                 205

Ser Leu Gln Pro Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Tyr Asp
    210                 215                 220
```

Asn Leu Pro Leu Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
225 230 235

<210> 927
<211> 717
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 927
caagtgaacc tgagagaaag cggcggagga cttgtgcaac ctggaggaag cctgagactg 60

tcatgtgccg cgtccggctt caccttctcg tcctacgaga tgaactgggt ccgccaggca 120

ccgggcaaag gactggaatg ggtgtcctac atttcctcgt ccgggtccac catctattac 180

gccgactccg tgaagggacg gttcaccatc tcccgggaca acgccaagaa ctccctctac 240

ctccaaatga actcactgag ggcagaggac actgcggtct actactgcgc ccgcgaagct 300

ttgggtagct cctgggagtg gggccaggga accactgtga ccgtgtcctc gggtggaggg 360

ggctccggtg gcgggggttc agggggtggc ggaagcgata tccagatgac tcagtcacca 420

agctccctga gcgcctcagt gggagatcgg gtcacaatca cgtgccaggc gtcccaggac 480

atttctaact acctcaattg gtaccagcag aagccgggga aggcccccaa gcttctgatc 540

tacgatgcct ccaacctgga aaccggcgtg ccctcccgct tctcgggatc gggcagcggc 600

actgacttca cctttaccat ctcgtccctg caacctgagg acatcgccac ctattactgc 660

cagcagtacg ataacctccc gctgactttc ggaggcggaa ctaagctgga gattaag 717

<210> 928
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 928
Gln Val Asn Leu Arg Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Glu Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

```
Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Glu Ala Leu Gly Ser Ser Trp Glu Trp Gly Gln Gly Thr Thr
            100                 105                 110

Val Thr Val Ser Ser
        115
```

<210> 929
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 929

```
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Gln Ala Ser Gln Asp Ile Ser Asn Tyr
            20                  25                  30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Asp Ala Ser Asn Leu Glu Thr Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Tyr Asp Asn Leu Pro Leu
                85                  90                  95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
            100                 105
```

<210> 930
<211> 483
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 930

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15

His Ala Ala Arg Pro Gln Val Asn Leu Arg Glu Ser Gly Gly Gly Leu
            20                  25                  30

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
        35                  40                  45

Thr Phe Ser Ser Tyr Glu Met Asn Trp Val Arg Gln Ala Pro Gly Lys
    50                  55                  60

Gly Leu Glu Trp Val Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr
65                  70                  75                  80

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala
                85                  90                  95

Lys Asn Ser Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Arg Glu Ala Leu Gly Ser Ser Trp Glu Trp
        115                 120                 125

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser
145                 150                 155                 160

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
                165                 170                 175

Gln Ala Ser Gln Asp Ile Ser Asn Tyr Leu Asn Trp Tyr Gln Gln Lys
            180                 185                 190

Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Glu
        195                 200                 205

Thr Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
    210                 215                 220
```

```
Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala Thr Tyr Tyr
225                 230                 235                 240

Cys Gln Gln Tyr Asp Asn Leu Pro Leu Thr Phe Gly Gly Gly Thr Lys
                245                 250                 255

Leu Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala
            260                 265                 270

Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg
        275                 280                 285

Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys
    290                 295                 300

Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu
305                 310                 315                 320

Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu
                325                 330                 335

Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln
            340                 345                 350

Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly
        355                 360                 365

Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr
    370                 375                 380

Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg
385                 390                 395                 400

Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met
                405                 410                 415

Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu
            420                 425                 430

Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys
        435                 440                 445

Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu
    450                 455                 460

Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu
465                 470                 475                 480
```

Pro Pro Arg

<210> 931
<211> 1449
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 931
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtga acctgagaga aagcggcgga ggacttgtgc aacctggagg aagcctgaga 120

ctgtcatgtg ccgcgtccgg cttcaccttc tcgtcctacg agatgaactg ggtccgccag 180

gcaccgggca aaggactgga atgggtgtcc tacatttcct cgtccgggtc caccatctat 240

tacgccgact ccgtgaaggg acggttcacc atctcccggg acaacgccaa gaactccctc 300

tacctccaaa tgaactcact gagggcagag gacactgcgg tctactactg cgcccgcgaa 360

gctttgggta gctcctggga gtggggccag ggaaccactg tgaccgtgtc ctcgggtgga 420

gggggctccg gtggcggggg ttcagggggt ggcggaagcg atatccagat gactcagtca 480

ccaagctccc tgagcgcctc agtgggagat cgggtcacaa tcacgtgcca ggcgtcccag 540

gacatttcta actacctcaa ttggtaccag cagaagccgg ggaaggcccc caagcttctg 600

atctacgatg cctccaacct ggaaaccggc gtgccctccc gcttctcggg atcgggcagc 660

ggcactgact tcacctttac catctcgtcc ctgcaacctg aggacatcgc cacctattac 720

tgccagcagt acgataacct cccgctgact ttcggaggcg gaactaagct ggagattaag 780

accactaccc cagcaccgag gccacccacc ccggctccta ccatcgcctc ccagcctctg 840

tccctgcgtc cggaggcatg tagacccgca gctggtgggg ccgtgcatac ccggggtctt 900

gacttcgcct gcgatatcta catttgggcc cctctggctg gtacttgcgg ggtcctgctg 960

ctttcactcg tgatcactct ttactgtaag cgcggtcgga agaagctgct gtacatcttt 1020

aagcaaccct tcatgaggcc tgtgcagact actcaagagg aggacggctg ttcatgccgg 1080

ttcccagagg aggaggaagg cggctgcgaa ctgcgcgtga aattcagccg cagcgcagat 1140

gctccagcct acaagcaggg gcagaaccag ctctacaacg aactcaatct tggtcggaga 1200

gaggagtacg acgtgctgga caagcggaga ggacgggacc cagaaatggg cgggaagccg 1260

cgcagaaaga atccccaaga gggcctgtac aacgagctcc aaaaggataa gatggcagaa 1320

gcctatagcg agattggtat gaaaggggaa cgcagaagag gcaaaggcca cgacggactg 1380

_SL
taccagggac tcagcaccgc caccaaggac acctatgacg ctcttcacat gcaggccctg 1440

ccgcctcgg 1449

<210> 932
<211> 247
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 932
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Ser Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Pro Phe Thr Gly Tyr
20 25 30

