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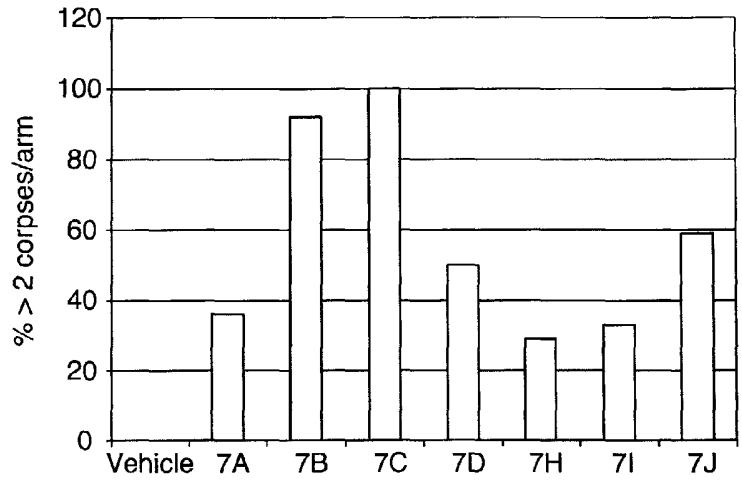
[Continued on next page]

(54) Title: MODULATORS OF RABGGT AND METHODS OF USE THEREOF



(57) Abstract: The present invention provides methods for inducing apoptosis in a cell, the methods generally involving contacting the cell with an agent that reduces the level and/or activity of RabGGT. The present invention further provides methods for treating a disorder related to unwanted cell proliferation in an individual, the methods generally involving administering to the individual an agent that reduces the level and/or activity of RabGGT. The present invention further provides methods for reducing apoptosis in a cell, the methods generally involving increasing the level and/or activity of RabGGT in the cell. The present invention further provides methods for treating disorders associated with excessive apoptosis. The present invention further provides methods for identifying a cell that is amenable to treatment with the methods of the present invention. The present invention further provides methods for modulating a binding event between RabGGT and a RabGGT interacting protein. The present invention further provides a 3-dimensional structure of RabGGT, and methods of use of the structure to identify compounds that modulate RabGGT activity.

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MODULATORS OF RABGGT AND METHODS OF USE THEREOF

[0001] This application claims benefit to provisional application U.S. Serial No. 60/401,604 filed August 7, 2002; and U.S. Serial No. 60/476,722 filed June 6, 2003; under 35 U.S.C. 119(e). The entire teachings of the referenced applications are incorporated herein by reference.

FIELD OF THE INVENTION

[0002] The present invention is in the field of modulators of enzyme activity, in particular modulators of Rab-geranylgeranyl transferase, and their use in controlling cell proliferation.

BACKGROUND OF THE INVENTION

[0003] Apoptosis is a coordinated program for induction of a cell suicide process. Conserved components of the apoptotic pathway such as cytochrome c, the Bcl-2 family, Apaf-1, and the caspases have been identified in most eukaryotic systems. Cytochrome c release from the mitochondria via a permeability transition pore is a key trigger for apoptosis. The Bcl-2 family are highly conserved mitochondrial proteins that can act to enhance (bax, bid, bak, bad, bcl-xs) or prevent (Bcl-2, bcl-xl) apoptosis; they may effect formation of the pore. Apaf-1 is a cytoplasmic protein that is triggered by cytochrome C to activate caspase 9, which then cleaves and activates caspase 3. Caspases are proteases that act in a cascade and cleave multiple substrates, resulting in the morphological changes associated with apoptosis. Examples of changes include chromatin condensation and aggregation to the nuclear margin, cytoplasmic shrinkage, DNA fragmentation, and the packaging of cellular components into membrane bound compartments. Such specific changes distinguish apoptotic death, which may affect single cells in otherwise healthy tissue, from necrosis, in which groups of cells lyse.

[0004] Apoptosis can be activated by a number of intrinsic or extrinsic signals. These signals include the following: mild physical signals, such as ionization radiation, ultraviolet radiation, or hyperthermia; low to medium doses of toxic compounds, such as azides or hydrogen peroxides; chemotherapeutic drugs, such as etoposides and teniposides, cytokines such as tumour necrosis factors and transforming growth factors; infection with human immunodeficiency virus (HIV); and stimulation of T-cell receptors. Various pathological processes, such as hormone deprivation, growth factor deprivation, thermal stress and metabolic stress, induce apoptosis. (Wyllie, A. H., in Bowen and Lockshin (eds.) *Cell Death in Biology and Pathology* (Chapman and Hall, 1981), at 9-34).

[0005] Unregulated apoptosis can cause, or be associated with, disease. An understanding of how apoptosis can be regulated by drugs is becoming of increasing importance to the pharmaceutical industry (Kinloch *et al.*, 1999, Trends in Pharmacological Science 20:35; Nicholson, 2000, Nature 407:810). For example, unregulated apoptosis is involved in diseases such as cancer, heart disease, neurodegenerative disorders, autoimmune disorders, and viral and bacterial infections. Cancer, for example, not only triggers cells to proliferate but also blocks apoptosis. Cancer is partly a failure of apoptosis in the sense that the signal(s) for the cells to kill themselves by apoptosis are blocked. Thus, inducing apoptosis may be a therapeutic strategy for the treatment of cancer.

[0006] In heart disease, damage caused by trauma (e.g, resulting in shock), and cardiac cells can be induced to undergo apoptosis. For example, cells deprived of oxygen after a heart attack release signals that induce apoptosis in cells in the heart. Apoptosis may also be involved in the destruction of neurons in people afflicted by strokes or neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease, and amyotrophic lateral sclerosis (ALS). There is also evidence suggesting that ischemia can kill neurons by inducing apoptosis. It has been shown that neurons that are resistant to apoptosis are also resistant to ischemic damage, thus, inhibition of apoptosis may be a therapeutic strategy for the treatment of neurodegenerative or cardiovascular disorders, e.g., stroke.

[0007] Rab-geranylgeranyl transferase (RabGGT; GGTII) is a protein-prenyl transferase enzyme composed of a single alpha and beta subunit. These subunits have limited homology to the alpha subunit shared by Farnesyl transferase (FT) and geranylgeranyl transferase I (GGTI), and to the beta subunits that are distinct to each of those enzymes. RabGGT is unique among prenlyation enzymes in requiring specific accessory proteins known as Rab escort proteins (REPs) for their prenylation function. However the three prenylating enzymes are similar in the structure of their active sites and in their mechanism of substrate modification. The only RabGGT substrates identified to date are a large family of Ras-related proteins called Rabs. Rab proteins are monomeric GTPases that regulate intracellular membrane traffic. RabGGT acts on the Rab proteins to attach a geranylgeranyl moiety to one or two cysteine residues at the C-terminus of the protein. This prenylation event is important for the subcellular targeting of Rabs to membranes.

[0008] There is an ongoing need in the art for agents and methods of modulating cell proliferation. The present invention addresses this need.

Literature

[0009] Hengartner (2000) *Nature* 407:770; Long et al. (2002) *Nature* 419:645; Seabra *et al.*, 2002, Trends in Molecular Medicine 8:23; Detter *et al.*, 2000, Proc. Natl. Acad. Sci. USA 97:4144; Ren *et al.*, 1997, Biochem. Pharmacol. 54:113; J.C. Reed, *Nature Reviews Drug Discovery*:1 pp111-121; Kinloch *et al.*, 1999, Trends in Pharmacological Science 20:35; Nicholson (2000) *Nature* 407:810; Thoma et al. (2000) *Biochem.* 39:12043-12052; Coxon et al. (2001) *J. Biol. Chem.* 276:48213-48222; Rose et al. (2001) *Cancer Res.* 61:7505-7517; Hunt et al. (2000) *J. Med. Chem.* 43:3587; Pylypenko et al. (2003) *Molec. Cell* 11:483-494.

SUMMARY OF THE INVENTION

[0010] The present invention provides methods for inducing apoptosis in a cell, the methods generally involving contacting the cell with an agent that reduces the level and/or activity of RabGGT. The present invention further provides methods for treating a disorder related to unwanted cell proliferation in an individual, the methods generally involving administering to the individual an agent that reduces the level and/or activity of RabGGT. The present invention further provides methods for reducing apoptosis in a cell, the methods generally involving increasing the level and/or activity of RabGGT in the cell. The present invention further provides methods for treating disorders associated with excessive apoptosis. The present invention further provides methods for identifying a cell that is amenable to treatment with the methods of the present invention. The present invention further provides methods for modulating a binding event between RabGGT and a RabGGT interacting protein. The present invention further provides a 3-dimensional structure of RabGGT, and methods of use of the structure to identify compounds that modulate RabGGT activity.

[0011] The invention also provides a computer for producing a three-dimensional representation of a molecule or molecular complex, wherein said molecule or molecular complex comprises the structural coorrdinates of the model RabGGT alpha or beta subunit in accordance with Table 11 or 12, or a three-dimensional representation of a homologue of said molecule or molecular complex, wherein said homologue comprises backbone atoms that have a root mean square deviation from the backbone atoms of not more than about 4.0, 3.0. 2.0, 1.0, 0.9, 0.8, 0.7, 0.6, 0.5, 0.4, 0.3, 0.2, or 0.1 Angstroms, wherein said computer comprises: A machine-readable data storage medium, comprising a data storage material encoded with machine readable data, wherein the data is defined by the set of structure coordinates of the model RabGGT alpha or beta subunit according to Table 11 or 12, or a homologue of said model, wherein said homologue comprises backbone atoms that have a root mean square

deviation from the backbone atoms of not more than about 4.0, 3.0. 2.0, 1.0, 0.9, 0.8, 0.7, 0.6, 0.5, 0.4, 0.3, 0.2, or 0.1 Angstroms; a working memory for storing instructions for processing said machine-readable data; a central-processing unit coupled to said working memory and to said machine-readable data storage medium for processing said machine readable data into said three-dimensional representation; and a display coupled to said central-processing unit for displaying said three-dimensional representation.

[0012] The invention also provides a machine readable storage medium which comprises the structure coordinates of RabGGT alpha or beta subunit, including all or any parts of conserved binding site regions. Such storage medium encoded with these data are capable of displaying on a computer screen or similar viewing device, a three-dimensional graphical representation of a molecule or molecular complex which comprises said regions or similarly shaped homologous regions.

[0013] The invention also provides methods for designing, evaluating and identifying compounds which bind to all or parts of the aforementioned regions. The methods include three dimensional model building (homology modeling) and methods of computer assisted-drug design which can be used to identify compounds which bind or modulate the forementioned regions of the RabGGT alpha or beta subunit polypeptide. Such compounds are potential inhibitors of RabGGT alpha or beta subunit or its homologues.

[0014] The invention also provides a machine-readable data storage medium, comprising a data storage material encoded with machine readable data, wherein the data is defined by the structure coordinates of the model RabGGT alpha or beta subunit according to Table 11 or 12 or a homologue of said model, wherein said homologue comprises any kind of surrogate atoms that have a root mean square deviation from the backbone atoms of the complex of not more than about 4.0, 3.0. 2.0, 1.0, 0.9, 0.8, 0.7, 0.6, 0.5, 0.4, 0.3, 0.2, 0.1, or less Angstroms.

[0015] The invention also provides a machine-readable data storage medium, comprising a data storage material encoded with machine readable data, wherein the data is defined by the structure coordinates of the model RabGGT alpha or beta subunit according to Table 11 or 12 or a homologue of said model, wherein said homologue comprises any kind of surrogate atoms that have a root mean square deviation from the backbone atoms of the complex of not more than about 4.0, 3.0. 2.0, 1.0, 0.9, 0.8, 0.7, 0.6, 0.5, 0.4, 0.3, 0.2, 0.1, or less Angstroms

[0016] The invention also provides a model comprising all or any part of the model defined by structure coordinates of RabGGT alpha or beta subunit according to Table 11 or 12, or a mutant or homologue of said molecule or molecular complex.

[0017] The invention also provides a method for identifying a mutant of RabGGT alpha or beta subunit with altered biological properties, function, or reactivity, the method comprising one or more of the following steps:

(a) use of the model or a homologue of said model according to Table 11 or 12, for the design of protein mutants with altered biological function or properties which exhibit any combination of therapeutic effects described herein; and/or (b) use of the model or a homologue of said model, for the design of a protein with mutations in the active site region according to Table 11 or 12 with altered biological function or properties which exhibit any combination of therapeutic effects described herein.

[0018] The method also relates to a method for identifying modulators of RabGGT alpha or beta subunit biological properties, function, or reactivity, the method comprising the step of modeling test compounds that fit spatially into the active site region defined by all or any portion of residues that embody this domain within the three-dimensional structural model according to Table 11 or 12, or using a homologue or portion thereof, or analogue in which the original C, N, and O atoms have been replaced with other elements

[0019] The invention also provides methods for designing, evaluating and identifying compounds which bind to all or parts of the aforementioned regions. The methods include three dimensional model building (homology modeling) and methods of computer assisted-drug design which can be used to identify compounds which bind or modulate the forementioned regions of the RabGGT alpha or beta subunit polypeptide. Such compounds are potential inhibitors of RabGGT alpha or beta subunit or its homologues.

[0020] The invention also relates to a method of using said structure coordinates as set forth in Table 11 or 12 to identify structural and chemical features of RabGGT alpha or beta subunit; employing identified structural or chemical features to design or select compounds as potential RabGGT alpha or beta subunit modulators; employing the three-dimensional structural model to design or select compounds as potential RabGGT alpha or beta subunit modulators; synthesizing the potential RabGGT alpha or beta subunit modulators; screening the potential RabGGT alpha or beta subunit modulators in an assay characterized by binding of a protein to the RabGGT alpha or beta subunit. The invention also relates to said method wherein the potential RabGGT alpha or beta subunit modulator is selected from a database. The invention further relates to said method wherein the potential RabGGT alpha or beta subunit modulator is designed de novo. The invention further relates to a method wherein the potential RabGGT alpha or beta subunit modulator is designed from a known modulator of activity.

BRIEF DESCRIPTION OF THE DRAWINGS

[0021] FIG. 1 provides a graphical display of data on the effects of compound treatments upon levels of apoptosis in the worm germline (The percentage of germline arms examined that contained greater than 2 apoptotic corpses is displayed. Compound treatments are shown on the X axis);

[0022] FIG. 2 provides a graphical display of data on the effects of compound treatments upon levels of apoptosis in the germline of apoptosis-defective mutant worms (Average number of apoptotic corpses per germline arm in worms treated with compound 7B or vehicle. Worm genotype is displayed on the X-axis. The error bars shown standard deviation.);

[0023] FIG. 3 provides a graphical display of data on the effects of RNAi treatments against RabGGT subunits upon levels of apoptosis in the worm germline (The percentage of germline arms that contained greater than 2 apoptotic corpses is displayed. RNAi treatments are shown on the X axis.);

[0024] FIG. 4 provides a graphical display of data on the effects of treatment with compound and/or RNAi against RabGGT subunit alpha upon levels of apoptosis in the worm germline (The percentage of germline arms examined that contained either less than three, three or four, or greater than four apoptotic corpses is displayed. Treatments are shown on the X axis.);

[0025] FIG. 5 provides a graphical display of data on the effects of treatment with RNAi against RabGGT alpha subunit upon levels of apoptosis in the germline of Wild Type or compound 7B-resistant mutant worms (The percentage of germline arms in wild-type or mutant worms that contained greater than two apoptotic corpses is displayed. Treatments are shown on the X axis.);

[0026] FIG. 6 provides a graphical display of data on the effects of treatment with RNAi against RabGGT subunits upon levels of proliferation in human cells (3H-uptake by HCT116 cells as percentage of control treatment. Treatments are shown on the X-axis.);

[0027] FIG. 7 provides a graphical display of results obtained by non-linear regression analysis of data obtained for compound 7B in a RabGGT inhibition assay (Results obtained by non-linear regression analysis of data obtained for compound 7B.);

[0028] FIG. 8a provides a graphical display of the data on RabGGT inhibition and apoptotic activity for the benzodiazepine class of compounds (Data from the benzodiazepine class of compounds: The IC90 for RabGGT inhibition in nanomoles is shown on the Y axis and the minimum concentration required for induce 50% apoptosis in an HCT116 cell culture is shown on the X axis.);

[0029] FIG. 8b provides a graphical display of the data on RabGGT inhibition and apoptotic activity for the tetrahydroquinolone class of compounds (Data from the tetrahydroquinolone class of compounds: The IC90 for RabGGT inhibition in nanomoles is shown on the Y axis and the minimum concentration required for induce 50% apoptosis in an HCT116 cell culture is shown on the X axis.);

[0030] FIG. 8c provides a graphical display of data on RabGGT inhibition and apoptotic activity for compounds 7A-7Q (Data from compounds 7A through 7Q. Compounds 7R, 7S, and 7T are represented in Fig. 9b, and have been omitted from this figure for graphical clarity rather than because they alter the trend of the observations. The IC90 for RabGGT inhibition in nanomoles is shown on the Y axis and the minimum concentration required for induce 50% apoptosis in an HCT116 cell culture is shown on the X axis.);

[0031] FIG. 9 provides a graphical display of data on FT inhibition and apoptotic activity for compounds 7A-7T (Data for compounds 7A through 7T. The IC50 for FT inhibition in nanomoles is shown on the Y axis and the minimum concentration required for induce 50% apoptosis in an HCT116 cell culture is shown on the X axis.);

[0032] FIG. 10 provides a superposition of the homology model of the *H. sapiens* RabGGT protein on the crystal structure of the rat RabGGT protein (Superposition of the homology model of the human RabGGT protein (dark) on the crystal of the rat RabGGT protein. The atom of zinc found in the binding site of the rat protein is shown as a white sphere.);

[0033] FIG. 11a provides free energy plots for the modeled human RabGGT alpha subunit and for the crystal structure of the rat RabGGT alpha subunit (Energy plots for the model of *H. sapiens* RabGGT alpha chain (dotted line), and for the crystal structure of the *R. norvegicus* RabGGT alpha chain (solid line)).

[0034] FIG. 11b provides free energy plots for the modeled human RabGGT beta subunit and for the crystal structure of the rat RabGGT beta subunit (Energy plots for the model of *H. sapiens* RabGGT beta chain (dotted line), and for crystal structure of the *R. norvegicus* RabGGT beta chain (solid line)).

[0035] FIG. 12 provides a superposition of the homology model of the *C.elegans* RabGGT protein on the crystal structure of the rat RabGGT protein (Superposition of the homology model of the *C. elegans* RabGGT protein (dark) on the crystal of the rat RabGGT protein. The atom of zinc found in the binding site of the rat protein is shown as a white sphere.);

[0036] FIG. 13a provides free energy plots for the modeled *C. elegans* RabGGT alpha subunit and for the crystal structure of the rat RabGGT alpha subunit (Energy plots for the model of *C.*

elegans RabGGT alpha chain (dotted line), and for the crystal structure of the *R. norvegicus* RabGGT alpha chain (solid line)).

[0037] FIG. 13b provides free energy plots for the modeled *C. elegans* RabGGT beta subunit and for the crystal structure of the rat RabGGT beta subunit (Energy plots for the model of *C. elegans* RabGGT beta chain (dotted line), and for the crystal structure of the *R. norvegicus* RabGGT beta chain (solid line)).

[0038] FIG. 14a provides a depiction of the binding site in the crystal structure of the rat RabGGT enzyme (Binding pocket from the crystal structure of rat RabGGT. The white sphere denotes the bound atom of zinc.);

[0039] FIG. 14b provides a depiction of the superimposition of the binding site in the crystal structure of the rat RabGGT enzyme upon the binding site in the model of the human RabGGT enzyme (Superposition of the residues within 5 Angstrom of the binding site in the homology model of the *H. sapiens* RabGGT protein (dark) on the crystal structure of the homologous residues of the rat protein. The atom of zinc found in the binding site of the rat protein is shown as a white sphere.);

[0040] FIG. 14c provides a depiction of the superimposition of the binding site in the crystal structure of the rat RabGGT enzyme upon the binding site in the model of the *C. elegans* RabGGT enzyme (Superposition of the residues within 5 Angstrom of the binding site in the homology model of the *C. elegans* RabGGT protein (dark) on the crystal structure of the homologous residues of the rat protein. The atom of zinc found in the binding site of the rat protein is shown as a white sphere).

[0041] FIG. 15A depicts binding of compound 7H docked into the putative binding site of RabGGT.

[0042] FIG. 15B depicts the binding site of the crystal structure of the complex between farnesyl transferase and the FT inhibitor U66.

[0043] FIG. 16A-B show the polynucleotide sequence (SEQ ID NO:15) and deduced amino acid sequence (SEQ ID NO:16) of the human RabGGT alpha subunit. The standard one-letter abbreviation for amino acids is used to illustrate the deduced amino acid sequence.

[0044] FIG. 17 show the polynucleotide sequence (SEQ ID NO:17) and deduced amino acid sequence (SEQ ID NO:18) of the human RabGGT beta subunit. The standard one-letter abbreviation for amino acids is used to illustrate the deduced amino acid sequence.

DEFINITIONS

[0045] As used herein, the term "disorder associated with undesired or uncontrolled cell proliferation" is any disorder that results from undesired or uncontrolled cell proliferation, and/or that is amenable to treatment by inducing apoptosis in the cell, such disorders including, but not limited to, cancer, viral infection, disorders associated with excessive or unwanted angiogenesis, and the like.

[0046] As used herein, the term "disorder associated with excessive apoptosis" is any disorder that results from an excessive amount of apoptosis, such disorders including, but not limited to, sepsis, atherosclerosis, muscle cachexia, ischemia/reperfusion injury, neurodegenerative disorders, and myocardial infarction.

[0047] As used herein, the terms "treatment", "treating", and the like, refer to obtaining a desired pharmacologic and/or physiologic effect. The effect may be prophylactic in terms of completely or partially preventing a disease or symptom thereof and/or may be therapeutic in terms of a partial or complete cure for a disease and/or adverse affect attributable to the disease. "Treatment", as used herein, covers any treatment of a disease in a mammal, particularly in a human, and includes: (a) preventing the disease from occurring in a subject which may be predisposed to the disease but has not yet been diagnosed as having it; (b) inhibiting the disease, i.e., arresting its development; and (c) relieving the disease, e.g., causing regression of the disease, *e.g.*, to completely or partially remove symptoms of the disease.

[0048] The term "biological sample" encompasses a variety of sample types obtained from an organism and can be used in a diagnostic or monitoring assay. The term encompasses blood and other liquid samples of biological origin, solid tissue samples, such as a biopsy specimen or tissue cultures or cells derived therefrom and the progeny thereof. The term encompasses samples that have been manipulated in any way after their procurement, such as by treatment with reagents, solubilization, or enrichment for certain components. The term encompasses a clinical sample, and also includes cells in cell culture, cell supernatants, cell lysates, serum, plasma, biological fluids, and tissue samples.

[0049] The terms "cancer", "neoplasm", "tumor", and "carcinoma", are used interchangeably herein to refer to cells which exhibit relatively autonomous growth, so that they exhibit an aberrant growth phenotype characterized by a significant loss of control of cell proliferation. Cancerous cells can be benign or malignant.

[0050] By "individual" or "host" or "subject" or "patient" is meant any mammalian subject for whom diagnosis, treatment, or therapy is desired, particularly humans. Other subjects may include cattle, dogs, cats, guinea pigs, rabbits, rats, mice, horses, and so on.

[0051] The term "binds specifically," in the context of antibody binding, refers to high avidity and/or high affinity binding of an antibody to a specific polypeptide i.e., epitope of a polypeptide, e.g., RabGGT. For example, antibody binding to an epitope on a specific RabGGT polypeptide or fragment thereof is stronger than binding of the same antibody to any other epitope, particularly those which may be present in molecules in association with, or in the same sample, as the specific polypeptide of interest, e.g., binds more strongly to a specific RabGGT epitope than to a different RabGGT epitope so that by adjusting binding conditions the antibody binds almost exclusively to the specific RabGGT epitope and not to any other RabGGT epitope, and not to any other RabGGT polypeptide (or fragment) or any other polypeptide which does not comprise the epitope. Antibodies which bind specifically to a polypeptide may be capable of binding other polypeptides at a weak, yet detectable, level (e.g., 10% or less of the binding shown to the polypeptide of interest). Such weak binding, or background binding, is readily discernible from the specific antibody binding to a subject polypeptide, e.g. by use of appropriate controls. In general, specific antibodies bind to a given polypeptide with a binding affinity of 10^{-7} M or more, e.g., 10^{-8} M or more (e.g., 10^{-9} M, 10^{-10} M, 10^{-11} M, etc.). In general, an antibody with a binding affinity of 10^{-6} M or less is not useful in that it will not bind an antigen at a detectable level using conventional methodology currently used.

[0052] Before the present invention is further described, it is to be understood that this invention is not limited to particular embodiments described, as such may, of course, vary. It is also to be understood that the terminology used herein is for the purpose of describing particular embodiments only, and is not intended to be limiting, since the scope of the present invention will be limited only by the appended claims.

[0053] Where a range of values is provided, it is understood that each intervening value, to the tenth of the unit of the lower limit unless the context clearly dictates otherwise, between the upper and lower limit of that range and any other stated or intervening value in that stated range, is encompassed within the invention. The upper and lower limits of these smaller ranges may independently be included in the smaller ranges, and are also encompassed within the invention, subject to any specifically excluded limit in the stated range. Where the stated range includes one or both of the limits, ranges excluding either or both of those included limits are also included in the invention.

[0054] 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 this invention belongs. Although any methods and materials similar or equivalent to those described herein

can also be used in the practice or testing of the present invention, the preferred methods and materials are now described. All publications mentioned herein are incorporated herein by reference to disclose and describe the methods and/or materials in connection with which the publications are cited.

0055] It must be noted that as used herein and in the appended claims, the singular forms "a", "and", and "the" include plural referents unless the context clearly dictates otherwise. Thus, for example, reference to "an agent" includes a plurality of such agents and reference to "the inhibitor" includes reference to one or more inhibitors and equivalents thereof known to those skilled in the art, and so forth.

0056] The publications discussed herein are provided solely for their disclosure prior to the filing date of the present application. Nothing herein is to be construed as an admission that the present invention is not entitled to antedate such publication by virtue of prior invention. Further, the dates of publication provided may be different from the actual publication dates which may need to be independently confirmed.

DETAILED DESCRIPTION OF THE INVENTION

[0057] The present invention provides methods for inducing apoptosis in a cell, the methods generally involving contacting the cell with an agent that reduces the level and/or activity of RabGGT. The present invention further provides methods for treating a disorder related to unwanted cell proliferation in an individual, the methods generally involving administering to the individual an agent that reduces the level and/or activity of RabGGT. The present invention further provides methods for reducing apoptosis in a cell, the methods generally involving increasing the level and/or activity of RabGGT in the cell. The present invention further provides methods for treating disorders associated with excessive apoptosis. The present invention further provides methods for identifying a cell that is amenable to treatment with the methods of the present invention. The present invention further provides methods for modulating a binding event between RabGGT and a RabGGT interacting protein. The present invention further provides a 3-dimensional structure of RabGGT, and methods of use of the structure to identify compounds that bind specifically to RabGGT.

[0058] The present invention is based in part on the observation that inhibitors of RabG GT levels and/or activity induce apoptosis and reduce cell proliferation. As discussed in the Examples section, inhibitors of RabGGT induced tumor regression in a human tumor xenograft model, and induced apoptosis of cells expressing RabGGT in cell cultures *in vitro* and *in vivo*.

TREATMENT METHODS

[0059] In some embodiments, the invention provides methods for inducing apoptosis in a cell and/or inhibiting proliferation of the cell. The methods generally involve contacting a cell with an effective amount of an agent that inhibits a level and/or activity of RabGGT or a RabGGT/REP complex. The invention also provides methods of treating a disorder amenable to treatment by inducing apoptosis and/or inhibiting cell proliferation, the methods generally involving administering an effective amount of an agent that inhibits a level and/or activity of RabGGT or a RabGGT/REP complex in a cell in the individual.

[0060] As used herein, the term "RabGGT" refers to a protein that includes a RabGGT α subunit and a RabGGT β subunit. As used herein, an "agent that reduces the level of a RabGGT protein" includes an agent that reduces the level of a RabGGT α subunit (and does not reduce the level of a RabGGT β subunit), an agent that reduces the level of a RabGGT β subunit (and does not reduce the level of a RabGGT β subunit), and an agent that reduces the level of both a RabGGT α subunit and a RabGGT β subunit. As used herein, an "agent that reduces the level of a RabGGT mRNA" includes an agent that reduces the level of an mRNA encoding a RabGGT α subunit (and does not reduce the level of an mRNA encoding a RabGGT β subunit), an agent that reduces the level of an mRNA encoding a RabGGT β subunit (and does not reduce the level of an mRNA encoding a RabGGT β subunit), and an agent that reduces the level of both an mRNA encoding a RabGGT α subunit and an mRNA encoding a RabGGT β subunit.

[0061] An "effective amount" of an agent that inhibits a level and/or activity of RabGGT is an amount that reduces a level of RabGGT mRNA and/or protein and/or is an amount that reduces an activity of a RabGGT protein by at least about 5%, at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 55%, at least about 60%, at least about 65%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, or at least about 90%, or more, when compare to the level or activity in the absence of the agent.

[0062] In other embodiments, the invention provides methods for reducing apoptosis in a cell. The methods generally involve contacting a cell with an effective amount of an agent that increases a level and/or activity of RabGGT or a RabGGT/REP complex. The invention also provides methods of treating a disorder amenable to treatment by reducing apoptosis, the methods generally involving administering an effective amount of an agent the increases a level and/or activity or RabGGT or a RabGGT/REP complex in a cell in the individual.

[0063] An "effective amount" of an agent that increases a level and/or activity of RabGGT is an amount that increases a level of RabGGT mRNA and/or protein and/or is an amount that increases an activity of a RabGGT protein by at least about 5%, at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 55%, at least about 60%, at least about 65%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, or at least about 90%, or more, when compared to the level or activity in the absence of the agent.

[0064] In some embodiments, the invention provides a method of inducing apoptosis in a eukaryotic cell, wherein the method generally involves identifying a compound that is a RabGGT inhibitor; testing the ability of the compound to modulate farnesyl transferase (FT) activity; modifying the compound, wherein the modified compound exhibits reduced modulation of FT activity compared to the unmodified compound, wherein inhibition of RabGGT is retained; and contacting the cell with the modified compound.

RabGGT Modulating Agents

[0065] As noted above, in some methods of the present invention, agents that reduce a level and/or activity of RabGGT are used. In other methods of the present invention, agents that increase a level and/or activity of RabGGT are used. Agents that reduce or increase a level and/or activity of RabGGT are referred to herein as "RabGGT modulators" or "RabGGT modulating agents" and include small molecule modulators, protein (or peptide) modulators, antibody modulators, and nucleic acid modulators. The RabGGT modulating agents are typically "specific" in their interaction with RabGGT, as that term is understand in the art.

[0066] Agents that reduce a level and/or activity of RabGGT include agents that reduce the protein prenyl transferase activity of RabGGT protein; agents that reduce an interaction between RabGGT and an interacting protein, where RabGGT interacting proteins include a Rab protein, an accessory protein (e.g., a REP), and a protein that binds to a Rab/RabGGT complex; agents that reduce the level of RabGGT mRNA in a cell; agents that reduce , but are not limited to, small molecule inhibitors of RabGGT enzymatic activity; antibodies specific for RabGGT; antisense RNA specific for RabGGT; interfering RNA (RNAi) specific for RabGGT; ribozymes specific for RabGGT; and the like.

[0067] In some embodiments, an agent that reduces a level and/or activity of RabGGT does not substantially reduce a level or activity of other proteins or mRNA, including farnesyl transferase, e.g., the agent reduces the level or activity of another protein or mRNA by less

than about 10%, less than about 5%, less than about 2%, or less than about 1%, compared to the activity or level of the protein or mRNA in the absence of the agent.

[0068] In some embodiments, agents that reduce a level and/or activity of a RabGGT/REP complex are used in a therapeutic method of the present invention. A RabGGT/REP complex includes RabGGT α and β subunits, and a Rab escort protein (REP) (e.g., REP-1, REP-2).

[0069] A RabGGT α subunit includes a protein having an amino acid sequence as set forth in SWISS-PROT Accession No. Q92696 (Genomics 38 (2), 133-140 (1996)), and homologs, analogs, and derivatives thereof, e.g., derivatives having one or more conservative amino acid substitutions. A RabGGT β subunit includes a protein having an amino acid sequence as set forth in SWISS-PROT Accession No. P53611 (Genomics 38 (2), 133-140 (1996)), and homologs, analogs, and derivatives thereof, e.g., derivatives having one or more conservative amino acid substitutions. A REP protein includes a protein having an amino acid sequence as set forth in GenBank Accession No. P24386 or P26374, and homologs, analogs, and derivatives thereof, e.g., derivatives having one or more conservative amino acid substitutions. Homologs include proteins that have from 1 to about 20 amino acid differences from a reference sequence. In general, homologs retain at least about 80%, or at least about 90% or more, of at least one activity of a protein having a reference sequence.

[0070] In some embodiments, an agent that reduces a level and/or activity of a RabGGT/REP complex does not substantially reduce a level or activity of other proteins or mRNA, including farnesyl transferase, e.g., the agent reduces the level or activity of another protein or mRNA by less than about 10%, less than about 5%, less than about 2%, or less than about 1%, compared to the activity or level of the protein or mRNA in the absence of the agent.

Biological modulators

[0071] Modulators suitable for use herein modulate a level and/or an activity of RabGGT or a RabGGT/REP complex. A suitable modulator exhibits one or more of the following activities: 1) modulates an enzymatic activity of RabGGT or a RabGGT/REP complex; 2) modulates a level of a RabGGT protein (α and/or β subunit) or the level of a RabGGT/REP protein complex; 3) modulates the level of an mRNA that encodes a RabGGT protein (α and/or β subunit), or an mRNA that encodes a REP protein; 4) modulates the level of apoptosis in a cell; and 5) modulates a binding event between a RabGGT protein and a protein that interacts with a RabGGT protein.

Modulating enzymatic activity

0072] In some embodiments, a RabGGT modulating agent modulates the protein prenyl transferase activity of RabGGT protein. In some of these embodiments, an agent increases the enzymatic activity of a RabGGT protein by at least about 5%, at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 55%, at least about 60%, at least about 65%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, or at least about 90%, or more, when compared to the enzymatic activity of the RabGGT protein in the absence of the agent.

[0073] In other embodiments, an agent reduces the enzymatic activity of a RabGGT protein by at least about 5%, at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 55%, at least about 60%, at least about 65%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, or at least about 90%, or more, when compared to the enzymatic activity of the RabGGT protein in the absence of the agent.

[0074] In some embodiments, an agent that reduces the activity of RabGGT inhibits the activity of a RabGGT/REP complex. A suitable agent reduces the level and/or activity of a RabGGT/REP complex by at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 40%, at least about 50%, at least about 60%, at least about 70%, at least about 80%, or at least about 90% or more, compared to the level or activity of the RabGGT/REP complex in the absence of the agent.

[0075] In many embodiments, an agent that reduces RabGGT enzymatic activity has an IC_{50} of less than 0.5 mM. Generally, a suitable agent that reduces RabGGT enzymatic activity has an IC_{50} of from about 0.5 nM to about 500 μM, e.g., from about 0.5 nM to about 1 nM, from about 1 nM to about 5 nM, from about 5 nM to about 10 nM, from 10 nM to about 25 nM, from about 25 nM to about 50 nM, from about 50 nM to about 100 nM, from about 100 nM to about 250 nM, from about 250 nM to about 500 nM, from about 500 nM to about 1 μM, from about 1 μM to about 5 μM, from about 5 μM to about 10 μM, from about 10 μM to about 25 μM, from about 25 μM to about 50 μM, from about 50 μM to about 100 μM, from about 100 μM to about 250 μM, or from about 250 μM to about 500 μM.

[0076] Whether a given agent modulates a level and/or activity of RabGGT can be determined using any known method. For example, RabGGT enzymatic activity is quantified using a filter binding assay that measures the transfer of (^{3}H) geranylgeranyl groups (GG) from all-trans-(^{3}H)geranylgeranyl pyrophosphate (^{3}H-GGPP) to recombinant Rab3A protein (Shen and

Seabra (1996) *J. Biol. Chem.* 271:3692; Armstrong *et al.* (1996) *Methods in Enzymology* 257:30), or as described in the Examples.

Protein level

[0077] In some embodiments, an agent modulates a level of RabGGT protein in a cell. In some of the embodiments, an agent increases the level of a RabGGT protein in a cell by at least about 5%, at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 55%, at least about 60%, at least about 65%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, or at least about 90%, or more, when compared to the level in a control cell in the absence of the agent.

[0078] In other embodiments, an agent decreases the level of a RabGGT protein in a cell by at least about 5%, at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 55%, at least about 60%, at least about 65%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, or at least about 90%, or more, when compared to the level in a control cell in the absence of the agent.

[0079] The level of RabGGT protein in a cell can be determined using a standard, well-known immunological assay, e.g., an enzyme-linked immunosorbent assay, a protein blot assay, a radioimmunoassay, and the like, using antibody specific for RabGGT, which antibody is directly or indirectly labeled.

[0080] Direct and indirect antibody labels are known in the art. An antibody may be labeled with a radioisotope, an enzyme, a fluorescer (e.g., a fluorescent protein or a fluorescent dye), a chemiluminescer, or other label for direct detection. Alternatively, a second stage antibody or reagent is used to amplify the signal. Such reagents are well known in the art. For example, the primary antibody may be conjugated to biotin, with horseradish peroxidase-conjugated avidin added as a second stage reagent. Final detection uses a substrate that undergoes a color change in the presence of the peroxidase. Alternatively, the secondary antibody conjugated to a fluorescent compound, *e.g.* fluorescein, rhodamine, Texas red, *etc.* The absence or presence of antibody binding may be determined by various methods, including flow cytometry of dissociated cells, microscopy, radiography, scintillation counting, *etc.*

[0081] Fluorescent proteins include, but are not limited to, a green fluorescent protein (GFP), e.g., a GFP derived from *Aequoria victoria* or a derivative thereof; a GFP from another species such as *Renilla reniformis, Renilla mulleri,* or *Ptilosarcus guernyi*, as described in, e.g., WO

99/49019 and Peelle et al. (2001) *J. Protein Chem.* 20:507-519; any of a variety of fluorescent and colored proteins from Anthozoan species, as described in, e.g., Matz et al. (1999) *Nature Biotechnol.* 17:969-973; and the like.

[0082] Enzyme labels include, but are not limited to, luciferase, β-galactosidase, horse radish peroxidase, and the like. Where the label is an enzyme that yields a detectable product, the product can be detected using an appropriate means, e.g., β-galactosidase can, depending on the substrate, yield colored product, which is detected spectrophotometrically, or a fluorescent product; luciferase can yield a luminescent product detectable with a luminometer; etc.

RabGGT mRNA level

[0083] In some embodiments, an agent modulates the level of a RabGGT mRNA in a cell, e.g., the agent modulates the level of mRNA that comprises a nucleotide sequence that encodes a RabGGT protein. Agents that modulate the level of a RabGGT mRNA include agents that modulate the rate of transcription of the mRNA, agents that modulate binding of a transcription factor(s) or other regulatory protein(s) to a RabGGT gene regulatory element (e.g., enhancer, promoter, and the like); agents that modulate the stability of RabGGT mRNA stability; and the like.

[0084] In some embodiments, an agent increases the level of RabGGT mRNA by at least about 5%, at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 55%, at least about 60%, at least about 65%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, or at least about 90%, or more, when compared to the level in the absence of the agent.

[0085] In other embodiments, an agent decreases the level of RabGGT mRNA by at least about 5%, at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 55%, at least about 60%, at least about 65%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, or at least about 90%, or more, when compared to the level in the absence of the agent.

[0086] The level of RabGGT mRNA in a cell is readily determined using any known method. In general, nucleic acids that hybridize specifically to a RabGGT mRNA are used. A number of methods are available for analyzing nucleic acids for the presence and/or level of a specific mRNA in a cell or in a sample. The mRNA may be assayed directly or reverse transcribed into

cDNA for analysis. Suitable methods include, but are not limited to, *in situ* nucleic acid hybridization methods, quantitative RT-PCR, nucleic acid blotting methods, and the like.

[0087] The nucleic acid may be amplified by conventional techniques, such as the polymerase chain reaction (PCR), to provide sufficient amounts for analysis. The mRNA may be reverse transcribed, then subjected to PCR (rtPCR). The use of the polymerase chain reaction is described in Saiki, *et al.* (1985), *Science* **239**:487, and a review of techniques may be found in Sambrook, *et al.* Molecular Cloning: A Laboratory Manual, CSH Press 1989, pp.14.2–14.33.

[0088] A detectable label may be included in an amplification reaction. Suitable labels include fluorochromes, *e.g.* fluorescein isothiocyanate (FITC), rhodamine, Texas Red, phycoerythrin, allophycocyanin, 6-carboxyfluorescein (6-FAM), 2', 7'-dimethoxy-4',5'-dichloro-6-carboxyfluorescein (JOE), 6-carboxy-X-rhodamine (ROX), 6-carboxy-2',4',7',4,7-hexachlorofluorescein (HEX), 5-carboxyfluorescein (5-FAM) or N,N,N',N'-tetramethyl-6-carboxyrhodamine (TAMRA), radioactive labels, *e.g.* ^{32}P, ^{35}S, ^{3}H; *etc.* The label may be a two stage system, where the amplified DNA is conjugated to biotin, haptens, *etc.* having a high affinity binding partner, *e.g.* avidin, specific antibodies, *etc.*, where the binding partner is conjugated to a detectable label. The label may be conjugated to one or both of the primers. Alternatively, the pool of nucleotides used in the amplification is labeled, so as to incorporate the label into the amplification product.

[0089] A variety of different methods for determining the nucleic acid abundance in a sample are known to those of skill in the art, where particular methods of interest include those described in: Pietu et al., Genome Res. (June 1996) 6: 492-503; Zhao et al., Gene (April 24, 1995) 156: 207-213; Soares, Curr. Opin. Biotechnol. (October 1997) 8: 542-546; Raval, J. Pharmacol Toxicol Methods (November 1994) 32: 125-127; Chalifour et al., Anal. Biochem (February 1, 1994) 216: 299-304; Stolz & Tuan, Mol. Biotechnol. (December 19960 6: 225-230; Hong et al., Bioscience Reports (1982) 2: 907; and McGraw, Anal. Biochem. (1984) 143: 298. Also of interest are the methods disclosed in WO 97/27317, the disclosure of which is herein incorporated by reference.

[0090] In some embodiments, RabGGT mRNA levels are quantitated using quantitative rtPCR. Methods of quantitating a given message using rtPCR are known in the art. In some of these embodiments, dye-labeled primers are used. In other embodiments, a double-stranded DNA-binding dye, such as SYBR®, is used, as described in the Examples. Quantitative fluorogenic RT-PCR assays are well known in the art, and can be used in the present methods to detect a level of RabGGT mRNA. See, e.g., Pinzani et al. (2001) *Regul. Pept.* 99:79-86; and Yin et al. (2001) *Immunol. Cell Biol.* 79:213-221.

Apoptosis

[0091] In some embodiments, an agent that modulates a level and/or activity of RabGGT mRNA and/or protein induces apoptosis in a eukaryotic cell.

[0092] Whether a given agent inhibits RabGGT and induces apoptosis in a eukaryotic cell can be determined using any known method. Assays can be conducted on cell populations or an individual cell, and include morphological assays and biochemical assays. A non-limiting example of a method of determining the level of apoptosis in a cell population is TUNEL (TdT-mediated dUTP nick-end labeling) labeling of the 3'-OH free end of DNA fragments produced during apoptosis (Gavrieli et al. (1992) *J. Cell Biol.* 119:493). The TUNEL method consists of catalytically adding a nucleotide, which has been conjugated to a chromogen system or a to a fluorescent tag, to the 3'-OH end of the 180-bp (base pair) oligomer DNA fragments in order to detect the fragments. The presence of a DNA ladder of 180-bp oligomers is indicative of apoptosis. Procedures to detect cell death based on the TUNEL method are available commercially, e.g., from Boehringer Mannheim (Cell Death Kit) and Oncor (Apoptag Plus). Another marker that is currently available is annexin, sold under the trademark APOPTEST™. This marker is used in the "Apoptosis Detection Kit," which is also commercially available, e.g., from R&D Systems. During apoptosis, a cell membrane's phospholipid asymmetry changes such that the phospholipids are exposed on the outer membrane. Annexins are a homologous group of proteins that bind phospholipids in the presence of calcium. A second reagent, propidium iodide (PI), is a DNA binding fluorochrome. When a cell population is exposed to both reagents, apoptotic cells stain positive for annexin and negative for PI, necrotic cells stain positive for both, live cells stain negative for both. Other methods of testing for apoptosis are known in the art and can be used, including, e.g., the method disclosed in U.S. Patent No. 6,048,703.

Modulating a binding event

[0093] In some embodiments, an agent that modulates a RabGGT activity modulates a binding event between RabGGT and a RabGGT interacting protein. RabGGT interacting proteins include, but are not limited to, a Rab protein; a Rab escort protein (REP); and a protein that binds to a Rab/RabGGT complex.

[0094] In some embodiments, an agent increases binding between RabGGT and a RabGGT interacting protein by at least about 5%, at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 55%, at least about 60%, at least about 65%, at

least about 70%, at least about 75%, at least about 80%, at least about 85%, or at least about 90%, or more, when compared to the binding in the absence of the agent.

[0095] In some embodiments, an agent reduces binding between RabGGT and a RabGGT interacting protein by at least about 5%, at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 55%, at least about 60%, at least about 65%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, or at least about 90%, or more, when compared to the binding in the absence of the agent.

[0096] In some embodiments, the agent reduces binding between RabGGT and a Rab protein. Rab proteins are known in the art. For example, at least 30 human Rab proteins are known, and include Rab1a, Rab1b, Rab2a, Rab2b, Rab3a, Rab3b, Rab3c, Rab3d, Rab4a, Rab4b, Rab5a, Rab5b, Rab5c, Rab6a, Rab6b, Rab6c, Rab7, Rab8a, Rab8b, Rab9a, Rab9b, Rab10, Rab11a, Rab11b, Rab12, Rab13, Rab14, Rab15, Rab17, Rab18, Rab19, Rab20, Rab21, Rab22a, Rab22b, Rab22c, Rab23, Rab24, Rab25, Rab26, Rab27a, Rab27b, Rab28, Rab29, Rab30, Rab32, Rab33a, Rab33b, Rab34, Rab35, Rab36, Rab37, Rab38, Rab39a, Rab39b. See, e.g., Seabra et al. (2002) *Trends Mol. Med.* 8:23-30.

[0097] In some embodiments, an agent inhibits binding between a Rab protein and REP protein. RabGGT prenylates Rab only when Rab is in a complex with REP. Therefore, an agent that reduces a Rab/REP interaction also reduces Rab/RabGGT binding. Accordingly, agents that reduce Rab/REP binding are suitable for use in a subject methods. Rab/REP interaction via a RabF motif is a target for inhibiting Rab/REP binding. The RabF motif has been described in the art. See, e.g., Pereira-Leal et al. (2003) *Biochem. Biophys. Res. Comm.* 301:92-97. An agent that inhibits binding of a REP protein to a RabF motif is suitable for use in a subject method. Human REP proteins are known in the art, and the amino acid sequences have been reported. See, e.g., GenBank Accession No. NP_000381 or P24386 for human REP-1; NP_001812 for human REP-2; etc.

[0098] Whether an agent modulates binding between two proteins, e.g., between a Rab protein and a RabGGT protein, between a Rab protein and a REP protein, between a Rab/REP complex and RabGGT, can be determined using standard methods that are well known in the art. Suitable methods include, but are not limited to, a yeast two-hybrid assay; a fluorescence resonance energy transfer (FRET) assay; a bioluminescence resonance energy transfer (BRET) assay; a fluorescence quenching assay; a fluorescence anisotropy assay; an immunological assay; and an assay involving binding of a detectably labeled protein to an immobilized protein.

[0099] FRET involves the transfer of energy from a donor fluorophore in an excited state to a nearby acceptor fluorophore. For this transfer to take place, the donor and acceptor molecules must in close proximity (e.g., less than 10 nanometers apart, usually between 10 and 100 Å apart), and the emission spectra of the donor fluorophore must overlap the excitation spectra of the acceptor fluorophore. In one non-limiting example, a fluorescently labeled RabGGT protein serves as a donor and/or acceptor in combination with a second fluorescent protein (e.g., a Rab protein) or dye, e.g., a fluorescent protein as described in Matz et al. (1999) *Nature Biotechnology* 17:969-973; a green fluorescent protein (GFP); a GFP from *Aequoria victoria* or fluorescent mutant thereof, e.g., as described in U.S. Patent No. 6,066,476; 6,020,192; 5,985,577; 5,976,796; 5,968,750; 5,968,738; 5,958,713; 5,919,445; 5,874,304, the disclosures of which are herein incorporated by reference; a GFP from another species such as *Renilla reniformis, Renilla mulleri,* or *Ptilosarcus guernyi*, as described in, e.g., WO 99/49019 and Peelle et al. (2001) *J. Protein Chem.* 20:507-519; "humanized" recombinant GFP (hrGFP) (Stratagene); other fluorescent dyes, e.g., coumarin and its derivatives, e.g. 7-amino-4-methylcoumarin, aminocoumarin, bodipy dyes, such as Bodipy FL, cascade blue, fluorescein and its derivatives, e.g. fluorescein isothiocyanate, Oregon green, rhodamine dyes, e.g. texas red, tetramethylrhodamine, eosins and erythrosins, cyanine dyes, e.g. Cy3 and Cy5, macrocyclic chelates of lanthanide ions, e.g. quantum dye, etc., chemilumescent dyes, e.g., luciferases.

[00100] BRET is a protein-protein interaction assay based on energy transfer from a bioluminescent donor to a fluorescent acceptor protein. The BRET signal is measured by the amount of light emitted by the acceptor to the amount of light emitted by the donor. The ratio of these two values increases as the two proteins are brought into proximity. The BRET assay has been amply described in the literature. See, e.g., U.S. Patent Nos. 6,020,192; 5,968,750; and 5,874,304; and Xu et al. (1999) *Proc. Natl. Acad. Sci.* USA 96:151-156. BRET assays may be performed by analyzing transfer between a bioluminescent donor protein and a fluorescent acceptor protein. Interaction between the donor and acceptor proteins can be monitored by a change in the ratio of light emitted by the bioluminescent and fluorescent proteins. In one non-limiting example, a RabGGT protein serves as donor and/or acceptor protein.

[00101] Fluorescent RabGGT can be produced by generating a construct encoding a protein comprising a RabGGT protein and a fluorescent fusion partner, e.g., a fluorescent protein as described in Matz et al. ((1999) *Nature Biotechnology* 17:969-973), a green fluorescent protein from any species or a derivative thereof; e.g., a GFP from another species such as *Renilla*

reniformis, Renilla mulleri, or *Ptilosarcus guernyi*, as described in, e.g., WO 99/49019 and Peelle et al. (2001) *J. Protein Chem.* 20:507-519; a GFP from *Aequoria victoria* or fluorescent mutant thereof, e.g., as described in U.S. Patent No. 6,066,476; 6,020,192; 5,985,577; 5,976,796; 5,968,750; 5,968,738; 5,958,713; 5,919,445; 5,874,304. Generation of such a construct, and production of a RabGGT/fluorescent protein fusion protein is well within the skill level of those of ordinary skill in the art.

[00102] Alternatively, binding may be assayed by fluorescence anisotropy. Fluorescence anisotropy assays are amply described in the literature. See, e.g., Jameson and Sawyer (1995) *Methods Enzymol.* 246:283-300.

[00103] In some embodiments, the method of determining whether an agent modulates a protein/protein interaction is a yeast two-hybrid assay system or a variation thereof. The yeast two-hybrid screen has been described in the literature. See, e.g., Zhu and Kahn (1997) *Proc. Natl. Acad. Sci. U.S.A.* 94:13063-13068; Fields and Song (1989) *Nature* 340:245-246; and U.S. Pat. No. 5,283,173; Chien et al. (1991) *Proc. Natl. Acad. Sci. U.S.A.* 88:9578-9581.

[00104] Protein/protein binding can also be assayed by other methods well known in the art, for example, immunoprecipitation with an antibody that binds to the protein in a complex, followed by analysis by size fractionation of the immunoprecipitated proteins (e.g. by denaturing or nondenaturing polyacrylamide gel electrophoresis); Western analysis; non-denaturing gel electrophoresis, etc.

Chemical features of modulators

[00105] In some embodiments, an agent that modulates a level and/or an activity of a RabGGT protein and/or a RabGGT/REP complex is a compound that binds to the binding pocket for the substrate prenyl moiety and/or the peptide substrate in the RabGGT active site. A suitable compound comprises moieties that provide for interactions with amino acid side chains that normally interact with substrate prenyl moiety and/or peptide substrate in the RabGGT active site. Features that a suitable compound possesses include one or more of: (1) zinc binding; (2) hydrogen bonding to specific amino acid side chains; (3) a hydrophobic moiety; (4) a size sufficient to occlude the binding site for the prenyl and/or the peptide substrate; and/or a size sufficient to interface with the size limitations embodied by the binding pocket of the RabGGT alpha and beta subunits, and defined by their respective structure coordinates.

[00106] In some embodiments, a suitable modulator of enzymatic activity of RabGGT or a RabGGT/REP complex is a benzodiazepine. In other embodiments, a suitable modulator of enzymatic activity of RabGGT or a RabGGT/REP complex is a tetrahydroquinoline.

[00107] In other embodiments, a suitable modulator of enzymatic activity of RabGGT or a RabGGT/REP complex may comprise one or more of the side chains, moieties, or groups, or any combinations thereof, of the compounds disclosed in USPN 6,011,029; USPN 6,387,926; and/or USPN 6,458,783, which are hereby incorporated by reference herein in their entirety.

[00108] In one embodiment, a suitable modulator of RabGGT or a RabGGT/REP complex may comprise a side chain, moiety, or group capable of chelating zinc, and/or coordinating with zinc. Examples of zinc chelators and/or cooridinators include, but are not limited to the following: thiol, cysteine, cysteine derivative, hydroxamic acid, hydroxamic acid derivative, barbituric acid, barbituric acid derivative, pyridyl, imidazolyl, methionine, nitrogen-containing heterocycles, or other groups known in the art that are capable of chelating and/or coordinating with zinc, or disclosed or referenced herein.

[00109] In another embodiment, a suitable modulator of RabGGT or a RabGGT/REP complex may comprise a hydrophobic or aromatic side chain, moiety, or group. Examples of such groups include, but are not limited to the following: phenyl, planar phenyl, aryl, substituted phenyl, cyano substituted phenyl, a cyanobenzene, substituted aryl, heteroaryl, substituted heteroaryl, or other hydrophobic or aromatic side chain, moiety, or group known in the art, or disclosed or referenced herein.

[00110] In another embodiment, a suitable modulator of RabGGT or a RabGGT/REP complex may comprise one, two, three, four, or more hydrophobic or aromatic side chains, moieties, or groups.

[00111] In another embodiment, a suitable modulator of RabGGT or a RabGGT/REP complex may comprise a side chain, moiety, or group capable of ligating with a water molecule and/or forming one or more hydrogen bonds with a water molecule.

[00112] In yet another embodiment, a suitable modulator of RabGGT or a RabGGT/REP complex may comprise a large multicyclic aromatic and/or hydrophobic side chain, moiety, or group. In yet another embodiment, a suitable modulator of RabGGT or a RabGGT/REP complex may not comprise a large multicyclic aromatic and/or hydrophobic side chain, moiety, or group. Examples of such multicyclic aromatic and/or hydrophobic side chains, moieties, or groups may be found in the teachings of I.M. Bell et al, J. Med. Chem. 45:2388 (2002), which is hereby incorporated herein by reference in its entirety.

[00113] A suitable modulator of RabGGT or a RabGGT/REP complex may comprise any combination of one, two, three, four, five, six, seven, eight, nine, ten, or more of the above specified characteristics.

Pharmacophores

[00114] Suitable modulators of RabGGT or RabGGT/REP activity are pharmacophores that possess appropriate size, volume, charge, and hydrophobicity features to allow interactions with amino acid side chains in the active site that normally interact with prenyl and/or peptide substrates. Such features may be used to identify compounds that are modulators of RabGGT or RabGGT/REP complex activity.