Tyr Ile Gln Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Asp Pro Asn Ser Gly Asn Thr Gly Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asn Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Ser Asp Ser Tyr Gly Tyr Tyr Tyr Gly Met Asp Val Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met
130 135 140

Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr
145 150 155 160

Phe Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Ala Leu Ala Trp Tyr
165 170 175

Gln Gln Lys Pro Gly Lys Pro Pro Lys Leu Leu Ile Tyr Asp Ala Ser
180 185 190

Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
195 200 205

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
210 215 220

Thr Tyr Tyr Cys Gln Gln Phe Asn Asn Tyr Pro Leu Thr Phe Gly Gly
225 230 235 240

Gly Thr Lys Val Glu Ile Lys
245

<210> 933
<211> 741
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 933
caagtgcaac tcgtccagtc cggtgcagaa gtgaaaaaga gcggagcctc agtgaaagtg 60

tcctgcaagg cctccggtta ccccttcact ggatactaca ttcagtgggt ccgccaagcc 120

ccgggacagg gtctggagtg gatggggtgg attgacccta actcgggaaa tacgggatac 180

gcgcagaagt tccagggccg cgtgaccatg accaggaaca cctcgatcag caccgcctac 240

atggaactgt cctccctgcg gtcggaggat actgccgtgt actactgcgc ctccgattcc 300

tatgggtact actacggaat ggacgtctgg ggacagggca ccctcgtgac cgtgtcctcg 360

ggaggcggag ggagcggcgg gggtggatcg ggaggaggcg gctccggcgg cggcggtagc 420

gacatccaga tgacccagtc accatcaagc cttagcgcct ccgtgggcga cagagtgaca 480

ttcacttgtc gggcgtccca gggaatctcc tccgctctgg cttggtatca gcagaagcct 540

gggaagcctc cgaagctgtt gatctacgac gcgagcagcc tggaatcagg ggtgccctcc 600

cggttttccg ggtccggttc tggcaccgat ttcaccctga ccatttcgtc cctccaaccc 660

gaggacttcg ccacttacta ctgccagcag ttcaacaact acccgctgac cttcggagga 720

ggcactaagg tcgagatcaa g 741

<210> 934
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

polypeptide"

<400> 934
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Ser Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Pro Phe Thr Gly Tyr
20 25 30

Tyr Ile Gln Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Asp Pro Asn Ser Gly Asn Thr Gly Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asn Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Ser Asp Ser Tyr Gly Tyr Tyr Tyr Gly Met Asp Val Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 935
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 935
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Phe Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Ala
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Pro Pro Lys Leu Leu Ile
35 40 45

Tyr Asp Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro

_SL
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Phe Asn Asn Tyr Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 936
<211> 491
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 936
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
20 25 30

Lys Lys Ser Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
35 40 45

Pro Phe Thr Gly Tyr Tyr Ile Gln Trp Val Arg Gln Ala Pro Gly Gln
50 55 60

Gly Leu Glu Trp Met Gly Trp Ile Asp Pro Asn Ser Gly Asn Thr Gly
65 70 75 80

Tyr Ala Gln Lys Phe Gln Gly Arg Val Thr Met Thr Arg Asn Thr Ser
85 90 95

Ile Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Ala Ser Asp Ser Tyr Gly Tyr Tyr Tyr Gly Met
115 120 125

Asp Val Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
130 135 140

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
145 150 155 160

Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val

_SL

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                165                 170                 175

Gly Asp Arg Val Thr Phe Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser
            180                 185                 190

Ala Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Pro Pro Lys Leu Leu
        195                 200                 205

Ile Tyr Asp Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser
    210                 215                 220

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln
225                 230                 235                 240

Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Phe Asn Asn Tyr Pro
                245                 250                 255

Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Thr Thr Thr Pro
            260                 265                 270

Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu
        275                 280                 285

Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His
    290                 295                 300

Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu
305                 310                 315                 320

Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr
                325                 330                 335

Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe
            340                 345                 350

Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg
        355                 360                 365

Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser
    370                 375                 380

Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr
385                 390                 395                 400

Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys
                405                 410                 415
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                                                _SL
Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn
            420                 425                 430

Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu
        435                 440                 445

Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly
    450                 455                 460

His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr
465                 470                 475                 480

Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
                485                 490
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<210> 937
<211> 1473
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 937

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atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg       60

ccccaagtgc aactcgtcca gtccggtgca gaagtgaaaa agagcggagc ctcagtgaaa      120

gtgtcctgca aggcctccgg ttacccttc actggatact acattcagtg ggtccgccaa      180

gccccgggac agggtctgga gtggatgggg tggattgacc ctaactcggg aaatacggga      240

tacgcgcaga agttccaggg ccgcgtgacc atgaccagga acacctcgat cagcaccgcc      300

tacatggaac tgtcctccct gcggtcggag gatactgccg tgtactactg cgcctccgat      360

tcctatgggt actactacgg aatggacgtc tggggacagg gcaccctcgt gaccgtgtcc      420

tcgggaggcg gagggagcgg cgggggtgga tcgggaggag gcggctccgg cggcggcggt      480

agcgacatcc agatgaccca gtcaccatca agccttagcg cctccgtggg cgacagagtg      540

acattcactt gtcgggcgtc ccagggaatc tcctccgctc tggcttggta tcagcagaag      600

cctgggaagc ctccgaagct gttgatctac gacgcgagca gcctggaatc aggggtgccc      660

tcccggtttt ccgggtccgg ttctggcacc gatttcaccc tgaccatttc gtccctccaa      720

cccgaggact tcgccactta ctactgccag cagttcaaca actacccgct gaccttcgga      780

ggaggcacta aggtcgagat caagaccact accccagcac cgaggccacc caccccggct      840

cctaccatcg cctcccagcc tctgtccctg cgtccggagg catgtagacc cgcagctggt      900

ggggccgtgc atacccgggg tcttgacttc gcctgcgata tctacatttg ggcccctctg      960
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gctggtactt gcggggtcct gctgctttca ctcgtgatca ctctttactg taagcgcggt 1020

cggaagaagc tgctgtacat ctttaagcaa cccttcatga ggcctgtgca gactactcaa 1080

gaggaggacg gctgttcatg ccggttccca gaggaggagg aaggcggctg cgaactgcgc 1140

gtgaaattca gccgcagcgc agatgctcca gcctacaagc aggggcagaa ccagctctac 1200

aacgaactca atcttggtcg gagagaggag tacgacgtgc tggacaagcg gagaggacgg 1260

gacccagaaa tgggcgggaa gccgcgcaga aagaatcccc aagagggcct gtacaacgag 1320

ctccaaaagg ataagatggc agaagcctat agcgagattg gtatgaaagg ggaacgcaga 1380

agaggcaaag gccacgacgg actgtaccag ggactcagca ccgccaccaa ggacacctat 1440

gacgctcttc acatgcaggc cctgccgcct cgg 1473

<210> 938
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 938
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Glu Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Pro Tyr Ser Ser Ser Trp His Asp Ala Phe Asp Ile Trp
100 105 110

Gly Gln Gly Thr Met Val Thr Val Ser Ser
115 120

<210> 939

<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 939
Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser
20 25 30

Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45

Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
50 55 60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65 70 75 80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro
85 90 95

Leu Thr Phe Gly Gly Gly Thr Lys Val Asp Ile Lys
100 105

<210> 940
<211> 489
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 940
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
20 25 30

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
35 40 45

Thr Phe Ser Ser Tyr Glu Met Asn Trp Val Arg Gln Ala Pro Gly Lys
50 55 60

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Gly Leu Glu Trp Val Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr
65                  70                  75                  80

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala
                85                  90                  95

Lys Asn Ser Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Arg Asp Pro Tyr Ser Ser Ser Trp His Asp
        115                 120                 125

Ala Phe Asp Ile Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile
145                 150                 155                 160

Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly Glu Arg
                165                 170                 175

Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser Tyr Leu
            180                 185                 190

Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr
        195                 200                 205

Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly Ser
    210                 215                 220

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu
225                 230                 235                 240

Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro Leu Thr
                245                 250                 255

Phe Gly Gly Gly Thr Lys Val Asp Ile Lys Thr Thr Thr Pro Ala Pro
            260                 265                 270

Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu
        275                 280                 285

Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg
    290                 295                 300

Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly
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305 310 315 320

Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys
325 330 335

Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg
340 345 350

Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro
355 360 365

Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser
370 375 380

Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu
385 390 395 400

Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg
405 410 415

Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln
420 425 430

Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr
435 440 445

Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp
450 455 460

Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala
465 470 475 480

Leu His Met Gln Ala Leu Pro Pro Arg
485

<210> 941
<211> 1467
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 941
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaagtgc aactcgtgga aagcggtgga ggtcttgtgc aacctggagg ttccttgcgc 120