[00115] Features can include topological indices, physicochemical properties, electrostatic field parameters, volume and surface parameters, etc. Other features include, but are not limited to, molecular volume and surface areas, dipole moments, octanol-water partition coefficients, molar refractivities, heats of formation, total energies, ionization potentials, molecular connectivity indices, substructure keys. Such descriptors and their use in the fields of Quantitative Structure-Activity Relationships (QSAR) and molecular diversity are reviewed in Kier, L. B. and Hall L. H., Molecular Connectivity in Chemistry and Drug Research, Academic Press, New York (1976); Kier, L. B. and Hall L. H., Molecular Connectivity in Structure-Activity Analysis, Research Studies Press, Wiley, Letchworth (1986); Kubinyi, H., Methods and Principles in Medicinal Chemistry, Vol. 1, VCH, Weinheim (1993); and P.V.R. Scheyler, Encyclopedia of Computational Chemistry, Wiley (1998).

[00116] In some embodiments, a modulator of an activity of RabGGT or a RabGGT/REP complex is identified by computational quantitative structure activity relationship (QSAR) modeling techniques as a screening device for potency as an inhibitor or activator. Structure-activity relationship (SAR) analysis is performed using any known method. See, e.g., U.S. Patent No. 6,344,334; U.S. Patent No. 6,208,942; U.S. Patent No. 6,453,246; U.S. Patent No. 6,421,612.

[00117] Suitable compounds can be identified using a selection approach that involves (1) identifying a set of compounds for analysis; (2) collecting, acquiring or synthesizing the identified compounds; (3) analyzing the compounds to determine one or more physical, chemical and/or bioactive properties (structure-property data); and (4) using the structure-property data to identify another set of compounds for analysis in the next iteration. These steps can be repeated multiple times, as necessary to derive suitable compounds with desired properties.

[00118] Suitable compounds may also be identified by subjecting putative modulators of the RabGGTase protein to virtual screens that predict the overall fit of the modulator to the putative binding site(s) of the RabGGTase protein, its alpha subunit, its beta subunit, the RabGGTase/Rep complex, and/or the RabGGTase/Rep/substrate ternary complex. The

DOCK3.5 algorithm, among others described herein, may be used for virtually screening RabGGTase modulators. DOCK3.5 is an automatic algorithm to screen small-molecule databases for ligands that could bind to a given receptor (Meng, E. C., et al., 1992, J. Comp. Chem. 15:505). DOCK3.5 characterizes the surface of the active site to be filled with sets of overlapping spheres. The generated sphere centers constitute an irregular grid that is matched to the atomic centers of the potential ligands. The quality of the fit of the ligand to the site is judged by either the shape complementarity or by a simplified estimated interaction energy. Putative RabGGTase modulators having the best shape complementarity scores and the best force field scores may be selected from the screen. The resulting virtual modulators may then be visually screened independently in the context of the RabGGTase binding pocket described herein using the molecular display software Insight II (Biosym Inc., San Diego, Calif.). Such compounds can then be confirmed to have RabGGTase modulating activity by subjecting these compounds to screening assays described herein.

[00119] Preferred RabGGTase modulators have a complementarity score of at least about 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, 225, 250, 275, 300, 325, 350, 375, 400, 425, 450, 475, 500, 525, 550, 575, 600, 625, 650, 675, 700, 725, 750, 775, 800, 825, 850, 875, 900, 925, 950, 975, 1000, or greater. In this context, "about" should be construed to represent 1 to 13 more or less than the stated complementarity score.

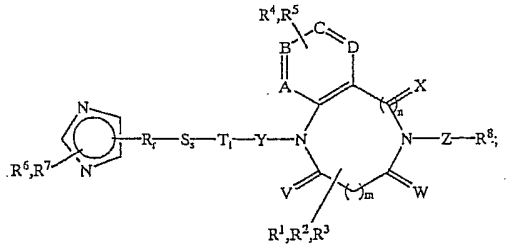
Small molecule modulators

[00120] In some embodiments, an agent that increases or reduces a level and/or an activity of RabGGT or a RabGGT/REP complex is a small molecule. Small molecule agents are generally small organic or inorganic compounds having a molecular weight of more than 50 and less than about 2,500 daltons. Specifically, small molecule agents may be at least about 50, 100, 150, 200, 250, 300, 350, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900, 950, 1000, 1050, 1100, 1150, 1200, 1250, 1300, 1350, 1400, 1450, 1500, 1550, 1600, 1650, 1700, 1750, 1800, 1850, 1900, 1950, 2000, 2050, 2100, 2150, 2200, 2250, 2300, 2350, 2400, 2450, or 2500. In this context, "about" should be construed to represent more or less than 1 to 25 daltons than the indicated amount.

[00121] Suitable agents may comprise functional groups necessary for structural interaction with proteins, particularly hydrogen bonding, and may include at least an amine, carbonyl, hydroxyl or carboxyl group, and may contain at least two of the functional chemical groups. The agents may comprise cyclical carbon or heterocyclic structures and/or aromatic or polyaromatic structures substituted with one or more of the above functional groups. Suitable

active agents are also found among biomolecules including peptides, saccharides, fatty acids, steroids, purines, pyrimidines, derivatives, structural analogs or combinations thereof.

[00122] In some embodiments, agents that reduce enzymatic activity of RabGGT or level of enzymatically active RabGGT are of the following formula:

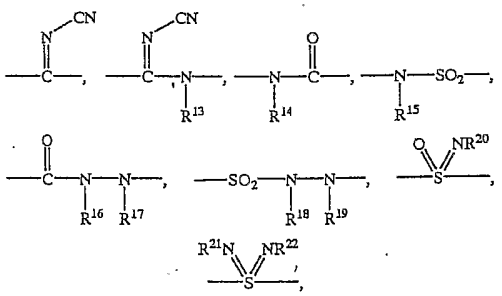


[00123] or an enantiomer, diastereomer, pharmaceutically acceptable salt, prodrug, or solvate thereof, where m, n, r, s, and 1 are 0 or 1;

[00124] p is 0, 1, or 2;

[00125] V, W, and X are selected from oxygen, hydrogen, R^1, R^2, or R^3;

[00126] Z and Y are selected from CHR^9, SO_2, SO_3, CO, CO_2, O, NR^{10}, SO_2NR^{11}, $CONR^{12}$,



[00127] or Z may be absent;

[00128] R^6, R^7, R^{10}, R^{11}, R^{12}, R^{13}, R^{14}, R^{15}, R^{16}, R^{17}, R^{18}, R^{19}, R^{20}, R^{21}, R^{22}, R^{23}, R^{24}, R^{25}, R^{26}, R^{27}, R^{28}, R^{29}, R^{30}, R^{31}, R^{32}, R^{33}, R^{34}, R^{35}, R^{36}, R^{37}, and R^{38}, are each independently selected from hydrogen, lower alkyl, substituted alkyl, aryl, or substituted aryl;

[00129] R^4 and R^5 are independently selected from hydrogen, halo, nitro, cyano, and U-R^{23};

[00130] U is selected from sulfur, oxygen, NR^{24}, CO, SO, SO_2, CO_2, $NR^{25}CO_2$, $NR^{26}CONR^{27}$, $NR^{28}SO_2$, $NR^{29}SO_2NR^{30}$, SO_2NR^{31}, $NR^{32}CO$, $CONR^{33}$, PO_2R^{34}, and PO_3R^{35} or U is absent;

[00131] R^1, R^2, and R^3 are each independently selected from hydrogen, alkyl, alkoxycarbonyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, arakyl, cycolalkyl, aryl, substituted aryl, heterocyclo, substituted heterocyclo, cyano, carboxyl, carbamyl (e.g., $CONH_2$) or substituted carbamyl further selected from CONH alkyl, CONH aryl, CONH

aralkyl or cases where there are two substituents on the nitrogen selected from alkyl, aryl, or aralkyl, ; R^8 and R^{23} are independently selected from hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, aalkynyl, substituted alkynyl, aralkyl, cycloalkyl, aryl, substituted aryl, heterocyclo, substituted heterocyclo;

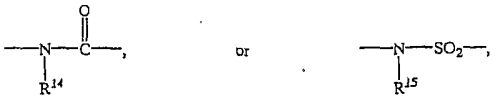
[00132] any two of R^1, r^2, and R^3 can be joined to form a cycloalkyl group;

[00133] R, S, and T are selected from CH_2, CO, and $CH(CH_2)pQ$, wherein Q is $NR^{36}R^{37}$, OR^{38}, or CN; and

[00134] A, B, and D are carbon, oxygen, sulfur or nitrogen, with the proviso that

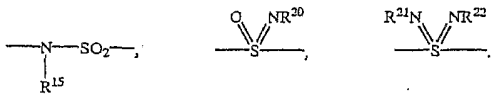
[00135] 1) when m is zero, then V and W are not both oxygen; or

[00136] 2) W and X together can be oxygen only if Z is either absent, O, NR^{10}, CHR^9,

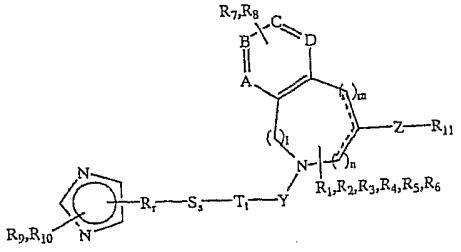


[00137] 3) R^{23} may be hydrogen except with U is SO_2, CO_2, or

[00138] 4) R^8 may be hydrogen except when Z is SO_2, CO_2 or



[00139] In other embodiments, agents that reduce enzymatic activity of RabGGT or level of enzymatically active RabGGT are of the following formula:



[00140] or an enantiomer, diastereomer, pharmaceutically acceptable salt, prodrug, or solvate thereof,

[00141] l, m. r. s. and t are 0 or 1;

[00142] N is 0, 1, or 2;

[00143] Y is selected from CHR^{12}, SO_2, SO_3, CO, CO_2, Y is selected from the group consisting of CHR^{12} SO_2, SO_3, CO, CO_2, O, NR^{13}, SO_2NR^{14}, $CONR^{15}$, C(NCN), $C(NCN)NR^{16}$, $NR^{17}CO$, $NR^{18}SO_2$, $CONR^{19}NR^{20}$, SO2NR21NR22, S(O)(NR^{23}), S(NR^{24})NR^{25}), or without Y;

[00144] Z is selected from the group consisting of CR^{12},S, SO, SO_2,SO_3,CO,CO_2, O,NR^{13},SO_2NR^{14},$CONR^{15}$,$NR^{26}NR^{27}$,ONR^{28},$NR^{29}O$,$NR^{30}SO_2NR^{31}$,$NR^{32}SO$,$NR^{33}C(NCN)$, NR^{34},$C(NCN)NR^{35}$, $NR^{36}CO$, $NR^{37}CO$, $NR^{37}CONR^{38}$, $NR^{39}CO_2$, $OCONR^{40}$, S(O)(NR^{41}), S(NR^{42})(NR^{43}) or CHR^{12};

[00145] or without Z;

[00146] R^7, R^8 are selected from the group consisting of hydrogen, halo, nitro, cyano and U-R^{44};

[00147] U is selected from the group consisting of S, O, NR^{45}, CO, SO, SO_2, CO_2, $NR^{46}CO_2$, $NR^{47}CONR^{48}$, $NR^{49}SO_2$, $NR^{50}SO_2NR^{51}$, SO_2NR^{52}, $NR^{53}CO$, $CONR^{54}$, PO_2R^{55} and PO_2R^{56} or without U;

[00148] R^9, R^{10}, R^{12}, R^{13}, R^{14}, R^{15}, R^{16}, R^{17}, R^{18}, R^{19}, R^{20}, R^{21}, R^{22}, R^{23}, R^{24}, R^{25}, R^{26}, R^{27}, R^{28}, R^{29}, R^{30}, R^{31}, R^{32}, R^{33}, R^{34}, R^{35}, R^{36}, R^{37}, R^{38}, R^{39}, R^{40}, R^{41}, R^{42}, R^{43}, R^{45}, R^{46}, R^{47}, R^{48}, R^{49}, R^{50}, R^{51}, R^{52}, R^{53}, R^{54}, R^{55}, R^{56}, R^{57}, R^{58} and R^{59} are selected from the group consisting of hydrogen, lower alkyl, aryl, heterocyclo, substituted alkyl or aryl or substituted heterocyclo;

[00149] $R^{11}$and R^{44} are selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, sub alkynyl, aralkyl, cycloalkyl, aryl, substituted aryl, heterocyclo, substituted heterocyclo;

[00150] R^1, R^2, R^3, R^4, R^5, and R^6 are selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, cycloalkyl, aryl, substituted aryl, heterocyclo, substituted heterocyclo, cyano, carboxy, carbamyl (e.g. $CONH_2$) substituted carbamyl (where nitrogen may be substituted by groups selected from hydrogen, alkyl, substituted alkyl, aryl or aralkyl, substituted aryl, heterocyclo, sub-situated heterocyclo) alkoxycarbonyl; any two of R^1, R^2, R^3, R^4, R^5, and R^6 can join to form a cycloalkyl group; any two of R^1, R^2, R^3, R^4, R^5, and R^6 together can by oxo, except when the carbon atom bearing the substituent is part of a double bond;

[00151] R, S, T are selected from the group consisting of CH_2, CO and $CH(CH_2)Q$ wherein Q is $NR^{57}R^{58}$, OR^{59}, or CN; and p is 0,1 or 2;

[00152] A, B, C are carbon, oxygen, sulfur or nitrogen; D is carbon, oxygen, sulfur or nitrogen or without D,

[00153] with the provisos that:

[00154] 1. When 1 and m are both 0, n is not 0;

[00155] 2. R^{11} may be hydrogen except when Z is SO, or when Z is O, NR^{13} or S and the carbon to which it is attached is part of a double bond or when Y is SO_2, CO_2, $NR^{18}SO_2$, $S(O)(NR^{23})$, or $S(NR^{24})(NR^{25})$; and

[00156] 3. R^{44} may be hydrogen except when U is SO, SO_2, $NR^{46}CO_2$ or $NR^{49}SO_2$.

[00157] In some embodiments, the agents disclosed in USPN 6,011,029; USPN 6,387,926; and/or USPN 6,458,783 are specifically excluded from the present invention.

Protein modulators

[00158] Agents that modulate an activity of a RabGGT include protein modulators. In some embodiments, an active agent is a peptide. Suitable peptides include peptides of from about 3 amino acids to about 50, from about 5 to about 30, or from about 10 to about 25 amino acids in length. In some embodiments, a peptide exhibits one or more of the following activities: inhibits binding of RabGGT to a RabGGT interacting protein; inhibits interaction between an α and a β subunit of RabGGT; inhibits an enzymatic activity of RabGGT.

[00159] Peptides can include naturally-occurring and non-naturally occurring amino acids. Peptides may comprise D-amino acids, a combination of D- and L-amino acids, and various "designer" amino acids (e.g., β-methyl amino acids, Cα-methyl amino acids, and Nα-methyl amino acids, etc.) to convey special properties to peptides. Additionally, peptide may be a cyclic peptide. Peptides may include non-classical amino acids in order to introduce particular conformational motifs. Any known non-classical amino acid can be used. Non-classical amino acids include, but are not limited to, 1,2,3,4-tetrahydroisoquinoline-3-carboxylate; (2S,3S)-methylphenylalanine, (2S,3R)-methyl-phenylalanine, (2R,3S)-methyl-phenylalanine and (2R,3R)-methyl-phenylalanine; 2-aminotetrahydronaphthalene-2-carboxylic acid; hydroxy-1,2,3,4-tetrahydroisoquinoline-3-carboxylate; β-carboline (D and L); HIC (histidine isoquinoline carboxylic acid); and HIC (histidine cyclic urea). Amino acid analogs and peptidomimetics may be incorporated into a peptide to induce or favor specific secondary structures, including, but not limited to, LL-Acp (LL-3-amino-2-propenidone-6-carboxylic acid), a β-turn inducing dipeptide analog; β-sheet inducing analogs; β-turn inducing analogs; α-

helix inducing analogs; γ-turn inducing analogs; Gly-Ala turn analog; amide bond isostere; tretrazol; and the like.

[00160] A peptide may be a depsipeptide, which may be a linear or a cyclic depsipeptide. Kuisle et al. (1999) *Tet. Letters* 40:1203-1206. "Depsipeptides" are compounds containing a sequence of at least two alpha-amino acids and at least one alpha-hydroxy carboxylic acid, which are bound through at least one normal peptide link and ester links, derived from the hydroxy carboxylic acids, where "linear depsipeptides" may comprise rings formed through S–S bridges, or through an hydroxy or a mercapto group of an hydroxy-, or mercapto-amino acid and the carboxyl group of another amino- or hydroxy-acid but do not comprise rings formed only through peptide or ester links derived from hydroxy carboxylic acids. "Cyclic depsipeptides" are peptides containing at least one ring formed only through peptide or ester links, derived from hydroxy carboxylic acids.

[00161] Peptides may be cyclic or bicyclic. For example, the C-terminal carboxyl group or a C-terminal ester can be induced to cyclize by internal displacement of the -OH or the ester (-OR) of the carboxyl group or ester respectively with the N-terminal amino group to form a cyclic peptide. For example, after synthesis and cleavage to give the peptide acid, the free acid is converted to an activated ester by an appropriate carboxyl group activator such as dicyclohexylcarbodiimide (DCC) in solution, for example, in methylene chloride (CH_2Cl_2), dimethyl formamide (DMF) mixtures. The cyclic peptide is then formed by internal displacement of the activated ester with the N-terminal amine. Internal cyclization as opposed to polymerization can be enhanced by use of very dilute solutions. Methods for making cyclic peptides are well known in the art

[00162] The term "bicyclic" refers to a peptide in which there exists two ring closures. The ring closures are formed by covalent linkages between amino acids in the peptide. A covalent linkage between two nonadjacent amino acids constitutes a ring closure, as does a second covalent linkage between a pair of adjacent amino acids which are already linked by a covalent peptide linkage. The covalent linkages forming the ring closures may be amide linkages, i.e., the linkage formed between a free amino on one amino acid and a free carboxyl of a second amino acid, or linkages formed between the side chains or "R" groups of amino acids in the peptides. Thus, bicyclic peptides may be "true" bicyclic peptides, i.e., peptides cyclized by the formation of a peptide bond between the N-terminus and the C-terminus of the peptide, or they may be "depsi-bicyclic" peptides, i.e., peptides in which the terminal amino acids are covalently linked through their side chain moieties.

[00163] A desamino or descarboxy residue can be incorporated at the terminii of the peptide, so that there is no terminal amino or carboxyl group, to decrease susceptibility to proteases or to restrict the conformation of the peptide. C-terminal functional groups include amide, amide lower alkyl, amide di(lower alkyl), lower alkoxy, hydroxy, and carboxy, and the lower ester derivatives thereof, and the pharmaceutically acceptable salts thereof.

[00164] In addition to the foregoing N-terminal and C-terminal modifications, a peptide or peptidomimetic can be modified with or covalently coupled to one or more of a variety of hydrophilic polymers to increase solubility and circulation half-life of the peptide. Suitable nonproteinaceous hydrophilic polymers for coupling to a peptide include, but are not limited to, polyalkylethers as exemplified by polyethylene glycol and polypropylene glycol, polylactic acid, polyglycolic acid, polyoxyalkenes, polyvinylalcohol, polyvinylpyrrolidone, cellulose and cellulose derivatives, dextran and dextran derivatives, etc. Generally, such hydrophilic polymers have an average molecular weight ranging from about 500 to about 100,000 daltons, from about 2,000 to about 40,000 daltons, or from about 5,000 to about 20,000 daltons. The peptide can be derivatized with or coupled to such polymers using any of the methods set forth in Zallipsky, S., Bioconjugate Chem., 6:150-165 (1995); Monfardini, C, et al., Bioconjugate Chem., 6:62-69 (1995); U.S. Pat. Nos. 4,640,835; 4,496,689; 4,301,144; 4,670,417; 4,791,192; 4,179,337 or WO 95/34326.

[00165] Another suitable agent for modulating an activity of RabGGT is a peptide aptamer. Peptide aptamers are peptides or small polypeptides that act as dominant inhibitors of protein function. Peptide aptamers specifically bind to target proteins, blocking their function ability. Kolonin and Finley, PNAS (1998) 95:14266-14271. Due to the highly selective nature of peptide aptamers, they may be used not only to target a specific protein, but also to target specific functions of a given protein (*e.g.* a signaling function). Further, peptide aptamers may be expressed in a controlled fashion by use of promoters which regulate expression in a temporal, spatial or inducible manner. Peptide aptamers act dominantly; therefore, they can be used to analyze proteins for which loss-of-function mutants are not available.

[00166] Peptide aptamers that bind with high affinity and specificity to a target protein may be isolated by a variety of techniques known in the art. Peptide aptamers can be isolated from random peptide libraries by yeast two-hybrid screens (Xu *et al.*, PNAS (1997) 94:12473-12478). They can also be isolated from phage libraries (Hoogenboom *et al.*, Immunotechnology (1998) 4:1-20) or chemically generated peptides/libraries.

Antibody modulators

[00167] In some embodiments, an agent that increases or reduces a level and/or activity of RabGGT is an antibody specific for RabGGT. Antibodies include naturally-occurring antibodies, artificial antibodies, intrabodies, antibody fragments, and the like, that specifically bind a RabGGT polypeptide. In some embodiments, a subject antibody binds specifically to native RabGGT protein, e.g., to native RabGGT protein present *in vivo* in an individual.

[00168] In many embodiments, a subject antibody is isolated, e.g., is in an environment other than its naturally-occurring environment. In some embodiments, a subject antibody is synthetic. Suitable antibodies are obtained by immunizing a host animal with peptides comprising all or a portion of the subject protein. Suitable host animals include mouse, rat, sheep, goat, hamster, rabbit, *etc.* The host animal is any mammal that is capable of mounting an immune response to a RabGGT protein, where representative host animals include, but are not limited to, *e.g.*, rabbits, goats, mice, *etc.*

[00169] The immunogen may comprise the complete protein, or fragments and derivatives thereof. Preferred immunogens comprise all or a part of the protein. Immunogens are produced in a variety of ways known in the art, *e.g.,* expression of cloned genes using conventional recombinant methods, followed by *in vitro* production of the RabGGT polypeptide; isolation of a RabGGT polypeptide; preparation of fragments of a RabGGT polypeptide using well-known methods, *etc.*

[00170] In some embodiments, a subject antibody is bound to a solid support or an insoluble support. Insoluble supports include, but are not limited to, beads (including plastic beads, magnetic beads, and the like); plastic plates (e.g., microtiter plates); membranes (e.g., polyvinyl pyrrolidone, nitrocellulose, and the like); and the like.

[00171] For preparation of polyclonal antibodies, the first step is immunization of the host animal with the target protein, where the target protein will preferably be in substantially pure form, comprising less than about 1% contaminant. The immunogen may comprise the complete target protein, fragments or derivatives thereof. To increase the immune response of the host animal, the target protein may be combined with an adjuvant, where suitable adjuvants include alum, dextran, sulfate, large polymeric anions, oil & water emulsions, e.g. Freund's adjuvant, Freund's complete adjuvant, and the like. The target protein may also be conjugated to a carrier, e.g., KLH, BSA, a synthetic carrier protein, and the like. A variety of hosts may be immunized to produce the polyclonal antibodies. Such hosts include rabbits, guinea pigs, rodents, e.g. mice, rats, sheep, goats, and the like. The target protein is administered to the host, e.g., intradermally, with an initial dosage followed by one or more, usually at least two,

additional booster dosages. Following immunization, the blood from the host will be collected, followed by separation of the serum from the blood cells. The Ig present in the resultant antiserum may be further fractionated using known methods, such as ammonium salt fractionation, DEAE chromatography, and the like.

[00172] Monoclonal antibodies are produced by conventional techniques. Generally, the spleen and/or lymph nodes of an immunized host animal provide a source of plasma cells. The plasma cells are immortalized by fusion with myeloma cells to produce hybridoma cells. Culture supernatant from individual hybridomas is screened using standard techniques to identify those producing antibodies with the desired specificity. Suitable animals for production of monoclonal antibodies to the human protein include mouse, rat, hamster, *etc.* The antibody may be purified from the hybridoma cell supernatants or ascites fluid by conventional techniques, *e.g.* affinity chromatography using protein bound to an insoluble support, protein A sepharose, *etc.*

[00173] The antibody may be produced as a single chain, instead of the normal multimeric structure. Single chain antibodies are described in Jost *et al.* (1994) *J. Biol. Chem.* 269:26267–73, and elsewhere. DNA sequences encoding the variable region of the heavy chain and the variable region of the light chain are ligated to a spacer encoding at least about 4 amino acids of small neutral amino acids, including glycine and/or serine. The protein encoded by this fusion allows assembly of a functional variable region that retains the specificity and affinity of the original antibody.

[00174] Also provided are "artificial" antibodies, e.g., antibodies and antibody fragments produced and selected *in vitro*. In some embodiments, such antibodies are displayed on the surface of a bacteriophage or other viral particle. In many embodiments, such artificial antibodies are present as fusion proteins with a viral or bacteriophage structural protein, including, but not limited to, M13 gene III protein. Methods of producing such artificial antibodies are well known in the art. See, e.g., U.S. Patent Nos. 5,516,637; 5,223,409; 5,658,727; 5,667,988; 5,498,538; 5,403,484; 5,571,698; and 5,625,033.

[00175] Also of interest are humanized antibodies. Methods of humanizing antibodies are known in the art. The humanized antibody may be the product of an animal having transgenic human immunoglobulin constant region genes (see for example International Patent Applications WO 90/10077 and WO 90/04036). Alternatively, the antibody of interest may be engineered by recombinant DNA techniques to substitute the CH1, CH2, CH3, hinge domains, and/or the framework domain with the corresponding human sequence (see WO 92/02190).

[00176] The use of Ig cDNA for construction of chimeric immunoglobulin genes is known in the art (Liu *et al.* (1987) *Proc. Natl. Acad. Sci. USA.* **84**:3439 and (1987) J. Immunol. **139**:3521). mRNA is isolated from a hybridoma or other cell producing the antibody and used to produce cDNA. The cDNA of interest may be amplified by the polymerase chain reaction using specific primers (U.S. Patent nos. 4,683,195 and 4,683,202). Alternatively, a library is made and screened to isolate the sequence of interest. The DNA sequence encoding the variable region of the antibody is then fused to human constant region sequences. The sequences of human constant regions genes may be found in Kabat *et al.* (1991) Sequences of Proteins of Immunological Interest, N.I.H. publication no. 91-3242. Human C region genes are readily available from known clones. The choice of isotype will be guided by the desired effector functions, such as complement fixation, or activity in antibody-dependent cellular cytotoxicity. Exemplary isotypes are IgG1, IgG3 and IgG4. Either of the human light chain constant regions, kappa or lambda, may be used. The chimeric, humanized antibody is then expressed by conventional methods. Other methods for preparing chimeric antibodies are described in, e.g., U.S. Patent No. 5,565,332.

[00177] Antibody fragments, such as Fv, $F(ab')_2$ and Fab may be prepared by cleavage of the intact protein, *e.g.* by protease or chemical cleavage. Alternatively, a truncated gene is designed. For example, a chimeric gene encoding a portion of the $F(ab')_2$ fragment would include DNA sequences encoding the CH1 domain and hinge region of the H chain, followed by a translational stop codon to yield the truncated molecule.

[00178] Consensus sequences of H and L J regions may be used to design oligonucleotides for use as primers to introduce useful restriction sites into the J region for subsequent linkage of V region segments to human C region segments. C region cDNA can be modified by site directed mutagenesis to place a restriction site at the analogous position in the human sequence.

[00179] Expression vectors include plasmids, retroviruses, YACs, BACs, EBV-derived episomes, and the like. A convenient vector is one that encodes a functionally complete human CH or CL immunoglobulin sequence, with appropriate restriction sites engineered so that any VH or VL sequence can be easily inserted and expressed. In such vectors, splicing usually occurs between the splice donor site in the inserted J region and the splice acceptor site preceding the human C region, and also at the splice regions that occur within the human CH exons. Polyadenylation and transcription termination occur at native chromosomal sites downstream of the coding regions. The resulting chimeric antibody may be joined to any strong promoter, including retroviral long terminal repeats (LTRs) and other promoters, *e.g.*

SV-40 early promoter, (Okayama *et al.* (1983) Mol. Cell. Bio. 3:280), Rous sarcoma virus LTR (Gorman *et al.* (1982) *Proc. Natl. Acad. Sci. USA* 79:6777), and moloney murine leukemia virus LTR (Grosschedl *et al.* (1985) *Cell* 41:885); native Ig promoters, *etc.*

[00180] Intrabodies that specifically bind RabGGT polypeptide are expressed in a cell in an individual, where they reduce levels of enzymatically active RabGGT. See, e.g., Marasco et al. (1999) *J. Immunol. Methods* 231:223-238. Intracellularly expressed antibodies, or intrabodies, are single-chain antibody molecules designed to specifically bind and inactivate target molecules inside cells. See, e.g., Chen *et al.*, Hum. Gen. Ther. (1994) 5:595-601; Hassanzadeh *et al.*, Febs Lett. (1998) 16(1, 2):75-80 and 81-86; Marasco (1997) *Gene Ther.* 4:11-15; and "Intrabodies: Basic Research and Clinical Gene Therapy Applications" W.A. Marasco, eg., (1998) Springer-Verlag, NY. Inducible expression vectors can be constructed that encode intrabodies that bind specifically to RabGGT polypeptide. These vectors are introduced into an individual, and production of the intrabody induced by administration to the individual of the inducer. Alternatively, the expression vector encoding the intrabody provides for constitutive production of the intrabody.

[00181] A subject antibody may be labeled. Suitable labels include radioisotopes; enzymes whose products are detectable (e.g., luciferase, β-galactosidase, and the like); fluorescent labels (e.g., fluorescein isothiocyanate, rhodamine, phycoerythrin, and the like); fluorescence emitting metals, e.g., ^{152}Eu, or others of the lanthanide series, attached to the antibody through metal chelating groups such as EDTA; chemiluminescent compounds, e.g., luminol, isoluminol, acridinium salts, and the like; bioluminescent compounds, e.g., luciferin, aequorin (a green fluorescent protein), and the like.

[00182] Suitable detectable moieties include, but are not limited to, fluorescent, metallic, enzymatic and radioactive markers such as fluorescent proteins, biotin, gold, ferritin, alkaline phosphatase, β-galactosidase, luciferase, horse radish peroxidase, peroxidase, urease, fluorescein, rhodamine, tritium, ^{14}C, and iodination. The binding agent, e.g., an antibody, can be used as a fusion protein, where the fusion partner is a fluorescent protein. Fluorescent proteins include, but are not limited to, a green fluorescent protein from *Aequoria victoria* or a mutant or derivative thereof e.g., as described in U.S. Patent No. 6,066,476; 6,020,192; 5,985,577; 5,976,796; 5,968,750; 5,968,738; 5,958,713; 5,919,445; 5,874,304; e.g., Enhanced GFP, many such GFP which are available commercially, e.g., from Clontech, Inc.; any of a variety of fluorescent and colored proteins from Anthozoan species, as described in, e.g., Matz et al. (1999) *Nature Biotechnol.* 17:969-973; and the like.

Nucleic acid modulators

[00183] In some embodiments, an agent that modulates a level of RabGGT is a nucleic acid. Nucleic acid modulators of RabGGT levels include RNAi, ribozymes, and antisense RNA.

[00184] In some embodiments, the active agent is an interfering RNA (RNAi). RNAi includes double-stranded RNA interference (dsRNAi). Use of RNAi to reduce a level of a particular mRNA and/or protein is based on the interfering properties of double-stranded RNA derived from the coding regions of gene. In one example of this method, complementary sense and antisense RNAs derived from a substantial portion of the RabGGT gene are synthesized *in vitro*. The resulting sense and antisense RNAs are annealed in an injection buffer, and the double-stranded RNA injected or otherwise introduced into the subject (such as in their food or by soaking in the buffer containing the RNA). See, e.g., WO99/32619. In another embodiment, dsRNA derived from a RabGGT gene is generated *in vivo* by simultaneous expression of both sense and antisense RNA from appropriately positioned promoters operably linked to RabGGT coding sequences in both sense and antisense orientations.

[00185] Antisense molecules can be used to down-regulate expression of the gene encoding RabGGT in cells. Antisense compounds include ribozymes, external guide sequence (EGS) oligonucleotides (oligozymes), and other short catalytic RNAs or catalytic oligonucleotides which hybridize to the target nucleic acid and modulate its expression.

[00186] The anti-sense reagent may be antisense oligonucleotides (ODN), particularly synthetic ODN having chemical modifications from native nucleic acids, or nucleic acid constructs that express such anti-sense molecules as RNA. The antisense sequence is complementary to the mRNA of the targeted gene, and inhibits expression of the targeted gene products. Antisense molecules inhibit gene expression through various mechanisms, *e.g.* by reducing the amount of mRNA available for translation, through activation of RNAse H, or steric hindrance. One or a combination of antisense molecules may be administered, where a combination may comprise multiple different sequences.

[00187] Antisense molecules may be produced by expression of all or a part of the target gene sequence in an appropriate vector, where the transcriptional initiation is oriented such that an antisense strand is produced as an RNA molecule. Alternatively, the antisense molecule is a synthetic oligonucleotide. Antisense oligonucleotides will generally be at least about 7, usually at least about 12, more usually at least about 20 nucleotides in length, and not more than about 500, usually not more than about 50, more usually not more than about 35 nucleotides in length, where the length is governed by efficiency of inhibition, specificity, including absence of cross-reactivity, and the like. It has been found that short

oligonucleotides, of from 7 to 8 bases in length, can be strong and selective inhibitors of gene expression (see Wagner *et al.* (1996), *Nature Biotechnol.* **14**:840-844).

[00188] A specific region or regions of the endogenous sense strand mRNA sequence is chosen to be complemented by the antisense sequence. Selection of a specific sequence for the oligonucleotide may use an empirical method, where several candidate sequences are assayed for inhibition of expression of the target gene in an *in vitro* or animal model. A combination of sequences may also be used, where several regions of the mRNA sequence are selected for antisense complementation.

[00189] Antisense oligonucleotides may be chemically synthesized by methods known in the art (see Wagner *et al.* (1993), *supra,* and Milligan *et al., supra.*) Preferred oligonucleotides are chemically modified from the native phosphodiester structure, in order to increase their intracellular stability and binding affinity. A number of such modifications have been described in the literature, which modifications alter the chemistry of the backbone, sugars or heterocyclic bases.

[00190] Among useful changes in the backbone chemistry are phosphorothioates; phosphorodithioates, where both of the non-bridging oxygens are substituted with sulfur; phosphoroamidites; alkyl phosphotriesters and boranophosphates. Achiral phosphate derivatives include 3'-O'-5'-S-phosphorothioate, 3'-S-5'-O-phosphorothioate, 3'-CH2-5'-O-phosphonate and 3'-NH-5'-O-phosphoroamidate. Peptide nucleic acids replace the entire ribose phosphodiester backbone with a peptide linkage. Sugar modifications are also used to enhance stability and affinity. The β-anomer of deoxyribose may be used, where the base is inverted with respect to the natural α-anomer. The 2'-OH of the ribose sugar may be altered to form 2'-O-methyl or 2'-O-allyl sugars, which provides resistance to degradation without comprising affinity. Modification of the heterocyclic bases must maintain proper base pairing. Some useful substitutions include deoxyuridine for deoxythymidine; 5-methyl-2'-deoxycytidine and 5-bromo-2'-deoxycytidine for deoxycytidine. 5- propynyl-2'-deoxyuridine and 5-propynyl-2'-deoxycytidine have been shown to increase affinity and biological activity when substituted for deoxythymidine and deoxycytidine, respectively.

[00191] Exemplary modified oligonucleotide backbones that do not include a phosphorus atom therein have backbones that are formed by short chain alkyl or cycloalkyl internucleoside linkages, mixed heteroatom and alkyl or cycloalkyl internucleoside linkages, or one or more short chain heteroatomic or heterocyclic internucleoside linkages. These include those having morpholino linkages (formed in part from the sugar portion of a nucleoside); siloxane backbones; sulfide, sulfoxide and sulfone backbones; formacetyl and thioformacetyl

backbones; methylene formacetyl and thioformacetyl backbones; riboacetyl backbones; alkene containing backbones; sulfamate backbones; methyleneimino and methylenehydrazino backbones; sulfonate and sulfonamide backbones; amide backbones; and others having mixed N, O, S and CH_2 component parts.

[00192] Oligonucleotides having a morpholino backbone structure (Summerton, J. E. and Weller D. D., U.S. Pat. No. 5,034,506) or a peptide nucleic acid (PNA) backbone (P. E. Nielson, M. Egholm, R. H. Berg, O. Buchardt, Science 1991, 254: 1497) can also be used. Morpholino antisense oligonucleotides are amply described in the literature. See, e.g., Partridge et al. (1996) *Antisense Nucl. Acid Drug Dev.* 6:169-175; and Summerton (1999) *Biochem. Biophys. Acta* 1489:141-158.

[00193] In another embodiment, the antisense oligomer is a phosphothioate morpholino oligomer (PMO). PMOs are assembled from four different morpholino subunits, each of which contain one of four genetic bases (A, C, G, or T) linked to a six-membered morpholine ring. Polymers of these subunits are joined by non-ionic phosphodiamidate intersubunit linkages. Details of how to make and use PMOs and other antisense oligomers are well known in the art (e.g. see WO99/18193; Probst JC, Antisense Oligodeoxynucleotide and Ribozyme Design, Methods. (2000) 22(3):271-281; Summerton J, and Weller D. 1997 Antisense Nucleic Acid Drug Dev. :7:187-95; US Pat. No. 5,235,033; and US Pat No. 5,378,841).

[00194] As an alternative to anti-sense inhibitors, catalytic nucleic acid compounds, *e.g.* ribozymes, anti-sense conjugates, *etc.* may be used to inhibit gene expression. Ribozymes may be synthesized *in vitro* and administered to the patient, or may be encoded on an expression vector, from which the ribozyme is synthesized in the targeted cell (for example, see International patent application WO 9523225, and Beigelman *et al.* (1995), *Nucl. Acids Res.* **23**:4434-42). Examples of oligonucleotides with catalytic activity are described in WO 9506764. Conjugates of anti-sense ODN with a metal complex, *e.g.* terpyridylCu(II), capable of mediating mRNA hydrolysis are described in Bashkin *et al.* (1995), *Appl. Biochem. Biotechnol.* **54**:43-56.

[00195] Alternative RabGGT nucleic acid modulators are double-stranded RNA species mediating RNA interference (RNAi). RNAi is the process of sequence-specific, post-transcriptional gene silencing in animals and plants, initiated by double-stranded RNA (dsRNA) that is homologous in sequence to the silenced gene. Methods relating to the use of RNAi to silence genes in *C. elegans*, *Drosophila*, plants, and humans are known in the art (Fire A, et al., 1998 Nature 391:806-811; Fire, A. Trends Genet. 15, 358-363 (1999); Sharp, P. A. RNA interference 2001. Genes Dev. 15, 485-490 (2001); Hammond, S. M., et al., Nature

Rev. Genet. 2, 110-1119 (2001); Tuschl, T. Chem. Biochem. 2, 239-245 (2001); Hamilton, A. et al., Science 286, 950-952 (1999); Hammond, S. M., et al., Nature 404, 293-296 (2000); Zamore, P. D., et al., Cell 101, 25-33 (2000); Bernstein, E., et al., Nature 409, 363-366 (2001); Elbashir, S. M., et al., Genes Dev. 15, 188-200 (2001); WO0129058; WO9932619; Elbashir SM, et al., 2001 Nature 411:494-498).

METHODS OF DETERMINING TUMOR SUSCEPTIBILITY

[00196] In some embodiments, the present invention provides methods for determining the susceptibility of a tumor to treatment by administration of a RabGGT inhibitor. In some embodiments, the methods comprise: a) detecting a level of RabGGT protein in a cell in an individual; and b) administering to the individual an effective amount of a RabGGT modulating agent. In other embodiments, the methods comprise: a) detecting a level of RabGGT enzymatic activity in a cell in an individual; and b) administering to the individual an effective amount of a RabGGT modulating agent. In other embodiments, the methods comprise: a) detecting a level of RabGGT mRNA in a cell in an individual; and b) administering to the individual an effective amount of a RabGGT modulating agent.

[00197] Methods of detecting a level of RabGGT protein, methods of detecting a level of RabGGT enzymatic activity, and methods of detecting a level of RabGGT mRNA are described above.

[00198] In some embodiments, the methods further comprise administering an effective amount of amount of a RabGGT inhibitor to an individual having a tumor that is susceptible to treatment with a RabGGT inhibitor.

DISORDERS AMENABLE TO TREATMENT

[00199] Disorders amenable to treatment with the methods of the present invention include disorders associated with or caused by uncontrolled cell proliferation; disorders amenable to treatment by inducing apoptosis; and disorders associated with or caused by excessive apoptosis.

[00200] Disorders which can be treated using methods of the invention for inducing apoptosis include, but are not limited to, undesired, excessive, or uncontrolled cellular proliferation, including, for example, neoplastic cells; as well as any undesired cell or cell type in which induction of cell death is desired, e.g., virus-infected cells and self-reactive immune cells. The methods may be used to treat follicular lymphomas, carcinomas associated with p53 mutations; autoimmune disorders, such as, for example, systemic lupus erythematosus (SLE),

immune-mediated glomerulonephritis; hormone-dependent tumors, such as, for example, breast cancer, prostate cancer and ovary cancer; and viral infections, such as, for example, herpesviruses, poxviruses and adenoviruses.

00201] Disorders which can be treated using the methods of the invention for reducing apoptosis in a eukaryotic cell, include, but are not limited to, cell death associated with Alzheimer's disease, Parkinson's disease, rheumatoid arthritis, septic shock, sepsis, stroke, central nervous system inflammation, osteoporosis, ischemia, reperfusion injury, cell death associated with cardiovascular disease, polycystic kidney disease, cell death of endothelial cells in cardiovascular disease, degenerative liver disease, multiple sclerosis, amyotropic lateral sclerosis, cerebellar degeneration, ischemic injury, cerebral infarction, myocardial infarction, acquired immunodeficiency syndrome (AIDS), myelodysplastic syndromes, aplastic anemia, male pattern baldness, and head injury damage. Also included are conditions in which DNA damage to a cell is induced by, e.g., irradiation, radiomimetic drugs, and the like. Also included are any hypoxic or anoxic conditions, e.g., conditions relating to or resulting from ischemia, myocardial infarction, cerebral infarction, stroke, bypass heart surgery, organ transplantation, neuronal damage, and the like.

Cancer

[00202] Generally, cells in a benign tumor retain their differentiated features and do not divide in a completely uncontrolled manner. A benign tumor is usually localized and nonmetastatic. Specific types benign tumors that can be treated using the present invention include hemangiomas, hepatocellular adenoma, cavernous haemangioma, focal nodular hyperplasia, acoustic neuromas, neurofibroma, bile duct adenoma, bile duct cystanoma, fibroma, lipomas, leiomyomas, mesotheliomas, teratomas, myxomas, nodular regenerative hyperplasia, trachomas and pyogenic granulomas.

[00203] In a malignant tumor cells become undifferentiated, do not respond to the body's growth control signals, and multiply in an uncontrolled manner. The malignant tumor is invasive and capable of spreading to distant sites (metastasizing). Malignant tumors are generally divided into two categories: primary and secondary. Primary tumors arise directly from the tissue in which they are found. A secondary tumor, or metastasis, is a tumor which originated elsewhere in the body but has now spread to a distant organ. The common routes for metastasis are direct growth into adjacent structures, spread through the vascular or lymphatic systems, and tracking along tissue planes and body spaces (peritoneal fluid, cerebrospinal fluid, etc.)

[00204] Specific types of cancers or malignant tumors, either primary or secondary, that can be treated using this invention include leukemia, breast cancer, skin cancer, bone cancer, prostate cancer, liver cancer, lung cancer, brain cancer, cancer of the larynx, gallbladder, pancreas, rectum, parathyroid, thyroid, adrenal, neural tissue, head and neck, colon, stomach, bronchi, kidneys, basal cell carcinoma, squamous cell carcinoma of both ulcerating and papillary type, metastatic skin carcinoma, osteosarcoma, Ewing's sarcoma, veticulum cell sarcoma, myeloma, giant cell tumor, small-cell lung tumor, gallstones, islet cell tumor, primary brain tumor, acute and chronic lymphocytic and granulocytic tumors, hairy-cell tumor, adenoma, hyperplasia, medullary carcinoma, pheochromocytoma, mucosal neuromas, intestinal ganglioneuromas, hyperplastic corneal nerve tumor, marfanoid habitus tumor, Wilm's tumor, seminoma, ovarian tumor, leiomyomater tumor, cervical dysplasia and in situ carcinoma, neuroblastoma, retinoblastoma, soft tissue sarcoma, malignant carcinoid, topical skin lesion, mycosis fungoide, rhabdomyosarcoma, Kaposi's sarcoma, osteogenic and other sarcoma, malignant hypercalcemia, renal cell tumor, polycythermia vera, adenocarcinoma, glioblastoma multiforme, leukemias, lymphomas, malignant melanomas, epidermoid carcinomas, and other carcinomas and sarcomas.

[00205] Subjects to be treated according to the methods of the invention include any individual having any of the above-mentioned disorders. Further included are individuals who are at risk of developing any of the above-mentioned disorders, including, but not limited to, an individual who has suffered a myocardial infarction, and is therefore at risk for experiencing a subsequent myocardial infarction; an individual who has undergone organ or tissue transplantation; an individual who has had a stroke and is at risk for having a subsequent stroke; and an individual at risk of developing an autoimmune disorder due to genetic predisposition, or due to the appearance of early symptoms of autoimmune disorder.

Determining efficacy of treatment

[00206] Whether a tumor load has been decreased can be determined using any known method, including, but not limited to, measuring solid tumor mass; counting the number of tumor cells using cytological assays; fluorescence-activated cell sorting (e.g., using antibody specific for a tumor-associated antigen); computed tomography scanning, magnetic resonance imaging, and/or x-ray imaging of the tumor to estimate and/or monitor tumor size; measuring the amount of tumor-associated antigen in a biological sample, e.g., blood; and the like.

FORMULATIONS, DOSAGES, AND ROUTES OF ADMINISTRATION

Formulations

[00207] An agent that modulates a level and/or activity of RabGGT may be formulated in a variety of ways. For example, and agent may include a buffer, which is selected according to the desired use of the agent, and may also include other substances appropriate to the intended use. Those skilled in the art can readily select an appropriate buffer, a wide variety of which are known in the art, suitable for an intended use. In some instances, the composition can comprise a pharmaceutically acceptable excipient, a variety of which are known in the art and need not be discussed in detail herein. Pharmaceutically acceptable excipients have been amply described in a variety of publications, including, for example, "Remington: The Science and Practice of Pharmacy", 19th Ed. (1995), or latest edition, Mack Publishing Co; A. Gennaro (2000) "Remington: The Science and Practice of Pharmacy", 20th edition, Lippincott, Williams, & Wilkins; Pharmaceutical Dosage Forms and Drug Delivery Systems (1999) H.C. Ansel et al., eds 7th ed., Lippincott, Williams, & Wilkins; and Handbook of Pharmaceutical Excipients (2000) A.H. Kibbe et al., eds., 3rd ed. Amer. Pharmaceutical Assoc.

[00208] In the subject methods, the active agent(s) may be administered to the host using any convenient means capable of resulting in the desired modulation in a level and/or an activity of RabGGT. Thus, the agent can be incorporated into a variety of formulations for therapeutic administration. More particularly, the agents of the present invention can be formulated into pharmaceutical compositions by combination with appropriate, pharmaceutically acceptable carriers or diluents, and may be formulated into preparations in solid, semi-solid, liquid or gaseous forms, such as tablets, capsules, powders, granules, ointments, solutions, suppositories, injections, inhalants and aerosols.

[00209] In pharmaceutical dosage forms, the agents may be administered in the form of their pharmaceutically acceptable salts, or they may also be used alone or in appropriate association, as well as in combination, with other pharmaceutically active compounds. The following methods and excipients are merely exemplary and are in no way limiting.

[00210] For oral preparations, the agents can be used alone or in combination with appropriate additives to make tablets, powders, granules or capsules, for example, with conventional additives, such as lactose, mannitol, corn starch or potato starch; with binders, such as crystalline cellulose, cellulose derivatives, acacia, corn starch or gelatins; with disintegrators, such as corn starch, potato starch or sodium carboxymethylcellulose; with lubricants, such as talc or magnesium stearate; and if desired, with diluents, buffering agents, moistening agents, preservatives and flavoring agents.

[00211] The agents can be formulated into preparations for injection by dissolving, suspending or emulsifying them in an aqueous or nonaqueous solvent, such as vegetable or other similar oils, synthetic aliphatic acid glycerides, esters of higher aliphatic acids or propylene glycol; and if desired, with conventional additives such as solubilizers, isotonic agents, suspending agents, emulsifying agents, stabilizers and preservatives.

[00212] The agents can be utilized in aerosol formulation to be administered via inhalation. The compounds of the present invention can be formulated into pressurized acceptable propellants such as dichlorodifluoromethane, propane, nitrogen and the like.

[00213] Furthermore, the agents can be made into suppositories by mixing with a variety of bases such as emulsifying bases or water-soluble bases. The compounds of the present invention can be administered rectally via a suppository. The suppository can include vehicles such as cocoa butter, carbowaxes and polyethylene glycols, which melt at body temperature, yet are solidified at room temperature.

[00214] Unit dosage forms for oral or rectal administration such as syrups, elixirs, and suspensions may be provided wherein each dosage unit, for example, teaspoonful, tablespoonful, tablet or suppository, contains a predetermined amount of the composition containing one or more inhibitors. Similarly, unit dosage forms for injection or intravenous administration may comprise the inhibitor(s) in a composition as a solution in sterile water, normal saline or another pharmaceutically acceptable carrier.

[00215] The term "unit dosage form," as used herein, refers to physically discrete units suitable as unitary dosages for human and animal subjects, each unit containing a predetermined quantity of compounds of the present invention calculated in an amount sufficient to produce the desired effect in association with a pharmaceutically acceptable diluent, carrier or vehicle. The specifications for the novel unit dosage forms of the present invention depend on the particular compound employed and the effect to be achieved, and the pharmacodynamics associated with each compound in the host.

[00216] Other modes of administration will also find use with the subject invention. For instance, an agent of the invention can be formulated in suppositories and, in some cases, aerosol and intranasal compositions. For suppositories, the vehicle composition will include traditional binders and carriers such as, polyalkylene glycols, or triglycerides. Such suppositories may be formed from mixtures containing the active ingredient in the range of about 0.5% to about 10% (w/w), preferably about 1% to about 2%.

[00217] Intranasal formulations will usually include vehicles that neither cause irritation to the nasal mucosa nor significantly disturb ciliary function. Diluents such as water, aqueous saline

or other known substances can be employed with the subject invention. The nasal formulations may also contain preservatives such as, but not limited to, chlorobutanol and benzalkonium chloride. A surfactant may be present to enhance absorption of the subject proteins by the nasal mucosa.

00218] An agent of the invention can be administered as injectables. Typically, injectable compositions are prepared as liquid solutions or suspensions; solid forms suitable for solution in, or suspension in, liquid vehicles prior to injection may also be prepared. The preparation may also be emulsified or the active ingredient encapsulated in liposome vehicles.

00219] Suitable excipient vehicles are, for example, water, saline, dextrose, glycerol, ethanol, or the like, and combinations thereof. In addition, if desired, the vehicle may contain minor amounts of auxiliary substances such as wetting or emulsifying agents or pH buffering agents. Actual methods of preparing such dosage forms are known, or will be apparent, to those skilled in the art. See, e.g., Remington's Pharmaceutical Sciences, Mack Publishing Company, Easton, Pennsylvania, 17th edition, 1985. The composition or formulation to be administered will, in any event, contain a quantity of the agent adequate to achieve the desired state in the subject being treated.

00220] The pharmaceutically acceptable excipients, such as vehicles, adjuvants, carriers or diluents, are readily available to the public. Moreover, pharmaceutically acceptable auxiliary substances, such as pH adjusting and buffering agents, tonicity adjusting agents, stabilizers, wetting agents and the like, are readily available to the public.

Dosages

00221] Although the dosage used will vary depending on the clinical goals to be achieved, a suitable dosage range is one which provides up to about 1 μg to about 1,000 μg or about 10,000 μg of an agent that reduces a level and/or an activity of RabGGT can be administered in a single dose. Alternatively, a target dosage of an agent that modulates a level and/or an activity of RabGGT can be considered to be about in the range of about 0.1-1000 μM, about 0.5-500 μM, about 1-100 μM, or about 5-50μM in a sample of host blood drawn within the first 24-48 hours after administration of the agent.

[00222] Those of skill will readily appreciate that dose levels can vary as a function of the specific compound, the severity of the symptoms and the susceptibility of the subject to side effects. Preferred dosages for a given compound are readily determinable by those of skill in the art by a variety of means.

Routes of administration

00223] An agent that modulates a level and/or activity of RabGGT may be administered (including self-administered) orally, parenterally, intraperitoneally, intravenously, intraarterially, transdermally, intratumorally, sublingually, intramuscularly, rectally, transbuccally, intranasally, liposomally, via inhalation, vaginally, intraoccularly, via local delivery (for example by catheter or stent), subcutaneously, intraadiposally, intraarticularly, or intrathecally.

00224] An agent that modulates a level and/or activity of RabGGT may be administered by a variety of routes, and may be administered in any conventional dosage form. In some embodiments, an agent that modulates a level and/or activity of RabGGT is administered in combination therapy (e.g., is "coadministered) with at least a second therapeutic agent. Coadministration in the context of this invention is defined to mean the administration of more than one therapeutic in the course of a coordinated treatment to achieve an improved clinical outcome. Such coadministration may also be coextensive, that is, occurring during overlapping periods of time.

00225] One route of administration or coadministration is local delivery. Local delivery of an effective amount of an agent that modulates an activity and/or level of RabGGT can be by a variety of techniques and devices that administer the agent(s) at or near a desired site. Examples of local delivery techniques and structures are not intended to be limiting but rather as illustrative of the techniques and structures available. Examples include local delivery catheters, site specific carriers, implants, direct injection, or direct applications.

[00226] Local delivery by a catheter allows the administration of an agent directly to the desired site. Examples of local delivery using a balloon catheter are described in EP 383 492 A2 and U.S. Pat. No. 4,636,195 to Wolinsky. Additional examples of local, catheter-based techniques and structures are disclosed in U.S. Pat. No. 5,049,132 to Shaffer et al. and U.S. Pat No. 5,286,254 to Shapland et al.

[00227] Generally, the catheter must be placed such that the agent is delivered at or near the desired site. Dosages delivered through the catheter can vary, according to determinations made by one of skill, but often are in amounts effective to generate the desired effect at the local site. Preferably, these total amounts are less than the total amounts for systemic administration of an agent, and are less than the maximum tolerated dose. The agent(s) delivered through catheters is generally formulated in a viscosity that enables delivery through a small treatment catheter, and may be formulated with pharmaceutically acceptable additional ingredients (active and inactive).

[00228] Local delivery by an implant describes the placement of a matrix that contains an agent into the desired site. The implant may be deposited by surgery or other means. The implanted matrix releases the agent by diffusion, chemical reaction, solvent activators, or other equivalent mechanisms. Examples are set forth in Lange, Science 249:1527-1533 (September, 1990). Often the implants may be in a form that releases the agent over time; these implants are termed time-release implants. The material of construction for the implants will vary according to the nature of the implant and the specific use to which it will be put. For example, biostable implants may have a rigid or semi-rigid support structure, with agent delivery taking place through a coating or a porous support structure. Other implants made be made of a liquid that stiffens after being implanted or may be made of a gel. The amounts of agent present in or on the implant may be in an amount effective to treat cell proliferation generally, or a specific proliferation indication, such as the indications discussed herein. One example of local delivery of an agent by an implant is use of a biostable or bioabsorbable plug or patch or similar geometry that can deliver the agent once placed in or near the desired site.