ctgtcatgtg cagcttccgg cttcactttc tcctcgtacg agatgaattg ggtgcggcag 180

gcgcctggaa aggggctgga atgggtgtcc tacatctcaa gctccggctc gaccatctac 240

tacgcggaca gcgtgaaggg gcggttcacg atttcgaggg acaacgccaa gaactcgctc 300

tatctgcaaa tgaactccct gagagccgag gacaccgctg tgtattactg cgcccgggac 360

ccctactcct cctcatggca cgacgccttt gatatctggg gccagggaac catggtcacc 420

gtcagcagcg ggggcggagg ttccgggggа gggggctccg gcggaggagg ctccgagatt 480

gtgttgactc agagcccggg taccctgtcg ctgagccccg gagagcgggc cacccttтca 540

tgccgcgcca gccagtccgt gtcctcatcc tacctcgcgt ggtaccagca gaaacctggc 600

caggccccgc ggctgctgat ctacggcgcc tcctcgcgcg caaccggaat ccccgaccgg 660

ttctccgggt ctggcagcgg aaccgacttc actctcacca tttcgaggct ggagccggaa 720

gatttcgccg tgtactactg ccagcagtac ggctcctcgc cactgacttt cggcggagga 780

accaaggtcg atatcaagac cactacccca gcaccgaggc cacccacccc ggctcctacc 840

atcgcctccc agcctctgtc cctgcgtccg gaggcatgta gacccgcagc tggtggggcc 900

gtgcataccc ggggtcttga cttcgcctgc gatatctaca tttgggcccc tctggctggt 960

acttgcgggg tcctgctgct ttcactcgtg atcactcttt actgtaagcg cggtcggaag 1020

aagctgctgt acatctttaa gcaacccttc atgaggcctg tgcagactac tcaagaggag 1080

gacggctgtt catgccggtt cccagaggag gaggaaggcg gctgcgaact gcgcgtgaaa 1140

ttcagccgca gcgcagatgc tccagcctac aagcaggggc agaaccagct ctacaacgaa 1200

ctcaatcttg gtcggagaga ggagtacgac gtgctggaca agcggagagg acgggaccca 1260

gaaatgggcg ggaagccgcg cagaaagaat ccccaagagg gcctgtacaa cgagctccaa 1320

aaggataaga tggcagaagc ctatagcgag attggtatga aaggggaacg cagaagaggc 1380

aaaggccacg acggactgta ccagggactc agcaccgcca ccaaggacac ctatgacgct 1440

cttcacatgc aggccctgcc gcctcgg 1467

<210> 942
<211> 354
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 942
gagcagctga aggagtccgg gggaggtctc ttcaagccaa cggataccct gacactcacc 60

tgcacagtct ctggattctc cctcagttac tatggagtga actgggtccg ccaggctcca 120

gggaacgggc tggaatggat cggaaccatt ggtggtagtg gtgacacata ctacgcgagc 180

tgggcgaaga gccgatccac catcatcaga aacaccaacg agaacacggt gactctgaaa 240

atgaccagtc tgacagccgc ggacacggcc acctatttct gtgtgagata tgctaatatt 300

ggttatgagt actttaacgt ctggggtcca ggcaccctgg tcaccgtctc ttca 354

<210> 943
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 943
Glu Gln Leu Lys Glu Ser Gly Gly Gly Leu Phe Lys Pro Thr Asp Thr
1 5 10 15

Leu Thr Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Ser Tyr Tyr Gly
20 25 30

Val Asn Trp Val Arg Gln Ala Pro Gly Asn Gly Leu Glu Trp Ile Gly
35 40 45

Thr Ile Gly Gly Ser Gly Asp Thr Tyr Tyr Ala Ser Trp Ala Lys Ser
50 55 60

Arg Ser Thr Ile Ile Arg Asn Thr Asn Glu Asn Thr Val Thr Leu Lys
65 70 75 80

Met Thr Ser Leu Thr Ala Ala Asp Thr Ala Thr Tyr Phe Cys Val Arg
85 90 95

Tyr Ala Asn Ile Gly Tyr Glu Tyr Phe Asn Val Trp Gly Pro Gly Thr
100 105 110

Leu Val Thr Val Ser Ser
115

<210> 944
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic oligonucleotide"

<400> 944
ggattctccc tcagttacta tgga 24

<210> 945
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 945
Gly Phe Ser Leu Ser Tyr Tyr Gly
1 5

<210> 946
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic oligonucleotide"

<400> 946
attggtggta gtggtgacac a 21

<210> 947
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 947
Ile Gly Gly Ser Gly Asp Thr
1 5

<210> 948
<211> 39
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic oligonucleotide"

<400> 948
gtgagatatg ctaatattgg ttatgagtac tttaacgtc 39

<210> 949
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 949
Val Arg Tyr Ala Asn Ile Gly Tyr Glu Tyr Phe Asn Val
1 5 10

<210> 950
<211> 333
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 950
cagtttgtgc tgactcagtc gccctctgca tctgctgccc tgggagcctc ggccaagctc 60

acctgcaccc tgagcagtgc ccacaagacc tacaccattg actggtatca gcagcagaaa 120

gggaaggccc ctcgctacct gatacaagtt aagagtgatg gaacctacac caaggcgacc 180

ggggtccctg atcgcttctc gggctccagc tctggggctg accgctacct gatcatcccc 240

agcgtccagg ctgatgacga agccgactac tattgtggta cagattatac cggtgggtat 300

gtgttcggcg gggggaccca gctgaccgtc aca 333

<210> 951
<211> 111
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 951
Gln Phe Val Leu Thr Gln Ser Pro Ser Ala Ser Ala Ala Leu Gly Ala
1 5 10 15

Ser Ala Lys Leu Thr Cys Thr Leu Ser Ser Ala His Lys Thr Tyr Thr
20 25 30

Ile Asp Trp Tyr Gln Gln Gln Lys Gly Lys Ala Pro Arg Tyr Leu Ile
35 40 45

Gln Val Lys Ser Asp Gly Thr Tyr Thr Lys Ala Thr Gly Val Pro Asp
50 55 60

Arg Phe Ser Gly Ser Ser Ser Gly Ala Asp Arg Tyr Leu Ile Ile Pro

_SL
65 70 75 80

Ser Val Gln Ala Asp Asp Glu Ala Asp Tyr Tyr Cys Gly Thr Asp Tyr
85 90 95

Thr Gly Gly Tyr Val Phe Gly Gly Gly Thr Gln Leu Thr Val Thr
100 105 110

<210> 952
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic oligonucleotide"

<400> 952
agtgcccaca agacctacac c 21

<210> 953
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 953
Ser Ala His Lys Thr Tyr Thr
1 5

<210> 954
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic oligonucleotide"

<400> 954
gttaagagtg atggaaccta c 21

<210> 955
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 955
Val Lys Ser Asp Gly Thr Tyr
1 5

<210> 956
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic oligonucleotide"

<400> 956
ggtacagatt ataccggtgg gtatgtg 27

<210> 957
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 957
Gly Thr Asp Tyr Thr Gly Gly Tyr Val
1 5