[00229] A non-limiting example of local delivery by an implant is the use of a stent. Stents are designed to mechanically prevent the collapse and reocclusion of the coronary arteries. Incorporating an agent into the stent may deliver the agent directly to or near the proliferative site. Certain aspects of local delivery by such techniques and structures are described in Kohn, Pharmaceutical Technology (October, 1990). Stents may be coated with the agent to be delivered. Examples of such techniques and structures may be found in U.S. Pat. No. 5,464,650 to Berg et al., U.S. Pat. No. 5,545,208 to Wolff et al., U.S. Pat. No. 5,649,977 to Campbell, U.S. Pat. No. 5,679,400 to Tuch, EP 0 716 836 to Tartaglia et al. Alternatively, the agent-loaded stent may be bioerodable, i.e. designed to dissolve, thus releasing the agent in or near the desired site, as disclosed in U.S. Pat. No. 5,527,337 to Stack et al. The present invention can be used with a wide variety of stent configurations, including, but not limited to shape memory alloy stents, expandable stents, and stents formed in situ.

[00230] Another example is a delivery system in which a polymer that contains an agent is injected into the target cells in liquid form. The polymer then cures to form the implant in situ. One variation of this technique and structure is described in WO 90/03768.

[00231] Another example is the delivery of an agent by polymeric endoluminal sealing. This technique and structure uses a catheter to apply a polymeric implant to the interior surface of the lumen. The agent incorporated into the biodegradable polymer implant is thereby released at the desired site. One example of this technique and structure is described in WO 90/01969.

[00232] Another example of local delivery by an implant is by direct injection of vesicles or microparticulates into the desired site. These microparticulates may comprise substances such as proteins, lipids, carbohydrates or synthetic polymers. These microparticulates have an agent incorporated throughout the microparticle or over the microparticle as a coating. Examples of delivery systems incorporating microparticulates are described in Lange, Science, 249:1527-1533 (September, 1990) and Mathiowitz, et al., J. App. Poly Sci. 26:809 (1981).

[00233] Local delivery by site specific carriers may involve linking an agent to a carrier which will direct the drug to the desired site. Examples of this delivery technique and structure include the use of carriers such as a protein ligand or a monoclonal antibody. Certain aspects of these techniques and structures are described in Lange, Science 249:1527-1533.

[00234] Local delivery also includes the use of topical applications. An example of a local delivery by topical application is applying an agent directly to an arterial bypass graft during a surgical procedure. Other equivalent examples will no doubt occur to one of skill in the art.

Combination therapies

[00235] An agent that reduces the level and/or activity of RabGGT may be administered in combination therapy with one or more additional therapeutic agents.

[00236] An agent that reduces the level and/or activity of RabGGT may be administered in combination therapy with one or more antiangiogenesis agents to inhibit undesirable and uncontrolled angiogenesis. Examples of anti-angiogenesis agents include, but are not limited to, retinoid acid and derivatives thereof, 2-methoxyestradiol, ANGIOSTATIN™ protein, ENDOSTATIN™ protein, suramin, squalamine, tissue inhibitor of metalloproteinase-I, tissue inhibitor of metalloproteinase-2, plasminogen activator inhibitor-1, plasminogen activator inhibitor-2, cartilage-derived inhibitor, paclitaxel, platelet factor 4, protamine sulphate (clupeine), sulfated chitin derivatives, sulfated polysaccharide peptidoglycan complex (sp-pg), staurosporine, modulators of matrix metabolism, including for example, proline analogs ((I-azetidine-2-carboxylic acid (LACA), cishydroxyproline, d,I-3,4-dehydroproline, thiaproline], α, α-dipyridyl, β.-aminopropionitrile fumarate, 4-propyl-5-(4-pyridinyl)-2(3h)-oxazolone; methotrexate, mitoxantrone, heparin, interferons, 2 macroglobulin-serum, chimp-3, chymostatin, β-cyclodextrin tetradecasulfate, eponemycin; fumagillin, gold sodium thiomalate, d-penicillamine (CDPT), β-1-anticollagenase-serum, α2-antiplasmin, bisantrene, lobenzarit disodium, n-(2-carboxyphenyl-4-chloroanthronilic acid disodium or "CCA", thalidomide; angostatic steroid, cargboxynaminolmidazole; metalloproteinase inhibitors such as BB94. Other anti-angiogenesis agents include antibodies, e.g., monoclonal antibodies against these

angiogenic growth factors: bFGF, aFGF, FGF-5, VEGF isoforms, VEGF-C, HGF/SF and Ang-1/Ang-2. Ferrara N. and Alitalo, K. "Clinical application of angiogenic growth factors and their inhibitors" (1999) Nature Medicine 5:1359-1364.

[00237] An agent that reduces the level and/or activity of RabGGT may be administered in combination therapy with one or more antiproliferative agents, or as an adjuvant to a standard cancer treatment. Standard cancer therapies include surgery (e.g., surgical removal of cancerous tissue), radiation therapy, bone marrow transplantation, chemotherapeutic treatment, biological response modifier treatment, and certain combinations of the foregoing.

[00238] Radiation therapy includes, but is not limited to, x-rays or gamma rays that are delivered from either an externally applied source such as a beam, or by implantation of small radioactive sources.

[00239] Chemotherapeutic agents are non-peptidic (i.e., non-proteinaceous) compounds that reduce proliferation of cancer cells, and encompass cytotoxic agents and cytostatic agents. Non-limiting examples of chemotherapeutic agents include alkylating agents, nitrosoureas, antimetabolites, antitumor antibiotics, plant (vinca) alkaloids, and steroid hormones.

[00240] Agents that act to reduce cellular proliferation are known in the art and widely used. Such agents include alkylating agents, such as nitrogen mustards, nitrosoureas, ethylenimine derivatives, alkyl sulfonates, and triazenes, including, but not limited to, mechlorethamine, cyclophosphamide (Cytoxan™), melphalan (L-sarcolysin), carmustine (BCNU), lomustine (CCNU), semustine (methyl-CCNU), streptozocin, chlorozotocin, uracil mustard, chlormethine, ifosfamide, chlorambucil, pipobroman, triethylenemelamine, triethylenethiophosphoramine, busulfan, dacarbazine, and temozolomide.

[00241] Antimetabolite agents include folic acid analogs, pyrimidine analogs, purine analogs, and adenosine deaminase inhibitors, including, but not limited to, cytarabine (CYTOSAR-U), cytosine arabinoside, fluorouracil (5-FU), floxuridine (FudR), 6-thioguanine, 6-mercaptopurine (6-MP), pentostatin, 5-fluorouracil (5-FU), methotrexate, 10-propargyl-5,8-dideazafolate (PDDF, CB3717), 5,8-dideazatetrahydrofolic acid (DDATHF), leucovorin, fludarabine phosphate, pentostatine, and gemcitabine.

[00242] Suitable natural products and their derivatives, (e.g., vinca alkaloids, antitumor antibiotics, enzymes, lymphokines, and epipodophyllotoxins), include, but are not limited to, Ara-C, paclitaxel (Taxol®), docetaxel (Taxotere®), deoxycoformycin, mitomycin-C, L-asparaginase, azathioprine; brequinar; alkaloids, *e.g.* vincristine, vinblastine, vinorelbine, vindesine, *etc.*; podophyllotoxins, *e.g.* etoposide, teniposide, *etc.*; antibiotics, *e.g.* anthracycline, daunorubicin hydrochloride (daunomycin, rubidomycin, cerubidine), idarubicin,

doxorubicin, epirubicin and morpholino derivatives, *etc.*; phenoxizone biscyclopeptides, *e.g.* dactinomycin; basic glycopeptides, *e.g.* bleomycin; anthraquinone glycosides, *e.g.* plicamycin (mithramycin); anthracenediones, *e.g.* mitoxantrone; azirinopyrrolo indolediones, *e.g.* mitomycin; macrocyclic immunosuppressants, *e.g.* cyclosporine, FK-506 (tacrolimus, prograf), rapamycin, *etc.*; and the like.

[00243] Other anti-proliferative cytotoxic agents are navelbene, CPT-11, anastrazole, letrazole, capecitabine, reloxafine, cyclophosphamide, ifosamide, and droloxafine.

[00244] Microtubule affecting agents that have antiproliferative activity are also suitable for use and include, but are not limited to, allocolchicine (NSC 406042), Halichondrin B (NSC 609395), colchicine (NSC 757), colchicine derivatives (e.g., NSC 33410), dolstatin 10 (NSC 376128), maytansine (NSC 153858), rhizoxin (NSC 332598), paclitaxel (Taxol®), Taxol® derivatives, docetaxel (Taxotere®), thiocolchicine (NSC 361792), trityl cysterin, vinblastine sulfate, vincristine sulfate, natural and synthetic epothilones including but not limited to, eopthilone A, epothilone B, discodermolide; estramustine, nocodazole, and the like.

[00245] Hormone modulators and steroids (including synthetic analogs) that are suitable for use include, but are not limited to, adrenocorticosteroids, *e.g.* prednisone, dexamethasone, *etc.*; estrogens and pregestins, *e.g.* hydroxyprogesterone caproate, medroxyprogesterone acetate, megestrol acetate, estradiol, clomiphene, tamoxifen; *etc.*; and adrenocortical suppressants, *e.g.* aminoglutethimide; 17α-ethinylestradiol; diethylstilbestrol, testosterone, fluoxymesterone, dromostanolone propionate, testolactone, methylprednisolone, methyl-testosterone, prednisolone, triamcinolone, chlorotrianisene, hydroxyprogesterone, aminoglutethimide, estramustine, medroxyprogesterone acetate, leuprolide, Flutamide (Drogenil), Toremifene (Fareston), and Zoladex®. Estrogens stimulate proliferation and differentiation, therefore compounds that bind to the estrogen receptor are used to block this activity. Corticosteroids may inhibit T cell proliferation.

[00246] Other chemotherapeutic agents include metal complexes, *e.g.* cisplatin (cis-DDP), carboplatin, *etc.*; ureas, *e.g.* hydroxyurea; and hydrazines, *e.g.* N-methylhydrazine; epidophyllotoxin; a topoisomerase inhibitor; procarbazine; mitoxantrone; leucovorin; tegafur; etc.. Other anti-proliferative agents of interest include immunosuppressants, *e.g.* mycophenolic acid, thalidomide, desoxyspergualin, azasporine, leflunomide, mizoribine, azaspirane (SKF 105685); Iressa® (ZD 1839, 4-(3-chloro-4-fluorophenylamino)-7-methoxy-6-(3-(4-morpholinyl)propoxy)quinazoline); etc.

[00247] "Taxanes" include paclitaxel, as well as any active taxane derivative or pro-drug. "Paclitaxel" (which should be understood herein to include analogues, formulations, and

derivatives such as, for example, docetaxel, TAXOL™, TAXOTERE™ (a formulation of docetaxel), 10-desacetyl analogs of paclitaxel and 3'N-desbenzoyl-3'N-t-butoxycarbonyl analogs of paclitaxel) may be readily prepared utilizing techniques known to those skilled in the art (see also WO 94/07882, WO 94/07881, WO 94/07880, WO 94/07876, WO 93/23555, WO 93/10076; U.S. Pat. Nos. 5,294,637; 5,283,253; 5,279,949; 5,274,137; 5,202,448; 5,200,534; 5,229,529; and EP 590,267), or obtained from a variety of commercial sources, including for example, Sigma Chemical Co., St. Louis, Mo. (T7402 from *Taxus brevifolia*; or T-1912 from *Taxus yannanensis*).

[00248] Paclitaxel should be understood to refer to not only the common chemically available form of paclitaxel, but analogs and derivatives (e.g., Taxotere™ docetaxel, as noted above) and paclitaxel conjugates (e.g., paclitaxel-PEG, paclitaxel-dextran, or paclitaxel-xylose).

[00249] Also included within the term "taxane" are a variety of known derivatives, including both hydrophilic derivatives, and hydrophobic derivatives. Taxane derivatives include, but not limited to, galactose and mannose derivatives described in International Patent Application No. WO 99/18113; piperazino and other derivatives described in WO 99/14209; taxane derivatives described in WO 99/09021, WO 98/22451, and U.S. Patent No. 5,869,680; 6-thio derivatives described in WO 98/28288; sulfenamide derivatives described in U.S. Patent No. 5,821,263; and taxol derivative described in U.S. Patent No. 5,415,869. It further includes prodrugs of paclitaxel including, but not limited to, those described in WO 98/58927; WO 98/13059; and U.S. Patent No. 5,824,701.

[00250] Biological response modifiers suitable for use in connection with the methods of the invention include, but are not limited to, (1) inhibitors of tyrosine kinase (RTK) activity; (2) inhibitors of serine/threonine kinase activity; (3) tumor-associated antigen antagonists, such as antibodies that bind specifically to a tumor antigen; (4) apoptosis receptor agonists; (5) interleukin-2; (6) IFN-α; (7) IFN-γ (8) colony-stimulating factors; (9) inhibitors of angiogenesis; and (10) antagonists of tumor necrosis factor.

SCREENING METHODS

[00251] The present invention provides methods of identifying an agent that induces apoptosis and/or inhibits cell proliferation. The method comprises screening a test agent in an assay system that detects changes in RabGGT level or activity. Any of the methods previously discussed for determining RagGGT protein level, RabGGT mRNA level, RabGGT enzymatic activity, RabGGT binding activity, etc. can be used in the assay system. For the discovery of small molecule modulators, the assay system may employ high-throughput screening of a

combinatorial library. A small molecule that is identified as reducing RabGGT levels or activity is then further tested to determine whether it induces apoptosis in a cell and/or inhibit cell proliferation. In an alternative embodiment, a compound already known to induce apoptosis and/or inhibit cell proliferation may serve as the test agent to determine whether the mechanism of action of the compound is through targeting RabGGT. A compound identified as inhibiting RabGGT activity and having an apoptotic and/or anti-proliferative effect on cells may serve as a "lead compound" from which further "analog compounds" are designed and synthesized in a drug development/optimization process to improve structure-activity relationship and other properties such as absorption, distribution, metabolism and excretion (ADME), etc. Typically, the analog compounds are synthesized to have an electronic configuration and a molecular conformation similar to that of the lead compound. Identification of analog compounds can be performed through use of techniques such as self-consistent field (SCF) analysis, configuration interaction (CI) analysis, and normal mode dynamics analysis. Computer programs for implementing these techniques are available. See, e.g., Rein et al., (1989) Computer-Assisted Modeling of Receptor-Ligand Interactions (Alan Liss, New York). Once analogs have been prepared, they can be screened using the methods disclosed herein to identify those analogs that exhibit an increased ability to modulate RabGGT activity. Such compounds can then be subjected to further analysis to identify those compounds that have the greatest potential as pharmaceutical agents. Alternatively, analogs shown to have activity through the screening methods can serve as lead compounds in the preparation of still further analogs, which can be screened by the methods described herein. The cycle of screening, synthesizing analogs and re-screening can be repeated multiple times.

[00252] Compounds identified as having the greatest potential as pharmaceutical agents are identified as "clinical compounds" and their safety and efficacy are further evaluated in clinical trials. Kits may be prepared comprising a clinical compound and instructions for administering the clinical compound to a patient afflicted with a disorder associated with undesired or uncontrolled cell proliferation.

[00253] The present invention further provides methods of identifying agents that selectively modulate a level and/or an activity, e.g., an enzymatic activity, of RabGGT. The present invention further provides methods of identifying agents that selectively modulate a level and/or activity of a RabGGT/REP complex.

[00254] An agent that selectively modulates a level and/or an enzymatic activity of RabGGT is an agent that does not substantially modulate a level or an enzymatic activity of another (non-RabGGT) enzyme, including farnesyl transferase, e.g., the agent modulates the level or activity

of another enzyme by less than about 10%, less than about 5%, less than about 2%, or less than about 1%, compared to the activity the enzyme in the absence of the agent. Thus, in some embodiments, an agent that selectively modulates a level and/or an enzymatic activity of RabGGT modulates the activity of a farnesyl transferase by less than about 10%, less than about 5%, less than about 2%, or less than about 1%, compared to the level or the activity the farnesyl transferase in the absence of the agent. An agent that selectively modulates the level and/or enzymatic activity of RabGGT is suitable for use in a method of the present invention.

[00255] Certain screening methods involve screening for a compound that modulates the expression of the RabGGT gene. Such methods generally involve conducting cell-based assays in which test compounds are contacted with one or more cells expressing RabGGT and then detecting an increase in RabGGT gene expression (either transcript or translation product). Some assays are performed with cells that express endogenous RabGGT. Other expression assays are conducted with cells that do not express endogenous RabGGT, but that express an exogenous RabGGT sequence.

[00256] RabGGT expression can be detected in a number of different ways. The expression level of a RabGGT in a cell can be determined by probing the mRNA expressed in a cell with a probe that specifically hybridizes with a transcript (or complementary nucleic acid derived therefrom) of RabGGT. Probing can be conducted by lysing the cells and conducting Northern blots or without lysing the cells using in situ-hybridization techniques. Alternatively, RabGGT protein can be detected using immunological methods in which a cell lysate is probe with antibodies that specifically bind to RabGGT protein.

[00257] Other cell-based assays are reporter assays conducted with cells that do not express RabGGT. Certain of these assays are conducted with a heterologous nucleic acid construct that includes a RabGGT promoter that is operably linked to a reporter gene that encodes a detectable product. A number of different reporter genes can be utilized. Some reporters are inherently detectable. An example of such a reporter is green fluorescent protein that emits fluorescence that can be detected with a fluorescence detector. Other reporters generate a detectable product. Often such reporters are enzymes. Exemplary enzyme reporters include, but are not limited to, β-glucuronidase, CAT (chloramphenicol acetyl transferase; Alton and Vapnek (1979) Nature 282:864-869), luciferase, β-galactosidase and alkaline phosphatase (Toh, et al. (1980) Eur. J. Biochem. 182:231-238; and Hall et al. (1983) J. Mol. Appl. Gen. 2:101).

[00258] In these assays, cells harboring the reporter construct are contacted with a test compound. A test compound that either activates the promoter by binding to it or triggers a

cascade that produces a molecule that activates the promoter causes expression of the detectable reporter. Certain other reporter assays are conducted with cells that harbor a heterologous construct that includes a transcriptional control element that activates expression of RabGGT and a reporter operably linked thereto. Here, too, an agent that binds to the transcriptional control element to activate expression of the reporter or that triggers the formation of an agent that binds to the transcriptional control element to activate reporter expression, can be identified by the generation of signal associated with reporter expression.

[00259] The level of expression or activity can be compared to a baseline value. As indicated above, the baseline value can be a value for a control sample or a statistical value that is representative of RabGGT expression levels for a control population (e.g., healthy individuals not at risk for neurological injury such as stroke). Expression levels can also be determined for cells that do not express a RabGGT as a negative control. Such cells generally are otherwise substantially genetically the same as the test cells.

[00260] A variety of different types of cells can be utilized in the reporter assays. In general, eukaryotic cells are used. The eukaryotic cells can be any of the cells typically utilized in generating cells that harbor recombinant nucleic acid constructs. Exemplary eukaryotic cells include, but are not limited to, yeast, and various higher eukaryotic cells such as the COS, CHO and HeLa cell lines.

[00261] Various controls can be conducted to ensure that an observed activity is authentic including running parallel reactions with cells that lack the reporter construct or by not contacting a cell harboring the reporter construct with test compound. Compounds can also be further validated as described below.

[00262] Compounds that are initially identified by any of the foregoing screening methods can be further tested to validate the apparent activity. The basic format of such methods involves administering a lead compound identified during an initial screen to a non-human animal that serves as a model for humans and then determining if a RabGGT activity is in fact modulated. The non-human animal models utilized in validation studies generally are mammals. Specific examples of suitable animals include, but are not limited to, primates, mice, and rats.

[00263] The present invention provides a method for identifying an agent that selectively modulates the enzymatic activity of a RabGGT enzyme, the method generally involving measuring the enzymatic activity of a RabGGT enzyme in the presence of a test agent; and measuring the enzymatic activity of a farnesyl transferase enzyme in the presence of the test agent. A test agent that modulates the enzymatic activity of the RabGGT enzyme, and that does not substantially modulate the enzymatic activity of the farnesyl transferase enzyme, is

considered to selectively modulate the enzymatic activity of the RabGGT enzyme. In general, a test agent that modulates the enzymatic activity of RabGGT by at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 55%, at least about 60%, at least about 65%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, or at least about 90%, or more, compared to the RabGGT enzymatic activity in the absence of the agent, and that modulates the enzymatic activity of the farnesyl transferase activity by less than about 10%, less than about 5%, less than about 2%, or less than about 1%, compared to the activity the farnesyl transferase in the absence of the agent, is considered to selectively modulate the enzymatic activity of the RabGGT enzyme.

00264] The enzymatic activity of RabGGT can be determined using any known method. For example, RabGGT enzymatic activity is quantified using a filter binding assay that measures the transfer of (^{3}H) geranylgeranyl groups (GG) from all-trans-(^{3}H)geranylgeranyl pyrophosphate (^{3}H-GGPP) to recombinant Rab3A protein (Shen and Seabra (1996) *J. Biol. Chem.* 271:3692; Armstrong *et al.* (1996) *Methods in Enzymology* 257:30), or as described in the Examples.

00265] The enzymatic activity of farnesyl transferase can be measured using any known method, e.g., the method described in Mann et al. (1995) *Drug Dev. Res.* 34:121, or in Ding et al. (1999) *J. Med. Chem.* 42:5241.

00266] The terms "candidate agent," "test agent," "agent", "substance" and "compound" are used interchangeably herein. Candidate agents encompass numerous chemical classes, typically synthetic, semi-synthetic, or naturally-occurring inorganic or organic molecules. Candidate agents include those found in large libraries of synthetic or natural compounds. For example, synthetic compound libraries are commercially available from Maybridge Chemical Co. (Trevillet, Cornwall, UK), ComGenex (South San Francisco, CA), and MicroSource (New Milford, CT). A rare chemical library is available from Aldrich (Milwaukee, Wis.). Alternatively, libraries of natural compounds in the form of bacterial, fungal, plant and animal extracts are available from Pan Labs (Bothell, WA) or are readily producible.

[00267] Candidate agents may be small organic or inorganic compounds having a molecular weight of more than 50 and less than about 2,500 daltons. Candidate agents may comprise functional groups necessary for structural interaction with proteins, particularly hydrogen bonding, and may include at least an amine, carbonyl, hydroxyl or carboxyl group, and may contain at least two of the functional chemical groups. The candidate agents may comprise cyclical carbon or heterocyclic structures and/or aromatic or polyaromatic structures

substituted with one or more of the above functional groups. Candidate agents are also found among biomolecules including peptides, saccharides, fatty acids, steroids, purines, pyrimidines, derivatives, structural analogs or combinations thereof.

00268] Of particular interest are agents that inhibit the enzymatic activity of RabGGT and that induce apoptosis in a cell. Thus, in some embodiments, the methods involve: a) measuring the enzymatic activity of a RabGGT enzyme in the presence of a test agent; b) measuring the enzymatic activity of a farnesyl transferase enzyme in the presence of the test agent; and c) determining whether the test agent induces apoptosis in a eukaryotic cell.

00269] A test agent that (1) reduces the enzymatic activity of RabGGT by at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 55%, at least about 60%, at least about 65%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, or at least about 90%, or more, compared to the RabGGT enzymatic activity in the absence of the agent; (2) reduces the enzymatic activity of the farnesyl transferase activity by less than about 10%, less than about 5%, less than about 2%, or less than about 1%, compared to the activity the farnesyl transferase in the absence of the agent; and (3) induces apoptosis in a eukaryotic cell is considered to be a candidate agent for the treatment of disorders amenable to treatment by inducing apoptosis, as described above.

[00270] Whether a given agent inhibits RabGGT and induces apoptosis in a eukaryotic cell can be determined using any known method. Assays can be conducted on cell populations or an individual cell, and include morphological assays and biochemical assays. A non-limiting example of a method of determining the level of apoptosis in a cell population is TUNEL (TdT-mediated dUTP nick-end labeling) labeling of the 3'-OH free end of DNA fragments produced during apoptosis (Gavrieli et al. (1992) *J. Cell Biol.* 119:493). The TUNEL method consists of catalytically adding a nucleotide, which has been conjugated to a chromogen system or a to a fluorescent tag, to the 3'-OH end of the 180-bp (base pair) oligomer DNA fragments in order to detect the fragments. The presence of a DNA ladder of 180-bp oligomers is indicative of apoptosis. Procedures to detect cell death based on the TUNEL method are available commercially, e.g., from Boehringer Mannheim (Cell Death Kit) and Oncor (Apoptag Plus). Another marker that is currently available is annexin, sold under the trademark APOPTEST™. This marker is used in the "Apoptosis Detection Kit," which is also commercially available, e.g., from R&D Systems. During apoptosis, a cell membrane's phospholipid asymmetry changes such that the phospholipids are exposed on the outer membrane. Annexins are a homologous group of proteins that bind phospholipids in the

presence of calcium. A second reagent, propidium iodide (PI), is a DNA binding fluorochrome. When a cell population is exposed to both reagents, apoptotic cells stain positive for annexin and negative for PI, necrotic cells stain positive for both, live cells stain negative for both. Other methods of testing for apoptosis are known in the art and can be used, including, e.g., the method disclosed in U.S. Patent No. 6,048,703.

RABGGT STRUCTURE

[00271] The present invention provides a three-dimensional (3-D) structure of RabGGT. A 3-D structure of a RabGGT is useful for predicting whether a given compound will bind to RabGGT, and is therefore useful for determining whether a given compound will modulate an activity of RabGGT. As discussed above, agents that modulate an activity of RabGGT are useful for the treatment of various disorders. Thus, a 3-D structure of RabGGT is useful for identifying agents that are useful for the treatment of disorders, as described herein.

[00272] The subject homology model is useful for drug design; for determining whether a given compound will modulate a RabGGT activity; and for determining whether a given compound will preferentially modulate a RabGGT activity, e.g., whether a compound will modulate a RabGGT activity, but will substantially not modulate an FT activity. Accordingly, in some embodiments, the present invention provides methods for identifying agents that modulate a RabGGT activity, but that do not substantially modulate an FT activity.

[00273] The subject 3-D structure is useful for structure-based drug design. Three dimensional structural information is useful to specify the characteristics of peptides and small molecules that might bind to or mimic a target of interest. These descriptors may then be used to search small molecule databases and to establish constraints for use in the design of combinatorial libraries. Accordingly, in some embodiments, the invention provides a method for structure-based drug design, the method comprising positioning a test compound in a subject 3-D structure of RabGGT; and modifying the test compound such that the fit within a target binding site within the 3-D structure is increased.

[00274] Target binding sites within the RabGGT 3-D structure include a Rab binding site; a prenyl moiety binding site; a REP binding site; and the like. A non-limiting example of a target binding site is a Rab binding pocket of human RabGGT. The Rab binding pocket of human RabGGT contains a bound Zn atom, coordinated by His B290, Cys B240, and Asp B238; the floor of the pocket is composed of Phe B289, Trp B52; and the back of the pocket is composed of Leu B45, Ser B48, and Tyr B44.

[00275] A test compound is positioned, using computer modeling, within the 3-D structure of RabGGT using any known program. A non-limiting example of a suitable program is Insight (Accelrys, San Diego, CA), as described in Example XIV. In these embodiments, positioning of a test compound within a binding site of the RabGGT 3-D structure is accomplished using a computer-generated model of the structure of the test compound. The computer-generated model of the test structure is positioned within the binding site of the RabGGT 3-D structure by rotating the structure until the best fit is achieved.

[00276] To arrive at the best fit within the active site, the structure of the test compound is altered using computer modeling. As such, the invention provides a method for rational drug design, comprising positioning a test compound within a 3-D structure of RabGGT; and altering, by computer modeling, the structure of the test compound, such that the altered test compound has an enhanced fit within the binding site of the RabGGT 3-D structure. In some embodiments, a test agent is modeled within the FT structure; and agents that modulate RabGGT activity, but that do not substantially modulate FT enzymatic activity, are identified and/or designed.

[00277] In some embodiments, rational drug design using computer modeling is carried out in conjunction with *in vitro* testing of the test compound, and/or the altered test compound. Thus, the present invention provides a method of identifying an agent that modulates RabGGT enzymatic activity, the method comprising selecting a test agent by performing rational drug design with a subject 3-D structure of RabGGT, wherein the selecting is performed in conjunction with computer modeling; and measuring the enzymatic activity of a RabGGT polypeptide contacted *in vitro* with the test agent. In some of these embodiments, the activity of the test compound and/or the altered test compound are further tested for their effect on FT enzymatic activity. In other embodiments, the activity of the test compound and/or the altered test compound are further tested for their effect on apoptosis.

[00278] In some embodiments, the invention provides methods of designing a compound such that it modulates an activity of RabGGT, but does not substantially modulate an activity of an FT. In some embodiments, the invention provides methods of identifying a compound that modulates an activity of RabGGT and that does not substantially modulate an activity of an FT.

[00279] A 3-D model ("homology model") of RabGGT was generated by homology modeling, as described in Example XIII and Example IV, and presented in Figures 11-15. The program LOOK was used for alignments, and the model-building module within LOOK, SEGMOD, was used to build the homology models. The 3-D model includes a model of the binding

pocket for modulators of RabGGT enzymatic activity. The structure information may be provided in a computer readable form, *e.g.* as a database of atomic coordinates, or as a three-dimensional model. The present invention provides three-dimensional coordinates for the RabGGTstructure. Such a data set may be provided in computer readable form. Methods of using such coordinates (including in computer readable form) in drug assays and drug screens as exemplified herein, are also part of the present invention. In a particular embodiment of this type, the coordinates contained in the data set of can be used to identify potential modulators of the RabGGT polypeptide.

[00280] In one embodiment, a potential agent for modulation of RabGGT is selected by performing rational drug design with the three-dimensional coordinates provided herein. Typically, the selection is performed in conjunction with computer modeling. The potential agent is then contacted with the RabGGT polypeptide *in vitro*, and the activity of the RabGGT is determined. A potential agent is identified as an agent that affects the enzymatic activity of RabGGT, or binding of RabGGT to one or more of Rab, REP, a Rab/REP complex, or other protein.

[00281] Computer analysis may be performed with one or more of the computer programs including: O (Jones *et al.* (1991) *Acta Cryst.* A47:110); QUANTA, CHARMM, INSIGHT, SYBYL, MACROMODEL; ICM, and CNS (Brunger *et al.* (1998) *Acta Cryst.* D54:905). In a further embodiment of this aspect of the invention, an initial drug screening assay is performed using the three-dimensional structure so obtained, preferably along with a docking computer program. Such computer modeling can be performed with one or more Docking programs such as DOC, GRAM and AUTO DOCK. See, for example, Dunbrack *et al.* (1997) *Folding & Design* 2:27-42.

[00282] It should be understood that in the drug screening and protein modification assays provided herein, a number of iterative cycles of any or all of the steps may be performed to optimize the selection. For example, assays and drug screens that monitor the activity of the RabGGT in the presence and/or absence of a potential modulator (or potential drug) are also included in the present invention and can be employed as the sole assay or drug screen, or more preferably as a single step in a multi-step protocol.

[00283] RabGGT structure models and databases of structure information are provided. The structure model may be implemented in hardware or software, or a combination of both. For most purposes, in order to use the structure coordinates generated for the structure, it is necessary to convert them into a three-dimensional shape. This is achieved through the use of

commercially available software that is capable of generating three-dimensional graphical representations of molecules or portions thereof from a set of structure coordinates.

[00284] In one embodiment of the invention, a machine-readable storage medium is provided, the medium comprising a data storage material encoded with machine readable data which, when using a machine programmed with instructions for using said data, is capable of displaying a graphical three-dimensional representation of any of the structures of this invention that have been described above. Specifically, the computer-readable storage medium is capable of displaying a graphical three-dimensional representation of the RabGGT protein, of a complex of a test agent bound to RabGGT protein, or RabGGT complexed to one or more of a prenyl moiety, a Rab protein, a Rab/REP complex, etc.

[00285] Thus, in accordance with the present invention, data providing structural coordinates, alone or in combination with software capable of displaying the resulting three dimensional structure of the enzyme, enzyme complex, and structural elements as described above, portions thereof, and their structurally similar homologues, is stored in a machine-readable storage medium. Such data may be used for a variety of purposes, such as drug discovery, identification of agents that modulate RabGGT activity, but do not substantially modulate FT activity, and the like.

[00286] Generally, the invention is implemented in computer programs executing on programmable computers, comprising a processor, a data storage system (including volatile and non-volatile memory and/or storage elements), at least one input device, and at least one output device. Program code is applied to input data to perform the functions described above and generate output information. The output information is applied to one or more output devices, in known fashion. The computer may be, for example, a personal computer, microcomputer, or workstation of conventional design.

[00287] Each program is preferably implemented in a high level procedural or object oriented programming language to communicate with a computer system. However, the programs can be implemented in assembly or machine language, if desired. In any case, the language may be a compiled or interpreted language.

[00288] Each such computer program is preferably stored on a storage media or device (e.g., ROM or magnetic diskette) readable by a general or special purpose programmable computer, for configuring and operating the computer when the storage media or device is read by the computer to perform the procedures described herein. The system may also be considered to be implemented as a computer-readable storage medium, configured with a computer program,

where the storage medium so configured causes a computer to operate in a specific and predefined manner to perform the functions described herein.

00289] The structure of the RabGGT polypeptide, complexes, and elements thereof, are useful in the design of agents that modulate the activity and/or specificity of the enzyme, which agents may then alter cellular proliferation and/or apoptosis. Agents of interest may comprise mimetics of the structural elements. Alternatively, the agents of interest may be binding agents, for example a structure that directly binds to a region of the RabGGT polypeptide by having a physical shape that provides the appropriate contacts and space filling.

00290] For example, the structure encoded by the data may be computationally evaluated for its ability to associate with chemical entities. This provides insight into an element's ability to associate with chemical entities. Chemical entities that are capable of associating with these domains may alter apoptosis. Such chemical entities are potential drug candidates. Alternatively, the structure encoded by the data may be displayed in a graphical format. This allows visual inspection of the structure, as well as visual inspection of the structure's association with chemical entities.

00291] In one embodiment of the invention, a invention is provided for evaluating the ability of a chemical entity to associate with any of the molecules or molecular complexes set forth above. This method comprises the steps of employing computational means to perform a fitting operation between the chemical entity and the interacting surface of the RabGGT polypeptide; and analyzing the results of the fitting operation to quantify the association. The term "chemical entity", as used herein, refers to chemical compounds, complexes of at least two chemical compounds, and fragments of such compounds or complexes.

[00292] Molecular design techniques are used to design and select chemical entities, including inhibitory compounds, capable of binding to a RabGGT structural or functional element. Such chemical entities may interact directly with certain key features of the structure, as described above. Such chemical entities and compounds may interact with one or more structural functional elements (e.g., binding sites), in whole or in part.

[00293] It will be understood by those skilled in the art that not all of the atoms present in a significant contact residue need be present in a binding agent. In fact, it is only those few atoms which shape the loops and actually form important contacts that are likely to be important for activity. Those skilled in the art will be able to identify these important atoms based on the structure model of the invention, which can be constructed using the structural data herein.

[00294] The design of compounds that bind to and modulate the activity of a RabGGT polypeptide according to this invention generally involves consideration of two factors. First, the compound must be capable of physically and structurally associating with the domains described above. Non-covalent molecular interactions important in this association include hydrogen bonding, van der Waals interactions, hydrophobic interactions and electrostatic interactions.

[00295] Second, the compound must be able to assume a conformation that allows it to associate or compete with a RabGGT structural element. Although certain portions of the compound will not directly participate in these associations, those portions of the may still influence the overall conformation of the molecule. This, in turn, may have a significant impact on potency. Such conformational requirements include the overall three-dimensional structure and orientation of the chemical entity in relation to all or a portion of a binding pocket, or the spacing between functional groups of an entity comprising several interacting chemical moieties.

[00296] Computer-based methods of analysis fall into two broad classes: database methods and *de novo* design methods. In database methods the compound of interest is compared to all compounds present in a database of chemical structures and compounds whose structure is in some way similar to the compound of interest are identified. The structures in the database are based on either experimental data, generated by NMR or x-ray crystallography, or modeled three-dimensional structures based on two-dimensional data. In *de novo* design methods, models of compounds whose structure is in some way similar to the compound of interest are generated by a computer program using information derived from known structures, *e.g.* data generated by x-ray crystallography and/or theoretical rules. Such design methods can build a compound having a desired structure in either an atom-by-atom manner or by assembling stored small molecular fragments. Selected fragments or chemical entities may then be positioned in a variety of orientations, or docked, within the interacting surface of the RNA. Docking may be accomplished using software such as Quanta (Molecular Simulations, San Diego, CA) and Sybyl, followed by energy minimization and molecular dynamics with standard molecular mechanics force fields, such as CHARMM and AMBER.

[00297] Specialized computer programs may also assist in the process of selecting fragments or chemical entities. These include: GRID (Goodford (1985) J. Med. Chem., 28, pp. 849-857; Oxford University, Oxford, UK; MCSS (Miranker *et al.* (1991) Proteins: Structure, Function and Genetics, 11, pp. 29-34; Molecular Simulations, San Diego, CA); AUTODOCK (Goodsell *et al.*, (1990) Proteins: Structure, Function, and Genetics, 8, pp. 195-202; Scripps Research

Institute, La Jolla, Calif.); and DOCK (Kuntz *et al.* (1982) J. Mol. Biol., 161:269-288; University of California, San Francisco, Calif.)

00298] Once suitable chemical entities or fragments have been selected, they can be assembled into a single compound or complex. Assembly may be preceded by visual inspection of the relationship of the fragments to each other on the three-dimensional image displayed on a computer screen in relation to the structure coordinates. Useful programs to aid one of skill in the art in connecting the individual chemical entities or fragments include: CAVEAT (Bartlett *et al.* (1989) In Molecular Recognition in Chemical and Biological Problems", Special Pub., Royal Chem. Soc., 78, pp. 182-196; University of California, Berkeley, Calif.); 3D Database systems such as MACCS-3D (MDL Information Systems, San Leandro, Calif); and HOOK (available from Molecular Simulations, San Diego, CA).

[00299] Other molecular modeling techniques may also be employed in accordance with this invention. See, e.g., N. C. Cohen et al., "Molecular Modeling Software and Methods for Medicinal Chemistry, J. Med. Chem., 33, pp. 883-894 (1990). See also, M. A. Navia et al., "The Use of Structural Information in Drug Design", Current Opinions in Structural Biology, 2, pp. 202-210 (1992).

[00300] Once the binding entity has been optimally selected or designed, as described above, substitutions may then be made in some of its atoms or side groups in order to improve or modify its binding properties. Generally, initial substitutions are conservative, i.e., the replacement group will have approximately the same size, shape, hydrophobicity and charge as the original group. It should, of course, be understood that components known in the art to alter conformation should be avoided. Such substituted chemical compounds may then be analyzed for efficiency of fit by the same computer methods described above.

[00301] Another approach made possible and enabled by this invention, is the computational screening of small molecule databases for chemical entities or compounds that can bind in whole, or in part, to the RabGGT polypeptide. In this screening, the quality of fit of such entities to the binding site may be judged either by shape complementarity or by estimated interaction energy. Generally the tighter the fit, the lower the steric hindrances, and the greater the attractive forces, the more potent the potential modulator since these properties are consistent with a tighter binding constant. Furthermore, the more specificity in the design of a potential drug the more likely that the drug will not interact as well with other proteins. This will minimize potential side effects due to unwanted interactions with other proteins.

[00302] Compounds known to bind RabGGT, including those described above, can be systematically modified by computer modeling programs until one or more promising potential

analogs are identified. In addition systematic modification of selected analogs can then be systematically modified by computer modeling programs until one or more potential analogs are identified. Alternatively a potential modulator could be obtained by initially screening a random peptide library, for example one produced by recombinant bacteriophage. A peptide selected in this manner would then be systematically modified by computer modeling programs as described above, and then treated analogously to a structural analog.

[00303] Once a potential modulator/inhibitor is identified it can be either selected from a library of chemicals as are commercially available from most large chemical companies including Merck, GlaxoWelcome, Bristol Meyers Squib, Monsanto/Searle, Eli Lilly, Novartis and Pharmacia Upjohn, or alternatively the potential modulator may be synthesized *de novo*. The *de novo* synthesis of one or even a relatively small group of specific compounds is reasonable in the art of drug design.

[00304] The success of both database and *de novo* methods in identifying compounds with activities similar to the compound of interest depends on the identification of the functionally relevant portion of the compound of interest. For drugs, the functionally relevant portion may be referred to as a pharmacophore, *i.e.* an arrangement of structural features and functional groups important for biological activity. Not all identified compounds having the desired pharmacophore will act as a modulator of apoptosis. The actual activity can be finally determined only by measuring the activity of the compound in relevant biological assays. However, the methods of the invention are extremely valuable because they can be used to greatly reduce the number of compounds which must be tested to identify an actual inhibitor.

[00305] In order to determine the biological activity of a candidate pharmacophore it is preferable to measure biological activity at several concentrations of candidate compound. The activity at a given concentration of candidate compound can be tested in a number of ways.

[00306] In some embodiments, the activity of the candidate compound is tested for its activity in modulating RabGGT enzymatic activity. RabGGT enzymatic activity is quantified using a filter binding assay that measures the transfer of (^{3}H) geranylgeranyl groups (GG) from all-trans-(^{3}H)geranylgeranyl pyrophosphate (^{3}H-GGPP) to recombinant Rab3A protein (Shen and Seabra (1996) *J. Biol. Chem.* 271:3692; Armstrong *et al.* (1996) *Methods in Enzymology* 257:30), or as described in the Examples.

[00307] In some embodiments, the activity of the candidate compound is tested for its activity in modulating an interaction between RabGGT and a RabGGT interacting protein, as described above. Suitable assays include a yeast two-hybrid assay, a FRET assay, a BRET assay, a

fluorescence quenching assay; a fluorescence anisotropy assay; an immunological assay; and an assay involving binding of a detectably labeled protein to an immobilized protein.

00308] In other embodiments, the activity of the candidate compound is tested for its activity in modulating FT enzymatic activity. The enzymatic activity of farnesyl transferase can be measured using any known method, e.g., the method described in Mann et al. (1995) *Drug Dev. Res.* 34:121, or in Ding et al. (1999) *J. Med. Chem.* 42:5241.

00309] In other embodiments, the activity of the candidate compound is tested for its activity in increasing or decreasing apoptosis. Assays can be conducted on cell populations or an individual cell, and include morphological assays and biochemical assays. A non-limiting example of a method of determining the level of apoptosis in a cell population is TUNEL (TdT-mediated dUTP nick-end labeling) labeling of the 3'-OH free end of DNA fragments produced during apoptosis (Gavrieli et al. (1992) *J. Cell Biol.* 119:493).

EXAMPLES

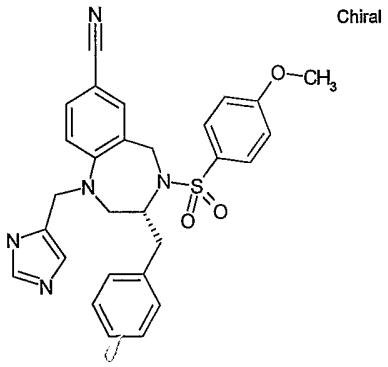
00310] The following examples are put forth so as to provide those of ordinary skill in the art with a complete disclosure and description of how to make and use the present invention, and are not intended to limit the scope of what the inventors regard as their invention nor are they intended to represent that the experiments below are all or the only experiments performed. Efforts have been made to ensure accuracy with respect to numbers used (e.g. amounts, temperature, etc.) but some experimental errors and deviations should be accounted for. Unless indicated otherwise, parts are parts by weight, molecular weight is weight average molecular weight, temperature is in degrees Celsius, and pressure is at or near atmospheric. Standard abbreviations may be used, e.g., bp, base pair(s); kb, kilobase(s); pl, picoliter(s); s, second(s); min, minute(s); hr, hour(s); and the like.

Example 1: Methods for Preparation of Compounds 7A-7T

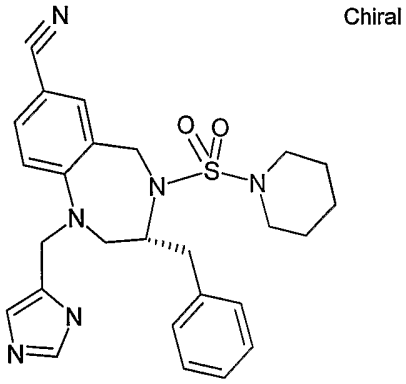
[00311] This example provides methods for synthesis of compounds 7A through 7T.

[00312] Compounds 7A, 7B, 7H, 7I, and 7J (structures shown below) may be prepared by the general procedures described by Ding *et al.*, in United States Patent No. 6,011,029, issued January 4th, 2000. Compounds 7C, 7D, 7N, 7O, 7P, 7Q, 7R, 7S, and 7T (structures shown below) may be prepared by the general procedures described by Bhide *et al.*, in United States Patent No. 6,387,926, issued May 14th, 2002. The contents of U.S. Patent Nos. 6,011,029, and 6,387,926 are hereby incorporated by reference in their entireties.

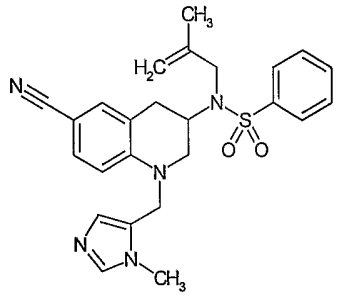
Compound 7A



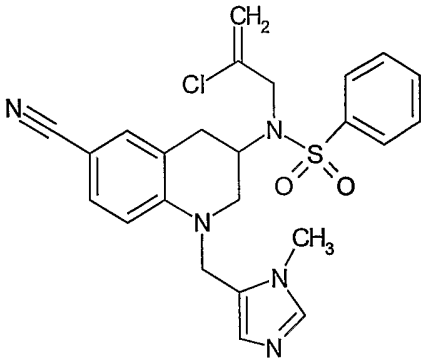
Compound 7B



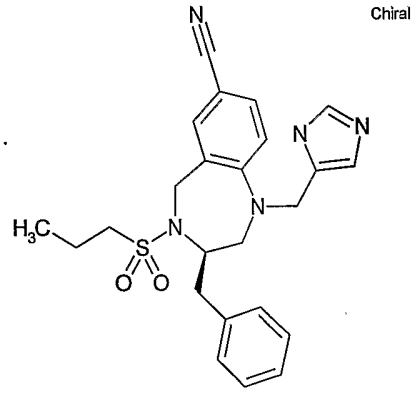
Compound 7c



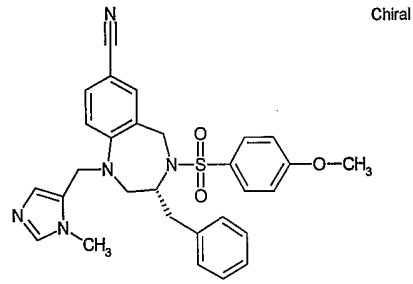
Compound 7D



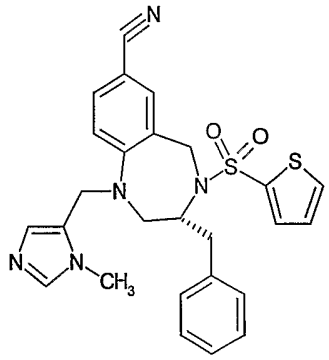
Compound 7H



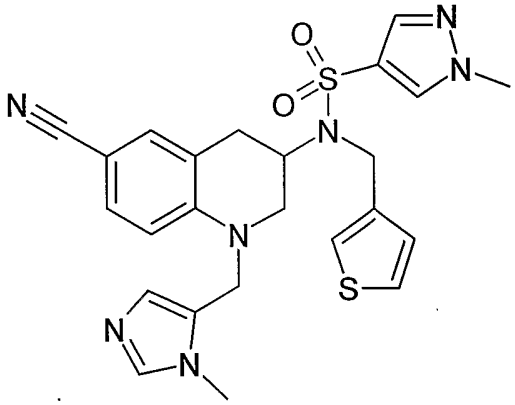
Compound 7I



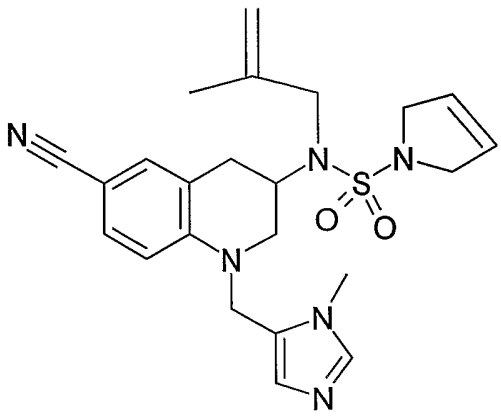
Compound 7J



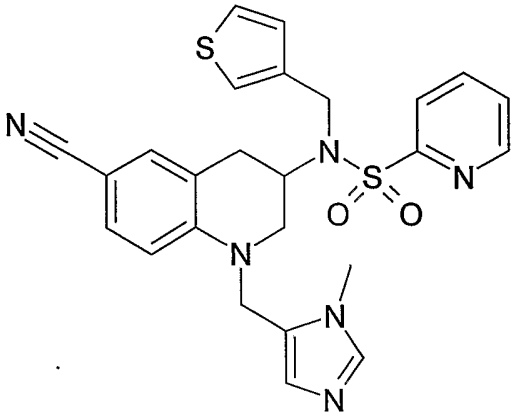
Compound 7N



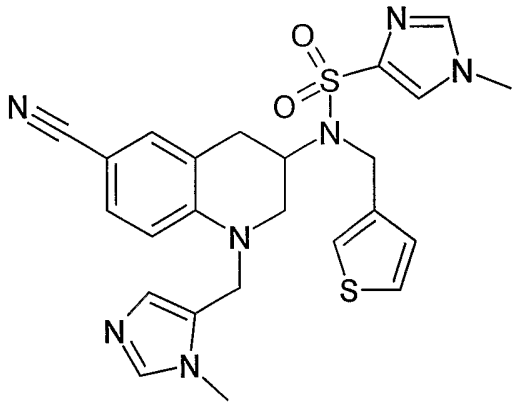
Compound 7O



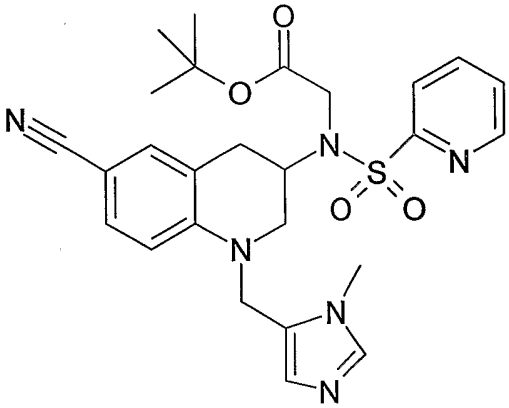
Compound 7P



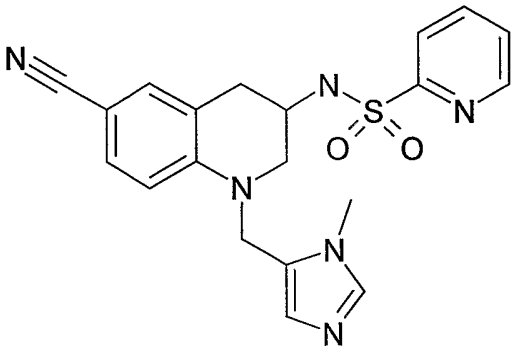
Compound 7Q



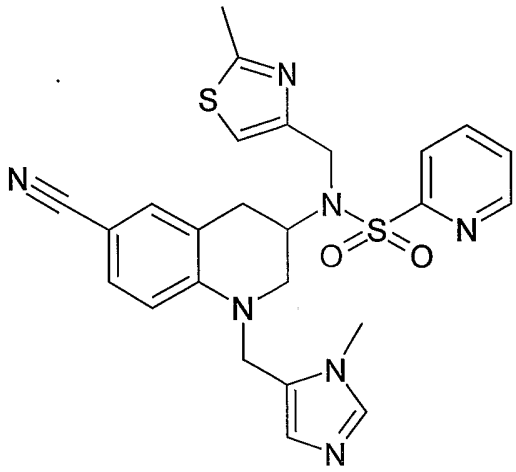
Compound 7R



Compound 7S



Compound 7T



Example II: Compound-induced apoptosis in HCT-116 human colon tumor cells

[00313] This example demonstrates that a specific apoptotic phenotype can be obtained by treatment of mammalian tissue culture cells with compounds that come from two major structural classes.

Methods

[00314] HCT-116 human colon tumor cells obtained from the American Type Culture Collection (ATCC) were grown in McCoy's 5A culture medium with 10% heat inactivated FBS, 1x penicillin/streptomycin, and 25 mM HEPES, in an incubator maintained at 37°C with CO_2 at 6-7% and humidity at 95%. Cells were treated with compounds using a dose range from 0.04 μM to 100 μM. After 48 hours they were examined by microscopy for signs of cell rounding, vaccuolation, and nuclear condensation. These are morphological markers associated

with apoptosis, and are consistent with results obtained by performing an assay for nucleosomal DNA, or a TdT-mediated dUTP nick end labeling (TUNEL) assay.

Results and Conclusions

[00315] Results of the apoptosis assay are presented in Table 1. The concentrations cited are the minimal concentration required to induce these morphological changes in 50% of the treated cells. Compounds 7A, 7B, 7D, 7H, 7I, 7J, and 7N induce apoptosis with varying potency: compound 7I is the most potent, with a minimum effective concentration of 40nM, while 7A, 7D and 7N require treatment at 3.7μM to produce apoptosis in 50% of cells. Compound 7C and compounds 7O through 7T are very weak effectors of apoptosis, requiring concentrations over 250 times higher than compounds 7B and 7H.

Table 1

Induction of apoptosis in HCT116 cells by compounds from two structural classes

Compound	Structural class	50% APOPTOTIC, μM
7A	Benzodiazepine	3.3
7B	Benzodiazepine	0.37
7C	Tetrahydroquinoline	10
7D	Tetrahydroquinoline	3.3
7H	Benzodiazepine	0.37
7I	Benzodiazepine	0.04
7J	Benzodiazepine	2.50
7N	Tetrahydroquinoline	3.3
7O	Tetrahydroquinoline	10
7P	Tetrahydroquinoline	25
7Q	Tetrahydroquinoline	30
7R	Tetrahydroquinoline	30
7S	Tetrahydroquinoline	50
7T	Tetrahydroquinoline	90

Example III: Compound induced regression of tumors in vivo

[00316] This example demonstrates that tumor regression resulting in complete cure was observed in a human tumor xenograft model in which one of the compounds was evaluated.

Methods

00317] Compound 7H was evaluated against a human tumor xenograft model; this data has been presented by Hunt *et al.* (2000, J. Med. Chem. 43:3587). Fragments of the HCT116 colon tumor were implanted subcutaneously in mice, and allowed to grow. The period of time required for tumor volume to double, TVDT, was determined. Compound administration was initiated when tumors were between 100 and 300 mg. Compound was dissolved in 10% ethanol and dosed orally once daily at 600 mg/kg for ten doses, Monday through Friday. Groups of eight mice were treated. Cures were evaluated after elapse of a post-treatment period that was greater than ten TVDT. A mouse was considered cured when no mass that was larger than 35 mg was present at the site of tumor implant. Drug-treated mice that died before the first death in the parallel control group were considered to have died from drug-related toxicity. Groups of mice with more than one death were not used in the evaluation of efficacy.

Results and Conclusions

[00318] Among the eight mice treated with compound 7H, seven mice experienced cure of the tumor, with one death that was attributed to drug related toxicity. The observation that treatment with compound 7H produces tumor regression resulting in complete cure is consistent with a model in which the compound acts on a cellular target to cause death.

Example IV: Compound-induced apoptosis in the *C. elegans* germline

[00319] This example demonstrates that treatment with the compounds also produces a specific apoptotic effect on the nematode *C. elegans*.

Methods

[00320] The compounds were applied to early larval and adult *C. elegans* hermaphrodites by mixing a concentrated DMSO solution of the compound with heat-killed OP50 bacteria in a salt solution. The bacteria were then applied to agar plates and worms of the appropriate age seeded onto the plates. Compounds 7A, 7B, 7C, 7D, 7H, 7I and 7J were applied to worms at a final concentration of 1.5 mM. and the resulting visible phenotypes analyzed. The phenotype of apoptosis in *C. elegans* was quantified as follows: Germ cells in the C. elegans hermaphrodite gonad progress through various stages of differentiation to become mature ova. At the pachytene stage of meiotic prophase, some germ cells undergo programmed cell death (apoptosis) as part of normal development. The apoptotic corpses resulting from this process can be visualized by high-resolution Nomarski optics and are readily distinguishable cells to the trained eye from viable germ cells by their compact, button-like appearance. Necrotic

cells, which are rarer, have a less compact appearance. Apoptosis is most reliably distinguished from necrosis, however, by its requirement for the core apoptotic machinery, such as a functional caspase/*ced-3* gene. Since *C. elegans* has symmetrical anterior and posterior gonad structures, referred to as "arms", apoptosis is scored by visually counting the apoptotic corpses present in a 1-2 day old adult in each germline arm. Normal, untreated worms rarely contain more than 2 corpses per arm. In a treated sample, the number of worms that contain more than 2 corpses provides a very accurate indicator of the apoptotic effect of the treatment.

Results and Conclusions

00321] Compounds 7A, 7B, 7C, 7D, 7H, 7I and 7J were applied to groups of 10-19 worms, and worms were examined for an apoptosis phenotype in the germline. The results are presented in Table 2. Adult worms treated with compound 7B showed the most striking increase in the number of apoptotic corpses in the adult germline. For example, while a typical germline arm in untreated wild-type adult worms contains 0-2 apoptotic corpses at any time (the average is 0.6 corpses/arm); treatment with compound 7B at 0.8 mM or higher increased the observed number of corpses to 5-7. Compounds 7A, 7C, 7D, 7H, 7I and 7J were found to have a similar effect to compound 7B, increasing the mean number of apoptotic corpses in the germline. In Figure 1, the percentage of the germline arms from each treated group that contain more than 2 apoptotic corpses is displayed.

Table 2

Frequency of observation of the stated number of apoptotic corpses per germline arm in wild-type worms treated with either compound or a vehicle control.

	Corpses/germline arm									
	0	**1**	**2**	**3**	**4**	**>4**	**N tested**	**mean**	**SD**	**% arms with >2 corpses**
Vehicle	7	4	0	0	0	0	11	0.4	0.5	0
7A	1	4	2	3	0	1	11	2.0	1.4	36
7B	0	0	1	1	0	10	12	6.9	2.8	92
7C	0	0	0	4	0	6	10	4.4	1.3	100
7D	0	2	3	2	2	1	10	3.0	2.1	50
7H	5	4	3	3	2	0	17	1.6	1.4	29
7I	1	3	3	1	2	1	12	2.3	1.7	33
7J	3	4	1	4	4	3	19	2.8	2.3	59
7K	5	3	6	3	1	1	19	1.7	1.4	26

Example V: The compounds mediate apoptosis via the canonical pathway

00322] This example demonstrates that the specific apoptotic effects of the compounds on *C. elegans* are abolished by a mutation in caspase/ced-3 or in APAF-1/ced-4, indicating that the compounds mediate their effects via the canonical apoptotic pathway.

Methods

00323] Early larval and adult *C. elegans* hermaphrodites were treated with compound and the phenotype of apoptosis in the germline arm was quantified as described in Example IV.

Results and Conclusions

00324] Early larval and adult *C. elegans* hermaphrodites that were mutant for the genes for caspase/ced-3 or APAF-1/ced-4 were treated with compound 7B at 1.6 mM, and the phenotype of apoptosis in the germline arm was quantified. Table 3 contains the numerical data from this experiment, and Figure 2 provides a graphical display of the data. While treatment of wild-type worms with compound 7B increases the average number of apoptotic corpses per germline arm from an average of 0.4 per arm to an average of 6.9 per arm, no increase in corpses was observed when caspase/ced-3 or in APAF-1/ced-4 mutants were treated. This observation shows that the drug-induced increase in frequency of germline corpses described in Example IV is dependent on the presence of functional components of the canonical apoptotic pathway, and supports the assertion that the increase in corpses is indeed due to an increase in apoptosis.

Table 3

Frequency of observation of the stated number of apoptotic corpses per germline arm in wild-type or mutant worms treated with 7B or vehicle.

		Corpses/germline arm									
Geno-type		**0**	**1**	**2**	**3**	**4**	**>4**	**N tested**	**mean**	**SD**	**% arms with >2 corpses**
WT	Vehicle	11	0	0	0	0	0	11	0	0	0
	7B	0	0	0	1	0	10	11	6.25	1.25	100
ced3	Vehicle	11	2	0	0	0	0	13	0.15	0.38	0
	7B	12	1	0	0	0	0	13	0.08	0.28	0
ced4	Vehicle	10	0	0	0	0	0	10	0	0	0
	7B	11	2	0	0	0	0	13	0.15	0.38	0

Example VI: RNAi of mRNA for RabGGT subunits causes apoptosis in *C.elegans*

00325] This example demonstrates that treatment of the nematode *C. elegans* with a reagent that destroys the messenger RNA (RNAi) against either subunit of RabGGT results in a specific apoptotic phenotype.

Methods

00326] DNA encoding GGTase alpha/M57.2 (GenBank entry NM_067966) and GGTase beta/ B0280.1 (GenBank entry NM_066158) was amplified from a *C. elegans* genomic DNA template by PCR (Takara *LA Taq* DNA polymerase) using oligonucleotides containing gene-specific priming sequences that were flanked by sequences encoding the T7 polymerase priming site. The gene-specific priming sequences targeted the first 5 exons of B0280.1 (product size ~2 kiloBases) and the first four exons of M57.2 (product size ~1 kiloBases). The PCR products were analyzed by gel electrophoresis to confirm that the correct product size was obtained. RNA was transcribed from the PCR product using the MEGAscript High Yield Transcription Kit (Ambion) according to manufacturer's instructions. Directly after transcription, the RNA was annealed by heating to 68°C for 20 minutes. The double stranded RNA (dsRNA) was checked for product quality by gel electrophoresis. The dsRNA was then ethanol-precipitated, washed once with 100% ethanol and twice with 70% ethanol and the pellet was allowed to air dry for 30 minutes. The dsRNA was re-suspended in 1x IM buffer (20mM KPO_4, 3mM potassium citrate, 2% PEG 6000) in volume equal to the original *in vitro* transcription reaction, and stored at –20°C.

[00327] For RNAi treatment of worms, wild type animals at the L2/L3 stage of development were collected in M9 buffer at ~ 50 animals/µl (M9 is 0.044 M KH_2PO_4, 0.085 M Na_2HPO_4, 0.18 M NaCl and 1 mM $MgSO_4$). 1µl of this nematode suspension was added to 3 µl of dsRNA and incubated for 24 hours in a sealed 96 well plate at 20°C in a humidified chamber. Animals were allowed to develop to adulthood before compound treatment and/or assay of germline apoptosis as described in Example IV.

Results and Conclusions

[00328] Use of an RNAi reagent against either the alpha or beta subunit of the nematode RabGGT enzyme was found to induce the formation of apoptotic corpses in the germline of *C. elegans*. While a typical germline arm in untreated adults contains, on average, less than one apoptotic corpse; treatment with an RNAi reagent against the RabGGT alpha subunit increased the average number observed to 2.4 corpses/arm. Treatment with an RNAi reagent against the

RabGGT beta subunit increased the average number observed to 9 corpses/arm. The graph displayed in Figure 3 shows the percentage of germline arms that contained greater than 2 apoptotic corpses. Ablation of the mRNA for a protein by RNAi or other methods has been demonstrated to result in a reduction of the quantity and hence cellular function of the encoded protein. Thus, it appears that a reduction in RabGGT function is sufficient to induce apoptosis in cells of the *C. elegans* germline.

Example VII: Genetic analysis of sensitivity connects the compound activity and Rab GGTase in inducing apoptosis

[00329] This example demonstrates that treatment of the nematode *C. elegans* with a low dose of RNAi against a RabGGT subunit acts in synergy with low doses of this same set of compounds, to result in a specific apoptotic phenotype.

Methods

[00330] Early larval and adult *C. elegans* hermaphrodites were treated with compound as described in Example IV. RNAi preparation and treatment was performed as described in Example VI. The phenotype of apoptosis in the germline arm was quantified as described in Example IV.

Results and Conclusions

[00331] To test the hypothesis that RabGGT is a direct target of the 7B compound, we examined the effect of a low dose of compound 7B (0.3mM) on the amount of apoptosis induced by a reduction in RabGGT function. The rationale behind the experiment is as follows: the effect of a submaximal compound dose will be substantially increased if the target activity is already partially compromised. Since RNAi directed against the alpha subunit of RabGGT induces a lower level of germline apoptosis than RNAi directed against the beta subunit, RNAi directed against the alpha subunit of RabGGT (RabGGT-alpha RNAi) was used to mimic a partial loss of function of the enzyme in adult worms. Table 4 contains data for each treatment administered separately, and for the treatments administered together. Co-administration of the RabGGT-alpha RNAi reagent with 0.3mM of compound 7B causes an increase in the level of observed apoptosis which is far greater than the additive value of the independent treatments. This can be seen very clearly when the number of germline arms containing more than four apoptotic corpses is quantified (Table 4) and displayed graphically (Figure 4). In compound

treated worms, 17% of arms have greater than four corpses, while in RNAi treated worms, 9% of arms have greater than four corpses. Co-administration of the RabGGT-alpha RNAi reagent with compound 7B increases the percentage of arms with more than 4 corpses to 88%. Thus, hypersensitivity to the compound is observed when RabGGT activity is compromised. These findings are consistent with a model in which compound 7B induces apoptosis in *C. elegans* by inhibiting the activity of the RabGGT enzyme.

Table 4

Frequency of observation of the stated number of apoptotic corpses per germline arm in wild-type worms treated with compound 7B and/or RNAi against the RabGGT alpha subunit.

	Corpses/arm											
	0	**1**	**2**	**3**	**4**	**>4**	**N tested**	**mean**	**SD**	**% arms with 0-2 corpses**	**% arms with 3-4 corpses**	**% arms with >4 corpses**
Vehicle	9	10	3	0	0	0	22	0.73	0.7	100	0	0
7B	5	5	2	5	3	4	24	2.3	1.8	50	33	17
RNAi	2	3	4	5	6	2	22	2.7	1.5	41	50	9
7B and RNAi	0	1	0	0	2	21	24	8.0	3.0	4	8	88

Example VIII: Genetic analysis of resistance connects the compound activity and Rab GGTase in inducing apoptosis

[00332] This example demonstrates that a mutation in the nematode *C. elegans* that confers resistance to the apoptotic effects of the compounds also confers resistance to the apoptotic effects of RNAi against a RabGGT subunit.

Methods

[00333] Early larval and adult *C. elegans* hermaphrodites were treated with compound as described in Example IV. RNAi preparation and treatment was performed as described in Example VI. The phenotype of apoptosis in the germline arm was quantified as described in Example IV.

Results and Conclusions

[00334] As a further genetic test of the interaction between compound 7B and RabGGT, we examined the effect of a reduction in RabGGT activity in mutants that are resistant to compound 7B. The rationale was as follows: if compound 7B induces apoptosis by inactivation of RabGGT, then the same mutations that decrease 7B-induced apoptosis would be expected to

decrease the apoptotic effect induced by lack of RabGGT. We examined a mutant strain that is strongly resistant to induction of apoptosis by compounds 7A-J. The resistance conferred by this mutation appears specific to compounds of the type exemplified by 7A-7J, since the mutant does not display any cross-resistance to the effects of a range of unrelated compounds (data not shown). RNAi treatment against the RabGGT alpha subunit was performed on this strain as described in Example VI. In the mutant strain the apoptotic effect of RNAi treatment against the RabGGT alpha subunit was strongly reduced (Figure 5). Thus we have shown that a mutant that is resistant to compound 7B-induced apoptosis is also insensitive to RabGGT (RNAi)-induced apoptosis. These findings are consistent with the model that compound 7B induces apoptosis in *C. elegans* by inactivating the RabGGT enzyme.

Example IX: RNAi of mRNA for RabGGT subunits inhibits proliferation in a human cell line

00335] This example demonstrates that RNAi treatment of a human cell line with reagents against either the alpha or the beta subunit of the RabGGT enzyme has an anti-proliferative effect.

Methods

00336] HCT-116 human colon tumor cells obtained from the ATCC were grown in RPMI culture medium supplemented with 10% heat inactivated FBS, 1x penicillin/streptomycin, and 25 mM HEPES, in an incubator maintained at 37°C with CO_2 at 6% and humidity at 95%. HCT116 cells were plated in 96 well plates at 2000 cells/ 100 µl media per well and incubated for 24 hours before RNAi treatment. For treatment, a 2X solution of Lipofectamine 2000/siRNA complexes was generated for each individual siRNA as follows. The siRNA oligonucleotides (Xeragon; Huntsville AL) were diluted to a final concentration of 1 µM in Optimem serum-free media (Invitrogen; Carlsbad, CA) and incubated for 5 minutes at room temperature. The Lipofectamine 2000 reagent (Invitrogen; Carlsbad, CA) was diluted to 10 µg/ml in Optimem serum-free media and incubated for 5 minutes at room temperature. Equal volumes of the 1µM siRNA oligonucleotides and the 10 µg/ml Lipofectamine 2000 were mixed together, giving a 5X stock of siRNA/Lipofectamine 2000 complexes. After incubation for 20 minutes at room temperature, 1.5 volumes of RPMI medium containing 10% heat inactivated FBS was added to the 5X stock, resulting in a 2X stock of siRNA/Lipofectamine 2000 complexes. For RNAi treatment, 100 µl of the 2X stock of siRNA/Lipofectamine 2000 complexes was added to each well containing HCT116 cells, to give a final concentration of

1X siRNA/Lipofectamine 2000 complexes. Cells were incubated for 72 hours prior to the proliferation assay. Three replicates were performed for each siRNA treatment.

00337] The effect of RNAi treatment directed against RabGGT subunits on cellular proliferation was assayed using a 3H-thymidine incorporation assay. The principle of this assay is as follows: During S-phase of the cell cycle, cells incorporate thymidine into the new strand of genomic DNA. Tritiated thymidine can be added to the culture medium and will be incorporated into genomic DNA in proportion to the number of rounds of DNA synthesis that occur. Incorporation can be quantified following lysis of the cells and removal of unincorporated nucleotides. RNAi-treated cells prepared as described above were assayed for 3H-thymidine uptake as follows. The cells were pulsed with 3H-thymidine by addition of 20 µl of a 44 µCi/ml solution of 3H-thymidine in RPMI to each well, to obtain a final concentration of 3H-thymidine of 4 µCi/ml. After incubation for 3h at 37°C, the medium was removed and 50 µl of 0.25% trypsin in phosphate buffered saline (140 mM NaCl, 2.7 mM KCl, 10 mM Na_2HPO_4 and 1.8 mM KH_2PO_4, pH 7.4) was added. After 10 minutes, the contents of the wells were harvested onto a 96-well GF/C filter plate (Whatman; Clifton NJ) using a Hewlett Packard Filtermate. The filter plate was washed 10 times with distilled water, then left to dry overnight. After the addition of 50 µl of Microscint-20 scintillation fluid (Perkin Elmer; Boston , MA) per well, the filter plates were sealed and the amount of radioactivity retained on the filter was determined by scintillation counting. The average of the three replicate samples is reported.

Results and Conclusions

[00338] We designed synthetic double-stranded oligonucleotides (siRNAs) suitable for performing RNAi treatment against either the alpha subunit (Genbank entry NM_004581) or beta subunit (Genbank entry NM_004582) of the human RabGGT enzyme (Table 5). Treatment of the HCT116 human colon cell line with siRNA reagents against the alpha subunit resulted in a reduction of 3H-thymidine incorporation that ranged from 17% to 63% of control values (Table 5). Treatment of the HCT116 human colon cell line with siRNA reagents against the beta subunit resulted in a reduction of 3H-thmidine incorporation that ranged from 36% to 77% of control values (Table 5). Thus, RNAi treatment with all six of the siRNA reagents against RabGGT resulted in a reduction in 3H-thymidine uptake. This result is displayed graphically in Figure 6. Varying efficacy among siRNAs targeting the same gene is not uncommon, since the characteristics that are required for effective destruction of the target mRNA are not understood (Elbashir *et al.*, 2002; Methods 26:199). The observed reduction in

3H-thymidine incorporation resulting from RNAi treatment against RabGGT could be the result of an inhibition of proliferation, or the result of increased cell death among the treated cells. This data is consistent with a model in which a reduction in function of the RabGGT enzyme results in apoptosis.

Table 5

Structure of siRNA reagents and effect on 3H-thymidine incorporation in HCT116 cells

siRNA	Gene targeted	siRNA sense strand	siRNA antisense strand	Bases of coding region targeted	3H-thy incorp. % of control
Alpha-1	RabGGT-alpha	GGCAGAACU GGGCUUCCU GTT (SEQ ID NO:01)	CAGGAAGCC CAGUUCUGC CTT (SEQ ID NO:02)	268-291	33
Alpha-2	RabGGT-alpha	AGAGCUGGA GCUGGUGCA GTT (SEQ ID NO:03)	CUGCACCAGC UCCAGCUCUT T (SEQ ID NO:04)	628-651	17
Alpha-3	RabGGT-alpha	GAUGGAGUA UGCCGAGGU GTT (SEQ ID NO:05)	CACCUCGGCA UACUCCAUCT T (SEQ ID NO:06)	1309-1332	63
Beta-1	RabGGT-beta	CUUUGGCUU UGUUGGGGA ATT (SEQ ID NO:07)	UUCCCCAACA AAGCCAAAGT T (SEQ ID NO:08)	493-516	77
Beta-2	RabGGT-beta	CGACAAUUA CCCUCAGGCG TT (SEQ ID NO:09)	CGCCUGAGG GUAAUUGUC GTT (SEQ ID NO:10)	662-685	39
Beta-3	RabGGT-beta	GAUGAAGAA ACGGGGGGA UTT (SEQ ID NO:11)	AUCCCCCCGU UUCUUCAUCT T (SEQ ID NO:12)	812-835	36
Non-silencing	none	UUCUCCGAA CGUGUCACG UTT (SEQ ID NO:13)	ACGUGACAC GUUCGGAGA ATT (SEQ ID NO:14)	none	100

Example X: Biochemical assay of compound inhibition of RabGGT activity in vitro

[00339] This example demonstrates that certain compounds inhibit RabGGT activity with nanomolar potency using a direct *in vitro* assay, and that different structural classes of compound may differ in the dose-response relationship for inhibition.

Methods

[00340] The effect of compounds 7A through 7T on RabGGT activity was quantified using a filter binding assay that measures the transfer of (3H) geranylgeranyl groups (GG) from all-trans-(3H)geranylgeranyl pyrophosphate (3H-GGPP) to recombinant Rab3A protein (Shen & Seabra, 1996, JBC, 271:3692; Armstrong *et al.*, 1996, Methods in Enzymology 257:30). Modifications to published protocols are noted explicitly below.

[00341] Recombinant rat RabGGT, expressed using the Sf9/baculovirus system, was purchased from Calbiochem (cat. no. 345855). Recombinant unprenylated human Rab3A was obtained from Panvera (cat. no. P2173). Human REP-1, expressed in Sf9 cells, was obtained from Calbiochem (cat. no. 554000). Tritium labeled geranylgeranyl pyrophosphate was purchased from Amersham Pharmacia Biotech (15 Ci/mmol). Unlabeled GGPP was purchased from Sigma (cat. no. G-6025).

[00342] The reaction buffer contained 50 mM HEPES pH7.4, 5 mM $MgCl_2$, 1 mM DTT, 1 mM NP-40. Solutions of RabGGT, Rab3A, REP-1, and GGPP were prepared in this reaction buffer. Final protein concentrations in the reaction mixture were modified from the published protocols, with the standard reaction mixture containing 2 μM Rab3A, 0.2 μM REP-1, 5 μM unlabeled GGPP, 0.5 μM labeled GGPP, and 10-50 nM RabGGT in a total volume of 20 μl. The specific activity of (3H)GGPP used in the assay was 3000 dpm/pmol.

[00343] Compounds were prepared as 50 mM stocks in DMSO and diluted to give an appropriate concentration for the assay as a 20% DMSO stock. 2 μl of the diluted compound stock was added to a 20 μl reaction to give a final DMSO concentration of 2% in the assay. The order of addition of reagents was altered from the published protocols. Reaction mixtures were prepared by sequentially adding Rab3A and REP-1 proteins to the reaction buffer, followed by compound and RabGGT enzyme to a volume of 18 μl. Reactions were initiated by the addition of 2 μl of a solution that contained unlabeled and labeled GGPP. After a 30 minute incubation at 37°C, 1 ml of stop solution (1 volume of concentrated HCl acid with 9 volumes of ethanol) was added and mixed. The solution was then incubated at room temperature for 1 hour to completely precipitate proteins.

[00344] The precipitate was collected by vacuum filtration using a vacuum filtration manifold (Millipore model 1225) onto 25mm GF/A filters (Whatman) that were prewetted with ethanol. The tubes were rinsed twice with 1 ml ethanol which was also poured over the filters. Each filter was subsequently washed three times with 2 mls of ethanol per wash, dried under vacuum, and then put in scintillation vials. Four milliliters of scintillation fluid was added and the radioactivity was quantified on a scintillation counter. Several types of blank reactions

were conducted including withholding the enzyme, the substrate, or the accessory protein REP-1, or replacing the compound solution with a 20% DMSO solution. For the substrate titration experiment, the equimolar amounts of Rab3A and REP-1 were mixed and preincubated for 30 min at room temperature before addition of the enzyme.

00345] The data was analyzed by non-linear regression analysis methods using the program PRIZM (GraphPad Software, Inc.). Inhibition constants were obtained by analyzing the data using the one site competition equation provided by the software. Figure 7 presents a typical data series obtained for compound 7B using these methods.

Results and Conclusions

00346] Data presented in Table 6 shows that compounds 7A, 7B, 7H, 7I, 7J, 7N, 7O, 7P, 7Q, and 7S inhibit the activity of rat RabGGT enzyme with IC50 values of less than 100 nM, while 7R and 7T are weaker inhibitors. IC90 values for inhibition of RabGGT are also presented in Table 6. The multiple of the IC90 value relative to the IC90 value is also presented in Table 6. For the benzodiazepine compounds 7A, 7B, 7H, 7I, and 7J, the IC90 value is between 5 and 9 times the IC50 value. For the tetrahydroquinoline compounds 7N, 7O, 7P, 7Q, 7R, 7S and 7T the IC90 value is between 12 and 49 times the IC50 value. The difference in the multiple of the IC90 value relative to the IC90 value for the two classes of compounds indicates that the dose-response relationship is different for each class. Such a difference in dose response may have consequences in an in vivo situation. If it is necessary to completely eliminate the function of an enzyme to produce a given measured effect, IC90 values for inhibition of that enzyme will show a closer relationship to that effect than IC50 values.

Table 6

Results of an *in vitro* assay that measures RabGGT activity in the presence of compounds.

Compound	Structural class	RabGGT IC50, nM	RabGGT IC90, nM	IC90/IC50
7A	Benzodiazepine	36	295	8
7B	Benzodiazepine	21	199	9
7H	Benzodiazepine	21	115	5
7I	Benzodiazepine	16	93	6
7J	Benzodiazepine	12	58	5
7N	Tetrahydroquinoline	25	309	12
7O	Tetrahydroquinoline	58	1117	19
7P	Tetrahydroquinoline	84	2162	26
7Q	Tetrahydroquinoline	47	2298	49
7R	Tetrahydroquinoline	541	10064	19
7S	Tetrahydroquinoline	73	1404	19
7T	Tetrahydroquinoline	1433	>15000	>10

Example XI: Relationship between inhibition of RabGGT in vitro and induction of apoptosis in vivo

00347] This example demonstrates a relationship between the level of inhibition of RabGGT enzyme activity in vitro and the ability of the compound to induce apoptosis in an HCT116 cell line.

Methods

00348] The assay for compound inhibition of RabGGT function is described in Example X. Methods for assaying apoptotic activity of compounds on HCT116 cells are described in Example II.

Results and Conclusions

00349] Table 7 provides the IC50 and IC90 values established by biochemical assays for inhibition of RabGGT, and also provides the minimum concentration required to achieve apoptosis of 50% of the HCT116 cells in a culture system. The data for IC90 values and apoptosis values are also presented in a graphical form in Figures 8a, 8b, and 8c. In Table 7, compounds are ranked according to their potency in the apoptosis assay and are presented according to structural class.

00350] When IC90 values for RabGGT inhibition are examined, a correlation between potency in the RabGGT inhibition assay and potency in the apoptosis assay is apparent. The square of the Pearson product moment correlation coefficient (the R-squared value) for the apoptosis values and the RabGGT IC90 values is 0.7, which can be interpreted as 70% of the variance in apoptosis values being attributable to the variance in RabGGT inhibition. Of the 12 compounds assayed, only two compounds deviate from their rank order position in Table 7: Compounds 7J and 7S show lower potency in the apoptosis assay than would be predicted by their potency in the RabGGT inhibition assay. Such occasional deviation (2 compounds out of 12) between rank in one assay and rank in another is not unexpected given the number of variables in each assay. We conclude that inhibition of RabGGT activity is related to the apoptotic activity of these compounds.

[00351] A correlation between potency in the RabGGT inhibition assay and potency in the apoptosis assay is also apparent when IC50 values for RabGGT inhibition are examined for their relationship to potency in the apoptosis assay. The R-squared value for the apoptosis values and the RabGGT IC90 values is 0.7, which can be interpreted as 70% of the variance in apoptosis values being attributable to the variance in RabGGT inhibition. Compounds 7J, 7P

and 7Q deviate from their rank order position. However we note that the tetrahydroquinoline class in general is less potent at inducing apoptosis than would be predicted based on their IC50 value as a measure of potency in the RabGGT inhibition assay. For example, compounds 7A and 7Q have similar IC50 values for RabGGT inhibition, whereas they show a 9-fold difference in potency in the apoptosis assay. The difference in potency in the apoptosis assay is in closer agreement with IC90 values for RabGGT inhibition by 7A and 7Q, which show an 8-fold difference. The observation that IC90 values for RabGGT inhibition show a better relationship to potency in the apoptosis assay than do IC50 values indicates that an almost total loss of cellular RabGGT activity may be required for induction of apoptosis. RabGGT cellular activity may be present in an amount that exceeds the general need, and a cell may be able to subsist with only 50% of that activity present.

Table 7

Results of an i*n vitro* assay upon RabGGT activity and results of an assay of apoptotic activity upon human cells.

Compound	Structural class	HCT116 50% apoptosis, μM	RabGGT IC50, nM	RabGGT IC90, nM
7I	Benzodiazepine	0.04	16	93
7H	Benzodiazepine	0.37	21	115
7B	Benzodiazepine	0.37	21	199
7J	Benzodiazepine	2.5	12	58
7A	Benzodiazepine	3.3	36	295
7N	Tetrahydroquinoline	3.3	25	309
7O	Tetrahydroquinoline	10	58	1117
7P	Tetrahydroquinoline	25	84	2162
7Q	Tetrahydroquinoline	30	47	2298
7R	Tetrahydroquinoline	30	541	10064
7S	Tetrahydroquinoline	50	73	1404
7T	Tetrahydroquinoline	90	1433	>15000

[00352] In Figure 8a, Data from the benzodiazepine class of compounds: The IC90 for RabGGT inhibition in nanomoles is shown on the Y axis and the minimum concentration required for induce 50% apoptosis in an HCT116 cell culture is shown on the X axis..

[00353] In Figure 8b, Data from the tetrahydroquinolone class of compounds: The IC90 for RabGGT inhibition in nanomoles is shown on the Y axis and the minimum concentration required for induce 50% apoptosis in an HCT116 cell culture is shown on the X axis.

[00354] In Figure 8c, Data from compounds 7A through 7Q. Compounds 7R, 7S, and 7T are represented in Fig. 8b, and have been omitted from this figure for graphical clarity rather than because they alter the trend of the observations. The IC90 for RabGGT inhibition in nanomoles is shown on the Y axis and the minimum concentration required for induce 50% apoptosis in an HCT116 cell culture is shown on the X axis.

Example XII: Lack of relationship between inhibition of farnesyl transferase (FT) in vitro and induction of apoptosis in vivo

[00355] This example demonstrates that there is no obvious relationship between the level of inhibition of FT enzyme activity in vitro and the ability of the compound to induce apoptosis in an HCT116 cell line.

Methods

[00356] Biochemical assays for inhibition of FT were performed as described by Mann *et al.* (1995, Drug Dev. Res. 34:121) with the modifications described by Ding *et al.* (1999, J. Med. Chem., 42:5241)

[00357] Methods for assaying apoptotic activity of compounds on HCT116 cells are described in Example II.

Results and Conclusions

[00358] Compounds 7A-7J are from a class of compounds that is predicted to have FT-inhibitory activity (Ding *et al.*, 1999, J. Med. Chem., 42:5241), while compounds 7N-7T also possess structural characteristics that make them potential FT inhibitors. We examined the possibility that inhibition of FT activity was related to the apoptotic activity of these compounds. Table 8 presents the compounds grouped according to structural class and provides the IC50 and IC90 values for inhibition of FT. Table 8 also provides the minimum concentration required to achieve apoptosis of 50% of the HCT116 cells in a culture system. The data for IC50 values and apoptosis values are also presented in a graphical form in Figure 9.

Table 8

Results of an *in vitro* assay upon FT activity and results of an assay of apoptotic activity upon human cells.

Compound	Structural class	HCT116 50% apoptosis, μM	FT IC50, nM	FT IC90, nM
7I	Benzodiazepine	0.04	1.4	11
7H	Benzodiazepine	0.37	4.1	360
7B	Benzodiazepine	0.37	7.8	110
7J	Benzodiazepine	2.5	0.8	7
7A	Benzodiazepine	3.3	2.4	30
7N	Tetrahydroquinoline	3.3	0.7	9
7O	Tetrahydroquinoline	10	1.4	8
7P	Tetrahydroquinoline	25	0.7	4
7Q	Tetrahydroquinoline	30	0.6	6
7R	Tetrahydroquinoline	30	1.5	9
7S	Tetrahydroquinoline	50	15.5	255
7T	Tetrahydroquinoline	90	3.7	48

[00359] In the data presented in Table 8, compounds are ranked according to their potency in the apoptosis assay. The compounds are all potent inhibitors of FT, with only a 20-fold range being observed in the IC50 values (0.7nM to 15.5 nM) whereas values in the apoptosis assay range over 2200-fold. When IC50 values for FT inhibition are examined for their relationship to potency in the apoptosis assay, no correlation is apparent. The R-squared value for the apoptosis values and the FT IC50 values is less than 0.1, which can be interpreted as less than 10% of the variance in apoptosis values being attributable to the variance in inhibition of 50% of FT activity. No general correlation with rank order position can be seen; at least 8 compounds deviate between ranking their potency for FT inhibition and ranking their potency for apoptosis induction. The conclusion that there is no correlation between potency in the apoptosis assay and potency in the FT inhibition assay is not altered by examination of IC90 values for FT inhibition. The R-squared value for the apoptosis values and the FT IC90 values is less than 0.01, indicating that none of the variance in apoptosis values is attributable to the variance in inhibiting 90% of FT activity.

[00360] Figure 9 provides a graphical display of the data from Table 8. No trend can be observed in the data by visual inspection. We conclude that inhibition of FT activity is not related to the apoptotic activity of these compounds.

Example XIII: Conservation of structure between the RabGGT enzymes from *C. elegans*, *R. norvegicus* and *H. sapiens*

00361] This example demonstrates that the active site of the RabGGT enzyme is conserved between *C. elegans*, *R. norvegicus* and *H. sapiens*, such that a compound which blocks the active site in one species would be reasonably expected to show the same activity in all species.

Methods

00362] Structural models of the RabGGT alpha subunits from *C. elegans* (GenBank entry NM_067966) and from *Homo sapiens* (GenBank entry NM_004581) were developed based on sequence alignment with the homologous protein rat RabGGT alpha (GenBank entry NM_031654) whose structure in the RabGGT complex is available in the Protein Data Bank as 1DCE (Zhang *et al.*, 2000, Structure 8:241). Sequence alignments of the RabGGT alpha subunit are shown in Table 9a and Table 10a.

00363] Structural models of the RabGGT beta subunits from *C. elegans* (GenBank entry NM_066158) and from *H. sapiens* (GenBank entry NM_004582) were developed based on sequence alignment with the homologous protein rat RabGGT beta (GenBank entry NM_138708) whose structure in the RabGGT complex is available in the Protein Data Bank as 1DCE (Zhang *et al.*, 2000, Structure 8:241). Sequence alignments of the RabGGT beta subunit are shown in Table 9b and Table 10b.

00364] The program LOOK was used for alignments and the model building module within LOOK, SEGMOD, was used to build the homology models (Levitt, (1992), *J. Mol. Biol.* 226: 507-533; Levitt, (1983), *J. Mol. Biol.* 170: 723-764). The co-ordinates for the structural model of *H. sapiens* RabGGT are presented in Table 11 (RabGGT alpha subunit) and Table 12 (RabGGT beta subunit). In both Tables 11 and 12, "Atom No" refers to the atom number within the RabGGT alpha or beta subunit homology model; "Atom name" refers to the element whose coordinates are measured, the first letter in the column defines the element; "Residue" refers to the amino acid within which the atom resides, with the number representing the amino acid number of the "residue"; "X Coord", "Y Coord", and "Z Coord" structurally define the atomic position of the element measured in three dimensions.

00365] The quality of the models was evaluated as follows: In order to recognize errors in three-dimensional structures knowledge based mean fields can be used to judge the quality of protein folds (Hendlich *et al.*, 1990, J. Mol. Biol. 216:167). These methods can be used to recognize misfolded structures as well as faulty parts of structural models. The technique

generates an energy graph where the energy distribution for a given protein fold is displayed on the y-axis and residue position in the protein fold is displayed on the x-axis. The knowledge based mean fields compose a force field derived from a set of globular protein structures taken as a subset from the Protein Data Bank (Bernstein *et al.*, 1977, J. Mol. Biol. 112:535). An energy value of less than zero is considered to represent a stable 3-dimensional structure. To analyze the quality of a model, the energy distribution of residues is plotted and compared to the energy distribution of the template from which the model was generated.

Results and Conclusions

00366] The amino acid sequence of the *H. sapiens* RabGGT alpha subunit (HsA) has 91% identity and 93% similarity with that of *Rattus norvegicus* (RatA). The proteins are both 567 amino acids in length. The amino acid sequence of the *H. sapiens* RabGGT beta subunit (HsB) has 95% identity and 97% similarity with that of *R. norvegicus* (RatB). The proteins are both 331 amino acids in length. The crystal structure of a RabGGT complex consisting of the rat alpha and beta subunits has been described at 2 angstrom (A) resolution (H Zhang *et al.*, 2000, Struct. Fold. Des. 8:241). The sequences of HsA and HsB were overlaid onto the crystal structure of the RatA/RatB complex (Figure 10). There were no insertions or deletions. The free energy plots for the models are shown in Figure 11. There is near identity between the energy distribution of the model and that of the template from which the model was generated, with the majority of residues having energy values below zero. This indicates that the human RabGGT as modeled represents a stable 3-dimensional structure of high quality.

[00367] The putative binding pocket for inhibitors of RabGGT activity can be hypothesized by comparison with farnesyl transferase (FT), a closely related enzyme that has very similar structure and function (Long *et al.*, 2002, Nature 419:645). The structure of FT in complex with known inhibitory compounds has been determined; in this example we used an overlay of an FT/inhibitor complex described by Long *et al.* (2001, Proc. Natl. Acad. Sci. USA, 98:12948). Of the residues lining the putative binding pocket, all three within the alpha subunit and all 12 within the beta subunit are identical between the two proteins and exist within a region of high conservation and high identity (Table 9a and b). In the enzyme from *R. norvegicus*, and the enzyme from *H. sapiens*, the residues within 5A of the active site are Asn A103, Lys A105, Tyr A107, Ser B42, Tyr B44, Leu B45, Trp B52, Arg B144, Asp B238, Cys B240, Tyr B241, Asp B280, Asp B287, Phe B289, His B290, where A refers to the alpha subunit and B to the beta subunit.

00368] The amino acid sequence of the *C. elegans* RabGGT alpha subunit (CeA) has 38% identity and 53% similarity with that of *R. norvegicus* (RatA). RatA is 567 amino acids in length and CeA is 580 amino acids. The amino acid sequence of the *C. elegans* RabGGT beta subunit (CeB) has 53% identity and 72% similarity with that of *R. norvegicus* (RatB). RatB is 331 amino acids in length and CeB is 335 amino acids. The sequences of CeA and CeB were overlaid onto the crystal structure of the RatA/RatB complex (Figure 12). One large insertion in CeA (80-94) corresponded to a loop between helices 3 and 4 in RatA. A substantial deletion in CeA at residue 316, corresponding to RatA residues 300-305, occurs within a beta-sheet at some distance from the proposed binding site and near a large loop. Another insertion in CeA (residues 439-442 at RatA 428) is also at some distance from the binding site and appears to occur with helix 17 of the RatA structure. The free energy plots for the models are shown in Figure 13. There is a strong correspondence between the energy distribution of the model and that of the template from which the model was generated, with the majority of residues having energy values below zero. This indicates that the *C.elegans* RabGGT as modeled represents a stable 3-dimensional structure of high quality.

00369] Of the residues lining the putative binding pocket of RabGGT, all three residues within the alpha subunit are identical between the two proteins and exist within a region of high conservation and high identity. Of the 12 residues in the beta subunit determined to be in the binding pocket, all but two were identical and existed in regions of high identity (Table 9a and 9b). In the enzyme from *C. elegans,* the residues within 5A of the active site are Asn A119, Lys A121, Tyr A123, Ala B48 (non-identity to rat), His B50 (non-identity to rat), Leu B51, Trp B58, Arg B150, Asp B244, Cys B246, Tyr B247, Asp B286, Asp 293, Phe B295, His B296, where A refers to the alpha subunit and B to the beta subunit.

00370] The data presented in this example demonstrates that high quality structural models of human and nematode RabGGT structure can be generated based on the crystal structure that has been obtained for the rat protein. In these models, the active site of the RabGGT enzyme is conserved between *C. elegans*, *R. norvegicus* and *H. sapiens*, such that a compound which blocks the active site in one species would be reasonably expected to show the same activity in all species. Therefore the observation that certain compounds inhibit the rat RabGGT enzyme with nanomolar potency (data presented in Example X), indicates that these compounds would have the same inhibitory effect when applied to the human RabGGT enzyme. The apoptotic effect of the same compounds when applied to *C. elegans* (data presented in Example IV) may also be interpreted as arising from inhibition of RabGGT, given that the active site of the nematode enzyme is conserved with respect to that of the rat enzyme, and that loss of the

enzyme function has been directly linked to an apoptotic effect (data presented in Example VI).

Example XIV: Modeling interaction of compounds with the active site of RabGGT

[00371] This example demonstrates that compounds with apoptotic activity and RabGGT inhibitory activity have the potential to block the active site of the RabGGT enzyme.

Methods

[00372] The program Insight (Accelrys, Inc., San Diego, CA) was used to visualize and compare possible binding interactions of compounds with the active site of RabGGT. The putative binding pocket for inhibitors of RabGGT activity can be hypothesized by comparison with farnesyl transferase (FT), a closely related enzyme that has very similar structure and function (Long *et al.*, 2002, Nature 419:645). The structure of FT in complex with known inhibitory compounds has been determined (for example Long *et al.*,2001, Proc. Natl. Acad. Sci. USA, 98:12948; Bell *et al.*, 2002, J. Med. Chem. 45:2388).

Results and Conclusions

[00373] The active site of RabGGT contains binding sites for a prenyl moiety and the peptide substrate of the enzyme. The crystal structure of the RabGGT complex from *R. norvegicus* is available in the Protein Data Bank as 1DCE (Zhang *et al.*, 2000, Structure 8:241). In the enzyme from *R. norvegicus*, the active site is composed of residues His B290, Cys B240, Asp B238, Tyr B241, Trp B244, Phe B289, Trp B52, Ser B48, Leu B45, Tyr B44, Asp A61, Arg B144, and Lys A105, where A refers to the alpha subunit and B to the beta subunit (Figure 14a). The derivation of the 3-dimensional model of the human enzyme from the rat enzyme crystal structure resulted in no significant change to the pocket. The pockets are constitutively identical: the only changes seen were those expected from use of different optimization procedures, which is known to result in slight shifts in amino acid side chain positions (Figure 14b).

[00374] The binding pocket of the predicted human RabGGT enzyme is large and substantially open to solvent on one side (the left side in Figures 14a-c). It contains a bound atom of zinc, coordinated by histidine B290, cysteine B240, and aspartic acid B238, identical to the motif found in the rat protein. The floor of the pocket (at the base in Figures 14a-c) is composed of phenylalanine B289 and tryptophan B52, and the back of the pocket (to the rear in Figures 14a-c) of leucine B45, serine B48, and tyrosine B44. In the crystal structure, the top of the pocket

(at the top in Figures 14a-c) contains a substantial quantity of bound water molecules in addition to aspartic acid A61; the homology model maintains this empty pocket that is occupied by the water molecules in the crystal structure. RabGGT contains substantial functional, sequence, and structural similarities to farnesyl transferase (FT). In FT, the side of the pocket opposite to that exposed to bulk solvent is known to be a binding site for a prenyl group. The geranyl-geranyl prenyl group that is bound and transferred by RabGGT should occupy the analogous location (to the right in Figures 14a-c) (Zhang *et al.*, 2000, Structure 8:241).

[00375] There is good indication that compounds 7A through 7T would bind in this pocket. FT and RabGGT are similar in the structure of their active sites and in their mechanism of substrate modification (Long *et al.*, 2002, Nature 419:645). Compounds 7A through 7T show the ability to inhibit FT with high potency (Table 8), indicating that they bind to the enzyme. Crystal structures of FT in complex with compounds structurally similar to 7A through 7H have been reported (Bell *et al.*, 2002, J. Med. Chem. 45:2388). Like 7A through 7H, these compounds contain an imidazole ring, a cyanobenzene, and an aromatic moiety, and they have been found to occlude the peptide-substrate binding site of the FT enzyme. The imidazole ring functions in its well-known role as a ligand for zinc, while the cyanobenzene moiety was found to form hydrophobic contacts with the prenyl group. As noted, the RabGGT pocket also contains a zinc ion at the analogous position, and a similar prenyl group is expected to bind to the pocket in the analogous location. The imidazole and cyanobenzene moieties of 7A through 7H are predicted to orient the compounds in an analogous manner within the RabGGT pocket, occluding the peptide-binding site of the enzyme. All the compounds have additional aromatic moieties that may form significant interactions with the enzymes. However, the substrate binding sites of FT and RabGGT have some differences that are expected to have a substantial influence on the type of molecules that can function as effective and specific inhibitors. The binding site of FT is more hydrophobic and, in particular, is more aromatic. It has been determined that the aromatic "back" region of the FT pocket is constrained and places strict orientation demands on ligands of high affinity (Bell *et al.*, 2002, J. Med. Chem 45:2388). The differences between the pockets of FT and RabGGT in this region, in particular the substitution of tryptophan B602 by leucine B54, would be expected to alter the binding specificity by making fewer requirements on orientation and aromaticity. Consequently, compounds of high-affinity for FT might not bind as tightly, if at all, to RabGGT and conversely, specific inhibitors of RabGGT can be designed.

[00376] Figure 15A depicts two views of compound 7H docked into the putative binding site of RABGGT. The left view is facing directly into the cavity opening viewed from outside of the protein, the right is viewed from a 90 degree rotation. The protein residues are heavy sticks. The ligand is represented by thin sticks. The putative bound atom of zinc is represented as a sphere.

[00377] Figure 15B depicts analogous views of the binding site of the crystal structure of the complex between farnesyl transferase (FT) and the FT inhibitor U66 (PDB 1LD7; Bell et al. (2002) *J. Med. Chem.* 45:2388). The views show similar binding patterns between the putative Rab ligand and the Rab binding site and that of the FT ligand and the FT binding site. Both show a liganding of an imidazole group to an atom of zinc, a close packing of a cyanophenyl group with a bound prenyl group (shown at the right hand side of the left images and in the middle of the right images) and additional hydrophobic functionality, a phenyl group in the putative Rab ligand and a napthyl group in the FT ligand.

[00378] While the present invention has been described with reference to the specific embodiments thereof, it should be understood by those skilled in the art that various changes may be made and equivalents may be substituted without departing from the true spirit and scope of the invention. In addition, many modifications may be made to adapt a particular situation, material, composition of matter, process, process step or steps, to the objective, spirit and scope of the present invention. All such modifications are intended to be within the scope of the claims appended hereto.

[00379] The entire disclosure of each document cited (including patents, patent applications, journal articles, abstracts, laboratory manuals, books, Genbank Accession Numbers, SWISS-PROT Accession Numbers, or other disclosures) in the Background of the Invention, Detailed Description, and Examples is hereby incorporated herein by reference. Further, the hard copy of the sequence listing submitted herewith and the corresponding computer readable form are both incorporated herein by reference in their entireties.

Tables 9a and 9b

Alignment of the indicated polypeptides chains. (a) RatA: *R. norvegicus* RabGGT alpha chain (SEQ ID NO:19), with HsA: *H. sapiens* RabGGT alpha chain (SEQ ID NO:16). (b) RatB: *R. norvegicus* RabGGT beta chain (SEQ ID NO:20), with HsB: *H. sapiens* RabGGT beta chain (SEQ ID NO:18). "^" indicates residues within 5 Angstrom of the binding site. "*" indicates identity. ":" indicates conserved properties.

Table 9a

```
RatA    ---HGRLKVKTSEEQAEAKRLEREQKLKLYQSATQAVFQKRQAGELDESVLELTSQILGA
HsA     M--HGRLKVKTSEEQAEAKRLEREQKLKLYQSATQAVFQKRQAGELDESVLELTSQILGA
           ************************************************************

RatA    NPDFATLWNCRREVLQHLETEKSPEESAALVKAELGFLESCLRVNPKSYGTWHHRCWLLS
HsA     NPDFATLWNCRREVLQQLETQKSPEELAALVKAELGFLESCLRVNPKSYGTWHHRCWLLG
        ****************:***:***** ******************************.
                                                  ^ ^ ^

RatA    RLPEPNWARELELCARFLEADERNFHCWDYRRFVAAQAAVAPAEELAFTDSLITRNFSNY
HsA     RLPEPNWTRELELCARFLEVDERNFHCWDYRRFVATQAAVPPAEELAFTDSLITRNFSNY
        *******:***********.***************:****.******************

RatA    SSWHYRSCLLPQLHPQPDSGPQGRLPENVLLKELELVQNAFFTDPNDQSAWFYHRWLLGR
HsA     SSWHYRSCLLPQLHPQPDSGPQGRLPEDVLLKELELVQNAFFTDPNDQSAWFYHRWLLGR
        ****************************:*******************************

RatA    AEPHDVLCCVHVSREEACLSVCFSRPLTVGSRMGTLLLMVDEAPLSVEWRTPDGRNRPSH
HsA     ADPQDALRCLHVSRDEACLTVSFSRPLLVGSRMEILLLMVDDSPLIVEWRTPDGRNRPSH
        *:*:*.* *:****:****:*.***** *****  ******::** **************

RatA    VWLCDLPAASLNDQLPQHTFRVIWTGSDSQKECVLLKDRPECWCRDSATDEQLFRCELSV
HsA     VWLCDLPAASLNDQLPQHTFRVIWTAGDVQKECVLLKGRQEGWCRDSTTDEQLFRCELSV
        *************************..* ********.* * *****:************

RatA    EKSTVLQSELESCKELQELEPENKWCLLTIILLMRALDPLLYEKETLQYFSTLKAVDPMR
HsA     EKSTVLQSELESCKELQELEPENKWCLLTIILLMRALDPLLYEKETLQYFQTLKAVDPMR
        ************************************************.*********

RatA    AAYLDDLRSKFLLENSVLKMEYADVRVLHLAHKDLTVLCHLEQLLLVTHLDLSHNRLRAL
HsA     ATYLDDLRSKFLLENSVLKMEYAEVRVLHLAHKDLTVLCHLEQLLLVTHLDLSHNRLRTL
        *:**********************:*********************************:*

RatA    PPALAALRCLEVLQASDNALENVDGVANLPRLQELLLCNNRLQQSAAIQPLVSCPRLVLL
HsA     PPALAALRCLEVLQASDNAIESLDGVTNLPRLQELLLCNNRLQQPAVLQPLASCPRLVLL
        ******************:*.:***:*****************.*.:***.********

RatA    NLQGNSLCQEEGIQERLAEMLPSVSSILT--------------------------------
HsA     NLQGNPLCQAVGILEQLAELLPSVSSVLT--------------------------------
        *****.***  ** *:***:******:**
```

Table 9b

```
                                                                    |
RatB    --------------------------------TQQKDVTIKSDAPDTLLLEKHADYIAS
HsB     -------------------------------MGTPQKDVIIKSDAPDTLLLEKHADYIAS
                                        * **** ********************


RatB    YGSKKDDYEYCMSEYLRMSGVYWGLTVMDLMGQLHRMNKEEILVFIKSCQHECGGVSASI
HsB     YGSKKDDYEYCMSEYLRMSGIYWGLTVMDLMGQLHRMNREEILAFIKSCQHECGGISASI
        ********************:*****************:****.***********:****
                     ^ ^^       ^

RatB    GHDPHLLYTLSAVQILTLYDSIHVINVDKVVAYVQSLQKEDGSFAGDIWGEIDTRFSFCA
HsB     GHDPHLLYTLSAVQILTLYDSINVIDVNKVVEYVKGLQKEDGSFAGDIWGEIDTRFSFCA
        ***********************:**:*:*** **:.************************
                                                                ^

RatB    VATLALLGKLDAINVEKAIEFVLSCMNFDGGFGCRPGSESHAGQIYCCTGFLAITSQLHQ
HsB     VATLALLGKLDAINVEKAIEFVLSCMNFDGGFGCRPGSESHAGQIYCCTGFLAITSQLHQ
        ************************************************************


RatB    VNSDLLGWWLCERQLPSGGLNGRPEKLPDVCYSWWVLASLKIIGRLHWIDREKLRSFILA
HsB     VNSDLLGWWLCERQLPSGGLNGRPEKLPDVCYSWWVLASLKIIGRLHWIDREKLRNFILA
        ************************************************.****
                                     ^ ^^

RatB    CQDEETGGFADRPGDMVDPFHTLFGIAGLSLLGEEQIKPVSPVFCMPEEVLQRVNVQPEL
HsB     CQDEETGGFADRPGDMVDPFHTLFGIAGLSLLGEEQIKPVNPVFCMPEEVLQRVNVQPEL
        ************************************.******************
                  ^       ^ ^^

RatB    VS-
HsB     VS-
        **
```

Tables 10a and 10b

Alignment of the polypeptides indicated. (a) RatA: *R. norvegicus* RabGGT alpha chain (SEQ ID NO:19), with CeA: *C. elegans* RabGGT alpha chain (SEQ ID NO:21). (b) RatB: *R. norvegicus* RabGGT beta chain (SEQ ID NO:20), with CeB: *C. elegans* RabGGT beta chain (SEQ ID NO:22). "^" indicates residues within 5 Angstrom of the binding site. "*" indicates identity. ":" indicates conserved properties.