<210> 958
<211> 744
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 958
ggatccgagc agctgaagga gtccggggga ggtctcttca agccaacgga taccctgaca 60

ctcacctgca cagtctctgg attctccctc agttactatg gagtgaactg ggtccgccag 120

gctccaggga acgggctgga atggatcgga accattggtg gtagtggtga cacatactac 180

gcgagctggg cgaagagccg atccaccatc atcagaaaca ccaacgagaa cacggtgact 240

ctgaaaatga ccagtctgac agccgcggac acggccacct atttctgtgt gagatatgct 300

aatattggtt atgagtactt taacgtctgg ggtccaggca ccctggtcac cgtctcttca 360

ggtggaggcg gttcaggcgg cggtggctct agcggtggtg gatcgcagtt tgtgctgact 420

cagtcgccct ctgcatctgc tgccctggga gcctcggcca agctcacctg caccctgagc 480

agtgcccaca gacctacac cattgactgg tatcagcagc agaaagggaa ggcccctcgc 540

tacctgatac aagttaagag tgatggaacc tacaccaagg cgaccggggt ccctgatcgc 600

ttctcgggct ccagctctgg ggctgaccgc tacctgatca tccccagcgt ccaggctgat 660

gacgaagccg actactattg tggtacagat ataccggtg ggtatgtgtt cggcgggggg 720

acccagctga ccgtcacagc tagc 744

<210> 959
<211> 744
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 959
ggatccgagc agctgaagga gtccggcgga ggcctgttta agcccaccga caccctgaca 60

ctgacctgca cagtgtccgg cttcagcctg agctactatg gcgtgaactg ggtgagacag 120

gcccctggca acggactgga gtggatcggc accattggcg gcagcggaga cacctactac 180

gccagctggg ccaagtccag gagcaccatc atcagaaaca ccaacgagaa caccgtgacc 240

ctgaagatga cctccctgac agccgccgac accgccacct acttctgcgt gaggtacgcc 300

aacatcggct acgagtactt caacgtgtgg ggccctggca ccctggtgac agtgtccagc 360

ggcggaggag gaagcggcgg cggcggctcc agcggaggcg gcagccagtt tgtgctgacc 420

cagagcccta gcgcttccgc cgccctgggc gccagcgcca agctcacctg taccctgagc 480

agcgcccaca agacctatac catcgactgg taccagcagc agaagggcaa ggcccccagg 540

tacctgatcc aggtgaagtc cgacggcacc tacaccaaag ccaccggcgt gcccgacaga 600

tttagcggca gcagctccgg cgccgacagg tatctgatca tcccttccgt gcaggccgac 660

gacgaggccg actactactg cggaaccgac tacaccggcg gatacgtgtt cggaggcggc 720

acccagctga ccgtgaccgc tagc 744

<210> 960
<211> 248
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 960
Gly Ser Glu Gln Leu Lys Glu Ser Gly Gly Gly Leu Phe Lys Pro Thr
1 5 10 15

_SL
Asp Thr Leu Thr Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Ser Tyr
            20   25   30

Tyr Gly Val Asn Trp Val Arg Gln Ala Pro Gly Asn Gly Leu Glu Trp
        35   40   45

Ile Gly Thr Ile Gly Gly Ser Gly Asp Thr Tyr Tyr Ala Ser Trp Ala
    50   55   60

Lys Ser Arg Ser Thr Ile Ile Arg Asn Thr Asn Glu Asn Thr Val Thr
65   70   75   80

Leu Lys Met Thr Ser Leu Thr Ala Ala Asp Thr Ala Thr Tyr Phe Cys
                85   90   95

Val Arg Tyr Ala Asn Ile Gly Tyr Glu Tyr Phe Asn Val Trp Gly Pro
            100   105   110

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115   120   125

Gly Ser Ser Gly Gly Gly Ser Gln Phe Val Leu Thr Gln Ser Pro Ser
    130   135   140

Ala Ser Ala Ala Leu Gly Ala Ser Ala Lys Leu Thr Cys Thr Leu Ser
145   150   155   160

Ser Ala His Lys Thr Tyr Thr Ile Asp Trp Tyr Gln Gln Gln Lys Gly
                165   170   175

Lys Ala Pro Arg Tyr Leu Ile Gln Val Lys Ser Asp Gly Thr Tyr Thr
            180   185   190

Lys Ala Thr Gly Val Pro Asp Arg Phe Ser Gly Ser Ser Ser Gly Ala
        195   200   205

Asp Arg Tyr Leu Ile Ile Pro Ser Val Gln Ala Asp Asp Glu Ala Asp
    210   215   220

Tyr Tyr Cys Gly Thr Asp Tyr Thr Gly Gly Tyr Val Phe Gly Gly Gly
225   230   235   240

Thr Gln Leu Thr Val Thr Ala Ser
                245

<210> 961
<211> 244
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 961

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Glu Gln Leu Lys Glu Ser Gly Gly Gly Leu Phe Lys Pro Thr Asp Thr
1               5                   10                  15

Leu Thr Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Ser Tyr Tyr Gly
            20                  25                  30

Val Asn Trp Val Arg Gln Ala Pro Gly Asn Gly Leu Glu Trp Ile Gly
        35                  40                  45

Thr Ile Gly Gly Ser Gly Asp Thr Tyr Tyr Ala Ser Trp Ala Lys Ser
    50                  55                  60

Arg Ser Thr Ile Ile Arg Asn Thr Asn Glu Asn Thr Val Thr Leu Lys
65                  70                  75                  80

Met Thr Ser Leu Thr Ala Ala Asp Thr Ala Thr Tyr Phe Cys Val Arg
                85                  90                  95

Tyr Ala Asn Ile Gly Tyr Glu Tyr Phe Asn Val Trp Gly Pro Gly Thr
            100                 105                 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125