Table 10a (i)

```
RatA      -HGRLKVKTSEEQAEAKRLEREQKLKLYQSATQAVFQKRQAGELDESVLELTSQILGANP
CeA       MHFVKKVPTTEEEKAAKQKEHTKRSQQFLHVRDKIVAKREKGEYDDEILSLTQAILEKNA
           *   ** *:**:  **: *: :: : :  . : :. **: ** *:.:*.**. **  *.

RatA      DFATLWNCRREVLQ-HLET---------------EKSPEESAALVKAELGFLE-SCLRVN
CeA       DIYTFWNIRRTTIELRMEANEKVQQSADAEEEEKTKSSQKIENLLAGEL-FLSYECIKSN
          *: *:** **. .:: ::*:                **.::   *: .** **. .*:: *
                                                                    ^

RatA      PKSYGTWHHRCWLLSRLPEPNWARELELCARFLEADERNFHCWDYRRFVAAQAAVAPAEE
CeA       PKSYSAWYQRAWALQRQSAPDFKKELALCEKALQLDCRNFHCWDHRRIVARMAKRSEAEE
          ****.:*::*.* *.* . *:: :** ** : *: * *******:**:**  *  : ***
           ^ ^

RatA      LAFTDSLITRNFSNYSSWHYRSCLLPQLHPQPDSGPQGRLPENVLLKELELVQNAFFTDP
CeA       LEFSNKLINDNFSNYSAWHYRSIALKNIHRDEKTGAP-KIDDELIASELQKVKNAFFMDA
          * *::.**. ******:*****  * ::* : .:*.  :: :::: .**: *:**** *.

RatA      NDQSAWFYHRWLLGRAEPHDVLCC-VHVSREEACLSVCFSRPLTVGSRMGTL--LLMVDE
CeA       EDQSAWTYTRWLLEVGSGKEFLRPESHTPIELISASFHGNNTTLVFSRAVTIQFLLTFVD
          :***** * **** .. ::.*    *.. *  . *.  ...  * **  *:  ** . :

RatA      APLSVEWRTPDGRNRPSHVWLCDLPAASLNDQLPQHTFRVIWTGSDSQKECVLLKDRPEC
CeA       TENTTGWRAFSSTS-PNPT------SSRVWQYLSDTPLRVV-TSNPTDLENISWTELNEQ
          :  :. **: .. . *. .      :: : : *.: .:**: *.. :: * :  .:  *
```

Table 10a (ii)

```
RatA      WCRDSATDEQLFRCELSVEKSTVLQSELESCKELQELEPENKWCLLTIILLMRALDPLLY
```

```
CeA       PYVNLDRLKTIYDV-VEVPQPAYIGELLEDCKQLIELEPKNKWPLYMRTLVLLEYQPIKS
             :    : ::   :.* :.: : . **.**:* ****:*** *    *::   :*:

RatA      EKETLQYFSTLKA-VDPMRAAYLDDLRSK----FLLENSVLKMEYADVRVLHLAHKDLTV
CeA       YEEIIKNLENLSENLDPKRSELYKSLISRQNLNFSIREQFERILGPDTDWLTCRYSKLTS
           :* :: :..*.  :** *:   ..* *:    * :.:.. ::  .*.  *   :..**

RatA      LCHLEQLL-LVTHLDLSHNRLRALPPALAALRCLEVLQASDNALENVDGVANLPRLQELL
CeA       LEGVEYLAGFVGSADFSGNRLKEIQR--IVLPNLKSLTINENPIESLPPSPCLSHLTFFS
          *  :* *  :*   *:* ***: :     .*  *: *  .:*.:*.:   . *.:*  :

RatA      LCNNRLQQSAAIQPLV-SCPRLVLLNLQGNSLCQE-EGIQERLAEMLPSVSSILT-----
CeA       IAGTQIASVSAVMPFFQTIPSLDRLVFCETPLVEKTEELRAQLPGVRLIPHWL-------
          :...:: . :*: *:. : * *  * :  ..* :: * :: :*. :      :
```

Table 10b

```
1DCE    ------------------------------------------------------------
Ceb     ------------------------------------------------------MSFAG

1DCE    ---TQQKDVTIKSDAPDTLLLEKHADYIASYGSKKDDYEYCMSEYLRMSGVYWGLTVMDL
Ceb     LLDFARKDVDLPQNSPNELLKDLHANFINQYEKNKNSYHYIMAEHLRVSGIYWCVNAMDL
             :*** : .::*: ** : **::* .* .:*:.*.* *:*:**:**:** :..***
                                                 ^ ^^      ^

1DCE    MGQLHRMNKEEILVFIKSCQHECGGVSASIGHDPHLLYTLSAVQILTLYDSIHVINVDKV
Ceb     SKQLERMSTEEIVNYVLGCRNTDGGYGPAPGHDSHLLHTLCAVQTLIIFNSIEKADADTI
          **.**..***: :: .*::  ** ..: ***.***:**.*** * :::**.  :.*.:

1DCE    VAYVQSLQKEDGSFAGDIWGEIDTRFSFCAVATLALLGKLDAINVEKAIEFVLSCMNFDG
Ceb     SEYVKGLQQEDGSFCGDLSGEVDTRFTLCSLATCHLLGRLSTLNIDSAVRFLMRCYNTDG
          **:.**:*****.**: **:****::*::**  ***:*.::*::.*:.*:: * * **
                                ^

1DCE    GFGCRPGSESHAGQIYCCTGFLAITSQLHQVNSDLLGWWLCERQLPSGGLNGRPEKLPDV
Ceb     GFGTRPGSESHSGQIYCCVGALAIAGRLDEIDRDRTAEWLAFRQCDSGGLNGRPEKLPDV
        *** *******:******.* ***:.:*.::: *  . **. **  **************
                                                                  ^

1DCE    CYSWWVLASLKIIGRLHWIDREKLRSFILACQDEETGGFADRPGDMVDPFHTLFGIAGLS
Ceb     CYSWWVLASLAILGRLNFIDSDAMKKFIYACQDDETGGFADRPGDCADPFHTVFGIAALS
        ********** *:***::** : ::.** ****:*********** .*****:****.**
        ^^                                      ^      ^ ^^

1DCE    LLGEEQIKPVSPVFCMPEEVLQRVNVQPELVS
Ceb     LFGDDTLESVDPIFCMTKRCLGDKQVEMYY--
        *:*:: ::.*.*:***.:. *   :*:
```

Table 11

Atom No.	Residue / Residue Position	Atom Type	X Coord.	Y Coord.	Z Coord.
1	MET1	N	40.653	31.02	43.155
2	MET1	CA	41.733	30.626	42.225
3	MET1	CB	42.562	29.486	42.796
4	MET1	CG	43.356	29.876	44.046
5	MET1	SD	44.746	31.016	43.814
6	MET1	CE	43.928	32.613	44.03
7	MET1	C	41.152	30.205	40.88
8	MET1	O	39.987	30.488	40.569
9	HIS2	N	41.95	29.458	40.134
10	HIS2	CA	41.596	29.033	38.771
11	HIS2	CB	42.849	28.472	38.107
12	HIS2	CG	44.026	29.429	38.102
13	HIS2	ND1	45.264	29.172	38.567
14	HIS2	CE1	46.039	30.263	38.397
15	HIS2	NE2	45.28	31.216	37.81
16	HIS2	CD2	44.038	30.716	37.619
17	HIS2	C	40.506	27.962	38.757
18	HIS2	O	40.782	26.764	38.881
19	GLY3	N	39.271	28.422	38.637
20	GLY3	CA	38.109	27.533	38.582
21	GLY3	C	37.613	27.167	39.979
22	GLY3	O	36.847	26.208	40.142
23	ARG4	N	38.005	27.948	40.972
24	ARG4	CA	37.645	27.604	42.351
25	ARG4	CB	38.847	27.832	43.257
26	ARG4	CG	39.963	26.85	42.922
27	ARG4	CD	39.495	25.415	43.127
28	ARG4	NE	40.539	24.455	42.74
29	ARG4	CZ	40.293	23.154	42.577
30	ARG4	NH1	39.058	22.681	42.765
31	ARG4	NH2	41.279	22.326	42.226
32	ARG4	C	36.45	28.404	42.847
33	ARG4	O	36.592	29.5	43.402
34	LEU5	N	35.275	27.83	42.652
35	LEU5	CA	34.042	28.459	43.133
36	LEU5	CB	32.87	27.909	42.325
37	LEU5	CG	31.585	28.69	42.577
38	LEU5	CD1	31.774	30.171	42.266
39	LEU5	CD2	30.432	28.116	41.762
40	LEU5	C	33.859	28.174	44.625
41	LEU5	O	33.747	27.017	45.052
42	LYS6	N	33.824	29.245	45.399
43	LYS6	CA	33.719	29.156	46.862
44	LYS6	CB	34.246	30.49	47.403
45	LYS6	CG	34.657	30.483	48.878
46	LYS6	CD	33.484	30.587	49.849
47	LYS6	CE	33.971	30.644	51.29
48	LYS6	NZ	34.837	31.811	51.512
49	LYS6	C	32.27	28.908	47.299
50	LYS6	O	31.495	29.848	47.504
51	VAL7	N	31.904	27.64	47.395
52	VAL7	CA	30.565	27.283	47.882
53	VAL7	CB	29.863	26.409	46.842
54	VAL7	CG1	28.404	26.162	47.222

Table 11

55	VAL7	CG2	29.927	27.039	45.457
56	VAL7	C	30.666	26.525	49.203
57	VAL7	O	30.582	27.136	50.279
58	LYS8	N	31.179	25.307	49.097
59	LYS8	CA	31.24	24.358	50.223
60	LYS8	CB	31.282	22.949	49.649
61	LYS8	CG	30.039	22.674	48.813
62	LYS8	CD	30.044	21.261	48.242
63	LYS8	CE	28.78	20.993	47.431
64	LYS8	NZ	28.78	19.623	46.893
65	LYS8	C	32.426	24.565	51.165
66	LYS8	O	32.687	23.736	52.04
67	THR9	N	33.147	25.655	50.966
68	THR9	CA	34.276	25.989	51.832
69	THR9	CB	35.443	26.463	50.975
70	THR9	OG1	35.045	27.648	50.305
71	THR9	CG2	35.826	25.426	49.923
72	THR9	C	33.877	27.077	52.829
73	THR9	O	34.734	27.613	53.54
74	SER10	N	32.62	27.49	52.776
75	SER10	CA	32.126	28.488	53.727
76	SER10	CB	31.028	29.322	53.074
77	SER10	OG	29.901	28.485	52.855
78	SER10	C	31.569	27.824	54.98
79	SER10	O	30.988	26.734	54.922
80	GLU11	N	31.487	28.619	56.037
81	GLU11	CA	30.953	28.127	57.32
82	GLU11	CB	31.451	29.033	58.442
83	GLU11	CG	32.976	29.108	58.496
84	GLU11	CD	33.598	27.741	58.789
85	GLU11	OE1	33.833	27.465	59.957
86	GLU11	OE2	33.935	27.06	57.831
87	GLU11	C	29.422	28.105	57.312
88	GLU11	O	28.797	27.338	58.054
89	GLU12	N	28.873	28.7	56.264
90	GLU12	CA	27.431	28.778	56.014
91	GLU12	CB	27.107	30.028	55.189
92	GLU12	CG	27.208	31.353	55.958
93	GLU12	CD	28.646	31.859	56.096
94	GLU12	OE1	29.481	31.411	55.317
95	GLU12	OE2	28.924	32.504	57.096
96	GLU12	C	26.907	27.542	55.276
97	GLU12	O	25.853	27.612	54.635
98	GLN13	N	27.726	26.505	55.185
99	GLN13	CA	27.257	25.216	54.675
100	GLN13	CB	28.354	24.607	53.805
101	GLN13	CG	28.79	25.554	52.684
102	GLN13	CD	27.804	25.627	51.511
103	GLN13	OE1	28.034	24.995	50.472
104	GLN13	NE2	26.775	26.45	51.643
105	GLN13	C	26.891	24.283	55.83
106	GLN13	O	26.528	23.124	55.596
107	ALA14	N	27.051	24.783	57.05
108	ALA14	CA	26.655	24.074	58.276
109	ALA14	CB	25.136	23.938	58.312
110	ALA14	C	27.309	22.706	58.395

Table 11

111	ALA14	O	26.639	21.669	58.356
112	GLU15	N	28.629	22.71	58.441
113	GLU15	CA	29.374	21.458	58.596
114	GLU15	CB	29.979	21.029	57.258
115	GLU15	CG	28.925	20.696	56.197
116	GLU15	CD	28.065	19.498	56.609
117	GLU15	OE1	27.15	19.183	55.861
118	GLU15	OE2	28.516	18.771	57.485
119	GLU15	C	30.468	21.636	59.641
120	GLU15	O	31.247	22.596	59.59
121	ALA16	N	30.475	20.747	60.618
122	ALA16	CA	31.461	20.839	61.701
123	ALA16	CB	30.865	20.228	62.964
124	ALA16	C	32.744	20.112	61.327
125	ALA16	O	32.85	18.902	61.557
126	LYS17	N	33.757	20.898	60.992
127	LYS17	CA	35.038	20.384	60.473
128	LYS17	CB	35.821	19.703	61.593
129	LYS17	CG	36.221	20.685	62.685
130	LYS17	CD	37.179	21.744	62.154
131	LYS17	CE	37.533	22.751	63.239
132	LYS17	NZ	36.321	23.416	63.742
133	LYS17	C	34.835	19.393	59.33
134	LYS17	O	34.484	19.784	58.21
135	ARG18	N	35.076	18.126	59.639
136	ARG18	CA	34.983	17.02	58.672
137	ARG18	CB	33.555	16.922	58.139
138	ARG18	CG	32.539	16.738	59.259
139	ARG18	CD	31.115	16.866	58.736
140	ARG18	NE	30.145	16.788	59.839
141	ARG18	CZ	29.063	16.006	59.802
142	ARG18	NH1	28.228	15.974	60.843
143	ARG18	NH2	28.821	15.251	58.727
144	ARG18	C	35.941	17.232	57.508
145	ARG18	O	35.532	17.176	56.341
146	LEU19	N	37.217	17.383	57.821
147	LEU19	CA	38.216	17.626	56.776
148	LEU19	CB	39.294	18.555	57.322
149	LEU19	CG	40.188	19.086	56.206
150	LEU19	CD1	39.359	19.788	55.134
151	LEU19	CD2	41.256	20.022	56.758
152	LEU19	C	38.82	16.302	56.311
153	LEU19	O	39.966	15.956	56.621
154	GLU20	N	38.012	15.553	55.586
155	GLU20	CA	38.441	14.242	55.117
156	GLU20	CB	37.259	13.285	55.047
157	GLU20	CG	36.922	12.721	56.43
158	GLU20	CD	37.967	11.695	56.89
159	GLU20	OE1	37.553	10.572	57.15
160	GLU20	OE2	39.15	11.962	56.735
161	GLU20	C	39.191	14.32	53.804
162	GLU20	O	39.491	15.417	53.319
163	ARG21	N	39.718	13.156	53.438
164	ARG21	CA	40.594	12.947	52.271
165	ARG21	CB	40.106	13.73	51.054
166	ARG21	CG	38.694	13.277	50.69

Table 11

167	ARG21	CD	37.921	14.351	49.933
168	ARG21	NE	36.489	14.008	49.895
169	ARG21	CZ	35.601	14.459	50.788
170	ARG21	NH1	35.978	15.32	51.738
171	ARG21	NH2	34.322	14.086	50.7
172	ARG21	C	42.011	13.319	52.69
173	ARG21	O	42.95	13.337	51.885
174	GLU22	N	42.179	13.227	54
175	GLU22	CA	43.451	13.502	54.655
176	GLU22	CB	43.173	14.109	56.032
177	GLU22	CG	42.12	13.321	56.807
178	GLU22	CD	41.759	14.027	58.115
179	GLU22	OE1	40.721	13.683	58.669
180	GLU22	OE2	42.607	14.746	58.625
181	GLU22	C	44.252	12.211	54.738
182	GLU22	O	45.486	12.239	54.779
183	GLN23	N	43.565	11.123	54.43
184	GLN23	CA	44.193	9.812	54.312
185	GLN23	CB	43.112	8.742	54.446
186	GLN23	CG	42.268	8.926	55.706
187	GLN23	CD	40.867	9.443	55.366
188	GLN23	OE1	40.706	10.528	54.78
189	GLN23	NE2	39.881	8.634	55.708
190	GLN23	C	44.858	9.694	52.946
191	GLN23	O	45.968	9.158	52.843
192	LYS24	N	44.33	10.45	51.994
193	LYS24	CA	44.931	10.514	50.664
194	LYS24	CB	43.893	11.031	49.677
195	LYS24	CG	44.535	11.295	48.322
196	LYS24	CD	43.591	12.014	47.368
197	LYS24	CE	44.325	12.404	46.09
198	LYS24	NZ	45.481	13.265	46.402
199	LYS24	C	46.113	11.47	50.685
200	LYS24	O	47.16	11.167	50.1
201	LEU25	N	46.041	12.449	51.573
202	LEU25	CA	47.154	13.382	51.743
203	LEU25	CB	46.684	14.573	52.567
204	LEU25	CG	45.593	15.352	51.844
205	LEU25	CD1	45.027	16.453	52.731
206	LEU25	CD2	46.11	15.926	50.529
207	LEU25	C	48.328	12.704	52.437
208	LEU25	O	49.436	12.76	51.894
209	LYS26	N	48.044	11.819	53.38
210	LYS26	CA	49.12	11.068	54.039
211	LYS26	CB	48.577	10.457	55.322
212	LYS26	CG	48.181	11.536	56.323
213	LYS26	CD	47.574	10.921	57.579
214	LYS26	CE	46.356	10.073	57.234
215	LYS26	NZ	45.742	9.501	58.439
216	LYS26	C	49.698	9.967	53.153
217	LYS26	O	50.908	9.723	53.218
218	LEU27	N	48.923	9.49	52.192
219	LEU27	CA	49.45	8.521	51.225
220	LEU27	CB	48.272	7.84	50.536
221	LEU27	CG	48.735	6.807	49.513
222	LEU27	CD1	49.589	5.727	50.169

Table 11

223	LEU27	CD2	47.543	6.184	48.795
224	LEU27	C	50.323	9.218	50.184
225	LEU27	O	51.427	8.739	49.894
226	TYR28	N	49.963	10.449	49.865
227	TYR28	CA	50.736	11.291	48.949
228	TYR28	CB	49.875	12.534	48.717
229	TYR28	CG	50.383	13.618	47.77
230	TYR28	CD1	49.901	13.677	46.468
231	TYR28	CE1	50.336	14.681	45.611
232	TYR28	CZ	51.246	15.628	46.064
233	TYR28	OH	51.649	16.648	45.23
234	TYR28	CE2	51.722	15.578	47.367
235	TYR28	CD2	51.283	14.576	48.223
236	TYR28	C	52.071	11.668	49.588
237	TYR28	O	53.133	11.412	49.002
238	GLN29	N	52.012	11.973	50.875
239	GLN29	CA	53.208	12.313	51.649
240	GLN29	CB	52.768	12.743	53.04
241	GLN29	CG	51.923	14.008	53.01
242	GLN29	CD	51.212	14.145	54.351
243	GLN29	OE1	50.063	14.599	54.429
244	GLN29	NE2	51.865	13.631	55.378
245	GLN29	C	54.145	11.124	51.799
246	GLN29	O	55.306	11.232	51.39
247	SER30	N	53.594	9.958	52.097
248	SER30	CA	54.429	8.777	52.335
249	SER30	CB	53.602	7.745	53.087
250	SER30	OG	53.224	8.332	54.326
251	SER30	C	54.976	8.167	51.051
252	SER30	O	56.117	7.686	51.052
253	ALA31	N	54.311	8.413	49.935
254	ALA31	CA	54.847	7.961	48.653
255	ALA31	CB	53.723	7.938	47.622
256	ALA31	C	55.966	8.886	48.187
257	ALA31	O	57	8.388	47.727
258	THR32	N	55.899	10.143	48.595
259	THR32	CA	56.954	11.105	48.259
260	THR32	CB	56.387	12.513	48.416
261	THR32	OG1	55.249	12.637	47.575
262	THR32	CG2	57.389	13.582	48.003
263	THR32	C	58.164	10.934	49.176
264	THR32	O	59.308	10.998	48.705
265	GLN33	N	57.913	10.463	50.387
266	GLN33	CA	58.996	10.184	51.33
267	GLN33	CB	58.392	10.07	52.725
268	GLN33	CG	57.783	11.402	53.151
269	GLN33	CD	56.975	11.254	54.437
270	GLN33	OE1	56.121	10.367	54.565
271	GLN33	NE2	57.181	12.2	55.336
272	GLN33	C	59.718	8.894	50.962
273	GLN33	O	60.957	8.892	50.913
274	ALA34	N	58.971	7.95	50.409
275	ALA34	CA	59.568	6.707	49.922
276	ALA34	CB	58.464	5.684	49.69
277	ALA34	C	60.351	6.933	48.634
278	ALA34	O	61.491	6.462	48.535

Table 11

279	VAL35	N	59.891	7.865	47.814
280	VAL35	CA	60.644	8.228	46.612
281	VAL35	CB	59.814	9.173	45.752
282	VAL35	CG1	60.666	9.824	44.671
283	VAL35	CG2	58.628	8.458	45.129
284	VAL35	C	61.954	8.92	46.961
285	VAL35	O	63.002	8.48	46.473
286	PHE36	N	61.943	9.761	47.984
287	PHE36	CA	63.167	10.481	48.344
288	PHE36	CB	62.82	11.684	49.212
289	PHE36	CG	62.135	12.83	48.472
290	PHE36	CD1	61.298	13.696	49.163
291	PHE36	CE1	60.678	14.743	48.495
292	PHE36	CZ	60.896	14.927	47.136
293	PHE36	CE2	61.739	14.066	46.446
294	PHE36	CD2	62.362	13.021	47.115
295	PHE36	C	64.174	9.605	49.079
296	PHE36	O	65.381	9.784	48.87
297	GLN37	N	63.717	8.563	49.754
298	GLN37	CA	64.677	7.682	50.42
299	GLN37	CB	64.069	7.128	51.704
300	GLN37	CG	62.783	6.351	51.47
301	GLN37	CD	62.066	6.161	52.799
302	GLN37	OE1	60.833	6.065	52.855
303	GLN37	NE2	62.85	6.168	53.863
304	GLN37	C	65.194	6.582	49.492
305	GLN37	O	66.371	6.218	49.604
306	LYS38	N	64.466	6.291	48.427
307	LYS38	CA	65	5.377	47.418
308	LYS38	CB	63.852	4.812	46.597
309	LYS38	CG	62.916	3.961	47.443
310	LYS38	CD	61.707	3.513	46.634
311	LYS38	CE	60.754	2.682	47.484
312	LYS38	NZ	61.43	1.484	48.004
313	LYS38	C	65.956	6.128	46.504
314	LYS38	O	67.062	5.638	46.237
315	ARG39	N	65.674	7.407	46.327
316	ARG39	CA	66.528	8.285	45.528
317	ARG39	CB	65.786	9.608	45.381
318	ARG39	CG	66.475	10.59	44.442
319	ARG39	CD	65.692	11.898	44.407
320	ARG39	NE	66.223	12.832	43.402
321	ARG39	CZ	65.737	14.064	43.238
322	ARG39	NH1	64.791	14.519	44.063
323	ARG39	NH2	66.234	14.861	42.29
324	ARG39	C	67.874	8.524	46.208
325	ARG39	O	68.909	8.289	45.571
326	GLN40	N	67.863	8.662	47.528
327	GLN40	CA	69.117	8.884	48.266
328	GLN40	CB	68.815	9.633	49.564
329	GLN40	CG	68.052	8.783	50.574
330	GLN40	CD	67.561	9.644	51.734
331	GLN40	OE1	67.735	9.301	52.909
332	GLN40	NE2	66.843	10.695	51.381
333	GLN40	C	69.871	7.582	48.561
334	GLN40	O	71.033	7.629	48.981

Table 11

335	ALA41	N	69.251	6.445	48.28
336	ALA41	CA	69.937	5.157	48.382
337	ALA41	CB	68.955	4.121	48.916
338	ALA41	C	70.486	4.698	47.029
339	ALA41	O	71.154	3.66	46.947
340	GLY42	N	70.172	5.441	45.977
341	GLY42	CA	70.682	5.123	44.638
342	GLY42	C	69.757	4.168	43.888
343	GLY42	O	70.156	3.534	42.903
344	GLU43	N	68.509	4.113	44.319
345	GLU43	CA	67.538	3.194	43.721
346	GLU43	CB	66.577	2.715	44.801
347	GLU43	CG	67.297	2.019	45.947
348	GLU43	CD	66.284	1.643	47.023
349	GLU43	OE1	65.116	1.52	46.683
350	GLU43	OE2	66.672	1.603	48.182
351	GLU43	C	66.732	3.886	42.633
352	GLU43	O	65.535	4.142	42.808
353	LEU44	N	67.353	4.083	41.483
354	LEU44	CA	66.677	4.749	40.359
355	LEU44	CB	67.705	5.54	39.562
356	LEU44	CG	68.365	6.614	40.419
357	LEU44	CD1	69.482	7.309	39.651
358	LEU44	CD2	67.34	7.626	40.925
359	LEU44	C	65.976	3.74	39.451
360	LEU44	O	66.282	3.62	38.261
361	ASP45	N	65.002	3.051	40.021
362	ASP45	CA	64.279	2.002	39.299
363	ASP45	CB	64.678	0.645	39.878
364	ASP45	CG	64.491	0.607	41.394
365	ASP45	OD1	65.474	0.774	42.102
366	ASP45	OD2	63.357	0.407	41.809
367	ASP45	C	62.766	2.216	39.355
368	ASP45	O	62.282	3.253	39.831
369	GLU46	N	62.03	1.164	39.029
370	GLU46	CA	60.569	1.259	38.905
371	GLU46	CB	59.99	0.088	38.099
372	GLU46	CG	59.955	-1.256	38.835
373	GLU46	CD	61.224	-2.072	38.594
374	GLU46	OE1	61.214	-2.877	37.677
375	GLU46	OE2	62.233	-1.729	39.201
376	GLU46	C	59.822	1.364	40.239
377	GLU46	O	58.672	1.808	40.215
378	SER47	N	60.487	1.206	41.376
379	SER47	CA	59.798	1.442	42.651
380	SER47	CB	60.593	0.822	43.798
381	SER47	OG	61.847	1.486	43.909
382	SER47	C	59.604	2.941	42.889
383	SER47	O	58.501	3.348	43.267
384	VAL48	N	60.503	3.743	42.337
385	VAL48	CA	60.365	5.194	42.441
386	VAL48	CB	61.735	5.823	42.227
387	VAL48	CG1	61.654	7.343	42.186
388	VAL48	CG2	62.713	5.367	43.297
389	VAL48	C	59.408	5.694	41.371
390	VAL48	O	58.499	6.475	41.681

Table 11

391	LEU49	N	59.39	4.974	40.262
392	LEU49	CA	58.535	5.333	39.133
393	LEU49	CB	58.97	4.47	37.957
394	LEU49	CG	58.603	5.097	36.621
395	LEU49	CD1	59.419	6.366	36.413
396	LEU49	CD2	58.864	4.12	35.48
397	LEU49	C	57.06	5.061	39.44
398	LEU49	O	56.222	5.948	39.242
399	GLU50	N	56.797	3.989	40.17
400	GLU50	CA	55.415	3.643	40.52
401	GLU50	CB	55.322	2.133	40.728
402	GLU50	CG	56.119	1.664	41.939
403	GLU50	CD	56.406	0.168	41.847
404	GLU50	OE1	56.595	-0.306	40.735
405	GLU50	OE2	56.612	-0.432	42.893
406	GLU50	C	54.902	4.393	41.753
407	GLU50	O	53.693	4.368	42.015
408	LEU51	N	55.766	5.115	42.449
409	LEU51	CA	55.286	5.967	43.535
410	LEU51	CB	56.301	5.97	44.668
411	LEU51	CG	56.423	4.605	45.329
412	LEU51	CD1	57.6	4.577	46.295
413	LEU51	CD2	55.129	4.217	46.036
414	LEU51	C	55.078	7.381	43.014
415	LEU51	O	53.993	7.949	43.208
416	THR52	N	55.95	7.783	42.1
417	THR52	CA	55.831	9.107	41.473
418	THR52	CB	57.125	9.492	40.758
419	THR52	OG1	57.453	8.479	39.818
420	THR52	CG2	58.296	9.648	41.714
421	THR52	C	54.69	9.156	40.467
422	THR52	O	54.066	10.211	40.337
423	SER53	N	54.244	8.003	39.996
424	SER53	CA	53.07	7.963	39.121
425	SER53	CB	52.986	6.583	38.476
426	SER53	OG	52.87	5.613	39.509
427	SER53	C	51.762	8.256	39.859
428	SER53	O	50.881	8.897	39.277
429	GLN54	N	51.732	8.049	41.166
430	GLN54	CA	50.515	8.354	41.916
431	GLN54	CB	50.509	7.501	43.177
432	GLN54	CG	50.595	6.019	42.839
433	GLN54	CD	50.702	5.198	44.119
434	GLN54	OE1	49.888	5.335	45.039
435	GLN54	NE2	51.725	4.365	44.168
436	GLN54	C	50.506	9.824	42.306
437	GLN54	O	49.529	10.54	42.039
438	ILEA55	N	51.695	10.312	42.617
439	ILEA55	CA	51.835	11.687	43.091
440	ILEA55	CB	53.197	11.803	43.752
441	ILEA55	CG2	53.298	13.124	44.5
442	ILEA55	CG1	53.417	10.646	44.715
443	ILEA55	CD1	54.876	10.568	45.136
444	ILEA55	C	51.741	12.694	41.951
445	ILEA55	O	51.023	13.689	42.09
446	LEU56	N	52.232	12.318	40.781

Table 11

447	LEU56	CA	52.15	13.19	39.605
448	LEU56	CB	53.305	12.867	38.67
449	LEU56	CG	54.641	13.172	39.333
450	LEU56	CD1	55.801	12.611	38.527
451	LEU56	CD2	54.807	14.667	39.551
452	LEU56	C	50.823	13.027	38.871
453	LEU56	O	50.382	13.961	38.19
454	GLY57	N	50.106	11.961	39.188
455	GLY57	CA	48.735	11.794	38.702
456	GLY57	C	47.828	12.818	39.377
457	GLY57	O	47.03	13.488	38.711
458	ALA58	N	48.031	13	40.674
459	ALA58	CA	47.297	14.026	41.428
460	ALA58	CB	47.194	13.566	42.879
461	ALA58	C	47.954	15.413	41.379
462	ALA58	O	47.393	16.379	41.911
463	ASN59	N	49.113	15.505	40.747
464	ASN59	CA	49.849	16.769	40.637
465	ASN59	CB	50.54	17.031	41.973
466	ASN59	CG	51.275	18.373	42.02
467	ASN59	OD1	51.473	19.056	41.004
468	ASN59	ND2	51.832	18.629	43.188
469	ASN59	C	50.893	16.689	39.525
470	ASN59	O	52.077	16.434	39.789
471	PRO60	N	50.507	17.158	38.348
472	PRO60	CA	51.395	17.139	37.175
473	PRO60	CB	50.48	17.388	36.018
474	PRO60	CG	49.117	17.82	36.534
475	PRO60	CD	49.189	17.722	38.046
476	PRO60	C	52.504	18.204	37.192
477	PRO60	O	53.34	18.238	36.283
478	ASP61	N	52.531	19.057	38.201
479	ASP61	CA	53.538	20.114	38.267
480	ASP61	CB	52.852	21.459	38.443
481	ASP61	CG	52.193	21.843	37.125
482	ASP61	OD1	52.927	22.254	36.234
483	ASP61	OD2	51.025	21.515	36.953
484	ASP61	C	54.559	19.886	39.373
485	ASP61	O	55.335	20.8	39.681
486	PHE62	N	54.549	18.711	39.984
487	PHE62	CA	55.586	18.388	40.973
488	PHE62	CB	55.057	17.277	41.876
489	PHE62	CG	55.701	17.16	43.259
490	PHE62	CD1	54.944	16.673	44.317
491	PHE62	CE1	55.506	16.558	45.581
492	PHE62	CZ	56.826	16.934	45.791
493	PHE62	CE2	57.583	17.426	44.736
494	PHE62	CD2	57.02	17.541	43.471
495	PHE62	C	56.86	17.95	40.242
496	PHE62	O	57.216	16.764	40.224
497	ALA63	N	57.653	18.947	39.876
498	ALA63	CA	58.828	18.75	39.018
499	ALA63	CB	59.249	20.105	38.46
500	ALA63	C	60.017	18.089	39.704
501	ALA63	O	60.829	17.463	39.017
502	THR64	N	59.961	17.957	41.018

Table 11

503	THR64	CA	61.016	17.233	41.725
504	THR64	CB	60.927	17.575	43.206
505	THR64	OG1	61.077	18.982	43.337
506	THR64	CG2	62.034	16.906	44.01
507	THR64	C	60.855	15.728	41.518
508	THR64	O	61.854	15.04	41.275
509	LEU65	N	59.624	15.306	41.271
510	LEU65	CA	59.362	13.895	41.001
511	LEU65	CB	57.995	13.532	41.551
512	LEU65	CG	57.951	13.757	43.057
513	LEU65	CD1	56.569	13.454	43.597
514	LEU65	CD2	58.991	12.912	43.783
515	LEU65	C	59.446	13.607	39.508
516	LEU65	O	59.743	12.472	39.119
517	TRP66	N	59.445	14.663	38.711
518	TRP66	CA	59.762	14.518	37.29
519	TRP66	CB	59.236	15.716	36.509
520	TRP66	CG	57.732	15.771	36.339
521	TRP66	CD1	56.893	16.775	36.765
522	TRP66	NE1	55.625	16.46	36.403
523	TRP66	CE2	55.582	15.281	35.758
524	TRP66	CZ2	54.544	14.556	35.195
525	TRP66	CH2	54.808	13.342	34.575
526	TRP66	CZ3	56.108	12.852	34.514
527	TRP66	CE3	57.154	13.574	35.073
528	TRP66	CD2	56.896	14.787	35.693
529	TRP66	C	61.271	14.404	37.092
530	TRP66	O	61.705	13.643	36.219
531	ASN67	N	62.04	14.936	38.033
532	ASN67	CA	63.489	14.714	38.034
533	ASN67	CB	64.164	15.667	39.012
534	ASN67	CG	63.947	17.128	38.648
535	ASN67	OD1	63.841	17.496	37.473
536	ASN67	ND2	63.977	17.959	39.675
537	ASN67	C	63.804	13.297	38.492
538	ASN67	O	64.677	12.645	37.903
539	CYS68	N	62.958	12.758	39.356
540	CYS68	CA	63.113	11.367	39.787
541	CYS68	CB	62.19	11.103	40.967
542	CYS68	SG	62.506	12.099	42.438
543	CYS68	C	62.777	10.399	38.659
544	CYS68	O	63.586	9.503	38.389
545	ARG69	N	61.794	10.741	37.839
546	ARG69	CA	61.474	9.9	36.68
547	ARG69	CB	60.095	10.27	36.155
548	ARG69	CG	59.026	10.002	37.203
549	ARG69	CD	57.633	10.262	36.647
550	ARG69	NE	57.328	9.369	35.519
551	ARG69	CZ	56.5	8.328	35.628
552	ARG69	NH1	56.247	7.554	34.571
553	ARG69	NH2	55.919	8.062	36.797
554	ARG69	C	62.497	10.045	35.557
555	ARG69	O	62.819	9.044	34.909
556	ARG70	N	63.174	11.18	35.497
557	ARG70	CA	64.273	11.339	34.543
558	ARG70	CB	64.652	12.813	34.459

Table 11

559	ARG70	CG	63.817	13.518	33.403
560	ARG70	CD	64.152	14.998	33.28
561	ARG70	NE	63.384	15.803	34.238
562	ARG70	CZ	62.513	16.729	33.832
563	ARG70	NH1	62.35	16.958	32.527
564	ARG70	NH2	61.823	17.44	34.725
565	ARG70	C	65.499	10.53	34.946
566	ARG70	O	66.071	9.84	34.094
567	GLU71	N	65.728	10.403	36.241
568	GLU71	CA	66.874	9.635	36.731
569	GLU71	CB	67.137	10.077	38.162
570	GLU71	CG	67.534	11.546	38.196
571	GLU71	CD	67.372	12.096	39.608
572	GLU71	OE1	66.439	11.673	40.277
573	GLU71	OE2	68.106	13.013	39.949
574	GLU71	C	66.603	8.135	36.687
575	GLU71	O	67.472	7.377	36.239
576	VAL72	N	65.347	7.763	36.875
577	VAL72	CA	64.952	6.359	36.753
578	VAL72	CB	63.543	6.191	37.316
579	VAL72	CG1	62.954	4.833	36.955
580	VAL72	CG2	63.511	6.411	38.823
581	VAL72	C	64.963	5.915	35.297
582	VAL72	O	65.538	4.866	34.987
583	LEU73	N	64.605	6.818	34.398
584	LEU73	CA	64.592	6.466	32.98
585	LEU73	CB	63.706	7.436	32.205
586	LEU73	CG	62.358	6.823	31.819
587	LEU73	CD1	61.513	6.447	33.033
588	LEU73	CD2	61.575	7.764	30.911
589	LEU73	C	65.989	6.457	32.38
590	LEU73	O	66.269	5.559	31.582
591	GLN74	N	66.91	7.236	32.924
592	GLN74	CA	68.289	7.195	32.427
593	GLN74	CB	68.987	8.495	32.804
594	GLN74	CG	68.389	9.663	32.028
595	GLN74	CD	68.938	10.988	32.545
596	GLN74	OE1	70.088	11.078	32.991
597	GLN74	NE2	68.087	11.998	32.522
598	GLN74	C	69.052	5.996	32.979
599	GLN74	O	69.75	5.315	32.214
600	GLN75	N	68.668	5.562	34.169
601	GLN75	CA	69.263	4.356	34.74
602	GLN75	CB	68.913	4.305	36.223
603	GLN75	CG	69.492	3.08	36.926
604	GLN75	CD	71.018	3.121	36.954
605	GLN75	OE1	71.615	3.822	37.781
606	GLN75	NE2	71.63	2.363	36.06
607	GLN75	C	68.732	3.111	34.034
608	GLN75	O	69.532	2.28	33.578
609	LEU76	N	67.473	3.187	33.639
610	LEU76	CA	66.824	2.1	32.9
611	LEU76	CB	65.31	2.293	32.988
612	LEU76	CG	64.619	1.454	34.069
613	LEU76	CD1	65.251	1.564	35.455
614	LEU76	CD2	63.136	1.797	34.139

Table 11

615	LEU76	C	67.244	2.069	31.43
616	LEU76	O	67.281	0.983	30.843
617	GLU77	N	67.808	3.16	30.935
618	GLU77	CA	68.313	3.201	29.558
619	GLU77	CB	68.343	4.649	29.082
620	GLU77	CG	66.937	5.128	28.743
621	GLU77	CD	66.889	6.644	28.596
622	GLU77	OE1	67.542	7.316	29.383
623	GLU77	OE2	66.078	7.107	27.806
624	GLU77	C	69.699	2.58	29.432
625	GLU77	O	70.152	2.304	28.316
626	THR78	N	70.336	2.311	30.559
627	THR78	CA	71.581	1.545	30.543
628	THR78	CB	72.6	2.207	31.464
629	THR78	OG1	72.204	1.988	32.81
630	THR78	CG2	72.709	3.707	31.218
631	THR78	C	71.35	0.107	31.011
632	THR78	O	72.324	-0.631	31.201
633	GLN79	N	70.106	-0.263	31.283
634	GLN79	CA	69.84	-1.599	31.833
635	GLN79	CB	69.275	-1.43	33.237
636	GLN79	CG	70.288	-0.799	34.178
637	GLN79	CD	69.644	-0.556	35.535
638	GLN79	OE1	68.737	0.275	35.667
639	GLN79	NE2	70.167	-1.233	36.541
640	GLN79	C	68.847	-2.427	31.023
641	GLN79	O	69.016	-3.647	30.897
642	LYS80	N	67.798	-1.789	30.536
643	LYS80	CA	66.708	-2.52	29.879
644	LYS80	CB	65.439	-1.675	29.918
645	LYS80	CG	64.964	-1.421	31.344
646	LYS80	CD	64.719	-2.726	32.094
647	LYS80	CE	64.104	-2.476	33.465
648	LYS80	NZ	62.786	-1.835	33.333
649	LYS80	C	67.016	-2.878	28.433
650	LYS80	O	67.642	-2.111	27.693
651	SER81	N	66.515	-4.036	28.038
652	SER81	CA	66.603	-4.479	26.642
653	SER81	CB	66.015	-5.883	26.544
654	SER81	OG	64.636	-5.801	26.877
655	SER81	C	65.808	-3.511	25.772
656	SER81	O	64.814	-2.948	26.245
657	PRO82	N	66.189	-3.344	24.514
658	PRO82	CA	65.751	-2.158	23.755
659	PRO82	CB	66.517	-2.216	22.468
660	PRO82	CG	67.431	-3.433	22.472
661	PRO82	CD	67.239	-4.099	23.824
662	PRO82	C	64.244	-2.083	23.478
663	PRO82	O	63.663	-1.003	23.629
664	GLU83	N	63.579	-3.224	23.382
665	GLU83	CA	62.128	-3.219	23.134
666	GLU83	CB	61.678	-4.471	22.361
667	GLU83	CG	61.622	-5.784	23.156
668	GLU83	CD	62.991	-6.447	23.294
669	GLU83	OE1	63.347	-7.205	22.407
670	GLU83	OE2	63.738	-6.003	24.159

Table 11

671	GLU83	C	61.34	-3.083	24.442
672	GLU83	O	60.24	-2.52	24.445
673	GLU84	N	62.014	-3.332	25.553
674	GLU84	CA	61.405	-3.181	26.871
675	GLU84	CB	62.162	-4.11	27.807
676	GLU84	CG	61.732	-4.009	29.262
677	GLU84	CD	62.705	-4.849	30.079
678	GLU84	OE1	63.841	-4.975	29.633
679	GLU84	OE2	62.305	-5.362	31.114
680	GLU84	C	61.571	-1.739	27.325
681	GLU84	O	60.652	-1.148	27.902
682	LEU85	N	62.621	-1.123	26.811
683	LEU85	CA	62.88	0.289	27.061
684	LEU85	CB	64.347	0.53	26.73
685	LEU85	CG	64.786	1.941	27.084
686	LEU85	CD1	64.585	2.206	28.573
687	LEU85	CD2	66.241	2.149	26.683
688	LEU85	C	61.987	1.159	26.179
689	LEU85	O	61.461	2.17	26.656
690	ALA86	N	61.603	0.627	25.028
691	ALA86	CA	60.646	1.324	24.164
692	ALA86	CB	60.728	0.728	22.763
693	ALA86	C	59.219	1.197	24.692
694	ALA86	O	58.455	2.169	24.621
695	ALA87	N	58.955	0.134	25.435
696	ALA87	CA	57.655	-0.005	26.095
697	ALA87	CB	57.457	-1.463	26.492
698	ALA87	C	57.573	0.885	27.333
699	ALA87	O	56.533	1.516	27.562
700	LEU88	N	58.721	1.151	27.938
701	LEU88	CA	58.786	2.087	29.068
702	LEU88	CB	60.133	1.931	29.775
703	LEU88	CG	60.042	1.16	31.092
704	LEU88	CD1	59.089	1.856	32.058
705	LEU88	CD2	59.64	-0.3	30.904
706	LEU88	C	58.638	3.531	28.595
707	LEU88	O	57.907	4.304	29.225
708	VAL89	N	59.101	3.808	27.387
709	VAL89	CA	58.939	5.143	26.805
710	VAL89	CB	59.923	5.275	25.646
711	VAL89	CG1	59.604	6.475	24.762
712	VAL89	CG2	61.36	5.335	26.149
713	VAL89	C	57.516	5.387	26.305
714	VAL89	O	56.978	6.481	26.521
715	LYS90	N	56.831	4.332	25.894
716	LYS90	CA	55.447	4.498	25.446
717	LYS90	CB	55.08	3.332	24.537
718	LYS90	CG	53.699	3.528	23.924
719	LYS90	CD	53.359	2.418	22.938
720	LYS90	CE	51.986	2.64	22.314
721	LYS90	NZ	51.679	1.594	21.326
722	LYS90	C	54.487	4.574	26.632
723	LYS90	O	53.552	5.386	26.608
724	ALA91	N	54.874	3.965	27.743
725	ALA91	CA	54.092	4.096	28.977
726	ALA91	CB	54.473	2.963	29.923

Table 11

727	ALA91	C	54.37	5.439	29.648
728	ALA91	O	53.458	6.05	30.219
729	GLU92	N	55.535	5.992	29.353
730	GLU92	CA	55.875	7.336	29.807
731	GLU92	CB	57.365	7.557	29.57
732	GLU92	CG	57.826	8.924	30.061
733	GLU92	CD	57.723	8.995	31.578
734	GLU92	OE1	58.446	8.25	32.224
735	GLU92	OE2	56.968	9.825	32.061
736	GLU92	C	55.078	8.38	29.036
737	GLU92	O	54.51	9.271	29.671
738	LEU93	N	54.824	8.14	27.758
739	LEU93	CA	54.006	9.076	26.974
740	LEU93	CB	54.212	8.792	25.491
741	LEU93	CG	55.632	9.145	25.074
742	LEU93	CD1	55.89	8.78	23.619
743	LEU93	CD2	55.9	10.625	25.314
744	LEU93	C	52.526	8.956	27.319
745	LEU93	O	51.839	9.981	27.423
746	GLY94	N	52.12	7.766	27.728
747	GLY94	CA	50.77	7.557	28.256
748	GLY94	C	50.555	8.376	29.525
749	GLY94	O	49.645	9.215	29.576
750	PHE95	N	51.505	8.288	30.443
751	PHE95	CA	51.4	9.018	31.709
752	PHE95	CB	52.444	8.461	32.667
753	PHE95	CG	52.37	9.072	34.059
754	PHE95	CD1	51.247	8.856	34.846
755	PHE95	CE1	51.171	9.414	36.114
756	PHE95	CZ	52.218	10.19	36.593
757	PHE95	CE2	53.339	10.41	35.804
758	PHE95	CD2	53.414	9.854	34.535
759	PHE95	C	51.607	10.529	31.555
760	PHE95	O	50.902	11.296	32.222
761	LEU96	N	52.356	10.949	30.548
762	LEU96	CA	52.511	12.383	30.278
763	LEU96	CB	53.657	12.582	29.292
764	LEU96	CG	55.01	12.297	29.932
765	LEU96	CD1	56.106	12.151	28.884
766	LEU96	CD2	55.372	13.366	30.952
767	LEU96	C	51.232	12.977	29.699
768	LEU96	O	50.773	14.018	30.184
769	GLU97	N	50.511	12.178	28.929
770	GLU97	CA	49.229	12.628	28.386
771	GLU97	CB	48.834	11.694	27.248
772	GLU97	CG	47.492	12.087	26.641
773	GLU97	CD	47.143	11.133	25.506
774	GLU97	OE1	46.517	11.58	24.555
775	GLU97	OE2	47.555	9.983	25.585
776	GLU97	C	48.145	12.615	29.457
777	GLU97	O	47.351	13.559	29.519
778	SER98	N	48.3	11.745	30.442
779	SER98	CA	47.346	11.687	31.551
780	SER98	CB	47.548	10.372	32.295
781	SER98	OG	47.35	9.313	31.368
782	SER98	C	47.547	12.851	32.516

Table 11

783	SER98	O	46.56	13.471	32.932
784	CYS99	N	48.78	13.318	32.636
785	CYS99	CA	49.05	14.482	33.48
786	CYS99	CB	50.516	14.473	33.876
787	CYS99	SG	51.009	13.115	34.954
788	CYS99	C	48.701	15.789	32.775
789	CYS99	O	48.227	16.717	33.439
790	LEU100	N	48.642	15.753	31.453
791	LEU100	CA	48.15	16.905	30.69
792	LEU100	CB	48.744	16.853	29.291
793	LEU100	CG	50.251	17.052	29.338
794	LEU100	CD1	50.885	16.8	27.975
795	LEU100	CD2	50.598	18.437	29.871
796	LEU100	C	46.624	16.927	30.609
797	LEU100	O	46.032	17.981	30.357
798	ARG101	N	45.996	15.819	30.965
799	ARG101	CA	44.541	15.79	31.121
800	ARG101	CB	44.048	14.377	30.842
801	ARG101	CG	44.279	13.988	29.388
802	ARG101	CD	43.923	12.526	29.153
803	ARG101	NE	42.535	12.26	29.558
804	ARG101	CZ	41.576	11.903	28.701
805	ARG101	NH1	41.86	11.758	27.405
806	ARG101	NH2	40.336	11.683	29.142
807	ARG101	C	44.134	16.204	32.535
808	ARG101	O	42.97	16.548	32.772
809	VAL102	N	45.094	16.212	33.449
810	VAL102	CA	44.85	16.749	34.79
811	VAL102	CB	45.724	15.989	35.788
812	VAL102	CG1	45.539	16.509	37.21
813	VAL102	CG2	45.437	14.493	35.74
814	VAL102	C	45.191	18.239	34.809
815	VAL102	O	44.574	19.022	35.544
816	ASN103	N	46.141	18.618	33.97
817	ASN103	CA	46.472	20.03	33.767
818	ASN103	CB	47.376	20.502	34.904
819	ASN103	CG	47.604	22.007	34.801
820	ASN103	OD1	46.99	22.68	33.966
821	ASN103	ND2	48.587	22.492	35.537
822	ASN103	C	47.172	20.235	32.422
823	ASN103	O	48.385	20.019	32.294
824	PRO104	N	46.439	20.82	31.486
825	PRO104	CA	46.962	21.09	30.137
826	PRO104	CB	45.746	21.394	29.316
827	PRO104	CG	44.546	21.556	30.237
828	PRO104	CD	45.041	21.234	31.637
829	PRO104	C	47.961	22.254	30.047
830	PRO104	O	48.514	22.492	28.964
831	LYS105	N	48.18	22.975	31.137
832	LYS105	CA	49.199	24.028	31.157
833	LYS105	CB	48.563	25.35	31.584
834	LYS105	CG	48.037	25.326	33.012
835	LYS105	CD	47.396	26.653	33.4
836	LYS105	CE	46.867	26.613	34.829
837	LYS105	NZ	46.241	27.892	35.198
838	LYS105	C	50.365	23.661	32.079

Table 11

839	LYS105	O	51.108	24.545	32.525
840	SER106	N	50.475	22.383	32.413
841	SER106	CA	51.538	21.926	33.315
842	SER106	CB	51.307	20.462	33.666
843	SER106	OG	52.457	20.016	34.375
844	SER106	C	52.926	22.04	32.712
845	SER106	O	53.342	21.16	31.951
846	TYR107	N	53.722	22.912	33.309
847	TYR107	CA	55.115	23.087	32.885
848	TYR107	CB	55.696	24.335	33.544
849	TYR107	CG	55.112	25.667	33.082
850	TYR107	CD1	54.097	26.279	33.808
851	TYR107	CE1	53.576	27.494	33.385
852	TYR107	CZ	54.08	28.098	32.24
853	TYR107	OH	53.526	29.276	31.787
854	TYR107	CE2	55.103	27.497	31.52
855	TYR107	CD2	55.621	26.28	31.943
856	TYR107	C	55.956	21.886	33.295
857	TYR107	O	56.807	21.445	32.513
858	GLY108	N	55.548	21.231	34.371
859	GLY108	CA	56.198	19.995	34.807
860	GLY108	C	56.077	18.91	33.739
861	GLY108	O	57.09	18.499	33.154
862	THR109	N	54.849	18.62	33.339
863	THR109	CA	54.631	17.534	32.383
864	THR109	CB	53.15	17.191	32.404
865	THR109	OG1	52.775	16.927	33.749
866	THR109	CG2	52.874	15.949	31.574
867	THR109	C	55.049	17.897	30.956
868	THR109	O	55.648	17.05	30.279
869	TRP110	N	54.989	19.174	30.607
870	TRP110	CA	55.441	19.594	29.277
871	TRP110	CB	54.961	21.015	28.985
872	TRP110	CG	53.507	21.137	28.567
873	TRP110	CD1	52.533	21.897	29.178
874	TRP110	NE1	51.371	21.738	28.496
875	TRP110	CE2	51.532	20.912	27.446
876	TRP110	CZ2	50.662	20.457	26.468
877	TRP110	CH2	51.124	19.59	25.485
878	TRP110	CZ3	52.453	19.18	25.477
879	TRP110	CE3	53.332	19.632	26.454
880	TRP110	CD2	52.875	20.495	27.438
881	TRP110	C	56.959	19.547	29.147
882	TRP110	O	57.448	19.012	28.145
883	HIS111	N	57.675	19.821	30.225
884	HIS111	CA	59.136	19.773	30.163
885	HIS111	CB	59.705	20.527	31.36
886	HIS111	CG	61.221	20.554	31.45
887	HIS111	ND1	62.102	20.501	30.43
888	HIS111	CE1	63.357	20.554	30.921
889	HIS111	NE2	63.266	20.638	32.268
890	HIS111	CD2	61.957	20.642	32.607
891	HIS111	C	59.638	18.334	30.165
892	HIS111	O	60.534	18.019	29.371
893	HIS112	N	58.902	17.437	30.798
894	HIS112	CA	59.326	16.038	30.802

Table 11

895	HIS112	CB	58.646	15.331	31.966
896	HIS112	CG	59.235	13.973	32.287
897	HIS112	ND1	60.228	13.722	33.16
898	HIS112	CE1	60.478	12.398	33.182
899	HIS112	NE2	59.635	11.807	32.308
900	HIS112	CD2	58.862	12.764	31.748
901	HIS112	C	58.985	15.35	29.479
902	HIS112	O	59.794	14.553	28.982
903	ARG113	N	57.969	15.848	28.791
904	ARG113	CA	57.638	15.283	27.483
905	ARG113	CB	56.165	15.532	27.186
906	ARG113	CG	55.722	14.677	26.008
907	ARG113	CD	54.223	14.765	25.757
908	ARG113	NE	53.847	13.857	24.663
909	ARG113	CZ	52.874	12.948	24.763
910	ARG113	NH1	52.149	12.874	25.879
911	ARG113	NH2	52.593	12.149	23.731
912	ARG113	C	58.517	15.874	26.38
913	ARG113	O	58.925	15.135	25.474
914	CYS114	N	59.017	17.083	26.593
915	CYS114	CA	59.991	17.661	25.659
916	CYS114	CB	60.117	19.162	25.902
917	CYS114	SG	58.678	20.174	25.491
918	CYS114	C	61.365	17.027	25.846
919	CYS114	O	62.069	16.776	24.862
920	TRP115	N	61.634	16.577	27.06
921	TRP115	CA	62.873	15.857	27.349
922	TRP115	CB	62.951	15.67	28.862
923	TRP115	CG	64.03	14.716	29.333
924	TRP115	CD1	65.378	14.974	29.432
925	TRP115	NE1	65.998	13.853	29.879
926	TRP115	CE2	65.115	12.858	30.088
927	TRP115	CZ2	65.256	11.546	30.517
928	TRP115	CH2	64.134	10.735	30.639
929	TRP115	CZ3	62.872	11.231	30.331
930	TRP115	CE3	62.721	12.541	29.896
931	TRP115	CD2	63.839	13.353	29.769
932	TRP115	C	62.889	14.502	26.651
933	TRP115	O	63.794	14.239	25.846
934	LEU116	N	61.768	13.801	26.724
935	LEU116	CA	61.703	12.465	26.134
936	LEU116	CB	60.459	11.764	26.663
937	LEU116	CG	60.431	10.303	26.232
938	LEU116	CD1	61.669	9.565	26.73
939	LEU116	CD2	59.166	9.619	26.73
940	LEU116	C	61.662	12.517	24.61
941	LEU116	O	62.497	11.864	23.974
942	LEU117	N	60.961	13.497	24.063
943	LEU117	CA	60.844	13.619	22.6
944	LEU117	CB	59.565	14.375	22.236
945	LEU117	CG	58.33	13.481	22.079
946	LEU117	CD1	58.584	12.359	21.084
947	LEU117	CD2	57.805	12.904	23.389
948	LEU117	C	62.052	14.316	21.964
949	LEU117	O	62.186	14.342	20.734
950	GLY118	N	62.945	14.82	22.797

Table 11

951	GLY118	CA	64.205	15.367	22.313
952	GLY118	C	65.251	14.265	22.199
953	GLY118	O	66	14.224	21.214
954	ARG119	N	65.264	13.362	23.168
955	ARG119	CA	66.284	12.304	23.193
956	ARG119	CB	66.677	12.04	24.643
957	ARG119	CG	65.511	11.518	25.473
958	ARG119	CD	65.918	11.317	26.926
959	ARG119	NE	67.026	10.356	27.04
960	ARG119	CZ	68.172	10.619	27.676
961	ARG119	NH1	69.145	9.706	27.703
962	ARG119	NH2	68.361	11.808	28.251
963	ARG119	C	65.871	10.988	22.523
964	ARG119	O	66.705	10.077	22.438
965	LEU120	N	64.632	10.863	22.074
966	LEU120	CA	64.237	9.645	21.352
967	LEU120	CB	62.726	9.625	21.152
968	LEU120	CG	61.997	9.268	22.438
969	LEU120	CD1	60.486	9.295	22.234
970	LEU120	CD2	62.449	7.905	22.951
971	LEU120	C	64.921	9.541	19.994
972	LEU120	O	64.866	10.47	19.184
973	PRO121	N	65.485	8.371	19.729
974	PRO121	CA	66.201	8.125	18.467
975	PRO121	CB	66.947	6.846	18.698
976	PRO121	CG	66.498	6.229	20.015
977	PRO121	CD	65.525	7.218	20.634
978	PRO121	C	65.279	7.991	17.249
979	PRO121	O	65.731	8.147	16.109
980	GLU122	N	64.007	7.712	17.485
981	GLU122	CA	63.011	7.743	16.406
982	GLU122	CB	62.948	6.356	15.764
983	GLU122	CG	62.595	6.386	14.274
984	GLU122	CD	61.173	6.881	14.012
985	GLU122	OE1	61.012	8.087	13.888
986	GLU122	OE2	60.294	6.042	13.877
987	GLU122	C	61.648	8.124	16.991
988	GLU122	O	60.804	7.245	17.196
989	PRO123	N	61.443	9.407	17.25
990	PRO123	CA	60.234	9.86	17.944
991	PRO123	CB	60.569	11.238	18.422
992	PRO123	CG	61.889	11.676	17.808
993	PRO123	CD	62.361	10.513	16.96
994	PRO123	C	59.012	9.875	17.027
995	PRO123	O	59.113	10.194	15.837
996	ASN124	N	57.865	9.525	17.588
997	ASN124	CA	56.624	9.531	16.807
998	ASN124	CB	55.643	8.532	17.417
999	ASN124	CG	54.414	8.344	16.524
1000	ASN124	OD1	54.074	9.207	15.703
1001	ASN124	ND2	53.732	7.232	16.724
1002	ASN124	C	56.02	10.931	16.787
1003	ASN124	O	55.146	11.264	17.597
1004	TRP125	N	56.283	11.629	15.697
1005	TRP125	CA	55.813	13.005	15.567
1006	TRP125	CB	56.693	13.727	14.556

Table 11

1007	TRP125	CG	58.12	13.919	15.033
1008	TRP125	CD1	59.271	13.659	14.322
1009	TRP125	NE1	60.339	13.96	15.104
1010	TRP125	CE2	59.946	14.4	16.313
1011	TRP125	CZ2	60.645	14.787	17.445
1012	TRP125	CH2	59.956	15.205	18.577
1013	TRP125	CZ3	58.567	15.227	18.583
1014	TRP125	CE3	57.859	14.824	17.459
1015	TRP125	CD2	58.541	14.406	16.327
1016	TRP125	C	54.343	13.124	15.179
1017	TRP125	O	53.71	14.098	15.606
1018	THR126	N	53.733	12.046	14.711
1019	THR126	CA	52.309	12.124	14.372
1020	THR126	CB	51.953	11.086	13.313
1021	THR126	OG1	52.041	9.785	13.876
1022	THR126	CG2	52.89	11.163	12.113
1023	THR126	C	51.467	11.918	15.627
1024	THR126	O	50.421	12.56	15.771
1025	ARG127	N	52.072	11.304	16.633
1026	ARG127	CA	51.42	11.171	17.937
1027	ARG127	CB	52.129	10.063	18.712
1028	ARG127	CG	51.631	9.955	20.149
1029	ARG127	CD	52.406	8.897	20.926
1030	ARG127	NE	52.217	7.562	20.335
1031	ARG127	CZ	53.161	6.618	20.334
1032	ARG127	NH1	52.898	5.411	19.828
1033	ARG127	NH2	54.356	6.868	20.874
1034	ARG127	C	51.524	12.472	18.723
1035	ARG127	O	50.556	12.874	19.378
1036	GLU128	N	52.551	13.251	18.426
1037	GLU128	CA	52.748	14.508	19.151
1038	GLU128	CB	54.218	14.896	19.076
1039	GLU128	CG	55.143	13.723	19.38
1040	GLU128	CD	54.91	13.144	20.77
1041	GLU128	OE1	54.929	13.924	21.708
1042	GLU128	OE2	54.929	11.925	20.878
1043	GLU128	C	51.899	15.613	18.53
1044	GLU128	O	51.288	16.408	19.257
1045	LEU129	N	51.662	15.497	17.233
1046	LEU129	CA	50.782	16.452	16.557
1047	LEU129	CB	51.068	16.43	15.061
1048	LEU129	CG	52.483	16.907	14.756
1049	LEU129	CD1	52.797	16.775	13.27
1050	LEU129	CD2	52.695	18.341	15.227
1051	LEU129	C	49.319	16.108	16.803
1052	LEU129	O	48.504	17.019	16.987
1053	GLU130	N	49.045	14.842	17.073
1054	GLU130	CA	47.681	14.446	17.422
1055	GLU130	CB	47.537	12.943	17.211
1056	GLU130	CG	46.086	12.494	17.341
1057	GLU130	CD	45.235	13.14	16.25
1058	GLU130	OE1	45.743	13.273	15.145
1059	GLU130	OE2	44.074	13.409	16.517
1060	GLU130	C	47.368	14.799	18.873
1061	GLU130	O	46.247	15.236	19.153
1062	LEU131	N	48.4	14.871	19.699

Table 11

1063	LEU131	CA	48.248	15.308	21.087
1064	LEU131	CB	49.599	15.155	21.775
1065	LEU131	CG	49.526	15.567	23.238
1066	LEU131	CD1	48.847	14.479	24.06
1067	LEU131	CD2	50.916	15.855	23.788
1068	LEU131	C	47.848	16.778	21.146
1069	LEU131	O	46.821	17.118	21.752
1070	CYS132	N	48.499	17.589	20.327
1071	CYS132	CA	48.159	19.011	20.295
1072	CYS132	CB	49.372	19.813	19.856
1073	CYS132	SG	50.526	20.07	21.215
1074	CYS132	C	46.941	19.328	19.438
1075	CYS132	O	46.283	20.339	19.701
1076	ALA133	N	46.502	18.385	18.622
1077	ALA133	CA	45.227	18.555	17.926
1078	ALA133	CB	45.149	17.557	16.776
1079	ALA133	C	44.07	18.318	18.892
1080	ALA133	O	43.158	19.151	18.96
1081	ARG134	N	44.256	17.384	19.813
1082	ARG134	CA	43.234	17.123	20.831
1083	ARG134	CB	43.594	15.848	21.581
1084	ARG134	CG	43.635	14.641	20.655
1085	ARG134	CD	44.109	13.399	21.402
1086	ARG134	NE	44.245	12.259	20.483
1087	ARG134	CZ	43.437	11.197	20.5
1088	ARG134	NH1	42.456	11.117	21.402
1089	ARG134	NH2	43.623	10.205	19.627
1090	ARG134	C	43.159	18.267	21.831
1091	ARG134	O	42.072	18.822	22.039
1092	PHE135	N	44.313	18.791	22.214
1093	PHE135	CA	44.322	19.9	23.171
1094	PHE135	CB	45.685	19.98	23.843
1095	PHE135	CG	45.901	18.877	24.874
1096	PHE135	CD1	47.119	18.216	24.95
1097	PHE135	CE1	47.303	17.21	25.89
1098	PHE135	CZ	46.271	16.866	26.754
1099	PHE135	CE2	45.055	17.531	26.681
1100	PHE135	CD2	44.871	18.537	25.741
1101	PHE135	C	43.949	21.244	22.552
1102	PHE135	O	43.353	22.06	23.258
1103	LEU136	N	44.026	21.36	21.237
1104	LEU136	CA	43.551	22.572	20.561
1105	LEU136	CB	44.343	22.767	19.273
1106	LEU136	CG	45.371	23.896	19.357
1107	LEU136	CD1	46.247	23.83	20.606
1108	LEU136	CD2	46.231	23.92	18.101
1109	LEU136	C	42.058	22.49	20.243
1110	LEU136	O	41.396	23.521	20.088
1111	GLU137	N	41.493	21.298	20.318
1112	GLU137	CA	40.042	21.181	20.166
1113	GLU137	CB	39.693	19.859	19.493
1114	GLU137	CG	40.277	19.773	18.086
1115	GLU137	CD	39.822	20.95	17.224
1116	GLU137	OE1	40.665	21.784	16.92
1117	GLU137	OE2	38.71	20.881	16.721
1118	GLU137	C	39.339	21.289	21.517

Table 11

1119	GLU137	O	38.125	21.514	21.567
1120	VAL138	N	40.1	21.161	22.593
1121	VAL138	CA	39.558	21.424	23.929
1122	VAL138	CB	40.229	20.461	24.907
1123	VAL138	CG1	39.785	20.708	26.345
1124	VAL138	CG2	39.964	19.011	24.515
1125	VAL138	C	39.846	22.871	24.332
1126	VAL138	O	39.072	23.509	25.056
1127	ASP139	N	40.929	23.394	23.786
1128	ASP139	CA	41.346	24.775	24.026
1129	ASP139	CB	42.022	24.83	25.398
1130	ASP139	CG	42.276	26.264	25.864
1131	ASP139	OD1	42.534	27.111	25.015
1132	ASP139	OD2	42.306	26.465	27.068
1133	ASP139	C	42.329	25.19	22.931
1134	ASP139	O	43.549	25.07	23.106
1135	GLU140	N	41.817	25.916	21.95
1136	GLU140	CA	42.637	26.322	20.793
1137	GLU140	CB	41.728	26.643	19.611
1138	GLU140	CG	40.745	27.764	19.924
1139	GLU140	CD	39.961	28.126	18.667
1140	GLU140	OE1	38.749	28.251	18.774
1141	GLU140	OE2	40.585	28.247	17.622
1142	GLU140	C	43.549	27.519	21.056
1143	GLU140	O	44.267	27.956	20.149
1144	ARG141	N	43.501	28.056	22.264
1145	ARG141	CA	44.365	29.164	22.649
1146	ARG141	CB	43.507	30.246	23.292
1147	ARG141	CG	42.483	30.799	22.305
1148	ARG141	CD	43.158	31.518	21.14
1149	ARG141	NE	43.932	32.669	21.628
1150	ARG141	CZ	43.547	33.936	21.459
1151	ARG141	NH1	42.481	34.215	20.703
1152	ARG141	NH2	44.276	34.926	21.978
1153	ARG141	C	45.454	28.699	23.613
1154	ARG141	O	46.132	29.54	24.217
1155	ASN142	N	45.558	27.393	23.824
1156	ASN142	CA	46.624	26.87	24.684
1157	ASN142	CB	46.345	25.411	25.046
1158	ASN142	CG	47.367	24.918	26.074
1159	ASN142	OD1	48.138	25.713	26.627
1160	ASN142	ND2	47.424	23.611	26.254
1161	ASN142	C	47.965	26.985	23.968
1162	ASN142	O	48.385	26.074	23.241
1163	PHE143	N	48.734	27.963	24.42
1164	PHE143	CA	50.018	28.287	23.797
1165	PHE143	CB	50.442	29.706	24.183
1166	PHE143	CG	50.738	29.965	25.664
1167	PHE143	CD1	52.031	29.809	26.147
1168	PHE143	CE1	52.309	30.05	27.486
1169	PHE143	CZ	51.294	30.457	28.343
1170	PHE143	CE2	50.003	30.627	27.859
1171	PHE143	CD2	49.727	30.387	26.519
1172	PHE143	C	51.11	27.289	24.161
1173	PHE143	O	52.043	27.124	23.37
1174	HIS144	N	50.844	26.427	25.13

Table 11

1175	HIS144	CA	51.796	25.373	25.466
1176	HIS144	CB	51.401	24.752	26.797
1177	HIS144	CG	51.393	25.704	27.973
1178	HIS144	ND1	50.32	26.334	28.486
1179	HIS144	CE1	50.706	27.099	29.527
1180	HIS144	NE2	52.039	26.934	29.679
1181	HIS144	CD2	52.476	26.074	28.732
1182	HIS144	C	51.787	24.286	24.4
1183	HIS144	O	52.864	23.85	23.979
1184	CYS145	N	50.645	24.081	23.761
1185	CYS145	CA	50.595	23.08	22.695
1186	CYS145	CB	49.227	22.418	22.653
1187	CYS145	SG	49.287	20.611	22.712
1188	CYS145	C	50.941	23.704	21.346
1189	CYS145	O	51.488	23.012	20.48
1190	TRP146	N	50.884	25.024	21.271
1191	TRP146	CA	51.406	25.709	20.084
1192	TRP146	CB	50.872	27.139	20.039
1193	TRP146	CG	49.412	27.26	19.648
1194	TRP146	CD1	48.326	27.378	20.487
1195	TRP146	NE1	47.202	27.46	19.73
1196	TRP146	CE2	47.497	27.407	18.418
1197	TRP146	CZ2	46.711	27.456	17.277
1198	TRP146	CH2	47.311	27.379	16.025
1199	TRP146	CZ3	48.692	27.259	15.912
1200	TRP146	CE3	49.486	27.212	17.051
1201	TRP146	CD2	48.892	27.285	18.302
1202	TRP146	C	52.934	25.722	20.119
1203	TRP146	O	53.574	25.364	19.121
1204	ASP147	N	53.479	25.817	21.324
1205	ASP147	CA	54.927	25.731	21.528
1206	ASP147	CB	55.266	26.173	22.951
1207	ASP147	CG	54.916	27.636	23.211
1208	ASP147	OD1	55.111	28.436	22.307
1209	ASP147	OD2	54.614	27.948	24.357
1210	ASP147	C	55.424	24.301	21.364
1211	ASP147	O	56.499	24.094	20.79
1212	TYR148	N	54.572	23.332	21.655
1213	TYR148	CA	54.969	21.938	21.479
1214	TYR148	CB	54.103	21.05	22.361
1215	TYR148	CG	54.695	19.657	22.55
1216	TYR148	CD1	55.754	19.493	23.433
1217	TYR148	CE1	56.32	18.239	23.614
1218	TYR148	CZ	55.826	17.153	22.909
1219	TYR148	OH	56.436	15.929	23.048
1220	TYR148	CE2	54.764	17.31	22.028
1221	TYR148	CD2	54.198	18.566	21.847
1222	TYR148	C	54.85	21.503	20.023
1223	TYR148	O	55.678	20.707	19.569
1224	ARG149	N	54.03	22.193	19.246
1225	ARG149	CA	53.995	21.917	17.81
1226	ARG149	CB	52.68	22.4	17.212
1227	ARG149	CG	52.637	22.043	15.732
1228	ARG149	CD	51.31	22.379	15.068
1229	ARG149	NE	51.341	21.93	13.667
1230	ARG149	CZ	50.659	20.876	13.211

Table 11

1231	ARG149	NH1	49.797	20.241	14.009
1232	ARG149	NH2	50.776	20.511	11.932
1233	ARG149	C	55.168	22.596	17.107
1234	ARG149	O	55.754	22.002	16.195
1235	ARG150	N	55.676	23.665	17.7
1236	ARG150	CA	56.909	24.276	17.193
1237	ARG150	CB	56.989	25.71	17.706
1238	ARG150	CG	55.952	26.568	16.992
1239	ARG150	CD	56.019	28.045	17.366
1240	ARG150	NE	55.239	28.349	18.575
1241	ARG150	CZ	54.219	29.213	18.563
1242	ARG150	NH1	53.582	29.513	19.696
1243	ARG150	NH2	53.873	29.821	17.426
1244	ARG150	C	58.144	23.472	17.608
1245	ARG150	O	59.082	23.335	16.811
1246	PHE151	N	58.024	22.739	18.703
1247	PHE151	CA	59.073	21.804	19.112
1248	PHE151	CB	58.804	21.379	20.553
1249	PHE151	CG	59.705	20.262	21.073
1250	PHE151	CD1	61.016	20.537	21.44
1251	PHE151	CE1	61.834	19.518	21.91
1252	PHE151	CZ	61.342	18.223	22.013
1253	PHE151	CE2	60.031	17.948	21.648
1254	PHE151	CD2	59.213	18.967	21.179
1255	PHE151	C	59.091	20.578	18.205
1256	PHE151	O	60.165	20.192	17.729
1257	VAL152	N	57.92	20.133	17.778
1258	VAL152	CA	57.848	19.003	16.848
1259	VAL152	CB	56.409	18.504	16.795
1260	VAL152	CG1	56.227	17.45	15.709
1261	VAL152	CG2	55.966	17.963	18.148
1262	VAL152	C	58.296	19.409	15.448
1263	VAL152	O	59.078	18.678	14.829
1264	ALA153	N	58.051	20.658	15.087
1265	ALA153	CA	58.495	21.16	13.788
1266	ALA153	CB	57.845	22.516	13.535
1267	ALA153	C	60.012	21.296	13.724
1268	ALA153	O	60.619	20.786	12.773
1269	THR154	N	60.627	21.713	14.817
1270	THR154	CA	62.091	21.823	14.821
1271	THR154	CB	62.537	22.756	15.944
1272	THR154	OG1	62.022	22.282	17.183
1273	THR154	CG2	62.02	24.173	15.731
1274	THR154	C	62.781	20.463	14.959
1275	THR154	O	63.717	20.197	14.196
1276	GLN155	N	62.148	19.534	15.659
1277	GLN155	CA	62.73	18.199	15.855
1278	GLN155	CB	62.137	17.62	17.13
1279	GLN155	CG	62.64	18.292	18.399
1280	GLN155	CD	64.077	17.875	18.689
1281	GLN155	OE1	64.975	18.722	18.756
1282	GLN155	NE2	64.261	16.588	18.934
1283	GLN155	C	62.459	17.229	14.701
1284	GLN155	O	62.994	16.113	14.693
1285	ALA156	N	61.582	17.612	13.789
1286	ALA156	CA	61.358	16.827	12.574

Table 11

1287	ALA156	CB	59.859	16.628	12.387
1288	ALA156	C	61.935	17.514	11.339
1289	ALA156	O	61.86	16.958	10.236
1290	ALA157	N	62.508	18.694	11.544
1291	ALA157	CA	63.024	19.542	10.457
1292	ALA157	CB	64.214	18.863	9.782
1293	ALA157	C	61.937	19.866	9.435
1294	ALA157	O	62.094	19.625	8.232
1295	VAL158	N	60.844	20.42	9.932
1296	VAL158	CA	59.705	20.785	9.087
1297	VAL158	CB	58.446	20.761	9.954
1298	VAL158	CG1	57.221	21.297	9.221
1299	VAL158	CG2	58.182	19.358	10.482
1300	VAL158	C	59.91	22.172	8.489
1301	VAL158	O	60.086	23.157	9.218
1302	PRO159	N	59.887	22.238	7.168
1303	PRO159	CA	60.044	23.514	6.469
1304	PRO159	CB	59.999	23.171	5.011
1305	PRO159	CG	59.775	21.675	4.848
1306	PRO159	CD	59.7	21.107	6.254
1307	PRO159	C	58.938	24.497	6.839
1308	PRO159	O	57.754	24.136	6.907
1309	PRO160	N	59.312	25.762	6.955
1310	PRO160	CA	58.363	26.806	7.37
1311	PRO160	CB	59.205	28.025	7.601
1312	PRO160	CG	60.643	27.732	7.2
1313	PRO160	CD	60.674	26.274	6.774
1314	PRO160	C	57.262	27.096	6.341
1315	PRO160	O	56.157	27.473	6.741
1316	ALA161	N	57.462	26.696	5.092
1317	ALA161	CA	56.412	26.85	4.078
1318	ALA161	CB	57.061	26.833	2.699
1319	ALA161	C	55.355	25.746	4.166
1320	ALA161	O	54.177	26.009	3.902
1321	GLU162	N	55.707	24.64	4.803
1322	GLU162	CA	54.748	23.555	5.02
1323	GLU162	CB	55.531	22.258	5.187
1324	GLU162	CG	54.62	21.064	5.447
1325	GLU162	CD	55.472	19.82	5.671
1326	GLU162	OE1	56.613	19.988	6.081
1327	GLU162	OE2	54.996	18.734	5.371
1328	GLU162	C	53.947	23.847	6.284
1329	GLU162	O	52.74	23.582	6.348
1330	GLU163	N	54.557	24.648	7.14
1331	GLU163	CA	53.888	25.114	8.348
1332	GLU163	CB	54.973	25.598	9.297
1333	GLU163	CG	54.478	25.655	10.731
1334	GLU163	CD	54.331	24.239	11.277
1335	GLU163	OE1	55.103	23.391	10.852
1336	GLU163	OE2	53.552	24.066	12.204
1337	GLU163	C	52.95	26.274	8.011
1338	GLU163	O	51.863	26.389	8.591
1339	LEU164	N	53.272	26.974	6.935
1340	LEU164	CA	52.412	28.042	6.435
1341	LEU164	CB	53.251	28.944	5.538
1342	LEU164	CG	52.483	30.186	5.107

Table 11

1343	LEU164	CD1	52.085	31.02	6.319
1344	LEU164	CD2	53.31	31.019	4.134
1345	LEU164	C	51.238	27.466	5.648
1346	LEU164	O	50.121	27.979	5.775
1347	ALA165	N	51.409	26.269	5.111
1348	ALA165	CA	50.288	25.578	4.465
1349	ALA165	CB	50.835	24.421	3.637
1350	ALA165	C	49.296	25.053	5.503
1351	ALA165	O	48.079	25.203	5.317
1352	PHE166	N	49.81	24.741	6.683
1353	PHE166	CA	48.945	24.352	7.798
1354	PHE166	CB	49.809	23.777	8.915
1355	PHE166	CG	49.04	23.487	10.2
1356	PHE166	CD1	48.052	22.512	10.216
1357	PHE166	CE1	47.348	22.255	11.385
1358	PHE166	CZ	47.632	22.974	12.539
1359	PHE166	CE2	48.62	23.95	12.523
1360	PHE166	CD2	49.324	24.207	11.354
1361	PHE166	C	48.153	25.545	8.329
1362	PHE166	O	46.93	25.44	8.475
1363	THR167	N	48.767	26.717	8.35
1364	THR167	CA	48.031	27.903	8.801
1365	THR167	CB	49.009	28.978	9.261
1366	THR167	OG1	49.822	29.369	8.167
1367	THR167	CG2	49.915	28.476	10.38
1368	THR167	C	47.093	28.45	7.722
1369	THR167	O	46.034	28.985	8.069
1370	ASP168	N	47.324	28.066	6.474
1371	ASP168	CA	46.403	28.41	5.386
1372	ASP168	CB	47.027	28.033	4.042
1373	ASP168	CG	48.284	28.841	3.731
1374	ASP168	OD1	49.134	28.313	3.023
1375	ASP168	OD2	48.321	30.008	4.094
1376	ASP168	C	45.096	27.635	5.528
1377	ASP168	O	44.02	28.244	5.475
1378	SER169	N	45.19	26.39	5.973
1379	SER169	CA	43.975	25.586	6.16
1380	SER169	CB	44.315	24.102	6.071
1381	SER169	OG	45.147	23.759	7.17
1382	SER169	C	43.286	25.888	7.493
1383	SER169	O	42.059	25.744	7.587
1384	LEU170	N	43.99	26.559	8.393
1385	LEU170	CA	43.356	27.006	9.636
1386	LEU170	CB	44.422	27.406	10.649
1387	LEU170	CG	45.301	26.236	11.069
1388	LEU170	CD1	46.375	26.708	12.039
1389	LEU170	CD2	44.476	25.113	11.689
1390	LEU170	C	42.461	28.215	9.386
1391	LEU170	O	41.373	28.3	9.972
1392	ILEA171	N	42.748	28.945	8.322
1393	ILEA171	CA	41.93	30.111	7.988
1394	ILEA171	CB	42.806	31.078	7.191
1395	ILEA171	CG2	42.05	32.347	6.808
1396	ILEA171	CG1	44.055	31.443	7.986
1397	ILEA171	CD1	43.711	32.088	9.325
1398	ILEA171	C	40.688	29.721	7.183

Table 11

1399	ILEA171	O	39.694	30.457	7.199
1400	THR172	N	40.654	28.499	6.674
1401	THR172	CA	39.519	28.101	5.838
1402	THR172	CB	40.002	27.177	4.726
1403	THR172	OG1	40.422	25.949	5.302
1404	THR172	CG2	41.166	27.783	3.953
1405	THR172	C	38.396	27.406	6.609
1406	THR172	O	37.29	27.311	6.066
1407	ARG173	N	38.646	26.949	7.83
1408	ARG173	CA	37.554	26.333	8.605
1409	ARG173	CB	37.2	24.98	7.987
1410	ARG173	CG	35.777	24.56	8.349
1411	ARG173	CD	35.427	23.175	7.816
1412	ARG173	NE	34.053	22.808	8.199
1413	ARG173	CZ	33.763	21.959	9.187
1414	ARG173	NH1	34.745	21.361	9.865
1415	ARG173	NH2	32.49	21.685	9.48
1416	ARG173	C	37.894	26.143	10.087
1417	ARG173	O	37.136	25.499	10.824
1418	ASN174	N	39.012	26.673	10.542
1419	ASN174	CA	39.328	26.506	11.962
1420	ASN174	CB	40.818	26.225	12.133
1421	ASN174	CG	41.146	25.798	13.56
1422	ASN174	OD1	42.199	26.154	14.103
1423	ASN174	ND2	40.255	25.011	14.14
1424	ASN174	C	38.902	27.755	12.723
1425	ASN174	O	37.811	27.768	13.307
1426	PHE175	N	39.693	28.81	12.615
1427	PHE175	CA	39.389	30.049	13.338
1428	PHE175	CB	39.488	29.769	14.839
1429	PHE175	CG	38.631	30.676	15.719
1430	PHE175	CD1	37.307	30.913	15.375
1431	PHE175	CE1	36.519	31.735	16.171
1432	PHE175	CZ	37.056	32.317	17.311
1433	PHE175	CE2	38.38	32.079	17.656
1434	PHE175	CD2	39.168	31.257	16.86
1435	PHE175	C	40.397	31.131	12.963
1436	PHE175	O	41.432	30.837	12.352
1437	SER176	N	40.043	32.376	13.245
1438	SER176	CA	41.016	33.472	13.148
1439	SER176	CB	40.335	34.823	13.39
1440	SER176	OG	39.504	34.778	14.544
1441	SER176	C	42.174	33.171	14.111
1442	SER176	O	43.208	32.702	13.626
1443	ASN177	N	42.096	33.622	15.358
1444	ASN177	CA	42.903	33.035	16.444
1445	ASN177	CB	43.037	31.518	16.252
1446	ASN177	CG	43.77	30.824	17.401
1447	ASN177	OD1	44.69	31.383	18.009
1448	ASN177	ND2	43.378	29.591	17.663
1449	ASN177	C	44.252	33.739	16.496
1450	ASN177	O	45.111	33.532	15.634
1451	TYR178	N	44.509	34.384	17.62
1452	TYR178	CA	45.681	35.254	17.732
1453	TYR178	CB	45.447	36.185	18.914
1454	TYR178	CG	46.53	37.232	19.138

Table 11

1455	TYR178	CD1	46.609	38.334	18.297
1456	TYR178	CE1	47.594	39.292	18.499
1457	TYR178	CZ	48.496	39.143	19.545
1458	TYR178	OH	49.463	40.099	19.756
1459	TYR178	CE2	48.419	38.042	20.388
1460	TYR178	CD2	47.434	37.085	20.184
1461	TYR178	C	46.995	34.492	17.9
1462	TYR178	O	48.028	34.994	17.446
1463	SER179	N	46.938	33.225	18.275
1464	SER179	CA	48.179	32.453	18.365
1465	SER179	CB	48.079	31.413	19.475
1466	SER179	OG	47.051	30.494	19.143
1467	SER179	C	48.497	31.79	17.024
1468	SER179	O	49.675	31.598	16.701
1469	SER180	N	47.5	31.677	16.158
1470	SER180	CA	47.78	31.182	14.807
1471	SER180	CB	46.608	30.373	14.261
1472	SER180	OG	45.499	31.234	14.081
1473	SER180	C	48.11	32.353	13.883
1474	SER180	O	48.948	32.201	12.987
1475	TRP181	N	47.678	33.546	14.266
1476	TRP181	CA	48.131	34.762	13.583
1477	TRP181	CB	47.196	35.919	13.912
1478	TRP181	CG	45.851	35.935	13.205
1479	TRP181	CD1	44.638	36.22	13.79
1480	TRP181	NE1	43.678	36.186	12.834
1481	TRP181	CE2	44.198	35.884	11.632
1482	TRP181	CZ2	43.638	35.777	10.367
1483	TRP181	CH2	44.444	35.458	9.28
1484	TRP181	CZ3	45.805	35.244	9.457
1485	TRP181	CE3	46.376	35.353	10.72
1486	TRP181	CD2	45.579	35.679	11.808
1487	TRP181	C	49.547	35.129	14.02
1488	TRP181	O	50.341	35.599	13.198
1489	HIS182	N	49.917	34.711	15.22
1490	HIS182	CA	51.3	34.84	15.683
1491	HIS182	CB	51.305	34.599	17.188
1492	HIS182	CG	52.675	34.403	17.806
1493	HIS182	ND1	53.777	35.149	17.596
1494	HIS182	CE1	54.794	34.652	18.331
1495	HIS182	NE2	54.327	33.576	19.005
1496	HIS182	CD2	53.023	33.411	18.692
1497	HIS182	C	52.21	33.828	14.994
1498	HIS182	O	53.326	34.183	14.594
1499	TYR183	N	51.661	32.68	14.637
1500	TYR183	CA	52.452	31.706	13.894
1501	TYR183	CB	51.724	30.369	13.925
1502	TYR183	CG	52.649	29.157	13.914
1503	TYR183	CD1	54.002	29.309	13.636
1504	TYR183	CE1	54.842	28.203	13.641
1505	TYR183	CZ	54.324	26.947	13.933
1506	TYR183	OH	55.156	25.847	13.943
1507	TYR183	CE2	52.976	26.793	14.221
1508	TYR183	CD2	52.138	27.9	14.214
1509	TYR183	C	52.645	32.18	12.454
1510	TYR183	O	53.784	32.165	11.968

Table 11

1511	ARG184	N	51.654	32.867	11.906
1512	ARG184	CA	51.812	33.424	10.558
1513	ARG184	CB	50.45	33.758	9.972
1514	ARG184	CG	49.584	32.516	9.848
1515	ARG184	CD	48.428	32.776	8.895
1516	ARG184	NE	48.966	33.118	7.57
1517	ARG184	CZ	48.43	32.69	6.427
1518	ARG184	NH1	47.289	32.001	6.445
1519	ARG184	NH2	48.999	33.01	5.264
1520	ARG184	C	52.675	34.682	10.538
1521	ARG184	O	53.419	34.874	9.572
1522	SER185	N	52.766	35.379	11.661
1523	SER185	CA	53.664	36.536	11.766
1524	SER185	CB	53.16	37.509	12.825
1525	SER185	OG	53.298	36.906	14.1
1526	SER185	C	55.098	36.122	12.096
1527	SER185	O	55.95	36.99	12.311
1528	CYS186	N	55.336	34.828	12.236
1529	CYS186	CA	56.701	34.315	12.241
1530	CYS186	CB	56.815	33.2	13.274
1531	CYS186	SG	56.497	33.68	14.987
1532	CYS186	C	57.028	33.764	10.856
1533	CYS186	O	57.937	34.281	10.19
1534	LEU187	N	56.113	32.961	10.335
1535	LEU187	CA	56.332	32.255	9.061
1536	LEU187	CB	55.159	31.312	8.82
1537	LEU187	CG	55.082	30.226	9.885
1538	LEU187	CD1	53.774	29.451	9.781
1539	LEU187	CD2	56.281	29.289	9.814
1540	LEU187	C	56.465	33.188	7.865
1541	LEU187	O	57.463	33.105	7.138
1542	LEU188	N	55.605	34.189	7.78
1543	LEU188	CA	55.699	35.159	6.677
1544	LEU188	CB	54.488	36.087	6.694
1545	LEU188	CG	53.19	35.313	6.489
1546	LEU188	CD1	51.984	36.192	6.772
1547	LEU188	CD2	53.102	34.709	5.094
1548	LEU188	C	57.024	35.945	6.684
1549	LEU188	O	57.732	35.831	5.675
1550	PRO189	N	57.439	36.622	7.757
1551	PRO189	CA	58.778	37.238	7.745
1552	PRO189	CB	58.861	38.065	8.988
1553	PRO189	CG	57.604	37.867	9.809
1554	PRO189	CD	56.732	36.914	9.015
1555	PRO189	C	59.978	36.274	7.672
1556	PRO189	O	61.06	36.728	7.283
1557	GLN190	N	59.793	34.982	7.894
1558	GLN190	CA	60.892	34.031	7.692
1559	GLN190	CB	60.682	32.845	8.626
1560	GLN190	CG	60.77	33.257	10.089
1561	GLN190	CD	60.446	32.066	10.986
1562	GLN190	OE1	59.278	31.708	11.192
1563	GLN190	NE2	61.496	31.47	11.521
1564	GLN190	C	60.967	33.509	6.257
1565	GLN190	O	61.983	32.913	5.88
1566	LEU191	N	59.931	33.738	5.466

Table 11

1567	LEU191	CA	59.911	33.216	4.095
1568	LEU191	CB	58.644	32.38	3.936
1569	LEU191	CG	58.635	31.149	4.833
1570	LEU191	CD1	57.247	30.52	4.874
1571	LEU191	CD2	59.685	30.138	4.388
1572	LEU191	C	59.885	34.29	3.01
1573	LEU191	O	60.181	33.987	1.847
1574	HIS192	N	59.477	35.501	3.346
1575	HIS192	CA	59.23	36.487	2.278
1576	HIS192	CB	57.736	36.807	2.239
1577	HIS192	CG	56.856	35.604	1.966
1578	HIS192	ND1	57.049	34.661	1.023
1579	HIS192	CE1	56.055	33.753	1.091
1580	HIS192	NE2	55.228	34.126	2.093
1581	HIS192	CD2	55.709	35.265	2.642
1582	HIS192	C	60.071	37.778	2.287
1583	HIS192	O	60.721	38.022	1.264
1584	PRO193	N	60.006	38.64	3.301
1585	PRO193	CA	60.485	40.018	3.097
1586	PRO193	CB	60.03	40.798	4.29
1587	PRO193	CG	59.33	39.868	5.26
1588	PRO193	CD	59.308	38.509	4.586
1589	PRO193	C	61.995	40.141	2.945
1590	PRO193	O	62.765	39.784	3.842
1591	GLN194	N	62.391	40.667	1.8
1592	GLN194	CA	63.785	41.058	1.582
1593	GLN194	CB	64.203	40.606	0.185
1594	GLN194	CG	63.131	40.924	-0.853
1595	GLN194	CD	63.603	40.51	-2.241
1596	GLN194	OE1	63.764	39.319	-2.532
1597	GLN194	NE2	63.819	41.505	-3.083
1598	GLN194	C	63.936	42.571	1.756
1599	GLN194	O	63.465	43.363	0.929
1600	PRO195	N	64.527	42.957	2.876
1601	PRO195	CA	64.609	44.373	3.243
1602	PRO195	CB	65.082	44.387	4.663
1603	PRO195	CG	65.422	42.966	5.091
1604	PRO195	CD	65.082	42.077	3.907
1605	PRO195	C	65.569	45.134	2.337
1606	PRO195	O	66.778	44.881	2.322
1607	ASP196	N	65.009	46.047	1.565
1608	ASP196	CA	65.821	46.875	0.675
1609	ASP196	CB	65.139	46.901	-0.693
1610	ASP196	CG	66.095	47.35	-1.797
1611	ASP196	OD1	65.967	48.504	-2.189
1612	ASP196	OD2	66.832	46.518	-2.303
1613	ASP196	C	65.983	48.264	1.305
1614	ASP196	O	66.663	48.385	2.33
1615	SER197	N	65.392	49.289	0.711
1616	SER197	CA	65.491	50.64	1.273
1617	SER197	CB	66.804	51.258	0.804
1618	SER197	OG	66.894	52.565	1.357
1619	SER197	C	64.326	51.519	0.825
1620	SER197	O	64.006	52.526	1.469
1621	GLY198	N	63.706	51.128	-0.276
1622	GLY198	CA	62.587	51.892	-0.847

Table 11

1623	GLY198	C	61.318	51.828	0.002
1624	GLY198	O	61.172	52.578	0.975
1625	PRO199	N	60.392	50.981	-0.419
1626	PRO199	CA	59.086	50.871	0.24
1627	PRO199	CB	58.296	49.916	-0.601
1628	PRO199	CG	59.169	49.406	-1.738
1629	PRO199	CD	60.507	50.11	-1.591
1630	PRO199	C	59.209	50.368	1.674
1631	PRO199	O	60.011	49.477	1.974
1632	GLN200	N	58.381	50.932	2.537
1633	GLN200	CA	58.395	50.591	3.965
1634	GLN200	CB	58.256	51.903	4.724
1635	GLN200	CG	58.723	51.821	6.17
1636	GLN200	CD	58.63	53.214	6.769
1637	GLN200	OE1	57.586	53.877	6.685
1638	GLN200	NE2	59.743	53.657	7.324
1639	GLN200	C	57.282	49.611	4.375
1640	GLN200	O	56.898	49.571	5.549
1641	GLY201	N	56.766	48.839	3.432
1642	GLY201	CA	55.678	47.894	3.741
1643	GLY201	C	56.143	46.831	4.733
1644	GLY201	O	57.35	46.602	4.872
1645	ARG202	N	55.213	46.298	5.508
1646	ARG202	CA	55.569	45.263	6.485
1647	ARG202	CB	54.336	44.894	7.3
1648	ARG202	CG	54.753	44.296	8.636
1649	ARG202	CD	55.572	45.324	9.405
1650	ARG202	NE	56.039	44.812	10.701
1651	ARG202	CZ	55.731	45.4	11.859
1652	ARG202	NH1	54.857	46.407	11.883
1653	ARG202	NH2	56.229	44.923	13.002
1654	ARG202	C	56.085	44.036	5.742
1655	ARG202	O	57.276	43.706	5.794
1656	LEU203	N	55.183	43.393	5.025
1657	LEU203	CA	55.57	42.332	4.094
1658	LEU203	CB	54.458	41.288	4.045
1659	LEU203	CG	54.283	40.571	5.377
1660	LEU203	CD1	53.088	39.627	5.32
1661	LEU203	CD2	55.547	39.811	5.764
1662	LEU203	C	55.774	42.959	2.717
1663	LEU203	O	55.332	44.094	2.498
1664	PRO204	N	56.453	42.26	1.816
1665	PRO204	CA	56.416	42.65	0.405
1666	PRO204	CB	57.184	41.598	-0.331
1667	PRO204	CG	57.659	40.546	0.659
1668	PRO204	CD	57.145	40.985	2.021
1669	PRO204	C	54.963	42.715	-0.04
1670	PRO204	O	54.164	41.847	0.332
1671	GLU205	N	54.649	43.632	-0.94
1672	GLU205	CA	53.236	43.949	-1.207
1673	GLU205	CB	53.168	45.225	-2.039
1674	GLU205	CG	51.748	45.779	-2.046
1675	GLU205	CD	51.635	47.007	-2.94
1676	GLU205	OE1	52.117	48.057	-2.536
1677	GLU205	OE2	51.076	46.876	-4.02
1678	GLU205	C	52.452	42.833	-1.908

Table 11

1679	GLU205	O	51.26	42.686	-1.621
1680	ASP206	N	53.147	41.887	-2.522
1681	ASP206	CA	52.469	40.754	-3.164
1682	ASP206	CB	53.434	40.083	-4.148
1683	ASP206	CG	54.714	39.593	-3.465
1684	ASP206	OD1	55.618	40.404	-3.302
1685	ASP206	OD2	54.748	38.436	-3.073
1686	ASP206	C	51.942	39.725	-2.154
1687	ASP206	O	50.943	39.058	-2.44
1688	VAL207	N	52.485	39.709	-0.945
1689	VAL207	CA	51.935	38.83	0.084
1690	VAL207	CB	53.048	37.972	0.694
1691	VAL207	CG1	54.289	38.775	1.057
1692	VAL207	CG2	52.559	37.162	1.89
1693	VAL207	C	51.209	39.665	1.133
1694	VAL207	O	50.206	39.219	1.703
1695	LEU208	N	51.519	40.95	1.147
1696	LEU208	CA	50.912	41.852	2.118
1697	LEU208	CB	51.742	43.128	2.16
1698	LEU208	CG	51.301	44.037	3.296
1699	LEU208	CD1	51.351	43.287	4.62
1700	LEU208	CD2	52.168	45.287	3.352
1701	LEU208	C	49.474	42.189	1.752
1702	LEU208	O	48.614	42.131	2.638
1703	LEU209	N	49.163	42.223	0.465
1704	LEU209	CA	47.787	42.54	0.069
1705	LEU209	CB	47.731	42.945	-1.4
1706	LEU209	CG	48.528	44.212	-1.68
1707	LEU209	CD1	48.351	44.644	-3.131
1708	LEU209	CD2	48.131	45.341	-0.737
1709	LEU209	C	46.853	41.359	0.29
1710	LEU209	O	45.751	41.562	0.817
1711	LYS210	N	47.375	40.148	0.177
1712	LYS210	CA	46.521	38.991	0.436
1713	LYS210	CB	46.984	37.78	-0.373
1714	LYS210	CG	48.387	37.307	-0.018
1715	LYS210	CD	48.792	36.106	-0.863
1716	LYS210	CE	50.17	35.59	-0.469
1717	LYS210	NZ	50.565	34.443	-1.301
1718	LYS210	C	46.451	38.683	1.93
1719	LYS210	O	45.401	38.223	2.385
1720	GLU211	N	47.388	39.204	2.708
1721	GLU211	CA	47.286	39.077	4.163
1722	GLU211	CB	48.653	39.288	4.793
1723	GLU211	CG	49.591	38.128	4.506
1724	GLU211	CD	48.954	36.827	4.974
1725	GLU211	OE1	48.749	35.975	4.122
1726	GLU211	OE2	48.813	36.661	6.178
1727	GLU211	C	46.311	40.096	4.732
1728	GLU211	O	45.496	39.74	5.594
1729	LEU212	N	46.22	41.241	4.073
1730	LEU212	CA	45.237	42.256	4.451
1731	LEU212	CB	45.526	43.533	3.669
1732	LEU212	CG	46.782	44.242	4.16
1733	LEU212	CD1	47.221	45.323	3.181
1734	LEU212	CD2	46.572	44.823	5.552

Table 11

1735	LEU212	C	43.828	41.779	4.133
1736	LEU212	O	42.959	41.86	5.007
1737	GLU213	N	43.702	41.006	3.065
1738	GLU213	CA	42.405	40.436	2.687
1739	GLU213	CB	42.462	40.152	1.194
1740	GLU213	CG	42.651	41.457	0.429
1741	GLU213	CD	43.107	41.172	-0.997
1742	GLU213	OE1	42.854	42.004	-1.857
1743	GLU213	OE2	43.787	40.171	-1.185
1744	GLU213	C	42.051	39.163	3.461
1745	GLU213	O	40.863	38.897	3.68
1746	LEU214	N	43.04	38.509	4.048
1747	LEU214	CA	42.752	37.347	4.896
1748	LEU214	CB	44.014	36.521	5.121
1749	LEU214	CG	44.386	35.713	3.885
1750	LEU214	CD1	45.669	34.925	4.119
1751	LEU214	CD2	43.251	34.777	3.485
1752	LEU214	C	42.195	37.784	6.24
1753	LEU214	O	41.133	37.29	6.641
1754	VAL215	N	42.739	38.857	6.793
1755	VAL215	CA	42.174	39.371	8.041
1756	VAL215	CB	43.223	40.157	8.817
1757	VAL215	CG1	44.223	39.223	9.478
1758	VAL215	CG2	43.942	41.175	7.947
1759	VAL215	C	40.932	40.216	7.778
1760	VAL215	O	39.994	40.149	8.582
1761	GLN216	N	40.798	40.707	6.555
1762	GLN216	CA	39.6	41.435	6.14
1763	GLN216	CB	39.866	42.025	4.757
1764	GLN216	CG	38.704	42.861	4.241
1765	GLN216	CD	39.031	43.462	2.876
1766	GLN216	OE1	40.14	43.297	2.35
1767	GLN216	NE2	38.087	44.232	2.359
1768	GLN216	C	38.397	40.504	6.095
1769	GLN216	O	37.415	40.754	6.806
1770	ASN217	N	38.596	39.316	5.552
1771	ASN217	CA	37.503	38.345	5.502
1772	ASN217	CB	37.813	37.294	4.441
1773	ASN217	CG	37.594	37.833	3.028
1774	ASN217	OD1	37.54	39.046	2.784
1775	ASN217	ND2	37.385	36.902	2.114
1776	ASN217	C	37.281	37.659	6.848
1777	ASN217	O	36.123	37.451	7.228
1778	ALA218	N	38.323	37.574	7.66
1779	ALA218	CA	38.178	36.97	8.987
1780	ALA218	CB	39.564	36.74	9.579
1781	ALA218	C	37.349	37.848	9.921
1782	ALA218	O	36.333	37.373	10.449
1783	PHE219	N	37.587	39.15	9.893
1784	PHE219	CA	36.793	40.037	10.744
1785	PHE219	CB	37.629	41.198	11.284
1786	PHE219	CG	38.335	42.163	10.326
1787	PHE219	CD1	37.643	42.816	9.314
1788	PHE219	CE1	38.307	43.706	8.478
1789	PHE219	CZ	39.661	43.954	8.662
1790	PHE219	CE2	40.349	43.317	9.685

Table 11

1791	PHE219	CD2	39.685	42.431	10.52
1792	PHE219	C	35.492	40.503	10.086
1793	PHE219	O	34.66	41.122	10.753
1794	PHE220	N	35.258	40.121	8.841
1795	PHE220	CA	33.926	40.327	8.262
1796	PHE220	CB	34.025	40.662	6.779
1797	PHE220	CG	34.533	42.072	6.498
1798	PHE220	CD1	35.065	42.386	5.255
1799	PHE220	CE1	35.528	43.671	5.007
1800	PHE220	CZ	35.454	44.642	5.996
1801	PHE220	CE2	34.903	44.335	7.231
1802	PHE220	CD2	34.437	43.052	7.478
1803	PHE220	C	33.048	39.096	8.466
1804	PHE220	O	31.825	39.165	8.298
1805	THR221	N	33.666	37.996	8.867
1806	THR221	CA	32.906	36.812	9.266
1807	THR221	CB	33.75	35.575	8.972
1808	THR221	OG1	34.03	35.562	7.58
1809	THR221	CG2	33.017	34.282	9.318
1810	THR221	C	32.601	36.901	10.758
1811	THR221	O	31.58	36.393	11.238
1812	ASP222	N	33.477	37.584	11.475
1813	ASP222	CA	33.202	37.911	12.878
1814	ASP222	CB	33.673	36.758	13.765
1815	ASP222	CG	33.321	36.993	15.236
1816	ASP222	OD1	32.643	37.977	15.514
1817	ASP222	OD2	33.99	36.386	16.057
1818	ASP222	C	33.884	39.222	13.262
1819	ASP222	O	35.012	39.218	13.773
1820	PRO223	N	33.077	40.274	13.286
1821	PRO223	CA	33.573	41.635	13.541
1822	PRO223	CB	32.432	42.527	13.165
1823	PRO223	CG	31.195	41.686	12.891
1824	PRO223	CD	31.64	40.24	12.999
1825	PRO223	C	33.964	41.906	14.992
1826	PRO223	O	34.672	42.875	15.279
1827	ASN224	N	33.582	41.021	15.895
1828	ASN224	CA	33.907	41.212	17.304
1829	ASN224	CB	32.695	40.769	18.115
1830	ASN224	CG	31.449	41.489	17.593
1831	ASN224	OD1	31.449	42.713	17.404
1832	ASN224	ND2	30.411	40.713	17.331
1833	ASN224	C	35.155	40.422	17.697
1834	ASN224	O	35.647	40.552	18.825
1835	ASP225	N	35.7	39.664	16.757
1836	ASP225	CA	36.896	38.87	17.038
1837	ASP225	CB	36.889	37.64	16.134
1838	ASP225	CG	37.893	36.588	16.6
1839	ASP225	OD1	39.022	36.962	16.894
1840	ASP225	OD2	37.568	35.416	16.489
1841	ASP225	C	38.143	39.709	16.788
1842	ASP225	O	38.667	39.745	15.666
1843	GLN226	N	38.764	40.091	17.893
1844	GLN226	CA	39.907	41.01	17.886
1845	GLN226	CB	40.109	41.461	19.325
1846	GLN226	CG	40.272	40.272	20.267

Table 11

1847	GLN226	CD	40.253	40.746	21.716
1848	GLN226	OE1	39.343	41.474	22.126
1849	GLN226	NE2	41.22	40.279	22.485
1850	GLN226	C	41.225	40.452	17.34
1851	GLN226	O	42.081	41.257	16.952
1852	SER227	N	41.296	39.159	17.054
1853	SER227	CA	42.549	38.59	16.555
1854	SER227	CB	42.491	37.069	16.682
1855	SER227	OG	41.519	36.528	15.791
1856	SER227	C	42.808	38.988	15.103
1857	SER227	O	43.943	39.351	14.773
1858	ALA228	N	41.742	39.245	14.36
1859	ALA228	CA	41.912	39.638	12.963
1860	ALA228	CB	40.653	39.262	12.196
1861	ALA228	C	42.182	41.134	12.836
1862	ALA228	O	42.936	41.544	11.946
1863	TRP229	N	41.835	41.875	13.877
1864	TRP229	CA	42.075	43.318	13.887
1865	TRP229	CB	41.114	43.966	14.876
1866	TRP229	CG	39.655	43.71	14.574
1867	TRP229	CD1	38.819	42.825	15.218
1868	TRP229	NE1	37.588	42.903	14.652
1869	TRP229	CE2	37.572	43.805	13.656
1870	TRP229	CZ2	36.568	44.244	12.807
1871	TRP229	CH2	36.852	45.213	11.856
1872	TRP229	CZ3	38.131	45.753	11.756
1873	TRP229	CE3	39.139	45.325	12.609
1874	TRP229	CD2	38.861	44.354	13.557
1875	TRP229	C	43.501	43.617	14.32
1876	TRP229	O	44.179	44.442	13.692
1877	PHE230	N	44.022	42.77	15.194
1878	PHE230	CA	45.406	42.931	15.641
1879	PHE230	CB	45.641	42.085	16.887
1880	PHE230	CG	44.918	42.563	18.143
1881	PHE230	CD1	44.407	41.637	19.044
1882	PHE230	CE1	43.751	42.07	20.189
1883	PHE230	CZ	43.611	43.429	20.438
1884	PHE230	CE2	44.13	44.355	19.542
1885	PHE230	CD2	44.785	43.923	18.397
1886	PHE230	C	46.379	42.504	14.552
1887	PHE230	O	47.341	43.234	14.277
1888	TYR231	N	45.994	41.509	13.768
1889	TYR231	CA	46.881	41.093	12.687
1890	TYR231	CB	46.587	39.653	12.302
1891	TYR231	CG	47.747	39.01	11.552
1892	TYR231	CD1	48.992	38.944	12.163
1893	TYR231	CE1	50.061	38.36	11.499
1894	TYR231	CZ	49.883	37.844	10.224
1895	TYR231	OH	50.938	37.234	9.584
1896	TYR231	CE2	48.643	37.915	9.605
1897	TYR231	CD2	47.574	38.502	10.271
1898	TYR231	C	46.745	42.007	11.47
1899	TYR231	O	47.764	42.285	10.829
1900	HIS232	N	45.615	42.688	11.338
1901	HIS232	CA	45.461	43.669	10.259
1902	HIS232	CB	43.99	44.052	10.129

Table 11

1903	HIS232	CG	43.697	45.029	9.004
1904	HIS232	ND1	43.473	44.723	7.712
1905	HIS232	CE1	43.25	45.855	7.015
1906	HIS232	NE2	43.336	46.891	7.88
1907	HIS232	CD2	43.608	46.398	9.11
1908	HIS232	C	46.28	44.922	10.544
1909	HIS232	O	46.973	45.404	9.639
1910	ARG233	N	46.433	45.256	11.816
1911	ARG233	CA	47.267	46.405	12.178
1912	ARG233	CB	46.906	46.85	13.593
1913	ARG233	CG	47.64	48.133	13.972
1914	ARG233	CD	47.261	48.62	15.366
1915	ARG233	NE	47.944	49.888	15.673
1916	ARG233	CZ	47.365	50.902	16.32
1917	ARG233	NH1	46.105	50.789	16.746
1918	ARG233	NH2	48.048	52.025	16.552
1919	ARG233	C	48.757	46.062	12.096
1920	ARG233	O	49.551	46.92	11.692
1921	TRP234	N	49.083	44.782	12.196
1922	TRP234	CA	50.475	44.357	12.02
1923	TRP234	CB	50.641	42.951	12.592
1924	TRP234	CG	52.071	42.442	12.578
1925	TRP234	CD1	53.023	42.667	13.548
1926	TRP234	NE1	54.175	42.056	13.172
1927	TRP234	CE2	54.031	41.43	11.99
1928	TRP234	CZ2	54.906	40.696	11.202
1929	TRP234	CH2	54.464	40.156	10
1930	TRP234	CZ3	53.152	40.351	9.583
1931	TRP234	CE3	52.271	41.09	10.365
1932	TRP234	CD2	52.706	41.632	11.563
1933	TRP234	C	50.859	44.347	10.542
1934	TRP234	O	51.943	44.83	10.197
1935	LEU235	N	49.892	44.062	9.683
1936	LEU235	CA	50.128	44.054	8.231
1937	LEU235	CB	49.029	43.219	7.592
1938	LEU235	CG	49.053	41.78	8.079
1939	LEU235	CD1	47.736	41.084	7.769
1940	LEU235	CD2	50.239	41.017	7.506
1941	LEU235	C	50.068	45.456	7.628
1942	LEU235	O	50.586	45.695	6.531
1943	LEU236	N	49.48	46.377	8.372
1944	LEU236	CA	49.418	47.78	7.966
1945	LEU236	CB	48.109	48.342	8.515
1946	LEU236	CG	47.73	49.673	7.878
1947	LEU236	CD1	47.582	49.517	6.369
1948	LEU236	CD2	46.442	50.214	8.487
1949	LEU236	C	50.611	48.555	8.533
1950	LEU236	O	50.86	49.705	8.148
1951	GLY237	N	51.377	47.894	9.387
1952	GLY237	CA	52.548	48.512	10.002
1953	GLY237	C	53.713	48.628	9.028
1954	GLY237	O	53.719	48.045	7.936
1955	ARG238	N	54.645	49.479	9.413
1956	ARG238	CA	55.831	49.742	8.605
1957	ARG238	CB	56.201	51.2	8.804
1958	ARG238	CG	55.042	52.123	8.46

Table 11

1959	ARG238	CD	55.354	53.55	8.891
1960	ARG238	NE	55.551	53.625	10.349
1961	ARG238	CZ	56.685	54.03	10.928
1962	ARG238	NH1	57.736	54.37	10.181
1963	ARG238	NH2	56.773	54.075	12.259
1964	ARG238	C	57.012	48.885	9.041
1965	ARG238	O	57.183	48.585	10.231
1966	ALA239	N	57.828	48.513	8.072
1967	ALA239	CA	59.082	47.814	8.364
1968	ALA239	CB	59.543	47.064	7.121
1969	ALA239	C	60.152	48.817	8.784
1970	ALA239	O	60.785	49.474	7.948
1971	ASP240	N	60.311	48.955	10.089
1972	ASP240	CA	61.326	49.852	10.65
1973	ASP240	CB	61.039	49.994	12.143
1974	ASP240	CG	61.91	51.072	12.786
1975	ASP240	OD1	62.053	52.121	12.173
1976	ASP240	OD2	62.265	50.892	13.942
1977	ASP240	C	62.72	49.272	10.421
1978	ASP240	O	62.982	48.112	10.757
1979	PRO241	N	63.578	50.06	9.791
1980	PRO241	CA	64.949	49.634	9.481
1981	PRO241	CB	65.488	50.691	8.564
1982	PRO241	CG	64.49	51.832	8.469
1983	PRO241	CD	63.287	51.406	9.292
1984	PRO241	C	65.824	49.515	10.73
1985	PRO241	O	65.342	49.265	11.844
1986	GLN242	N	67.125	49.509	10.497
1987	GLN242	CA	68.084	49.557	11.604
1988	GLN242	CB	68.549	48.129	11.896
1989	GLN242	CG	69.303	47.973	13.222
1990	GLN242	CD	68.403	48.002	14.469
1991	GLN242	OE1	68.922	47.941	15.59
1992	GLN242	NE2	67.092	48.044	14.287
1993	GLN242	C	69.238	50.486	11.231
1994	GLN242	O	70.248	50.627	11.932
1995	ASP243	N	69	51.201	10.149
1996	ASP243	CA	70.014	52.057	9.542
1997	ASP243	CB	70.642	51.301	8.359
1998	ASP243	CG	69.608	50.707	7.389
1999	ASP243	OD1	69.053	49.66	7.707
2000	ASP243	OD2	69.395	51.305	6.346
2001	ASP243	C	69.398	53.384	9.107
2002	ASP243	O	68.97	53.542	7.957
2003	ALA244	N	69.354	54.331	10.028
2004	ALA244	CA	68.753	55.627	9.701
2005	ALA244	CB	67.237	55.496	9.777
2006	ALA244	C	69.216	56.773	10.598
2007	ALA244	O	68.821	56.88	11.768
2008	LEU245	N	70.074	57.61	10.037
2009	LEU245	CA	70.447	58.874	10.688
2010	LEU245	CB	71.886	59.232	10.341
2011	LEU245	CG	72.877	58.161	10.772
2012	LEU245	CD1	74.278	58.508	10.283
2013	LEU245	CD2	72.865	57.98	12.282
2014	LEU245	C	69.524	59.942	10.132

Table 11

2015	LEU245	O	69.834	60.565	9.112
2016	ARG246	N	68.46	60.23	10.857
2017	ARG246	CA	67.362	60.966	10.239
2018	ARG246	CB	66.064	60.592	10.94
2019	ARG246	CG	65.84	59.084	10.872
2020	ARG246	CD	64.398	58.74	11.217
2021	ARG246	NE	64.16	57.288	11.279
2022	ARG246	CZ	63.746	56.522	10.264
2023	ARG246	NH1	63.595	57.041	9.042
2024	ARG246	NH2	63.542	55.217	10.46
2025	ARG246	C	67.53	62.479	10.221
2026	ARG246	O	66.905	63.123	9.372
2027	CYS247	N	68.428	63.035	11.015
2028	CYS247	CA	68.612	64.49	10.941
2029	CYS247	CB	67.529	65.167	11.774
2030	CYS247	SG	67.568	66.973	11.773
2031	CYS247	C	69.98	64.963	11.417
2032	CYS247	O	70.23	65.06	12.626
2033	LEU248	N	70.838	65.291	10.466
2034	LEU248	CA	72.111	65.945	10.799
2035	LEU248	CB	73.143	65.761	9.694
2036	LEU248	CG	73.587	64.325	9.478
2037	LEU248	CD1	74.794	64.332	8.548
2038	LEU248	CD2	73.96	63.659	10.795
2039	LEU248	C	71.908	67.444	10.943
2040	LEU248	O	71.003	68.019	10.322
2041	HIS249	N	72.738	68.059	11.762
2042	HIS249	CA	72.762	69.519	11.843
2043	HIS249	CB	71.626	69.992	12.736
2044	HIS249	CG	71.601	71.497	12.858
2045	HIS249	ND1	71.255	72.362	11.889
2046	HIS249	CE1	71.367	73.619	12.357
2047	HIS249	NE2	71.802	73.545	13.635
2048	HIS249	CD2	71.954	72.242	13.959
2049	HIS249	C	74.075	70.056	12.405
2050	HIS249	O	74.352	69.914	13.602
2051	VAL250	N	74.86	70.695	11.556
2052	VAL250	CA	76.046	71.392	12.057
2053	VAL250	CB	77.219	71.283	11.084
2054	VAL250	CG1	77.82	69.889	11.094
2055	VAL250	CG2	76.869	71.712	9.665
2056	VAL250	C	75.737	72.859	12.328
2057	VAL250	O	75.3	73.615	11.45
2058	SER251	N	75.893	73.233	13.579
2059	SER251	CA	75.807	74.64	13.93
2060	SER251	CB	75.082	74.8	15.256
2061	SER251	OG	75.196	76.17	15.615
2062	SER251	C	77.203	75.22	14.054
2063	SER251	O	77.958	74.851	14.961
2064	ARG252	N	77.463	76.245	13.263
2065	ARG252	CA	78.733	76.962	13.347
2066	ARG252	CB	78.946	77.742	12.053
2067	ARG252	CG	80.243	78.544	12.083
2068	ARG252	CD	80.45	79.341	10.798
2069	ARG252	NE	80.612	78.455	9.634
2070	ARG252	CZ	80.957	78.9	8.424