Ser Gly Gly Gly Ser Gln Phe Val Leu Thr Gln Ser Pro Ser Ala Ser
    130                 135                 140

Ala Ala Leu Gly Ala Ser Ala Lys Leu Thr Cys Thr Leu Ser Ser Ala
145                 150                 155                 160

His Lys Thr Tyr Thr Ile Asp Trp Tyr Gln Gln Gln Lys Gly Lys Ala
                165                 170                 175

Pro Arg Tyr Leu Ile Gln Val Lys Ser Asp Gly Thr Tyr Thr Lys Ala
            180                 185                 190

Thr Gly Val Pro Asp Arg Phe Ser Gly Ser Ser Ser Gly Ala Asp Arg
        195                 200                 205

Tyr Leu Ile Ile Pro Ser Val Gln Ala Asp Asp Glu Ala Asp Tyr Tyr
    210                 215                 220
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Cys Gly Thr Asp Tyr Thr Gly Gly Tyr Val Phe Gly Gly Gly Thr Gln
225 230 235 240

Leu Thr Val Thr

<210> 962
<211> 369
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 962
cagtcagtga aggagtccga gggaggtctc ttcaagccaa cggataccct gacactcacc 60

tgcacggtct ctggattctc cctcagtaga catgcactga cctgggtccg ccaggctcca 120

gggaacgggc tggaatggat cggagccatt gataacgctg gtaccacata ctacgcgagc 180

tgggcgaaaa gccgctccac catcaccaga aacaccgacc tgcacacggt gactctgaaa 240

atgaccagtc tgacagcctc ggacacggct acctatttct gtgcgagagt cttttatgat 300

attaatagtg gttattatct ggacggcatg gacctctggg gcccagggac cctcgtcacc 360

gtctcttca 369

<210> 963
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 963
Gln Ser Val Lys Glu Ser Glu Gly Gly Leu Phe Lys Pro Thr Asp Thr
1 5 10 15

Leu Thr Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Ser Arg His Ala
20 25 30

Leu Thr Trp Val Arg Gln Ala Pro Gly Asn Gly Leu Glu Trp Ile Gly
35 40 45

Ala Ile Asp Asn Ala Gly Thr Thr Tyr Tyr Ala Ser Trp Ala Lys Ser
50 55 60

Arg Ser Thr Ile Thr Arg Asn Thr Asp Leu His Thr Val Thr Leu Lys

_SL
65 70 75 80

Met Thr Ser Leu Thr Ala Ser Asp Thr Ala Thr Tyr Phe Cys Ala Arg
85 90 95

Val Phe Tyr Asp Ile Asn Ser Gly Tyr Tyr Leu Asp Gly Met Asp Leu
100 105 110

Trp Gly Pro Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 964
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic oligonucleotide"

<400> 964
ggattctccc tcagtagaca tgca 24

<210> 965
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 965
Gly Phe Ser Leu Ser Arg His Ala
1 5

<210> 966
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic oligonucleotide"

<400> 966
attgataacg ctggtaccac a 21

<210> 967
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 967
Ile Asp Asn Ala Gly Thr Thr
1 5

<210> 968
<211> 54
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic oligonucleotide"

<400> 968
gcgagagtct tttatgatat taatagtggt tattatctgg acggcatgga cctc 54

<210> 969
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 969
Ala Arg Val Phe Tyr Asp Ile Asn Ser Gly Tyr Tyr Leu Asp Gly Met
1 5 10 15

Asp Leu

<210> 970
<211> 333
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 970
cagtttgtgc tgactcagtc gccctctgtg tctgccgccc tgggagcctc tgccaagctc 60

acctgcaccc tgagcagtgc ccacaagacc tacaccattg actggtatca gcagcagcaa 120

ggggaggccc ctcggtacct gatgcaagtt aagagtgatg gaagctacac caaggggacc 180

ggggtccctg atcgcttctc gggctccagc tctggggctg accgctactt gatcatcccc 240

agcgtccagg ctgatgacga agccggctac gtttgtggtg cagatgataa cggtgggtat 300

gtgttcggcg gagggaccca gctgaccgtc aca 333

<210> 971
<211> 111
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 971
Gln Phe Val Leu Thr Gln Ser Pro Ser Val Ser Ala Ala Leu Gly Ala
1 5 10 15

Ser Ala Lys Leu Thr Cys Thr Leu Ser Ser Ala His Lys Thr Tyr Thr
20 25 30

Ile Asp Trp Tyr Gln Gln Gln Gln Gly Glu Ala Pro Arg Tyr Leu Met
35 40 45

Gln Val Lys Ser Asp Gly Ser Tyr Thr Lys Gly Thr Gly Val Pro Asp
50 55 60

Arg Phe Ser Gly Ser Ser Ser Gly Ala Asp Arg Tyr Leu Ile Ile Pro
65 70 75 80

Ser Val Gln Ala Asp Asp Glu Ala Gly Tyr Val Cys Gly Ala Asp Asp
85 90 95

Asn Gly Gly Tyr Val Phe Gly Gly Gly Thr Gln Leu Thr Val Thr
100 105 110

<210> 972
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic oligonucleotide"

<400> 972
agtgcccaca agacctacac c 21

<210> 973
<211> 7
<212> PRT
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 973
Ser Ala His Lys Thr Tyr Thr
1 5

<210> 974
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic oligonucleotide"

<400> 974
gttaagagtg atggaagcta c 21

<210> 975
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 975
Val Lys Ser Asp Gly Ser Tyr
1 5

<210> 976
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic oligonucleotide"