Table 11

2071	ARG252	NH1	81.165	80.204	8.229
2072	ARG252	NH2	81.096	78.044	7.409
2073	ARG252	C	78.678	77.919	14.53
2074	ARG252	O	79.661	78.042	15.269
2075	ASP253	N	77.46	78.314	14.873
2076	ASP253	CA	77.229	79.174	16.042
2077	ASP253	CB	75.749	79.533	16.11
2078	ASP253	CG	75.244	80.072	14.78
2079	ASP253	OD1	75.759	81.09	14.334
2080	ASP253	OD2	74.352	79.447	14.223
2081	ASP253	C	77.579	78.458	17.343
2082	ASP253	O	78.358	78.977	18.148
2083	GLU254	N	77.107	77.227	17.485
2084	GLU254	CA	77.392	76.458	18.705
2085	GLU254	CB	76.258	75.46	18.94
2086	GLU254	CG	74.87	76.092	18.939
2087	GLU254	CD	74.739	77.163	20.015
2088	GLU254	OE1	74.231	76.836	21.078
2089	GLU254	OE2	74.933	78.316	19.656
2090	GLU254	C	78.69	75.653	18.632
2091	GLU254	O	79.071	75.06	19.649
2092	ALA255	N	79.38	75.703	17.5
2093	ALA255	CA	80.48	74.774	17.202
2094	ALA255	CB	81.725	75.192	17.978
2095	ALA255	C	80.078	73.348	17.566
2096	ALA255	O	80.707	72.716	18.427
2097	CYS256	N	79.048	72.842	16.905
2098	CYS256	CA	78.488	71.546	17.312
2099	CYS256	CB	77.596	71.801	18.524
2100	CYS256	SG	76.875	70.343	19.312
2101	CYS256	C	77.675	70.849	16.22
2102	CYS256	O	76.751	71.424	15.631
2103	LEU257	N	78.014	69.591	15.994
2104	LEU257	CA	77.259	68.727	15.075
2105	LEU257	CB	78.249	67.886	14.271
2106	LEU257	CG	77.613	66.691	13.551
2107	LEU257	CD1	76.533	67.087	12.548
2108	LEU257	CD2	78.685	65.868	12.857
2109	LEU257	C	76.311	67.821	15.859
2110	LEU257	O	76.743	66.985	16.661
2111	THR258	N	75.025	68.01	15.625
2112	THR258	CA	73.992	67.195	16.266
2113	THR258	CB	72.887	68.15	16.701
2114	THR258	OG1	73.503	69.235	17.382
2115	THR258	CG2	71.885	67.492	17.642
2116	THR258	C	73.438	66.148	15.296
2117	THR258	O	73.237	66.436	14.111
2118	VAL259	N	73.334	64.916	15.767
2119	VAL259	CA	72.716	63.842	14.978
2120	VAL259	CB	73.729	62.711	14.815
2121	VAL259	CG1	73.15	61.553	14.008
2122	VAL259	CG2	75.01	63.216	14.165
2123	VAL259	C	71.456	63.294	15.655
2124	VAL259	O	71.509	62.756	16.771
2125	SER260	N	70.328	63.495	14.995
2126	SER260	CA	69.067	62.891	15.433

Table 11

2127	SER260	CB	67.901	63.797	15.068
2128	SER260	OG	68.052	65.009	15.792
2129	SER260	C	68.877	61.516	14.8
2130	SER260	O	68.975	61.329	13.578
2131	PHE261	N	68.63	60.561	15.673
2132	PHE261	CA	68.479	59.158	15.294
2133	PHE261	CB	69.106	58.285	16.376
2134	PHE261	CG	70.629	58.247	16.383
2135	PHE261	CD1	71.359	59.184	17.102
2136	PHE261	CE1	72.746	59.131	17.098
2137	PHE261	CZ	73.401	58.138	16.383
2138	PHE261	CE2	72.672	57.199	15.669
2139	PHE261	CD2	71.285	57.256	15.668
2140	PHE261	C	67.025	58.749	15.148
2141	PHE261	O	66.088	59.556	15.208
2142	SER262	N	66.872	57.467	14.883
2143	SER262	CA	65.551	56.852	14.838
2144	SER262	CB	65.662	55.551	14.057
2145	SER262	OG	66.344	55.819	12.841
2146	SER262	C	65.142	56.523	16.263
2147	SER262	O	64.689	57.384	17.029
2148	ARG263	N	65.399	55.274	16.61
2149	ARG263	CA	65.213	54.751	17.966
2150	ARG263	CB	65.281	53.231	17.834
2151	ARG263	CG	66.659	52.799	17.349
2152	ARG263	CD	66.622	51.472	16.597
2153	ARG263	NE	65.873	51.613	15.335
2154	ARG263	CZ	66.434	51.961	14.173
2155	ARG263	NH1	65.669	52.158	13.097
2156	ARG263	NH2	67.749	52.189	14.102
2157	ARG263	C	66.323	55.284	18.88
2158	ARG263	O	67.296	55.858	18.374
2159	PRO264	N	66.121	55.222	20.19
2160	PRO264	CA	67.153	55.67	21.132
2161	PRO264	CB	66.502	55.637	22.479
2162	PRO264	CG	65.129	54.996	22.355
2163	PRO264	CD	64.929	54.711	20.876
2164	PRO264	C	68.37	54.753	21.089
2165	PRO264	O	68.331	53.608	21.553
2166	LEU265	N	69.455	55.284	20.559
2167	LEU265	CA	70.68	54.501	20.401
2168	LEU265	CB	71.122	54.572	18.944
2169	LEU265	CG	70.174	53.763	18.065
2170	LEU265	CD1	70.431	53.992	16.581
2171	LEU265	CD2	70.256	52.278	18.404
2172	LEU265	C	71.793	54.969	21.327
2173	LEU265	O	71.618	55.877	22.15
2174	LEU266	N	72.871	54.209	21.294
2175	LEU266	CA	74.073	54.517	22.074
2176	LEU266	CB	74.288	53.411	23.1
2177	LEU266	CG	73.487	53.636	24.372
2178	LEU266	CD1	73.473	52.383	25.239
2179	LEU266	CD2	74.06	54.818	25.141
2180	LEU266	C	75.303	54.588	21.181
2181	LEU266	O	75.776	53.556	20.691
2182	VAL267	N	75.832	55.784	20.996

Table 11

2183	VAL267	CA	77.076	55.924	20.233
2184	VAL267	CB	77.193	57.348	19.706
2185	VAL267	CG1	78.505	57.552	18.961
2186	VAL267	CG2	76.017	57.669	18.797
2187	VAL267	C	78.262	55.569	21.124
2188	VAL267	O	78.675	56.337	22.001
2189	GLY268	N	78.771	54.374	20.893
2190	GLY268	CA	79.857	53.813	21.69
2191	GLY268	C	79.424	52.467	22.258
2192	GLY268	O	80.055	51.944	23.185
2193	SER269	N	78.349	51.921	21.713
2194	SER269	CA	77.838	50.639	22.216
2195	SER269	CB	76.318	50.592	22.095
2196	SER269	OG	75.952	50.738	20.73
2197	SER269	C	78.459	49.448	21.493
2198	SER269	O	79.583	49.522	20.978
2199	ARG270	N	77.746	48.334	21.568
2200	ARG270	CA	78.146	47.075	20.922
2201	ARG270	CB	76.969	46.117	21.051
2202	ARG270	CG	76.525	46.016	22.505
2203	ARG270	CD	75.191	45.294	22.634
2204	ARG270	NE	75.271	43.924	22.109
2205	ARG270	CZ	74.368	42.988	22.405
2206	ARG270	NH1	73.33	43.287	23.189
2207	ARG270	NH2	74.494	41.757	21.905
2208	ARG270	C	78.444	47.339	19.454
2209	ARG270	O	79.601	47.279	19.018
2210	MET271	N	77.404	47.668	18.709
2211	MET271	CA	77.628	48.268	17.399
2212	MET271	CB	76.418	48.048	16.514
2213	MET271	CG	76.871	47.441	15.193
2214	MET271	SD	77.802	45.897	15.313
2215	MET271	CE	78.163	45.671	13.558
2216	MET271	C	77.905	49.738	17.681
2217	MET271	O	77.05	50.461	18.204
2218	GLU272	N	79.098	50.166	17.325
2219	GLU272	CA	79.709	51.303	18.015
2220	GLU272	CB	81.211	51.206	17.803
2221	GLU272	CG	81.745	49.951	18.486
2222	GLU272	CD	83.235	49.796	18.214
2223	GLU272	OE1	84.012	50.428	18.916
2224	GLU272	OE2	83.551	49.206	17.189
2225	GLU272	C	79.214	52.716	17.704
2226	GLU272	O	78.275	53.193	18.352
2227	ILEA273	N	79.793	53.344	16.697
2228	ILEA273	CA	79.841	54.816	16.691
2229	ILEA273	CB	81.266	55.255	17.032
2230	ILEA273	CG2	81.596	55.043	18.504
2231	ILEA273	CG1	82.283	54.546	16.143
2232	ILEA273	CD1	83.706	54.986	16.468
2233	ILEA273	C	79.476	55.466	15.362
2234	ILEA273	O	78.996	54.819	14.423
2235	LEU274	N	79.593	56.786	15.371
2236	LEU274	CA	79.457	57.608	14.164
2237	LEU274	CB	78.585	58.814	14.488
2238	LEU274	CG	77.168	58.442	14.898

Table 11

2239	LEU274	CD1	76.456	59.647	15.498
2240	LEU274	CD2	76.391	57.891	13.711
2241	LEU274	C	80.821	58.138	13.722
2242	LEU274	O	81.483	58.875	14.465
2243	LEU275	N	81.214	57.793	12.511
2244	LEU275	CA	82.468	58.308	11.946
2245	LEU275	CB	82.974	57.331	10.892
2246	LEU275	CG	83.284	55.962	11.482
2247	LEU275	CD1	83.634	54.967	10.38
2248	LEU275	CD2	84.406	56.045	12.512
2249	LEU275	C	82.248	59.666	11.29
2250	LEU275	O	81.483	59.777	10.323
2251	LEU276	N	82.896	60.685	11.824
2252	LEU276	CA	82.789	62.02	11.231
2253	LEU276	CB	82.933	63.068	12.331
2254	LEU276	CG	82.772	64.494	11.805
2255	LEU276	CD1	81.464	64.671	11.042
2256	LEU276	CD2	82.864	65.51	12.934
2257	LEU276	C	83.846	62.221	10.147
2258	LEU276	O	85.047	62.019	10.362
2259	MET277	N	83.365	62.531	8.958
2260	MET277	CA	84.233	62.836	7.823
2261	MET277	CB	83.872	61.907	6.671
2262	MET277	CG	84.065	60.444	7.048
2263	MET277	SD	85.759	59.958	7.445
2264	MET277	CE	86.561	60.426	5.894
2265	MET277	C	84.057	64.287	7.385
2266	MET277	O	83.119	64.63	6.652
2267	VAL278	N	84.986	65.118	7.821
2268	VAL278	CA	84.992	66.531	7.44
2269	VAL278	CB	85.671	67.349	8.532
2270	VAL278	CG1	85.705	68.831	8.17
2271	VAL278	CG2	84.967	67.144	9.865
2272	VAL278	C	85.745	66.681	6.126
2273	VAL278	O	86.983	66.76	6.096
2274	ASP279	N	84.966	66.841	5.067
2275	ASP279	CA	85.418	66.838	3.66
2276	ASP279	CB	86.325	68.045	3.421
2277	ASP279	CG	85.555	69.337	3.689
2278	ASP279	OD1	84.686	69.646	2.888
2279	ASP279	OD2	85.732	69.902	4.761
2280	ASP279	C	86.114	65.533	3.248
2281	ASP279	O	85.553	64.745	2.48
2282	ASP280	N	87.344	65.341	3.695
2283	ASP280	CA	88.073	64.1	3.426
2284	ASP280	CB	89.095	64.333	2.312
2285	ASP280	CG	90.094	65.433	2.678
2286	ASP280	OD1	91.145	65.101	3.206
2287	ASP280	OD2	89.794	66.586	2.392
2288	ASP280	C	88.763	63.594	4.694
2289	ASP280	O	89.252	62.46	4.735
2290	SER281	N	88.755	64.417	5.73
2291	SER281	CA	89.447	64.072	6.976
2292	SER281	CB	89.944	65.361	7.62
2293	SER281	OG	90.424	65.028	8.916
2294	SER281	C	88.543	63.356	7.968

Table 11

2295	SER281	O	87.474	63.865	8.324
2296	PRO282	N	88.987	62.199	8.426
2297	PRO282	CA	88.39	61.591	9.612
2298	PRO282	CB	89.085	60.275	9.769
2299	PRO282	CG	90.232	60.197	8.77
2300	PRO282	CD	90.185	61.492	7.974
2301	PRO282	C	88.608	62.486	10.826
2302	PRO282	O	89.73	62.922	11.108
2303	LEU283	N	87.517	62.816	11.49
2304	LEU283	CA	87.592	63.658	12.682
2305	LEU283	CB	86.774	64.922	12.441
2306	LEU283	CG	87.028	65.97	13.521
2307	LEU283	CD1	88.51	66.32	13.601
2308	LEU283	CD2	86.201	67.226	13.276
2309	LEU283	C	87.076	62.903	13.904
2310	LEU283	O	85.901	62.517	13.984
2311	ILEA284	N	87.973	62.71	14.857
2312	ILEA284	CA	87.634	61.998	16.097
2313	ILEA284	CB	88.909	61.386	16.676
2314	ILEA284	CG2	88.602	60.61	17.953
2315	ILEA284	CG1	89.585	60.468	15.661
2316	ILEA284	CD1	88.72	59.253	15.334
2317	ILEA284	C	86.993	62.948	17.11
2318	ILEA284	O	87.676	63.646	17.868
2319	VAL285	N	85.676	63.022	17.041
2320	VAL285	CA	84.904	63.88	17.942
2321	VAL285	CB	83.859	64.6	17.108
2322	VAL285	CG1	84.475	65.756	16.333
2323	VAL285	CG2	83.153	63.622	16.177
2324	VAL285	C	84.232	63.096	19.064
2325	VAL285	O	83.856	61.928	18.909
2326	GLU286	N	84.108	63.751	20.205
2327	GLU286	CA	83.45	63.126	21.358
2328	GLU286	CB	84.006	63.74	22.637
2329	GLU286	CG	83.389	63.107	23.881
2330	GLU286	CD	84.006	63.726	25.13
2331	GLU286	OE1	85.143	64.168	25.033
2332	GLU286	OE2	83.336	63.747	26.152
2333	GLU286	C	81.938	63.324	21.306
2334	GLU286	O	81.44	64.442	21.483
2335	TRP287	N	81.24	62.236	21.029
2336	TRP287	CA	79.774	62.238	21.005
2337	TRP287	CB	79.294	61.061	20.163
2338	TRP287	CG	79.727	61.099	18.712
2339	TRP287	CD1	80.763	60.396	18.134
2340	TRP287	NE1	80.811	60.711	16.813
2341	TRP287	CE2	79.848	61.593	16.489
2342	TRP287	CZ2	79.505	62.214	15.299
2343	TRP287	CH2	78.429	63.094	15.266
2344	TRP287	CZ3	77.699	63.357	16.421
2345	TRP287	CE3	78.04	62.743	17.62
2346	TRP287	CD2	79.114	61.869	17.657
2347	TRP287	C	79.177	62.105	22.404
2348	TRP287	O	79.64	61.312	23.237
2349	ARG288	N	78.163	62.913	22.651
2350	ARG288	CA	77.409	62.823	23.9

Table 11

2351	ARG288	CB	78.091	63.697	24.944
2352	ARG288	CG	78.003	65.162	24.55
2353	ARG288	CD	78.842	66.052	25.455
2354	ARG288	NE	78.645	67.466	25.1
2355	ARG288	CZ	79.319	68.105	24.14
2356	ARG288	NH1	80.286	67.482	23.46
2357	ARG288	NH2	79.042	69.384	23.882
2358	ARG288	C	75.959	63.271	23.712
2359	ARG288	O	75.628	64.067	22.825
2360	THR289	N	75.085	62.681	24.503
2361	THR289	CA	73.684	63.108	24.531
2362	THR289	CB	72.874	61.951	25.118
2363	THR289	OG1	71.533	62.353	25.348
2364	THR289	CG2	73.441	61.506	26.448
2365	THR289	C	73.604	64.386	25.37
2366	THR289	O	74.442	64.57	26.262
2367	PRO290	N	72.637	65.263	25.112
2368	PRO290	CA	72.676	66.641	25.651
2369	PRO290	CB	71.577	67.375	24.946
2370	PRO290	CG	70.809	66.41	24.061
2371	PRO290	CD	71.552	65.09	24.138
2372	PRO290	C	72.481	66.777	27.169
2373	PRO290	O	72.536	67.892	27.695
2374	ASP291	N	72.238	65.679	27.865
2375	ASP291	CA	72.142	65.708	29.323
2376	ASP291	CB	71.039	64.747	29.765
2377	ASP291	CG	71.378	63.309	29.379
2378	ASP291	OD1	72.021	62.66	30.188
2379	ASP291	OD2	71.028	62.914	28.274
2380	ASP291	C	73.47	65.342	29.996
2381	ASP291	O	73.531	65.284	31.23
2382	GLY292	N	74.489	65.016	29.212
2383	GLY292	CA	75.804	64.687	29.781
2384	GLY292	C	76.004	63.179	29.936
2385	GLY292	O	76.975	62.609	29.422
2386	ARG293	N	75.155	62.581	30.754
2387	ARG293	CA	75.162	61.129	30.957
2388	ARG293	CB	74.095	60.812	31.993
2389	ARG293	CG	74.328	61.556	33.3
2390	ARG293	CD	73.082	61.481	34.171
2391	ARG293	NE	72.602	60.094	34.259
2392	ARG293	CZ	71.454	59.756	34.849
2393	ARG293	NH1	70.698	60.694	35.424
2394	ARG293	NH2	71.069	58.479	34.875
2395	ARG293	C	74.782	60.419	29.667
2396	ARG293	O	73.629	60.509	29.238
2397	ASN294	N	75.697	59.623	29.137
2398	ASN294	CA	75.471	58.925	27.859
2399	ASN294	CB	76.823	58.646	27.211
2400	ASN294	CG	77.337	59.92	26.541
2401	ASN294	OD1	76.558	60.842	26.27
2402	ASN294	ND2	78.608	59.907	26.176
2403	ASN294	C	74.645	57.638	27.97
2404	ASN294	O	75.152	56.522	27.81
2405	ARG295	N	73.36	57.832	28.215
2406	ARG295	CA	72.36	56.761	28.228

Table 11

2407	ARG295	CB	71.46	57.001	29.44
2408	ARG295	CG	71.077	58.468	29.59
2409	ARG295	CD	70.343	58.698	30.905
2410	ARG295	NE	70.17	60.133	31.174
2411	ARG295	CZ	69.229	60.618	31.986
2412	ARG295	NH1	68.371	59.788	32.583
2413	ARG295	NH2	69.144	61.933	32.198
2414	ARG295	C	71.601	56.795	26.9
2415	ARG295	O	71.81	57.745	26.139
2416	PRO296	N	70.869	55.736	26.565
2417	PRO296	CA	70.252	55.621	25.233
2418	PRO296	CB	69.44	54.364	25.268
2419	PRO296	CG	69.705	53.64	26.578
2420	PRO296	CD	70.673	54.516	27.358
2421	PRO296	C	69.41	56.842	24.882
2422	PRO296	O	68.479	57.228	25.598
2423	SER297	N	69.777	57.445	23.768
2424	SER297	CA	69.204	58.731	23.378
2425	SER297	CB	70.203	59.808	23.794
2426	SER297	OG	69.762	61.074	23.317
2427	SER297	C	68.945	58.822	21.882
2428	SER297	O	69.599	58.168	21.061
2429	HIS298	N	67.961	59.634	21.542
2430	HIS298	CA	67.679	59.937	20.145
2431	HIS298	CB	66.243	60.424	20.032
2432	HIS298	CG	65.151	59.469	20.463
2433	HIS298	ND1	64.566	58.527	19.702
2434	HIS298	CE1	63.621	57.893	20.424
2435	HIS298	NE2	63.611	58.443	21.659
2436	HIS298	CD2	64.545	59.42	21.697
2437	HIS298	C	68.559	61.066	19.608
2438	HIS298	O	68.541	61.308	18.397
2439	VAL299	N	69.31	61.751	20.457
2440	VAL299	CA	70.083	62.894	19.979
2441	VAL299	CB	69.338	64.168	20.381
2442	VAL299	CG1	68.827	64.108	21.817
2443	VAL299	CG2	70.159	65.427	20.133
2444	VAL299	C	71.503	62.852	20.537
2445	VAL299	O	71.717	62.825	21.757
2446	TRP300	N	72.448	62.713	19.622
2447	TRP300	CA	73.868	62.663	19.983
2448	TRP300	CB	74.427	61.292	19.623
2449	TRP300	CG	73.938	60.18	20.529
2450	TRP300	CD1	72.742	59.5	20.45
2451	TRP300	NE1	72.694	58.598	21.461
2452	TRP300	CE2	73.812	58.643	22.207
2453	TRP300	CZ2	74.212	57.959	23.344
2454	TRP300	CH2	75.459	58.216	23.898
2455	TRP300	CZ3	76.302	59.164	23.326
2456	TRP300	CE3	75.898	59.871	22.201
2457	TRP300	CD2	74.655	59.618	21.647
2458	TRP300	C	74.649	63.753	19.265
2459	TRP300	O	74.679	63.819	18.031
2460	LEU301	N	75.269	64.614	20.047
2461	LEU301	CA	76.007	65.742	19.48
2462	LEU301	CB	75.338	67.094	19.801

Table 11

2463	LEU301	CG	75.01	67.483	21.256
2464	LEU301	CD1	73.752	66.832	21.819
2465	LEU301	CD2	76.17	67.425	22.241
2466	LEU301	C	77.483	65.716	19.863
2467	LEU301	O	77.886	65.074	20.838
2468	CYS302	N	78.288	66.298	18.997
2469	CYS302	CA	79.722	66.416	19.259
2470	CYS302	CB	80.471	65.48	18.322
2471	CYS302	SG	80.335	65.886	16.567
2472	CYS302	C	80.204	67.839	19.016
2473	CYS302	O	79.676	68.553	18.153
2474	ASP303	N	81.211	68.241	19.771
2475	ASP303	CA	81.831	69.547	19.523
2476	ASP303	CB	82.799	69.912	20.64
2477	ASP303	CG	82.027	70.362	21.874
2478	ASP303	OD1	80.913	70.836	21.707
2479	ASP303	OD2	82.546	70.173	22.966
2480	ASP303	C	82.56	69.543	18.188
2481	ASP303	O	83.279	68.6	17.839
2482	LEU304	N	82.315	70.596	17.435
2483	LEU304	CA	82.884	70.743	16.099
2484	LEU304	CB	81.737	71.093	15.16
2485	LEU304	CG	82.093	70.894	13.696
2486	LEU304	CD1	82.455	69.436	13.433
2487	LEU304	CD2	80.922	71.316	12.819
2488	LEU304	C	83.927	71.857	16.11
2489	LEU304	O	83.593	73.038	16.249
2490	PRO305	N	85.18	71.465	15.962
2491	PRO305	CA	86.304	72.39	16.138
2492	PRO305	CB	87.534	71.54	16.057
2493	PRO305	CG	87.136	70.102	15.763
2494	PRO305	CD	85.617	70.088	15.722
2495	PRO305	C	86.339	73.486	15.081
2496	PRO305	O	85.788	73.339	13.983
2497	ALA306	N	87.175	74.481	15.342
2498	ALA306	CA	87.363	75.608	14.414
2499	ALA306	CB	88.061	76.74	15.157
2500	ALA306	C	88.173	75.239	13.167
2501	ALA306	O	88.073	75.919	12.14
2502	ALA307	N	88.752	74.048	13.168
2503	ALA307	CA	89.4	73.515	11.967
2504	ALA307	CB	90.358	72.404	12.383
2505	ALA307	C	88.377	72.966	10.965
2506	ALA307	O	88.714	72.738	9.799
2507	SER308	N	87.129	72.859	11.394
2508	SER308	CA	86.035	72.469	10.512
2509	SER308	CB	85.326	71.285	11.153
2510	SER308	OG	86.292	70.261	11.345
2511	SER308	C	85.041	73.616	10.321
2512	SER308	O	83.977	73.41	9.73
2513	LEU309	N	85.338	74.774	10.892
2514	LEU309	CA	84.414	75.916	10.814
2515	LEU309	CB	83.877	76.213	12.21
2516	LEU309	CG	83.025	75.082	12.771
2517	LEU309	CD1	82.625	75.378	14.209
2518	LEU309	CD2	81.788	74.849	11.912

Table 11

2519	LEU309	C	85.08	77.187	10.288
2520	LEU309	O	84.451	78.251	10.264
2521	ASN310	N	86.354	77.089	9.95
2522	ASN310	CA	87.14	78.264	9.558
2523	ASN310	CB	88.615	77.87	9.489
2524	ASN310	CG	88.841	76.726	8.502
2525	ASN310	OD1	88.575	76.853	7.299
2526	ASN310	ND2	89.425	75.658	9.009
2527	ASN310	C	86.721	78.879	8.228
2528	ASN310	O	86.128	78.234	7.358
2529	ASP311	N	87.234	80.078	8.014
2530	ASP311	CA	87.017	80.838	6.772
2531	ASP311	CB	87.177	82.326	7.089
2532	ASP311	CG	88.546	82.608	7.715
2533	ASP311	OD1	88.6	82.705	8.932
2534	ASP311	OD2	89.522	82.647	6.976
2535	ASP311	C	87.982	80.467	5.638
2536	ASP311	O	88.142	81.248	4.695
2537	GLN312	N	88.694	79.36	5.775
2538	GLN312	CA	89.706	78.993	4.786
2539	GLN312	CB	90.858	78.324	5.528
2540	GLN312	CG	91.489	79.25	6.567
2541	GLN312	CD	92.454	80.232	5.905
2542	GLN312	OE1	93.593	79.867	5.594
2543	GLN312	NE2	92.026	81.475	5.765
2544	GLN312	C	89.125	78.029	3.759
2545	GLN312	O	89.592	77.968	2.616
2546	LEU313	N	88.075	77.329	4.151
2547	LEU313	CA	87.389	76.449	3.203
2548	LEU313	CB	87.452	75.022	3.737
2549	LEU313	CG	86.969	73.997	2.716
2550	LEU313	CD1	87.886	73.971	1.498
2551	LEU313	CD2	86.902	72.611	3.339
2552	LEU313	C	85.939	76.892	3.024
2553	LEU313	O	85.143	76.838	3.966
2554	PRO314	N	85.584	77.215	1.787
2555	PRO314	CA	84.272	77.808	1.464
2556	PRO314	CB	84.414	78.307	0.058
2557	PRO314	CG	85.751	77.863	-0.512
2558	PRO314	CD	86.469	77.153	0.62
2559	PRO314	C	83.062	76.863	1.554
2560	PRO314	O	81.93	77.311	1.33
2561	GLN315	N	83.278	75.599	1.879
2562	GLN315	CA	82.177	74.646	2.027
2563	GLN315	CB	81.639	74.257	0.653
2564	GLN315	CG	82.732	73.871	-0.339
2565	GLN315	CD	82.079	73.408	-1.634
2566	GLN315	OE1	82.749	73.205	-2.653
2567	GLN315	NE2	80.767	73.26	-1.577
2568	GLN315	C	82.62	73.411	2.808
2569	GLN315	O	83.112	72.429	2.237
2570	HIS316	N	82.391	73.447	4.107
2571	HIS316	CA	82.761	72.312	4.953
2572	HIS316	CB	82.947	72.788	6.383
2573	HIS316	CG	84.253	73.511	6.615
2574	HIS316	ND1	85.467	72.936	6.71

Table 11

2575	HIS316	CE1	86.395	73.89	6.927
2576	HIS316	NE2	85.757	75.082	6.96
2577	HIS316	CD2	84.437	74.866	6.766
2578	HIS316	C	81.721	71.202	4.901
2579	HIS316	O	80.642	71.28	5.5
2580	THR317	N	82.059	70.182	4.138
2581	THR317	CA	81.231	68.98	4.03
2582	THR317	CB	81.738	68.197	2.823
2583	THR317	OG1	81.674	69.05	1.688
2584	THR317	CG2	80.913	66.949	2.531
2585	THR317	C	81.368	68.146	5.3
2586	THR317	O	82.48	67.947	5.8
2587	PHE318	N	80.247	67.711	5.846
2588	PHE318	CA	80.271	66.885	7.057
2589	PHE318	CB	79.684	67.668	8.222
2590	PHE318	CG	80.46	68.921	8.605
2591	PHE318	CD1	79.917	70.176	8.365
2592	PHE318	CE1	80.622	71.316	8.725
2593	PHE318	CZ	81.869	71.201	9.32
2594	PHE318	CE2	82.413	69.946	9.556
2595	PHE318	CD2	81.708	68.805	9.201
2596	PHE318	C	79.477	65.598	6.877
2597	PHE318	O	78.239	65.586	6.951
2598	ARG319	N	80.206	64.522	6.647
2599	ARG319	CA	79.581	63.204	6.54
2600	ARG319	CB	80.305	62.369	5.495
2601	ARG319	CG	80.353	63.087	4.154
2602	ARG319	CD	80.774	62.145	3.032
2603	ARG319	NE	82.084	61.526	3.288
2604	ARG319	CZ	82.259	60.203	3.339
2605	ARG319	NH1	81.204	59.388	3.277
2606	ARG319	NH2	83.479	59.699	3.534
2607	ARG319	C	79.608	62.478	7.88
2608	ARG319	O	80.578	62.564	8.641
2609	VAL320	N	78.503	61.829	8.188
2610	VAL320	CA	78.393	61.032	9.413
2611	VAL320	CB	77.323	61.646	10.311
2612	VAL320	CG1	77.124	60.823	11.577
2613	VAL320	CG2	77.677	63.083	10.675
2614	VAL320	C	78.04	59.59	9.062
2615	VAL320	O	76.934	59.303	8.587
2616	ILEA321	N	79.013	58.713	9.257
2617	ILEA321	CA	78.853	57.29	8.934
2618	ILEA321	CB	80.152	56.803	8.304
2619	ILEA321	CG2	80.017	55.356	7.837
2620	ILEA321	CG1	80.548	57.7	7.137
2621	ILEA321	CD1	81.844	57.228	6.49
2622	ILEA321	C	78.533	56.444	10.169
2623	ILEA321	O	79.388	56.218	11.034
2624	TRP322	N	77.302	55.969	10.223
2625	TRP322	CA	76.856	55.09	11.313
2626	TRP322	CB	75.329	55.048	11.235
2627	TRP322	CG	74.543	54.331	12.322
2628	TRP322	CD1	73.333	53.698	12.124
2629	TRP322	NE1	72.909	53.189	13.308
2630	TRP322	CE2	73.783	53.463	14.295

Table 11

2631	TRP322	CZ2	73.79	53.169	15.651
2632	TRP322	CH2	74.848	53.59	16.447
2633	TRP322	CZ3	75.899	54.31	15.888
2634	TRP322	CE3	75.9	54.606	14.531
2635	TRP322	CD2	74.849	54.188	13.73
2636	TRP322	C	77.468	53.7	11.14
2637	TRP322	O	77.334	53.08	10.081
2638	THR323	N	78.152	53.222	12.167
2639	THR323	CA	78.831	51.919	12.078
2640	THR323	CB	80.155	51.944	12.839
2641	THR323	OG1	79.908	51.984	14.234
2642	THR323	CG2	81.011	53.144	12.454
2643	THR323	C	77.986	50.731	12.551
2644	THR323	O	78.551	49.664	12.821
2645	ALA324	N	76.699	50.932	12.783
2646	ALA324	CA	75.818	49.78	12.999
2647	ALA324	CB	74.682	50.146	13.941
2648	ALA324	C	75.261	49.363	11.649
2649	ALA324	O	75.547	48.279	11.128
2650	GLY325	N	74.453	50.251	11.104
2651	GLY325	CA	74.069	50.174	9.696
2652	GLY325	C	74.764	51.357	9.043
2653	GLY325	O	74.565	52.486	9.504
2654	ASP326	N	75.535	51.102	7.994
2655	ASP326	CA	76.438	52.107	7.385
2656	ASP326	CB	77.444	51.389	6.492
2657	ASP326	CG	78.39	50.525	7.326
2658	ASP326	OD1	79.453	51.023	7.668
2659	ASP326	OD2	78.082	49.354	7.5
2660	ASP326	C	75.76	53.216	6.577
2661	ASP326	O	75.896	53.297	5.351
2662	VAL327	N	75.113	54.114	7.297
2663	VAL327	CA	74.469	55.282	6.706
2664	VAL327	CB	73.305	55.671	7.608
2665	VAL327	CG1	72.549	56.877	7.069
2666	VAL327	CG2	72.362	54.494	7.782
2667	VAL327	C	75.463	56.424	6.642
2668	VAL327	O	76.061	56.777	7.661
2669	GLN328	N	75.675	56.948	5.448
2670	GLN328	CA	76.599	58.068	5.272
2671	GLN328	CB	77.55	57.723	4.135
2672	GLN328	CG	78.262	56.408	4.429
2673	GLN328	CD	79.182	56.022	3.279
2674	GLN328	OE1	79.176	56.651	2.216
2675	GLN328	NE2	79.955	54.975	3.506
2676	GLN328	C	75.839	59.352	4.96
2677	GLN328	O	75.788	59.803	3.81
2678	LYS329	N	75.256	59.932	5.995
2679	LYS329	CA	74.521	61.19	5.83
2680	LYS329	CB	73.659	61.431	7.059
2681	LYS329	CG	72.332	60.692	6.97
2682	LYS329	CD	71.494	61.233	5.818
2683	LYS329	CE	70.104	60.61	5.791
2684	LYS329	NZ	70.178	59.15	5.64
2685	LYS329	C	75.498	62.338	5.622
2686	LYS329	O	76.609	62.312	6.157

Table 11

2687	GLU330	N	75.113	63.313	4.819
2688	GLU330	CA	76.046	64.401	4.504
2689	GLU330	CB	76.628	64.131	3.121
2690	GLU330	CG	77.58	65.24	2.685
2691	GLU330	CD	78.049	64.999	1.255
2692	GLU330	OE1	79.085	64.369	1.096
2693	GLU330	OE2	77.377	65.467	0.347
2694	GLU330	C	75.397	65.782	4.506
2695	GLU330	O	74.627	66.121	3.601
2696	CYS331	N	75.759	66.585	5.491
2697	CYS331	CA	75.379	68.002	5.476
2698	CYS331	CB	74.959	68.449	6.872
2699	CYS331	SG	76.146	68.153	8.198
2700	CYS331	C	76.56	68.819	4.957
2701	CYS331	O	77.671	68.29	4.827
2702	VAL332	N	76.298	70.036	4.516
2703	VAL332	CA	77.398	70.876	4.021
2704	VAL332	CB	77.485	70.762	2.497
2705	VAL332	CG1	76.152	71.042	1.811
2706	VAL332	CG2	78.597	71.634	1.921
2707	VAL332	C	77.253	72.327	4.483
2708	VAL332	O	76.302	73.041	4.135
2709	LEU333	N	78.228	72.755	5.264
2710	LEU333	CA	78.225	74.107	5.815
2711	LEU333	CB	78.87	74.04	7.19
2712	LEU333	CG	78.602	75.292	8.01
2713	LEU333	CD1	77.107	75.559	8.108
2714	LEU333	CD2	79.203	75.142	9.399
2715	LEU333	C	78.991	75.064	4.904
2716	LEU333	O	80.221	75.197	4.984
2717	LEU334	N	78.243	75.681	4.006
2718	LEU334	CA	78.797	76.665	3.068
2719	LEU334	CB	77.698	77.069	2.091
2720	LEU334	CG	77.111	75.871	1.354
2721	LEU334	CD1	75.824	76.254	0.633
2722	LEU334	CD2	78.118	75.268	0.383
2723	LEU334	C	79.263	77.906	3.817
2724	LEU334	O	78.781	78.186	4.921
2725	LYS335	N	80.216	78.616	3.241
2726	LYS335	CA	80.699	79.86	3.848
2727	LYS335	CB	81.797	80.455	2.972
2728	LYS335	CG	81.324	80.67	1.539
2729	LYS335	CD	82.408	81.31	0.684
2730	LYS335	CE	81.949	81.47	-0.76
2731	LYS335	NZ	83.018	82.05	-1.588
2732	LYS335	C	79.557	80.857	4.023
2733	LYS335	O	78.725	81.054	3.131
2734	GLY336	N	79.415	81.319	5.252
2735	GLY336	CA	78.353	82.27	5.58
2736	GLY336	C	77.187	81.594	6.301
2737	GLY336	O	76.427	82.255	7.019
2738	ARG337	N	77.028	80.299	6.083
2739	ARG337	CA	75.944	79.565	6.731
2740	ARG337	CB	75.735	78.232	6.024
2741	ARG337	CG	75.365	78.432	4.561
2742	ARG337	CD	74.039	79.168	4.414

Table 11

2743	ARG337	NE	73.756	79.443	2.998
2744	ARG337	CZ	73.41	80.652	2.553
2745	ARG337	NH1	73.293	81.67	3.409
2746	ARG337	NH2	73.17	80.841	1.253
2747	ARG337	C	76.289	79.325	8.19
2748	ARG337	O	77.355	78.8	8.529
2749	GLN338	N	75.374	79.726	9.051
2750	GLN338	CA	75.571	79.535	10.484
2751	GLN338	CB	74.838	80.664	11.191
2752	GLN338	CG	75.341	82.022	10.721
2753	GLN338	CD	74.497	83.125	11.349
2754	GLN338	OE1	73.733	83.809	10.658
2755	GLN338	NE2	74.591	83.237	12.662
2756	GLN338	C	75.01	78.195	10.943
2757	GLN338	O	75.391	77.685	12.006
2758	GLU339	N	74.146	77.62	10.119
2759	GLU339	CA	73.51	76.327	10.413
2760	GLU339	CB	72.156	76.589	11.07
2761	GLU339	CG	72.293	77.182	12.471
2762	GLU339	CD	70.923	77.452	13.078
2763	GLU339	OE1	70.351	78.481	12.745
2764	GLU339	OE2	70.449	76.601	13.817
2765	GLU339	C	73.312	75.515	9.13
2766	GLU339	O	72.672	75.987	8.182
2767	GLY340	N	73.838	74.302	9.12
2768	GLY340	CA	73.742	73.425	7.941
2769	GLY340	C	73.234	72.025	8.296
2770	GLY340	O	73.964	71.184	8.837
2771	TRP341	N	71.989	71.769	7.945
2772	TRP341	CA	71.357	70.492	8.295
2773	TRP341	CB	69.985	70.768	8.902
2774	TRP341	CG	69.062	71.626	8.061
2775	TRP341	CD1	68.229	71.199	7.051
2776	TRP341	NE1	67.576	72.278	6.548
2777	TRP341	CE2	67.936	73.407	7.186
2778	TRP341	CZ2	67.564	74.734	7.034
2779	TRP341	CH2	68.12	75.705	7.858
2780	TRP341	CZ3	69.047	75.353	8.834
2781	TRP341	CE3	69.424	74.026	8.994
2782	TRP341	CD2	68.875	73.055	8.171
2783	TRP341	C	71.224	69.53	7.116
2784	TRP341	O	71.519	69.866	5.963
2785	CYS342	N	70.88	68.302	7.465
2786	CYS342	CA	70.591	67.233	6.497
2787	CYS342	CB	71.858	66.44	6.209
2788	CYS342	SG	71.677	65.093	5.019
2789	CYS342	C	69.526	66.305	7.08
2790	CYS342	O	69.838	65.288	7.718
2791	ARG343	N	68.276	66.687	6.88
2792	ARG343	CA	67.147	65.981	7.498
2793	ARG343	CB	66.281	67.039	8.178
2794	ARG343	CG	65.123	66.42	8.949
2795	ARG343	CD	64.16	67.468	9.484
2796	ARG343	NE	63.042	66.812	10.175
2797	ARG343	CZ	61.85	66.603	9.612
2798	ARG343	NH1	61.607	67.049	8.377

Table 11

2799	ARG343	NH2	60.89	65.983	10.3
2800	ARG343	C	66.291	65.19	6.501
2801	ARG343	O	65.952	65.676	5.417
2802	ASP344	N	65.973	63.964	6.883
2803	ASP344	CA	64.991	63.142	6.171
2804	ASP344	CB	65.065	61.717	6.715
2805	ASP344	CG	66.4	61.059	6.388
2806	ASP344	OD1	66.826	61.23	5.253
2807	ASP344	OD2	66.783	60.177	7.146
2808	ASP344	C	63.585	63.666	6.445
2809	ASP344	O	63.187	63.803	7.607
2810	SER345	N	62.833	63.93	5.392
2811	SER345	CA	61.455	64.379	5.581
2812	SER345	CB	60.942	65.099	4.337
2813	SER345	OG	60.414	64.125	3.444
2814	SER345	C	60.566	63.179	5.861
2815	SER345	O	60.749	62.087	5.304
2816	THR346	N	59.503	63.44	6.598
2817	THR346	CA	58.547	62.387	6.931
2818	THR346	CB	57.641	62.895	8.046
2819	THR346	OG1	56.845	63.966	7.554
2820	THR346	CG2	58.451	63.406	9.231
2821	THR346	C	57.695	61.992	5.732
2822	THR346	O	57.308	60.82	5.624
2823	THR347	N	57.624	62.884	4.756
2824	THR347	CA	56.861	62.628	3.542
2825	THR347	CB	56.594	63.963	2.854
2826	THR347	OG1	55.892	64.8	3.764
2827	THR347	CG2	55.738	63.799	1.603
2828	THR347	C	57.595	61.701	2.579
2829	THR347	O	57.116	60.587	2.334
2830	ASP348	N	58.813	62.056	2.191
2831	ASP348	CA	59.478	61.34	1.1
2832	ASP348	CB	60.322	62.349	0.326
2833	ASP348	CG	59.494	63.58	-0.036
2834	ASP348	OD1	58.651	63.463	-0.913
2835	ASP348	OD2	59.618	64.573	0.671
2836	ASP348	C	60.389	60.221	1.593
2837	ASP348	O	61.026	59.531	0.791
2838	GLU349	N	60.563	60.132	2.9
2839	GLU349	CA	61.417	59.073	3.439
2840	GLU349	CB	62.563	59.668	4.259
2841	GLU349	CG	63.789	60.04	3.415
2842	GLU349	CD	63.561	61.254	2.512
2843	GLU349	OE1	62.904	62.188	2.963
2844	GLU349	OE2	64.113	61.273	1.423
2845	GLU349	C	60.617	58.081	4.273
2846	GLU349	O	61.183	57.063	4.697
2847	GLN350	N	59.313	58.315	4.379
2848	GLN350	CA	58.415	57.475	5.187
2849	GLN350	CB	58.423	56.061	4.621
2850	GLN350	CG	58.036	56.037	3.153
2851	GLN350	CD	58.521	54.741	2.52
2852	GLN350	OE1	57.727	53.957	1.975
2853	GLN350	NE2	59.814	54.509	2.667
2854	GLN350	C	58.862	57.443	6.644

Table 11

2855	GLN350	O	59.626	56.562	7.059
2856	LEU351	N	58.432	58.437	7.403
2857	LEU351	CA	58.807	58.482	8.825
2858	LEU351	CB	59.121	59.913	9.224
2859	LEU351	CG	60.588	60.116	9.574
2860	LEU351	CD1	60.982	59.146	10.676
2861	LEU351	CD2	61.493	59.96	8.356
2862	LEU351	C	57.697	57.966	9.731
2863	LEU351	O	57.924	57.694	10.915
2864	PHE352	N	56.503	57.877	9.173
2865	PHE352	CA	55.345	57.353	9.902
2866	PHE352	CB	54.837	58.377	10.921
2867	PHE352	CG	54.688	59.82	10.436
2868	PHE352	CD1	53.766	60.151	9.451
2869	PHE352	CE1	53.645	61.467	9.026
2870	PHE352	CZ	54.437	62.455	9.595
2871	PHE352	CE2	55.348	62.128	10.589
2872	PHE352	CD2	55.472	60.812	11.011
2873	PHE352	C	54.248	56.963	8.923
2874	PHE352	O	53.099	56.724	9.312
2875	ARG353	N	54.63	56.865	7.661
2876	ARG353	CA	53.661	56.562	6.608
2877	ARG353	CB	52.87	57.838	6.294
2878	ARG353	CG	51.652	57.607	5.394
2879	ARG353	CD	51.974	57.749	3.91
2880	ARG353	NE	50.811	57.414	3.074
2881	ARG353	CZ	50.799	57.584	1.751
2882	ARG353	NH1	51.842	58.152	1.143
2883	ARG353	NH2	49.724	57.237	1.04
2884	ARG353	C	54.382	56.03	5.374
2885	ARG353	O	55.081	56.779	4.677
2886	CYS354	N	54.256	54.728	5.176
2887	CYS354	CA	54.743	54.07	3.961
2888	CYS354	CB	54.431	52.581	4.074
2889	CYS354	SG	54.646	51.606	2.567
2890	CYS354	C	54.037	54.639	2.737
2891	CYS354	O	52.808	54.766	2.716
2892	GLU355	N	54.818	54.979	1.727
2893	GLU355	CA	54.251	55.537	0.498
2894	GLU355	CB	55.334	56.37	-0.179
2895	GLU355	CG	55.695	57.55	0.726
2896	GLU355	CD	56.902	58.322	0.2
2897	GLU355	OE1	56.733	59.068	-0.754
2898	GLU355	OE2	57.982	58.126	0.744
2899	GLU355	C	53.716	54.409	-0.383
2900	GLU355	O	54.47	53.672	-1.028
2901	LEU356	N	52.398	54.291	-0.371
2902	LEU356	CA	51.706	53.151	-0.987
2903	LEU356	CB	50.222	53.198	-0.632
2904	LEU356	CG	49.906	53.466	0.834
2905	LEU356	CD1	48.395	53.548	1.003
2906	LEU356	CD2	50.484	52.409	1.768
2907	LEU356	C	51.768	53.16	-2.508
2908	LEU356	O	51.848	54.213	-3.149
2909	SER357	N	51.722	51.965	-3.069
2910	SER357	CA	51.506	51.821	-4.511

Table 11

2911	SER357	CB	51.815	50.395	-4.934
2912	SER357	OG	50.721	49.6	-4.493
2913	SER357	C	50.031	52.07	-4.789
2914	SER357	O	49.215	52.008	-3.862
2915	VAL358	N	49.667	52.128	-6.059
2916	VAL358	CA	48.256	52.34	-6.413
2917	VAL358	CB	48.181	52.647	-7.904
2918	VAL358	CG1	46.738	52.839	-8.359
2919	VAL358	CG2	49.021	53.872	-8.252
2920	VAL358	C	47.409	51.106	-6.098
2921	VAL358	O	46.312	51.241	-5.547
2922	GLU359	N	48.047	49.948	-6.138
2923	GLU359	CA	47.387	48.681	-5.809
2924	GLU359	CB	48.292	47.496	-6.178
2925	GLU359	CG	48.511	47.274	-7.68
2926	GLU359	CD	49.659	48.115	-8.241
2927	GLU359	OE1	50.339	48.749	-7.439
2928	GLU359	OE2	49.679	48.302	-9.447
2929	GLU359	C	47.091	48.602	-4.315
2930	GLU359	O	45.937	48.366	-3.931
2931	LYS360	N	48.052	49.021	-3.504
2932	LYS360	CA	47.85	49.002	-2.054
2933	LYS360	CB	49.21	49.147	-1.387
2934	LYS360	CG	49.128	48.929	0.118
2935	LYS360	CD	50.512	48.968	0.756
2936	LYS360	CE	50.435	48.743	2.262
2937	LYS360	NZ	51.764	48.885	2.881
2938	LYS360	C	46.916	50.117	-1.583
2939	LYS360	O	46.097	49.873	-0.69
2940	SER361	N	46.839	51.197	-2.342
2941	SER361	CA	45.907	52.273	-2
2942	SER361	CB	46.299	53.526	-2.774
2943	SER361	OG	47.621	53.884	-2.401
2944	SER361	C	44.473	51.899	-2.358
2945	SER361	O	43.564	52.149	-1.557
2946	THR362	N	44.318	51.073	-3.379
2947	THR362	CA	42.983	50.644	-3.799
2948	THR362	CB	43.086	50.014	-5.184
2949	THR362	OG1	43.541	51.012	-6.087
2950	THR362	CG2	41.732	49.515	-5.68
2951	THR362	C	42.39	49.636	-2.824
2952	THR362	O	41.261	49.839	-2.358
2953	VAL363	N	43.216	48.736	-2.314
2954	VAL363	CA	42.685	47.755	-1.364
2955	VAL363	CB	43.541	46.488	-1.391
2956	VAL363	CG1	45.012	46.782	-1.145
2957	VAL363	CG2	43.032	45.439	-0.407
2958	VAL363	C	42.578	48.333	0.049
2959	VAL363	O	41.624	47.985	0.758
2960	LEU364	N	43.309	49.401	0.326
2961	LEU364	CA	43.186	50.061	1.629
2962	LEU364	CB	44.437	50.89	1.898
2963	LEU364	CG	45.393	50.244	2.901
2964	LEU364	CD1	45.868	48.859	2.474
2965	LEU364	CD2	46.589	51.153	3.152
2966	LEU364	C	41.958	50.964	1.663

Table 11

2967	LEU364	O	41.223	50.952	2.66
2968	GLN365	N	41.583	51.481	0.503
2969	GLN365	CA	40.363	52.282	0.403
2970	GLN365	CB	40.404	53.074	-0.899
2971	GLN365	CG	39.306	54.131	-0.963
2972	GLN365	CD	39.646	55.295	-0.035
2973	GLN365	OE1	40.748	55.85	-0.104
2974	GLN365	NE2	38.698	55.663	0.809
2975	GLN365	C	39.131	51.381	0.398
2976	GLN365	O	38.118	51.727	1.02
2977	SER366	N	39.296	50.157	-0.079
2978	SER366	CA	38.203	49.181	-0.04
2979	SER366	CB	38.544	48.025	-0.967
2980	SER366	OG	37.551	47.028	-0.773
2981	SER366	C	37.983	48.632	1.364
2982	SER366	O	36.83	48.505	1.796
2983	GLU367	N	39.054	48.538	2.136
2984	GLU367	CA	38.936	48.114	3.534
2985	GLU367	CB	40.324	47.727	4.037
2986	GLU367	CG	40.864	46.5	3.312
2987	GLU367	CD	42.364	46.363	3.553
2988	GLU367	OE1	43.015	47.397	3.63
2989	GLU367	OE2	42.856	45.244	3.526
2990	GLU367	C	38.379	49.243	4.394
2991	GLU367	O	37.537	48.989	5.263
2992	LEU368	N	38.634	50.472	3.974
2993	LEU368	CA	38.104	51.643	4.672
2994	LEU368	CB	38.827	52.869	4.12
2995	LEU368	CG	38.433	54.137	4.86
2996	LEU368	CD1	38.702	53.986	6.348
2997	LEU368	CD2	39.175	55.347	4.308
2998	LEU368	C	36.601	51.787	4.453
2999	LEU368	O	35.853	51.89	5.435
3000	GLU369	N	36.15	51.502	3.24
3001	GLU369	CA	34.716	51.609	2.948
3002	GLU369	CB	34.467	51.537	1.444
3003	GLU369	CG	35.245	52.579	0.652
3004	GLU369	CD	34.964	53.994	1.145
3005	GLU369	OE1	33.806	54.382	1.149
3006	GLU369	OE2	35.941	54.713	1.315
3007	GLU369	C	33.951	50.465	3.593
3008	GLU369	O	32.907	50.702	4.213
3009	SER370	N	34.595	49.316	3.692
3010	SER370	CA	33.934	48.154	4.273
3011	SER370	CB	34.606	46.911	3.716
3012	SER370	OG	34.433	46.935	2.305
3013	SER370	C	33.947	48.159	5.801
3014	SER370	O	32.996	47.648	6.405
3015	CYS371	N	34.828	48.941	6.407
3016	CYS371	CA	34.771	49.096	7.862
3017	CYS371	CB	36.149	49.437	8.408
3018	CYS371	SG	36.71	48.37	9.751
3019	CYS371	C	33.768	50.179	8.245
3020	CYS371	O	33.097	50.046	9.277
3021	LYS372	N	33.469	51.065	7.307
3022	LYS372	CA	32.377	52.02	7.516

Table 11

3023	LYS372	CB	32.531	53.174	6.533
3024	LYS372	CG	33.813	53.949	6.804
3025	LYS372	CD	34.021	55.07	5.796
3026	LYS372	CE	35.283	55.86	6.119
3027	LYS372	NZ	35.517	56.919	5.123
3028	LYS372	C	31.029	51.338	7.303
3029	LYS372	O	30.096	51.566	8.083
3030	GLU373	N	31.028	50.308	6.473
3031	GLU373	CA	29.825	49.493	6.285
3032	GLU373	CB	29.989	48.674	5.01
3033	GLU373	CG	30.057	49.582	3.787
3034	GLU373	CD	30.41	48.774	2.541
3035	GLU373	OE1	31.594	48.677	2.237
3036	GLU373	OE2	29.494	48.273	1.906
3037	GLU373	C	29.588	48.563	7.473
3038	GLU373	O	28.439	48.428	7.91
3039	LEU374	N	30.657	48.174	8.15
3040	LEU374	CA	30.506	47.379	9.37
3041	LEU374	CB	31.813	46.664	9.673
3042	LEU374	CG	31.612	45.162	9.838
3043	LEU374	CD1	32.918	44.498	10.253
3044	LEU374	CD2	30.517	44.846	10.85
3045	LEU374	C	30.123	48.257	10.558
3046	LEU374	O	29.314	47.816	11.381
3047	GLN375	N	30.449	49.538	10.493
3048	GLN375	CA	29.968	50.497	11.495
3049	GLN375	CB	30.783	51.776	11.35
3050	GLN375	CG	30.289	52.858	12.301
3051	GLN375	CD	30.87	54.208	11.905
3052	GLN375	OE1	31.523	54.341	10.862
3053	GLN375	NE2	30.607	55.201	12.737
3054	GLN375	C	28.489	50.83	11.28
3055	GLN375	O	27.755	51.059	12.248
3056	GLU376	N	28.017	50.64	10.059
3057	GLU376	CA	26.594	50.819	9.754
3058	GLU376	CB	26.455	51.072	8.258
3059	GLU376	CG	27.144	52.365	7.842
3060	GLU376	CD	27.224	52.44	6.32
3061	GLU376	OE1	26.191	52.286	5.686
3062	GLU376	OE2	28.333	52.56	5.811
3063	GLU376	C	25.761	49.591	10.128
3064	GLU376	O	24.531	49.684	10.207
3065	LEU377	N	26.418	48.472	10.391
3066	LEU377	CA	25.709	47.277	10.855
3067	LEU377	CB	26.354	46.054	10.213
3068	LEU377	CG	26.279	46.11	8.691
3069	LEU377	CD1	27.122	45.007	8.062
3070	LEU377	CD2	24.834	46.039	8.203
3071	LEU377	C	25.82	47.164	12.37
3072	LEU377	O	24.919	46.656	13.049
3073	GLU378	N	26.957	47.605	12.877
3074	GLU378	CA	27.215	47.67	14.316
3075	GLU378	CB	28.193	46.562	14.711
3076	GLU378	CG	27.663	45.153	14.464
3077	GLU378	CD	28.728	44.126	14.849
3078	GLU378	OE1	29.898	44.431	14.673