<400> 976
ggtgcagatg ataacggtgg gtatgtg 27

<210> 977
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 977

_SL
Gly Ala Asp Asp Asn Gly Gly Tyr Val
1 5

<210> 978
<211> 759
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 978
ggatcccagt cagtgaagga gtccgaggga ggtctcttca agccaacgga taccctgaca 60

ctcacctgca cggtctctgg attctccctc agtagacatg cactgacctg ggtccgccag 120

gctccaggga acgggctgga atggatcgga gccattgata acgctggtac cacatactac 180

gcgagctggg cgaaaagccg ctccaccatc accagaaaca ccgacctgca cacggtgact 240

ctgaaaatga ccagtctgac agcctcggac acggctacct atttctgtgc gagagtcttt 300

tatgatatta atagtggtta ttatctggac ggcatggacc tctggggccc agggaccctc 360

gtcaccgtct cttcaggtgg aggcggttca ggcggcggtg gctctagcgg tggtggatcg 420

cagtttgtgc tgactcagtc gccctctgtg tctgccgccc tgggagcctc tgccaagctc 480

acctgcaccc tgagcagtgc ccacaagacc tacaccattg actggtatca gcagcagcaa 540

ggggaggccc ctcggtacct gatgcaagtt aagagtgatg gaagctacac caaggggacc 600

ggggtccctg atcgcttctc gggctccagc tctggggctg accgctactt gatcatcccc 660

agcgtccagg ctgatgacga agccggctac gtttgtggtg cagatgataa cggtgggtat 720

gtgttcggcg gagggaccca gctgaccgtc acagctagc 759

<210> 979
<211> 759
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 979
ggatcccagt ccgtgaagga gagcgagggc ggcctgttca agcccaccga caccctgacc 60

ctgacctgca cagtgagcgg cttcagcctg tccagacacg ccctgacatg ggtgagacag 120

gcccctggca acggcctgga atggatcggc gccatcgaca acgccggcac cacctactac 180

gccagctggg ccaagtccag gtccaccatc accaggaaca ccgacctcca caccgtgacc 240

ctgaagatga caagcctgac cgcctccgac accgccacct acttctgcgc cagggtgttc 300

tacgacatca acagcggcta ctacctggat ggcatggacc tgtggggacc tggcacactg 360

gtgaccgtga gcagcggagg cggcggcagc ggcggcggcg gcagcagcgg cggcggaagc 420

cagttcgtgc tgacacagag ccctagcgtg agcgccgccc tgggagcctc cgctaaactg 480

acctgcaccc tgagcagcgc ccacaagacc tacaccatcg actggtacca acagcagcag 540

ggcgaggccc ccaggtatct gatgcaggtg aagtccgacg gcagctacac caaaggcacc 600

ggcgtgcctg acaggttcag cggcagctcc agcggagccg acaggtacct gatcatcccc 660

tccgtgcagg ccgacgacga ggctggctac gtgtgtggcg ccgacgacaa tggcggctac 720

gtgttcggag gcggcaccca gctgaccgtg acagctagc 759

<210> 980
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 980

Gly	Ser	Gln	Ser	Val	Lys	Glu	Ser	Glu	Gly	Gly	Leu	Phe	Lys	Pro	Thr
1				5				10					15		
Asp	Thr	Leu	Thr	Leu	Thr	Cys	Thr	Val	Ser	Gly	Phe	Ser	Leu	Ser	Arg
			20					25				30			
His	Ala	Leu	Thr	Trp	Val	Arg	Gln	Ala	Pro	Gly	Asn	Gly	Leu	Glu	Trp
		35					40					45			
Ile	Gly	Ala	Ile	Asp	Asn	Ala	Gly	Thr	Thr	Tyr	Tyr	Ala	Ser	Trp	Ala
	50					55					60				
Lys	Ser	Arg	Ser	Thr	Ile	Thr	Arg	Asn	Thr	Asp	Leu	His	Thr	Val	Thr
65					70					75					80
Leu	Lys	Met	Thr	Ser	Leu	Thr	Ala	Ser	Asp	Thr	Ala	Thr	Tyr	Phe	Cys
				85					90					95	
Ala	Arg	Val	Phe	Tyr	Asp	Ile	Asn	Ser	Gly	Tyr	Tyr	Leu	Asp	Gly	Met
			100					105					110		
Asp	Leu	Trp	Gly	Pro	Gly	Thr	Leu	Val	Thr	Val	Ser	Ser	Gly	Gly	Gly
		115					120					125			
Gly	Ser	Gly	Gly	Gly	Gly	Ser	Ser	Gly	Gly	Gly	Ser	Gln	Phe	Val	Leu
	130					135					140				

Thr Gln Ser Pro Ser Val Ser Ala Ala Leu Gly Ala Ser Ala Lys Leu
145 150 155 160

Thr Cys Thr Leu Ser Ser Ala His Lys Thr Tyr Thr Ile Asp Trp Tyr
165 170 175

Gln Gln Gln Gln Gly Glu Ala Pro Arg Tyr Leu Met Gln Val Lys Ser
180 185 190

Asp Gly Ser Tyr Thr Lys Gly Thr Gly Val Pro Asp Arg Phe Ser Gly
195 200 205

Ser Ser Ser Gly Ala Asp Arg Tyr Leu Ile Ile Pro Ser Val Gln Ala
210 215 220

Asp Asp Glu Ala Gly Tyr Val Cys Gly Ala Asp Asp Asn Gly Gly Tyr
225 230 235 240

Val Phe Gly Gly Gly Thr Gln Leu Thr Val Thr Ala Ser
245 250

<210> 981
<211> 249
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 981
Gln Ser Val Lys Glu Ser Glu Gly Gly Leu Phe Lys Pro Thr Asp Thr
1 5 10 15

Leu Thr Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Ser Arg His Ala
20 25 30

Leu Thr Trp Val Arg Gln Ala Pro Gly Asn Gly Leu Glu Trp Ile Gly
35 40 45

Ala Ile Asp Asn Ala Gly Thr Thr Tyr Tyr Ala Ser Trp Ala Lys Ser
50 55 60

Arg Ser Thr Ile Thr Arg Asn Thr Asp Leu His Thr Val Thr Leu Lys
65 70 75 80

Met Thr Ser Leu Thr Ala Ser Asp Thr Ala Thr Tyr Phe Cys Ala Arg
85 90 95

```
Val Phe Tyr Asp Ile Asn Ser Gly Tyr Tyr Leu Asp Gly Met Asp Leu
            100                 105                 110

Trp Gly Pro Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser
        115                 120                 125

Gly Gly Gly Gly Ser Ser Gly Gly Gly Ser Gln Phe Val Leu Thr Gln
    130                 135                 140

Ser Pro Ser Val Ser Ala Ala Leu Gly Ala Ser Ala Lys Leu Thr Cys
145                 150                 155                 160

Thr Leu Ser Ser Ala His Lys Thr Tyr Thr Ile Asp Trp Tyr Gln Gln
                165                 170                 175

Gln Gln Gly Glu Ala Pro Arg Tyr Leu Met Gln Val Lys Ser Asp Gly
            180                 185                 190

Ser Tyr Thr Lys Gly Thr Gly Val Pro Asp Arg Phe Ser Gly Ser Ser
        195                 200                 205

Ser Gly Ala Asp Arg Tyr Leu Ile Ile Pro Ser Val Gln Ala Asp Asp
    210                 215                 220

Glu Ala Gly Tyr Val Cys Gly Ala Asp Asp Asn Gly Gly Tyr Val Phe
225                 230                 235                 240

Gly Gly Gly Thr Gln Leu Thr Val Thr
                245
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<210> 982
<211> 521
<212> DNA
<213> Homo sapiens

<400> 982
accctctct ccagccacta agccagttgc tccctcggct gacggctgca cgcgaggcct 60

ccgaacgtct tacgccttgt ggcgcgcccg tccttgtccc gggtgtgatg gcggggtgtg 120

gggcggaggg cgtggcgggg aagggccggc gacgagagcc gcgcgggacg actcgtcggc 180

gataaccggt gtcgggtagc gccagccgcg cgacggtaac gagggaccgc gacaggcaga 240

cgctcccatg atcactctgc acgccgaagg caaatagtgc aggccgtgcg gcgcttggcg 300

ttccttggaa gggctgaatc cccgcctcgt ccttcgcagc ggccccccgg gtgttcccat 360

cgccgcttct aggcccactg cgacgcttgc ctgcacttct tacacgctct gggtcccagc 420

cgcggcgacg caaagggcct tggtgcgggt ctcgtcggcg cagggacgcg tttgggtccc 480

_SL
gacggaacct tttccgcgtt ggggttgggg caccataagc t 521

<210> 983
<211> 118
<212> DNA
<213> Homo sapiens

<400> 983
acccctctct ccagccacta agccagttgc tccctcggct gacggctgca cgcgaggcct 60

ccgaacgtct tacgccttgt ggcgcgcccg tccttgtccc gggtgtgatg gcggggtg 118

<210> 984
<211> 221
<212> DNA
<213> Homo sapiens

<400> 984
acccctctct ccagccacta agccagttgc tccctcggct gacggctgca cgcgaggcct 60

ccgaacgtct tacgccttgt ggcgcgcccg tccttgtccc gggtgtgatg gcggggtgtg 120

gggcggaggg cgtggcgggg aagggccggc gacgagagcc gcgcgggacg actcgtcggc 180

gataaccggt gtcgggtagc gccagccgcg cgacggtaac g 221

<210> 985
<211> 324
<212> DNA
<213> Homo sapiens

<400> 985
acccctctct ccagccacta agccagttgc tccctcggct gacggctgca cgcgaggcct 60

ccgaacgtct tacgccttgt ggcgcgcccg tccttgtccc gggtgtgatg gcggggtgtg 120

gggcggaggg cgtggcgggg aagggccggc gacgagagcc gcgcgggacg actcgtcggc 180

gataaccggt gtcgggtagc gccagccgcg cgacggtaac gagggaccgc gacaggcaga 240

cgctcccatg atcactctgc acgccgaagg caaatagtgc aggccgtgcg gcgcttggcg 300

ttccttggaa gggctgaatc cccg 324

<210> 986
<211> 422
<212> DNA
<213> Homo sapiens

<400> 986
acccctctct ccagccacta agccagttgc tccctcggct gacggctgca cgcgaggcct 60

ccgaacgtct tacgccttgt ggcgcgcccg tccttgtccc gggtgtgatg gcggggtgtg 120

gggcggaggg cgtggcgggg aagggccggc gacgagagcc gcgcgggacg actcgtcggc 180

gataaccggt gtcgggtagc gccagccgcg cgacggtaac gagggaccgc gacaggcaga 240

cgctcccatg atcactctgc acgccgaagg caaatagtgc aggccgtgcg gcgcttggcg 300

ttccttggaa gggctgaatc cccgcctcgt ccttcgcagc ggccccccgg gtgttcccat 360

cgccgcttct aggcccactg cgacgcttgc ctgcacttct tacacgctct gggtcccagc 420

cg 422