Table 11

3079	GLU378	OE2	28.353	43.04	15.278
3080	GLU378	C	27.872	49.003	14.653
3081	GLU378	O	29.107	49.069	14.708
3082	PRO379	N	27.078	49.97	15.091
3083	PRO379	CA	27.594	51.326	15.356
3084	PRO379	CB	26.368	52.177	15.49
3085	PRO379	CG	25.134	51.287	15.512
3086	PRO379	CD	25.629	49.868	15.289
3087	PRO379	C	28.459	51.432	16.618
3088	PRO379	O	29.132	52.447	16.831
3089	GLU380	N	28.463	50.382	17.423
3090	GLU380	CA	29.303	50.319	18.617
3091	GLU380	CB	28.471	49.777	19.771
3092	GLU380	CG	27.321	50.715	20.115
3093	GLU380	CD	26.455	50.095	21.205
3094	GLU380	OE1	26.65	50.437	22.362
3095	GLU380	OE2	25.589	49.307	20.848
3096	GLU380	C	30.534	49.434	18.42
3097	GLU380	O	31.172	49.066	19.413
3098	ASN381	N	30.802	48.991	17.2
3099	ASN381	CA	31.996	48.168	16.992
3100	ASN381	CB	31.838	47.299	15.745
3101	ASN381	CG	33.053	46.383	15.596
3102	ASN381	OD1	34.117	46.832	15.151
3103	ASN381	ND2	32.922	45.147	16.041
3104	ASN381	C	33.225	49.067	16.892
3105	ASN381	O	33.609	49.542	15.814
3106	LYS382	N	33.958	49.089	17.993
3107	LYS382	CA	35.127	49.958	18.129
3108	LYS382	CB	35.398	50.128	19.619
3109	LYS382	CG	35.696	48.803	20.31
3110	LYS382	CD	35.811	48.991	21.816
3111	LYS382	CE	36.287	47.716	22.498
3112	LYS382	NZ	37.641	47.369	22.042
3113	LYS382	C	36.372	49.438	17.408
3114	LYS382	O	37.276	50.232	17.115
3115	TRP383	N	36.296	48.225	16.888
3116	TRP383	CA	37.418	47.665	16.153
3117	TRP383	CB	37.253	46.156	16.11
3118	TRP383	CG	37.381	45.445	17.443
3119	TRP383	CD1	36.452	44.608	18.021
3120	TRP383	NE1	36.947	44.169	19.205
3121	TRP383	CE2	38.171	44.68	19.44
3122	TRP383	CZ2	39.06	44.542	20.495
3123	TRP383	CH2	40.283	45.202	20.458
3124	TRP383	CZ3	40.617	46.003	19.371
3125	TRP383	CE3	39.727	46.154	18.313
3126	TRP383	CD2	38.505	45.498	18.347
3127	TRP383	C	37.439	48.227	14.738
3128	TRP383	O	38.488	48.713	14.299
3129	CYS384	N	36.261	48.433	14.169
3130	CYS384	CA	36.189	49.08	12.859
3131	CYS384	CB	34.873	48.766	12.157
3132	CYS384	SG	35.036	47.735	10.681
3133	CYS384	C	36.341	50.582	12.986
3134	CYS384	O	36.976	51.168	12.109

Table 11

3135	LEU385	N	36.062	51.139	14.153
3136	LEU385	CA	36.294	52.576	14.347
3137	LEU385	CB	35.661	53.019	15.663
3138	LEU385	CG	34.149	52.822	15.667
3139	LEU385	CD1	33.559	53.159	17.03
3140	LEU385	CD2	33.484	53.651	14.576
3141	LEU385	C	37.792	52.878	14.379
3142	LEU385	O	38.26	53.72	13.599
3143	LEU386	N	38.545	51.992	15.014
3144	LEU386	CA	39.999	52.146	15.073
3145	LEU386	CB	40.512	51.246	16.191
3146	LEU386	CG	42.024	51.337	16.369
3147	LEU386	CD1	42.466	52.766	16.672
3148	LEU386	CD2	42.488	50.389	17.47
3149	LEU386	C	40.667	51.762	13.753
3150	LEU386	O	41.58	52.469	13.31
3151	THR387	N	40.06	50.848	13.016
3152	THR387	CA	40.623	50.446	11.724
3153	THR387	CB	40.072	49.071	11.37
3154	THR387	OG1	40.515	48.169	12.373
3155	THR387	CG2	40.595	48.567	10.032
3156	THR387	C	40.306	51.458	10.624
3157	THR387	O	41.174	51.714	9.782
3158	ILEA388	N	39.24	52.222	10.803
3159	ILEA388	CA	38.938	53.324	9.888
3160	ILEA388	CB	37.51	53.803	10.143
3161	ILEA388	CG2	37.242	55.138	9.464
3162	ILEA388	CG1	36.492	52.778	9.668
3163	ILEA388	CD1	35.087	53.151	10.126
3164	ILEA388	C	39.924	54.463	10.108
3165	ILEA388	O	40.519	54.94	9.133
3166	ILEA389	N	40.328	54.645	11.356
3167	ILEA389	CA	41.343	55.65	11.682
3168	ILEA389	CB	41.408	55.77	13.2
3169	ILEA389	CG2	42.61	56.595	13.642
3170	ILEA389	CG1	40.115	56.361	13.745
3171	ILEA389	CD1	40.132	56.425	15.267
3172	ILEA389	C	42.711	55.26	11.129
3173	ILEA389	O	43.319	56.064	10.409
3174	LEU390	N	43.03	53.977	11.193
3175	LEU390	CA	44.323	53.499	10.693
3176	LEU390	CB	44.54	52.079	11.202
3177	LEU390	CG	44.637	52.026	12.721
3178	LEU390	CD1	44.618	50.585	13.216
3179	LEU390	CD2	45.87	52.766	13.229
3180	LEU390	C	44.398	53.495	9.168
3181	LEU390	O	45.414	53.933	8.612
3182	LEU391	N	43.278	53.253	8.508
3183	LEU391	CA	43.273	53.26	7.044
3184	LEU391	CB	42.081	52.451	6.555
3185	LEU391	CG	42.263	50.977	6.889
3186	LEU391	CD1	40.962	50.204	6.739
3187	LEU391	CD2	43.372	50.354	6.05
3188	LEU391	C	43.222	54.675	6.483
3189	LEU391	O	43.926	54.95	5.506
3190	MET392	N	42.679	55.608	7.247

Table 11

3191	MET392	CA	42.705	57.007	6.816
3192	MET392	CB	41.664	57.792	7.603
3193	MET392	CG	40.253	57.411	7.174
3194	MET392	SD	38.92	58.381	7.91
3195	MET392	CE	39.254	58.041	9.65
3196	MET392	C	44.084	57.625	7.019
3197	MET392	O	44.577	58.32	6.119
3198	ARG393	N	44.804	57.127	8.01
3199	ARG393	CA	46.17	57.597	8.246
3200	ARG393	CB	46.538	57.309	9.698
3201	ARG393	CG	45.714	58.177	10.64
3202	ARG393	CD	45.967	59.645	10.332
3203	ARG393	NE	45.148	60.544	11.153
3204	ARG393	CZ	45.574	61.761	11.491
3205	ARG393	NH1	46.814	62.13	11.172
3206	ARG393	NH2	44.801	62.569	12.221
3207	ARG393	C	47.186	56.94	7.312
3208	ARG393	O	48.235	57.534	7.038
3209	ALA394	N	46.824	55.811	6.725
3210	ALA394	CA	47.703	55.167	5.75
3211	ALA394	CB	47.566	53.657	5.895
3212	ALA394	C	47.39	55.575	4.311
3213	ALA394	O	48.242	55.403	3.434
3214	LEU395	N	46.216	56.138	4.075
3215	LEU395	CA	45.86	56.586	2.724
3216	LEU395	CB	44.368	56.359	2.512
3217	LEU395	CG	44.035	54.885	2.33
3218	LEU395	CD1	42.538	54.64	2.471
3219	LEU395	CD2	44.552	54.38	0.989
3220	LEU395	C	46.169	58.062	2.514
3221	LEU395	O	46.704	58.444	1.467
3222	ASP396	N	45.834	58.872	3.504
3223	ASP396	CA	46.112	60.314	3.447
3224	ASP396	CB	45.347	60.952	2.282
3225	ASP396	CG	45.863	62.36	1.974
3226	ASP396	OD1	46.057	63.113	2.925
3227	ASP396	OD2	45.87	62.717	0.807
3228	ASP396	C	45.689	60.964	4.761
3229	ASP396	O	44.6	61.552	4.84
3230	PRO397	N	46.654	61.102	5.656
3231	PRO397	CA	46.372	61.58	7.015
3232	PRO397	CB	47.658	61.374	7.755
3233	PRO397	CG	48.738	60.889	6.802
3234	PRO397	CD	48.059	60.73	5.456
3235	PRO397	C	45.954	63.054	7.088
3236	PRO397	O	45.132	63.411	7.942
3237	LEU398	N	46.326	63.841	6.09
3238	LEU398	CA	45.992	65.267	6.074
3239	LEU398	CB	46.916	65.943	5.072
3240	LEU398	CG	48.375	65.824	5.483
3241	LEU398	CD1	49.292	66.086	4.298
3242	LEU398	CD2	48.695	66.758	6.643
3243	LEU398	C	44.556	65.499	5.632
3244	LEU398	O	43.758	66.073	6.385
3245	LEU399	N	44.18	64.823	4.56
3246	LEU399	CA	42.849	65.006	3.97

Table 11

3247	LEU399	CB	42.88	64.392	2.574
3248	LEU399	CG	41.55	64.535	1.845
3249	LEU399	CD1	41.2	66.004	1.632
3250	LEU399	CD2	41.588	63.797	0.512
3251	LEU399	C	41.777	64.313	4.801
3252	LEU399	O	40.699	64.872	5.037
3253	TYR400	N	42.171	63.22	5.428
3254	TYR400	CA	41.259	62.481	6.29
3255	TYR400	CB	41.597	61.002	6.199
3256	TYR400	CG	41.286	60.365	4.846
3257	TYR400	CD1	42.225	59.545	4.237
3258	TYR400	CE1	41.946	58.959	3.01
3259	TYR400	CZ	40.725	59.195	2.396
3260	TYR400	OH	40.441	58.591	1.188
3261	TYR400	CE2	39.783	60.016	3
3262	TYR400	CD2	40.064	60.602	4.228
3263	TYR400	C	41.306	62.938	7.746
3264	TYR400	O	40.54	62.397	8.551
3265	GLU401	N	42.008	64.023	8.041
3266	GLU401	CA	42.178	64.478	9.43
3267	GLU401	CB	43.059	65.718	9.422
3268	GLU401	CG	43.166	66.335	10.812
3269	GLU401	CD	43.942	67.643	10.732
3270	GLU401	OE1	45.163	67.565	10.687
3271	GLU401	OE2	43.308	68.678	10.596
3272	GLU401	C	40.873	64.854	10.12
3273	GLU401	O	40.642	64.391	11.243
3274	LYS402	N	39.938	65.442	9.39
3275	LYS402	CA	38.681	65.842	10.026
3276	LYS402	CB	37.965	66.845	9.13
3277	LYS402	CG	36.675	67.33	9.782
3278	LYS402	CD	35.949	68.346	8.911
3279	LYS402	CE	34.668	68.828	9.584
3280	LYS402	NZ	33.968	69.81	8.74
3281	LYS402	C	37.774	64.641	10.277
3282	LYS402	O	37.179	64.558	11.359
3283	GLU403	N	37.954	63.602	9.475
3284	GLU403	CA	37.155	62.388	9.619
3285	GLU403	CB	37.187	61.637	8.296
3286	GLU403	CG	36.7	62.503	7.142
3287	GLU403	CD	36.891	61.757	5.825
3288	GLU403	OE1	37.009	60.541	5.874
3289	GLU403	OE2	37.062	62.428	4.817
3290	GLU403	C	37.754	61.503	10.702
3291	GLU403	O	37.013	60.984	11.543
3292	THR404	N	39.062	61.615	10.867
3293	THR404	CA	39.767	60.847	11.89
3294	THR404	CB	41.256	60.844	11.567
3295	THR404	OG1	41.442	60.293	10.271
3296	THR404	CG2	42.024	59.987	12.562
3297	THR404	C	39.56	61.459	13.266
3298	THR404	O	39.419	60.722	14.246
3299	LEU405	N	39.273	62.749	13.297
3300	LEU405	CA	38.948	63.406	14.565
3301	LEU405	CB	39.136	64.913	14.412
3302	LEU405	CG	40.427	65.427	15.055

Table 11

3303	LEU405	CD1	41.684	64.76	14.501
3304	LEU405	CD2	40.53	66.94	14.91
3305	LEU405	C	37.511	63.103	14.979
3306	LEU405	O	37.271	62.822	16.161
3307	GLN406	N	36.652	62.855	14.001
3308	GLN406	CA	35.27	62.498	14.327
3309	GLN406	CB	34.35	62.666	13.119
3310	GLN406	CG	34.427	64.043	12.464
3311	GLN406	CD	34.233	65.184	13.462
3312	GLN406	OE1	33.285	65.203	14.255
3313	GLN406	NE2	35.166	66.12	13.412
3314	GLN406	C	35.215	61.049	14.788
3315	GLN406	O	34.616	60.769	15.834
3316	TYR407	N	36.07	60.226	14.202
3317	TYR407	CA	36.164	58.824	14.608
3318	TYR407	CB	36.782	58.007	13.48
3319	TYR407	CG	35.786	57.61	12.398
3320	TYR407	CD1	35.772	58.254	11.167
3321	TYR407	CE1	34.855	57.878	10.196
3322	TYR407	CZ	33.956	56.853	10.458
3323	TYR407	OH	33.067	56.448	9.484
3324	TYR407	CE2	33.969	56.206	11.686
3325	TYR407	CD2	34.887	56.584	12.656
3326	TYR407	C	36.958	58.618	15.893
3327	TYR407	O	36.66	57.665	16.617
3328	PHE408	N	37.774	59.582	16.289
3329	PHE408	CA	38.422	59.5	17.6
3330	PHE408	CB	39.641	60.411	17.638
3331	PHE408	CG	40.956	59.677	17.414
3332	PHE408	CD1	41.786	60.022	16.355
3333	PHE408	CE1	42.983	59.345	16.164
3334	PHE408	CZ	43.351	58.325	17.032
3335	PHE408	CE2	42.523	57.982	18.092
3336	PHE408	CD2	41.326	58.659	18.283
3337	PHE408	C	37.463	59.891	18.712
3338	PHE408	O	37.428	59.208	19.742
3339	GLN409	N	36.522	60.768	18.401
3340	GLN409	CA	35.486	61.115	19.377
3341	GLN409	CB	34.801	62.395	18.916
3342	GLN409	CG	35.771	63.57	18.884
3343	GLN409	CD	35.105	64.765	18.212
3344	GLN409	OE1	35.266	65.915	18.638
3345	GLN409	NE2	34.379	64.475	17.147
3346	GLN409	C	34.452	59.998	19.489
3347	GLN409	O	34.075	59.62	20.606
3348	THR410	N	34.228	59.305	18.385
3349	THR410	CA	33.288	58.181	18.384
3350	THR410	CB	32.95	57.837	16.936
3351	THR410	OG1	32.383	58.99	16.327
3352	THR410	CG2	31.934	56.705	16.847
3353	THR410	C	33.891	56.958	19.067
3354	THR410	O	33.246	56.373	19.944
3355	LEU411	N	35.189	56.778	18.897
3356	LEU411	CA	35.89	55.648	19.506
3357	LEU411	CB	37.218	55.515	18.769
3358	LEU411	CG	38.034	54.309	19.206

Table 11

3359	LEU411	CD1	37.219	53.03	19.101
3360	LEU411	CD2	39.3	54.202	18.368
3361	LEU411	C	36.123	55.867	21
3362	LEU411	O	35.942	54.925	21.781
3363	LYS412	N	36.212	57.124	21.404
3364	LYS412	CA	36.354	57.46	22.822
3365	LYS412	CB	36.878	58.893	22.886
3366	LYS412	CG	37.07	59.396	24.31
3367	LYS412	CD	37.628	60.815	24.317
3368	LYS412	CE	37.835	61.328	25.739
3369	LYS412	NZ	38.358	62.705	25.736
3370	LYS412	C	35.018	57.353	23.558
3371	LYS412	O	34.98	56.877	24.7
3372	ALA413	N	33.93	57.558	22.832
3373	ALA413	CA	32.595	57.425	23.426
3374	ALA413	CB	31.632	58.321	22.655
3375	ALA413	C	32.079	55.986	23.408
3376	ALA413	O	31.189	55.641	24.194
3377	VAL414	N	32.66	55.149	22.563
3378	VAL414	CA	32.315	53.725	22.568
3379	VAL414	CB	32.429	53.189	21.14
3380	VAL414	CG1	32.297	51.672	21.082
3381	VAL414	CG2	31.391	53.838	20.232
3382	VAL414	C	33.236	52.96	23.515
3383	VAL414	O	32.857	51.926	24.081
3384	ASP415	N	34.409	53.516	23.759
3385	ASP415	CA	35.307	52.919	24.744
3386	ASP415	CB	36.366	52.112	23.995
3387	ASP415	CG	37.098	51.161	24.94
3388	ASP415	OD1	37.234	51.507	26.11
3389	ASP415	OD2	37.609	50.164	24.456
3390	ASP415	C	35.958	53.997	25.612
3391	ASP415	O	37.147	54.301	25.44
3392	PRO416	N	35.279	54.33	26.701
3393	PRO416	CA	35.788	55.333	27.645
3394	PRO416	CB	34.602	55.689	28.488
3395	PRO416	CG	33.483	54.69	28.227
3396	PRO416	CD	33.984	53.779	27.119
3397	PRO416	C	36.94	54.837	28.533
3398	PRO416	O	37.689	55.663	29.066
3399	MET417	N	37.208	53.539	28.531
3400	MET417	CA	38.308	52.997	29.331
3401	MET417	CB	38.027	51.516	29.546
3402	MET417	CG	36.645	51.304	30.152
3403	MET417	SD	36.105	49.583	30.254
3404	MET417	CE	36.11	49.189	28.489
3405	MET417	C	39.618	53.157	28.57
3406	MET417	O	40.664	53.471	29.15
3407	ARG418	N	39.48	53.181	27.255
3408	ARG418	CA	40.607	53.398	26.353
3409	ARG418	CB	40.369	52.58	25.09
3410	ARG418	CG	41.644	51.903	24.606
3411	ARG418	CD	42.063	50.797	25.569
3412	ARG418	NE	41.007	49.775	25.666
3413	ARG418	CZ	40.523	49.319	26.824
3414	ARG418	NH1	41.04	49.747	27.978

Table 11

3415	ARG418	NH2	39.552	48.403	26.827
3416	ARG418	C	40.725	54.867	25.962
3417	ARG418	O	41.636	55.216	25.202
3418	ALA419	N	39.935	55.729	26.587
3419	ALA419	CA	39.842	57.132	26.168
3420	ALA419	CB	38.795	57.822	27.032
3421	ALA419	C	41.154	57.894	26.284
3422	ALA419	O	41.573	58.501	25.291
3423	THR420	N	41.935	57.597	27.312
3424	THR420	CA	43.225	58.282	27.478
3425	THR420	CB	43.737	58.049	28.897
3426	THR420	OG1	43.951	56.657	29.09
3427	THR420	CG2	42.729	58.522	29.938
3428	THR420	C	44.268	57.808	26.462
3429	THR420	O	44.94	58.659	25.862
3430	TYR421	N	44.133	56.571	26.009
3431	TYR421	CA	45.043	56.039	24.996
3432	TYR421	CB	44.96	54.516	25
3433	TYR421	CG	45.623	53.866	23.788
3434	TYR421	CD1	47.005	53.9	23.646
3435	TYR421	CE1	47.603	53.321	22.534
3436	TYR421	CZ	46.815	52.713	21.565
3437	TYR421	OH	47.405	52.167	20.447
3438	TYR421	CE2	45.435	52.675	21.705
3439	TYR421	CD2	44.839	53.253	22.818
3440	TYR421	C	44.669	56.56	23.616
3441	TYR421	O	45.56	56.964	22.86
3442	LEU422	N	43.39	56.841	23.428
3443	LEU422	CA	42.922	57.4	22.158
3444	LEU422	CB	41.417	57.185	22.071
3445	LEU422	CG	41.083	55.702	22.17
3446	LEU422	CD1	39.586	55.478	22.334
3447	LEU422	CD2	41.638	54.924	20.983
3448	LEU422	C	43.241	58.887	22.067
3449	LEU422	O	43.668	59.347	21.003
3450	ASP423	N	43.354	59.529	23.219
3451	ASP423	CA	43.766	60.934	23.269
3452	ASP423	CB	43.44	61.492	24.652
3453	ASP423	CG	41.951	61.379	24.969
3454	ASP423	OD1	41.156	61.541	24.053
3455	ASP423	OD2	41.633	61.25	26.146
3456	ASP423	C	45.27	61.065	23.035
3457	ASP423	O	45.71	61.971	22.318
3458	ASP424	N	46.012	60.04	23.423
3459	ASP424	CA	47.46	60.028	23.198
3460	ASP424	CB	48.091	58.993	24.128
3461	ASP424	CG	47.868	59.352	25.596
3462	ASP424	OD1	47.843	60.539	25.895
3463	ASP424	OD2	47.81	58.432	26.403
3464	ASP424	C	47.798	59.659	21.755
3465	ASP424	O	48.654	60.307	21.138
3466	LEU425	N	46.965	58.822	21.158
3467	LEU425	CA	47.178	58.392	19.775
3468	LEU425	CB	46.375	57.111	19.573
3469	LEU425	CG	46.664	56.449	18.231
3470	LEU425	CD1	48.144	56.104	18.104

Table 11

3471	LEU425	CD2	45.808	55.2	18.05
3472	LEU425	C	46.719	59.465	18.79
3473	LEU425	O	47.377	59.687	17.765
3474	ARG426	N	45.777	60.283	19.228
3475	ARG426	CA	45.335	61.422	18.426
3476	ARG426	CB	43.961	61.834	18.932
3477	ARG426	CG	43.405	63.039	18.189
3478	ARG426	CD	42.048	63.42	18.768
3479	ARG426	NE	42.121	63.464	20.239
3480	ARG426	CZ	42.439	64.553	20.942
3481	ARG426	NH1	42.659	65.713	20.32
3482	ARG426	NH2	42.501	64.488	22.274
3483	ARG426	C	46.313	62.587	18.543
3484	ARG426	O	46.562	63.268	17.541
3485	SER427	N	47.051	62.632	19.642
3486	SER427	CA	48.124	63.623	19.782
3487	SER427	CB	48.648	63.604	21.211
3488	SER427	OG	47.599	63.964	22.09
3489	SER427	C	49.28	63.28	18.855
3490	SER427	O	49.718	64.13	18.068
3491	LYS428	N	49.555	61.989	18.763
3492	LYS428	CA	50.604	61.484	17.879
3493	LYS428	CB	50.703	59.984	18.118
3494	LYS428	CG	51.857	59.354	17.353
3495	LYS428	CD	51.883	57.848	17.575
3496	LYS428	CE	51.959	57.519	19.061
3497	LYS428	NZ	51.938	56.066	19.282
3498	LYS428	C	50.271	61.741	16.414
3499	LYS428	O	51.036	62.436	15.731
3500	PHE429	N	49.037	61.453	16.033
3501	PHE429	CA	48.621	61.629	14.639
3502	PHE429	CB	47.283	60.925	14.452
3503	PHE429	CG	47.345	59.403	14.376
3504	PHE429	CD1	46.236	58.65	14.733
3505	PHE429	CE1	46.282	57.265	14.658
3506	PHE429	CZ	47.437	56.63	14.22
3507	PHE429	CE2	48.544	57.384	13.851
3508	PHE429	CD2	48.496	58.77	13.924
3509	PHE429	C	48.473	63.093	14.222
3510	PHE429	O	48.938	63.462	13.135
3511	LEU430	N	48.099	63.954	15.152
3512	LEU430	CA	47.916	65.364	14.809
3513	LEU430	CB	46.953	65.956	15.829
3514	LEU430	CG	46.363	67.28	15.366
3515	LEU430	CD1	45.871	67.181	13.927
3516	LEU430	CD2	45.227	67.696	16.294
3517	LEU430	C	49.251	66.112	14.801
3518	LEU430	O	49.446	67.011	13.97
3519	LEU431	N	50.231	65.557	15.496
3520	LEU431	CA	51.586	66.104	15.444
3521	LEU431	CB	52.335	65.63	16.69
3522	LEU431	CG	53.656	66.362	16.92
3523	LEU431	CD1	53.952	66.49	18.409
3524	LEU431	CD2	54.832	65.726	16.183
3525	LEU431	C	52.276	65.633	14.166
3526	LEU431	O	52.953	66.436	13.511

Table 11

3527	GLU432	N	51.872	64.47	13.681
3528	GLU432	CA	52.381	63.959	12.403
3529	GLU432	CB	51.895	62.529	12.22
3530	GLU432	CG	52.527	61.594	13.238
3531	GLU432	CD	51.87	60.222	13.152
3532	GLU432	OE1	51.442	59.865	12.064
3533	GLU432	OE2	51.697	59.61	14.197
3534	GLU432	C	51.881	64.799	11.235
3535	GLU432	O	52.702	65.259	10.431
3536	ASN433	N	50.634	65.235	11.317
3537	ASN433	CA	50.093	66.124	10.287
3538	ASN433	CB	48.591	66.227	10.458
3539	ASN433	CG	47.889	65.099	9.726
3540	ASN433	OD1	48.513	64.222	9.115
3541	ASN433	ND2	46.58	65.231	9.688
3542	ASN433	C	50.668	67.53	10.347
3543	ASN433	O	50.95	68.101	9.287
3544	SER434	N	51.084	67.971	11.522
3545	SER434	CA	51.693	69.298	11.625
3546	SER434	CB	51.649	69.751	13.076
3547	SER434	OG	50.284	69.827	13.464
3548	SER434	C	53.135	69.289	11.127
3549	SER434	O	53.557	70.266	10.498
3550	VAL435	N	53.779	68.132	11.169
3551	VAL435	CA	55.123	68.004	10.597
3552	VAL435	CB	55.816	66.803	11.232
3553	VAL435	CG1	57.185	66.563	10.611
3554	VAL435	CG2	55.95	66.986	12.738
3555	VAL435	C	55.056	67.826	9.08
3556	VAL435	O	55.892	68.388	8.359
3557	LEU436	N	53.947	67.286	8.6
3558	LEU436	CA	53.722	67.207	7.153
3559	LEU436	CB	52.506	66.328	6.884
3560	LEU436	CG	52.774	64.867	7.215
3561	LEU436	CD1	51.489	64.048	7.172
3562	LEU436	CD2	53.821	64.28	6.277
3563	LEU436	C	53.473	68.592	6.571
3564	LEU436	O	54.192	68.996	5.649
3565	LYS437	N	52.704	69.4	7.286
3566	LYS437	CA	52.418	70.771	6.84
3567	LYS437	CB	51.28	71.316	7.695
3568	LYS437	CG	50.023	70.468	7.552
3569	LYS437	CD	48.97	70.867	8.58
3570	LYS437	CE	47.756	69.948	8.516
3571	LYS437	NZ	46.775	70.306	9.552
3572	LYS437	C	53.63	71.688	6.985
3573	LYS437	O	53.894	72.488	6.079
3574	MET438	N	54.495	71.372	7.937
3575	MET438	CA	55.739	72.122	8.121
3576	MET438	CB	56.323	71.717	9.471
3577	MET438	CG	57.636	72.428	9.765
3578	MET438	SD	58.438	71.992	11.324
3579	MET438	CE	58.669	70.223	11.034
3580	MET438	C	56.751	71.823	7.014
3581	MET438	O	57.447	72.741	6.56
3582	GLU439	N	56.641	70.648	6.414

Table 11

3583	GLU439	CA	57.507	70.292	5.29
3584	GLU439	CB	57.588	68.776	5.211
3585	GLU439	CG	58.283	68.224	6.441
3586	GLU439	CD	58.201	66.706	6.461
3587	GLU439	OE1	57.871	66.112	5.442
3588	GLU439	OE2	58.624	66.14	7.457
3589	GLU439	C	56.973	70.823	3.968
3590	GLU439	O	57.77	71.284	3.144
3591	TYR440	N	55.664	71.001	3.877
3592	TYR440	CA	55.071	71.506	2.63
3593	TYR440	CB	53.63	71.016	2.517
3594	TYR440	CG	53.47	69.497	2.55
3595	TYR440	CD1	54.404	68.674	1.931
3596	TYR440	CE1	54.261	67.294	1.989
3597	TYR440	CZ	53.175	66.742	2.654
3598	TYR440	OH	53.096	65.376	2.822
3599	TYR440	CE2	52.222	67.562	3.241
3600	TYR440	CD2	52.366	68.941	3.183
3601	TYR440	C	55.106	73.032	2.575
3602	TYR440	O	54.901	73.629	1.513
3603	ALA441	N	55.358	73.646	3.719
3604	ALA441	CA	55.625	75.083	3.769
3605	ALA441	CB	54.872	75.677	4.953
3606	ALA441	C	57.119	75.373	3.908
3607	ALA441	O	57.524	76.539	3.806
3608	GLU442	N	57.919	74.313	3.955
3609	GLU442	CA	59.365	74.349	4.261
3610	GLU442	CB	60.23	74.51	2.996
3611	GLU442	CG	59.991	75.764	2.148
3612	GLU442	CD	59.111	75.467	0.934
3613	GLU442	OE1	59.262	76.169	-0.057
3614	GLU442	OE2	58.406	74.467	0.97
3615	GLU442	C	59.715	75.389	5.328
3616	GLU442	O	60.44	76.361	5.079
3617	VAL443	N	59.199	75.161	6.524
3618	VAL443	CA	59.423	76.095	7.631
3619	VAL443	CB	58.098	76.742	8.02
3620	VAL443	CG1	57.662	77.79	7.003
3621	VAL443	CG2	57.007	75.702	8.238
3622	VAL443	C	60.051	75.414	8.842
3623	VAL443	O	60.146	74.186	8.92
3624	ARG444	N	60.565	76.243	9.737
3625	ARG444	CA	61.135	75.758	11.001
3626	ARG444	CB	62.499	76.408	11.217
3627	ARG444	CG	63.371	76.224	9.977
3628	ARG444	CD	64.806	76.694	10.189
3629	ARG444	NE	65.557	75.752	11.033
3630	ARG444	CZ	66.74	76.044	11.579
3631	ARG444	NH1	67.263	77.262	11.422
3632	ARG444	NH2	67.38	75.133	12.313
3633	ARG444	C	60.197	76.043	12.177
3634	ARG444	O	60.617	76.031	13.344
3635	VAL445	N	58.987	76.468	11.85
3636	VAL445	CA	57.945	76.673	12.86
3637	VAL445	CB	57.195	77.971	12.557
3638	VAL445	CG1	58.147	79.159	12.543

Table 11

3639	VAL445	CG2	56.444	77.908	11.232
3640	VAL445	C	56.981	75.485	12.87
3641	VAL445	O	56.641	74.929	11.819
3642	LEU446	N	56.597	75.069	14.062
3643	LEU446	CA	55.655	73.954	14.198
3644	LEU446	CB	56.353	72.786	14.884
3645	LEU446	CG	55.487	71.531	14.853
3646	LEU446	CD1	55.189	71.125	13.416
3647	LEU446	CD2	56.153	70.383	15.598
3648	LEU446	C	54.429	74.382	14.999
3649	LEU446	O	54.512	74.717	16.191
3650	HIS447	N	53.294	74.375	14.323
3651	HIS447	CA	52.042	74.804	14.951
3652	HIS447	CB	51.262	75.64	13.948
3653	HIS447	CG	52.022	76.876	13.511
3654	HIS447	ND1	52.232	77.286	12.246
3655	HIS447	CE1	52.958	78.422	12.259
3656	HIS447	NE2	53.213	78.73	13.551
3657	HIS447	CD2	52.643	77.787	14.334
3658	HIS447	C	51.212	73.619	15.429
3659	HIS447	O	50.802	72.749	14.652
3660	LEU448	N	51.055	73.576	16.74
3661	LEU448	CA	50.26	72.565	17.434
3662	LEU448	CB	51.209	71.637	18.18
3663	LEU448	CG	51.959	70.717	17.226
3664	LEU448	CD1	53.12	70.028	17.927
3665	LEU448	CD2	51.008	69.698	16.611
3666	LEU448	C	49.315	73.228	18.434
3667	LEU448	O	48.931	72.614	19.438
3668	ALA449	N	49.046	74.503	18.212
3669	ALA449	CA	48.176	75.268	19.109
3670	ALA449	CB	48.369	76.752	18.841
3671	ALA449	C	46.711	74.916	18.907
3672	ALA449	O	46.262	74.753	17.765
3673	HIS450	N	45.994	74.831	20.018
3674	HIS450	CA	44.56	74.502	20.034
3675	HIS450	CB	43.757	75.577	19.301
3676	HIS450	CG	43.689	76.941	19.957
3677	HIS450	ND1	42.738	77.361	20.813
3678	HIS450	CE1	42.996	78.633	21.178
3679	HIS450	NE2	44.122	79.022	20.538
3680	HIS450	CD2	44.558	77.991	19.778
3681	HIS450	C	44.285	73.169	19.354
3682	HIS450	O	43.405	73.087	18.489
3683	LYS451	N	45.039	72.144	19.713
3684	LYS451	CA	44.853	70.848	19.054
3685	LYS451	CB	46.182	70.387	18.473
3686	LYS451	CG	46.684	71.316	17.376
3687	LYS451	CD	45.718	71.402	16.201
3688	LYS451	CE	46.264	72.329	15.124
3689	LYS451	NZ	47.573	71.854	14.649
3690	LYS451	C	44.329	69.805	20.028
3691	LYS451	O	44.011	68.675	19.636
3692	ASP452	N	44.315	70.19	21.295
3693	ASP452	CA	43.867	69.351	22.414
3694	ASP452	CB	42.432	68.895	22.157

Table 11

3695	ASP452	CG	41.763	68.503	23.465
3696	ASP452	OD1	42	69.203	24.438
3697	ASP452	OD2	40.966	67.576	23.449
3698	ASP452	C	44.816	68.162	22.596
3699	ASP452	O	44.406	67.053	22.954
3700	LEU453	N	46.099	68.437	22.426
3701	LEU453	CA	47.126	67.396	22.532
3702	LEU453	CB	48.434	67.897	21.934
3703	LEU453	CG	48.301	68.306	20.475
3704	LEU453	CD1	49.619	68.877	19.971
3705	LEU453	CD2	47.857	67.142	19.597
3706	LEU453	C	47.381	67.045	23.985
3707	LEU453	O	47.506	67.937	24.831
3708	THR454	N	47.537	65.761	24.242
3709	THR454	CA	47.783	65.28	25.602
3710	THR454	CB	46.856	64.099	25.882
3711	THR454	OG1	47.061	63.099	24.89
3712	THR454	CG2	45.396	64.522	25.816
3713	THR454	C	49.241	64.868	25.792
3714	THR454	O	49.812	65.054	26.874
3715	VAL455	N	49.867	64.441	24.708
3716	VAL455	CA	51.276	64.027	24.774
3717	VAL455	CB	51.31	62.512	24.998
3718	VAL455	CG1	50.636	61.756	23.861
3719	VAL455	CG2	52.721	61.979	25.228
3720	VAL455	C	52.035	64.425	23.504
3721	VAL455	O	51.5	64.334	22.392
3722	LEU456	N	53.229	64.965	23.69
3723	LEU456	CA	54.09	65.311	22.553
3724	LEU456	CB	55.107	66.35	23.003
3725	LEU456	CG	54.441	67.656	23.405
3726	LEU456	CD1	55.47	68.63	23.964
3727	LEU456	CD2	53.697	68.269	22.223
3728	LEU456	C	54.835	64.086	22.03
3729	LEU456	O	55.579	63.429	22.766
3730	CYS457	N	54.634	63.798	20.757
3731	CYS457	CA	55.31	62.661	20.125
3732	CYS457	CB	54.251	61.735	19.546
3733	CYS457	SG	53.099	61.052	20.762
3734	CYS457	C	56.279	63.12	19.039
3735	CYS457	O	56.304	64.301	18.679
3736	HIS458	N	57.136	62.196	18.624
3737	HIS458	CA	58.131	62.408	17.551
3738	HIS458	CB	57.409	62.56	16.212
3739	HIS458	CG	56.641	61.337	15.753
3740	HIS458	ND1	57.146	60.28	15.089
3741	HIS458	CE1	56.162	59.389	14.852
3742	HIS458	NE2	55.018	59.896	15.367
3743	HIS458	CD2	55.296	61.098	15.921
3744	HIS458	C	59.014	63.636	17.757
3745	HIS458	O	59.415	64.275	16.775
3746	LEU459	N	59.535	63.79	18.964
3747	LEU459	CA	60.282	65.009	19.3
3748	LEU459	CB	60.256	65.183	20.812
3749	LEU459	CG	58.834	65.391	21.323
3750	LEU459	CD1	58.787	65.358	22.845

Table 11

3751	LEU459	CD2	58.241	66.692	20.793
3752	LEU459	C	61.721	64.962	18.796
3753	LEU459	O	62.298	66.004	18.472
3754	GLU460	N	62.158	63.766	18.438
3755	GLU460	CA	63.492	63.579	17.863
3756	GLU460	CB	63.997	62.158	18.141
3757	GLU460	CG	63.548	61.058	17.168
3758	GLU460	CD	62.096	60.619	17.347
3759	GLU460	OE1	61.52	60.948	18.38
3760	GLU460	OE2	61.509	60.243	16.339
3761	GLU460	C	63.539	63.871	16.36
3762	GLU460	O	64.628	63.868	15.779
3763	GLN461	N	62.396	64.153	15.749
3764	GLN461	CA	62.395	64.568	14.346
3765	GLN461	CB	61.121	64.051	13.677
3766	GLN461	CG	60.967	62.534	13.772
3767	GLN461	CD	62.079	61.821	13.005
3768	GLN461	OE1	62.41	62.189	11.872
3769	GLN461	NE2	62.576	60.75	13.598
3770	GLN461	C	62.401	66.092	14.282
3771	GLN461	O	62.903	66.686	13.322
3772	LEU462	N	62.104	66.695	15.421
3773	LEU462	CA	61.88	68.138	15.498
3774	LEU462	CB	60.734	68.368	16.474
3775	LEU462	CG	59.476	67.62	16.044
3776	LEU462	CD1	58.393	67.709	17.112
3777	LEU462	CD2	58.958	68.127	14.701
3778	LEU462	C	63.11	68.937	15.934
3779	LEU462	O	62.951	70.078	16.38
3780	LEU463	N	64.299	68.449	15.607
3781	LEU463	CA	65.56	69.094	16.02
3782	LEU463	CB	66.699	68.213	15.499
3783	LEU463	CG	68.084	68.859	15.598
3784	LEU463	CD1	68.502	69.107	17.041
3785	LEU463	CD2	69.135	68.004	14.9
3786	LEU463	C	65.73	70.508	15.458
3787	LEU463	O	66.175	71.405	16.189
3788	LEU464	N	65.166	70.733	14.279
3789	LEU464	CA	65.273	72.018	13.58
3790	LEU464	CB	65.297	71.738	12.082
3791	LEU464	CG	66.441	70.812	11.691
3792	LEU464	CD1	66.343	70.429	10.221
3793	LEU464	CD2	67.794	71.443	11.994
3794	LEU464	C	64.117	72.977	13.866
3795	LEU464	O	64.02	74.013	13.199
3796	VAL465	N	63.203	72.613	14.749
3797	VAL465	CA	62.09	73.516	15.046
3798	VAL465	CB	60.939	72.724	15.657
3799	VAL465	CG1	59.812	73.638	16.121
3800	VAL465	CG2	60.411	71.698	14.663
3801	VAL465	C	62.554	74.616	15.99
3802	VAL465	O	62.85	74.373	17.164
3803	THR466	N	62.584	75.826	15.461
3804	THR466	CA	63.041	76.984	16.226
3805	THR466	CB	63.764	77.95	15.292
3806	THR466	OG1	62.851	78.394	14.299

Table 11

3807	THR466	CG2	64.937	77.28	14.589
3808	THR466	C	61.87	77.695	16.888
3809	THR466	O	62.048	78.374	17.91
3810	HIS467	N	60.676	77.462	16.372
3811	HIS467	CA	59.482	78.061	16.976
3812	HIS467	CB	58.976	79.183	16.077
3813	HIS467	CG	60.007	80.268	15.83
3814	HIS467	ND1	60.513	81.111	16.749
3815	HIS467	CE1	61.412	81.926	16.163
3816	HIS467	NE2	61.474	81.591	14.855
3817	HIS467	CD2	60.613	80.573	14.634
3818	HIS467	C	58.401	77.009	17.17
3819	HIS467	O	57.755	76.571	16.209
3820	LEU468	N	58.212	76.615	18.416
3821	LEU468	CA	57.249	75.559	18.735
3822	LEU468	CB	57.956	74.512	19.588
3823	LEU468	CG	57.095	73.282	19.84
3824	LEU468	CD1	56.61	72.671	18.532
3825	LEU468	CD2	57.859	72.248	20.657
3826	LEU468	C	56.048	76.138	19.473
3827	LEU468	O	56.161	76.648	20.596
3828	ASP469	N	54.904	76.068	18.817
3829	ASP469	CA	53.677	76.613	19.393
3830	ASP469	CB	52.998	77.475	18.337
3831	ASP469	CG	51.761	78.159	18.908
3832	ASP469	OD1	51.666	78.263	20.123
3833	ASP469	OD2	50.892	78.489	18.114
3834	ASP469	C	52.753	75.49	19.853
3835	ASP469	O	51.954	74.961	19.076
3836	LEU470	N	52.815	75.224	21.145
3837	LEU470	CA	52.035	74.18	21.815
3838	LEU470	CB	52.951	73.423	22.767
3839	LEU470	CG	54.147	72.799	22.071
3840	LEU470	CD1	55.11	72.226	23.102
3841	LEU470	CD2	53.703	71.727	21.084
3842	LEU470	C	50.929	74.771	22.682
3843	LEU470	O	50.43	74.073	23.574
3844	SER471	N	50.691	76.064	22.558
3845	SER471	CA	49.681	76.727	23.391
3846	SER471	CB	49.627	78.201	23.015
3847	SER471	OG	49.205	78.281	21.661
3848	SER471	C	48.289	76.121	23.23
3849	SER471	O	47.916	75.653	22.148
3850	HIS472	N	47.573	76.091	24.342
3851	HIS472	CA	46.179	75.632	24.401
3852	HIS472	CB	45.31	76.469	23.47
3853	HIS472	CG	45.168	77.919	23.894
3854	HIS472	ND1	44.186	78.428	24.66
3855	HIS472	CE1	44.389	79.751	24.824
3856	HIS472	NE2	45.511	80.081	24.146
3857	HIS472	CD2	46	78.963	23.563
3858	HIS472	C	46.059	74.15	24.076
3859	HIS472	O	45.613	73.764	22.986
3860	ASN473	N	46.572	73.354	24.997
3861	ASN473	CA	46.5	71.89	24.923
3862	ASN473	CB	47.777	71.334	24.291

Table 11

3863	ASN473	CG	47.782	71.539	22.778
3864	ASN473	OD1	46.778	71.289	22.105
3865	ASN473	ND2	48.906	71.975	22.25
3866	ASN473	C	46.304	71.314	26.327
3867	ASN473	O	46.094	72.054	27.296
3868	ARG474	N	46.329	69.995	26.417
3869	ARG474	CA	46.148	69.308	27.699
3870	ARG474	CB	44.999	68.311	27.603
3871	ARG474	CG	43.67	69.007	27.344
3872	ARG474	CD	42.499	68.06	27.573
3873	ARG474	NE	42.597	66.86	26.73
3874	ARG474	CZ	41.575	66.021	26.551
3875	ARG474	NH1	40.408	66.253	27.156
3876	ARG474	NH2	41.719	64.947	25.772
3877	ARG474	C	47.41	68.576	28.15
3878	ARG474	O	47.32	67.676	28.994
3879	LEU475	N	48.55	68.945	27.583
3880	LEU475	CA	49.838	68.334	27.944
3881	LEU475	CB	50.949	69.109	27.239
3882	LEU475	CG	50.74	69.225	25.732
3883	LEU475	CD1	51.635	70.307	25.137
3884	LEU475	CD2	50.967	67.894	25.032
3885	LEU475	C	50.054	68.477	29.442
3886	LEU475	O	49.805	69.558	29.982
3887	ARG476	N	50.469	67.411	30.108
3888	ARG476	CA	50.679	67.473	31.567
3889	ARG476	CB	50.319	66.118	32.169
3890	ARG476	CG	48.859	65.738	31.941
3891	ARG476	CD	47.905	66.681	32.666
3892	ARG476	NE	48.198	66.735	34.108
3893	ARG476	CZ	47.448	66.136	35.036
3894	ARG476	NH1	47.778	66.235	36.325
3895	ARG476	NH2	46.364	65.444	34.676
3896	ARG476	C	52.128	67.786	31.931
3897	ARG476	O	52.436	68.26	33.036
3898	THR477	N	53.001	67.589	30.962
3899	THR477	CA	54.429	67.822	31.164
3900	THR477	CB	55.01	66.64	31.944
3901	THR477	OG1	56.419	66.806	32.054
3902	THR477	CG2	54.756	65.309	31.243
3903	THR477	C	55.136	67.94	29.823
3904	THR477	O	54.678	67.383	28.818
3905	LEU478	N	56.181	68.746	29.805
3906	LEU478	CA	57.105	68.751	28.676
3907	LEU478	CB	57.807	70.1	28.61
3908	LEU478	CG	56.811	71.191	28.235
3909	LEU478	CD1	57.427	72.581	28.333
3910	LEU478	CD2	56.245	70.954	26.839
3911	LEU478	C	58.102	67.618	28.882
3912	LEU478	O	58.938	67.657	29.798
3913	PRO479	N	57.987	66.617	28.023
3914	PRO479	CA	58.706	65.348	28.189
3915	PRO479	CB	58.109	64.426	27.167
3916	PRO479	CG	57.115	65.19	26.31
3917	PRO479	CD	57.077	66.597	26.874
3918	PRO479	C	60.195	65.546	27.952

Table 11

3919	PRO479	O	60.573	66.488	27.251
3920	PRO480	N	61.03	64.668	28.491
3921	PRO480	CA	62.492	64.822	28.366
3922	PRO480	CB	63.073	63.768	29.258
3923	PRO480	CG	61.952	62.923	29.843
3924	PRO480	CD	60.655	63.52	29.324
3925	PRO480	C	63.038	64.685	26.933
3926	PRO480	O	64.095	65.252	26.635
3927	ALA481	N	62.218	64.188	26.016
3928	ALA481	CA	62.581	64.126	24.595
3929	ALA481	CB	61.715	63.072	23.917
3930	ALA481	C	62.422	65.472	23.873
3931	ALA481	O	62.878	65.607	22.731
3932	LEU482	N	61.965	66.494	24.587
3933	LEU482	CA	61.858	67.849	24.036
3934	LEU482	CB	60.922	68.644	24.941
3935	LEU482	CG	60.638	70.043	24.412
3936	LEU482	CD1	59.822	69.977	23.127
3937	LEU482	CD2	59.901	70.869	25.457
3938	LEU482	C	63.233	68.525	23.975
3939	LEU482	O	63.453	69.369	23.098
3940	ALA483	N	64.208	67.91	24.635
3941	ALA483	CA	65.611	68.335	24.546
3942	ALA483	CB	66.366	67.787	25.752
3943	ALA483	C	66.3	67.884	23.249
3944	ALA483	O	67.48	68.185	23.039
3945	ALA484	N	65.571	67.196	22.378
3946	ALA484	CA	66.07	66.89	21.037
3947	ALA484	CB	65.395	65.619	20.535
3948	ALA484	C	65.783	68.042	20.068
3949	ALA484	O	66.313	68.057	18.951
3950	LEU485	N	65.005	69.016	20.515
3951	LEU485	CA	64.757	70.242	19.745
3952	LEU485	CB	63.353	70.788	20.03
3953	LEU485	CG	62.198	70.015	19.394
3954	LEU485	CD1	61.754	68.803	20.21
3955	LEU485	CD2	61.006	70.947	19.212
3956	LEU485	C	65.757	71.308	20.17
3957	LEU485	O	65.375	72.318	20.767
3958	ARG486	N	66.998	71.161	19.738
3959	ARG486	CA	68.063	72.03	20.249
3960	ARG486	CB	69.383	71.283	20.135
3961	ARG486	CG	69.268	69.908	20.783
3962	ARG486	CD	70.612	69.196	20.856
3963	ARG486	NE	71.472	69.773	21.902
3964	ARG486	CZ	72.658	70.339	21.667
3965	ARG486	NH1	73.069	70.535	20.413
3966	ARG486	NH2	73.395	70.785	22.687
3967	ARG486	C	68.152	73.375	19.53
3968	ARG486	O	68.753	74.316	20.068
3969	CYS487	N	67.447	73.5	18.414
3970	CYS487	CA	67.363	74.78	17.702
3971	CYS487	CB	67.248	74.499	16.209
3972	CYS487	SG	68.608	73.545	15.499
3973	CYS487	C	66.159	75.607	18.155
3974	CYS487	O	65.956	76.718	17.649

Table 11

3975	LEU488	N	65.386	75.07	19.088
3976	LEU488	CA	64.205	75.758	19.613
3977	LEU488	CB	63.524	74.798	20.58
3978	LEU488	CG	62.208	75.339	21.113
3979	LEU488	CD1	61.272	75.661	19.96
3980	LEU488	CD2	61.568	74.334	22.062
3981	LEU488	C	64.603	77.03	20.344
3982	LEU488	O	65.341	76.979	21.329
3983	GLU489	N	64.125	78.153	19.836
3984	GLU489	CA	64.426	79.46	20.409
3985	GLU489	CB	64.814	80.388	19.268
3986	GLU489	CG	66.055	79.878	18.549
3987	GLU489	CD	66.25	80.642	17.248
3988	GLU489	OE1	65.244	80.885	16.591
3989	GLU489	OE2	67.394	80.786	16.837
3990	GLU489	C	63.211	80.022	21.123
3991	GLU489	O	63.337	80.694	22.157
3992	VAL490	N	62.042	79.715	20.59
3993	VAL490	CA	60.796	80.149	21.232
3994	VAL490	CB	60.09	81.171	20.343
3995	VAL490	CG1	58.719	81.55	20.896
3996	VAL490	CG2	60.943	82.421	20.151
3997	VAL490	C	59.88	78.96	21.501
3998	VAL490	O	59.407	78.289	20.572
3999	LEU491	N	59.678	78.691	22.779
4000	LEU491	CA	58.761	77.633	23.199
4001	LEU491	CB	59.472	76.723	24.195
4002	LEU491	CG	58.585	75.567	24.651
4003	LEU491	CD1	58.036	74.783	23.465
4004	LEU491	CD2	59.343	74.641	25.596
4005	LEU491	C	57.516	78.244	23.833
4006	LEU491	O	57.55	78.765	24.956
4007	GLN492	N	56.434	78.204	23.077
4008	GLN492	CA	55.144	78.695	23.56
4009	GLN492	CB	54.456	79.441	22.414
4010	GLN492	CG	52.988	79.785	22.685
4011	GLN492	CD	52.811	80.661	23.922
4012	GLN492	OE1	53.034	80.212	25.051
4013	GLN492	NE2	52.348	81.877	23.698
4014	GLN492	C	54.297	77.519	24.029
4015	GLN492	O	53.707	76.812	23.21
4016	ALA493	N	54.238	77.32	25.332
4017	ALA493	CA	53.495	76.192	25.891
4018	ALA493	CB	54.465	75.248	26.589
4019	ALA493	C	52.405	76.656	26.856
4020	ALA493	O	51.894	75.858	27.656
4021	SER494	N	52.066	77.931	26.779
4022	SER494	CA	51.014	78.512	27.622
4023	SER494	CB	50.852	79.983	27.268
4024	SER494	OG	52.058	80.648	27.622
4025	SER494	C	49.669	77.813	27.464
4026	SER494	O	49.409	77.111	26.476
4027	ASP495	N	48.849	77.984	28.487
4028	ASP495	CA	47.498	77.419	28.563
4029	ASP495	CB	46.611	78.07	27.511
4030	ASP495	CG	46.546	79.577	27.752

Table 11

4031	ASP495	OD1	45.696	79.991	28.527
4032	ASP495	OD2	47.301	80.289	27.101
4033	ASP495	C	47.556	75.913	28.397
4034	ASP495	O	47.255	75.368	27.325
4035	ASN496	N	48.137	75.292	29.405
4036	ASN496	CA	48.326	73.839	29.425
4037	ASN496	CB	49.661	73.468	28.783
4038	ASN496	CG	49.534	73.059	27.318
4039	ASN496	OD1	49.184	71.912	27.013
4040	ASN496	ND2	49.944	73.957	26.442
4041	ASN496	C	48.339	73.337	30.858
4042	ASN496	O	48.654	74.079	31.796
4043	ALA497	N	48.235	72.026	30.98
4044	ALA497	CA	48.265	71.371	32.292
4045	ALA497	CB	47.429	70.102	32.209
4046	ALA497	C	49.689	71.045	32.759
4047	ALA497	O	49.879	70.412	33.803
4048	ILEA498	N	50.665	71.479	31.974
4049	ILEA498	CA	52.087	71.271	32.253
4050	ILEA498	CB	52.887	71.968	31.159
4051	ILEA498	CG2	54.384	71.81	31.393
4052	ILEA498	CG1	52.511	71.413	29.794
4053	ILEA498	CD1	53.219	72.166	28.676
4054	ILEA498	C	52.511	71.804	33.613
4055	ILEA498	O	52.459	73.011	33.887
4056	GLU499	N	52.842	70.855	34.471
4057	GLU499	CA	53.388	71.137	35.796
4058	GLU499	CB	52.518	70.418	36.822
4059	GLU499	CG	52.157	69.009	36.367
4060	GLU499	CD	51.21	68.36	37.371
4061	GLU499	OE1	50.031	68.681	37.337
4062	GLU499	OE2	51.673	67.503	38.112
4063	GLU499	C	54.845	70.692	35.888
4064	GLU499	O	55.54	70.982	36.869
4065	SER500	N	55.296	69.995	34.858
4066	SER500	CA	56.692	69.547	34.802
4067	SER500	CB	56.703	68.03	34.895
4068	SER500	OG	57.999	67.589	34.523
4069	SER500	C	57.389	69.998	33.521
4070	SER500	O	56.949	69.678	32.41
4071	LEU501	N	58.53	70.646	33.687
4072	LEU501	CA	59.279	71.207	32.549
4073	LEU501	CB	59.611	72.655	32.889
4074	LEU501	CG	58.354	73.464	33.183
4075	LEU501	CD1	58.7	74.809	33.807
4076	LEU501	CD2	57.506	73.644	31.93
4077	LEU501	C	60.586	70.457	32.293
4078	LEU501	O	61.601	71.081	31.954
4079	ASP502	N	60.513	69.137	32.243
4080	ASP502	CA	61.749	68.338	32.274
4081	ASP502	CB	61.42	66.89	32.626
4082	ASP502	CG	60.866	66.765	34.044
4083	ASP502	OD1	61.01	67.71	34.811
4084	ASP502	OD2	60.208	65.767	34.301
4085	ASP502	C	62.507	68.356	30.953
4086	ASP502	O	63.729	68.541	30.966

Table 11

4087	GLY503	N	61.778	68.477	29.856
4088	GLY503	CA	62.409	68.487	28.532
4089	GLY503	C	62.806	69.873	28.037
4090	GLY503	O	63.112	70.041	26.853
4091	VAL504	N	62.773	70.853	28.925
4092	VAL504	CA	63.266	72.183	28.588
4093	VAL504	CB	62.384	73.202	29.299
4094	VAL504	CG1	62.736	74.624	28.889
4095	VAL504	CG2	60.913	72.933	29.014
4096	VAL504	C	64.716	72.303	29.055
4097	VAL504	O	65.472	73.164	28.588
4098	THR505	N	65.119	71.341	29.868
4099	THR505	CA	66.477	71.301	30.412
4100	THR505	CB	66.507	70.206	31.477
4101	THR505	OG1	65.481	70.494	32.418
4102	THR505	CG2	67.827	70.125	32.238
4103	THR505	C	67.487	71.029	29.296
4104	THR505	O	67.307	70.116	28.481
4105	ASN506	N	68.575	71.782	29.345
4106	ASN506	CA	69.638	71.783	28.332
4107	ASN506	CB	70.383	70.451	28.36
4108	ASN506	CG	70.893	70.14	29.767
4109	ASN506	OD1	71.343	71.022	30.507
4110	ASN506	ND2	70.741	68.884	30.143
4111	ASN506	C	69.112	72.058	26.927
4112	ASN506	O	69.24	71.221	26.025
4113	LEU507	N	68.481	73.209	26.761
4114	LEU507	CA	68.08	73.652	25.42
4115	LEU507	CB	66.586	73.948	25.365
4116	LEU507	CG	65.771	72.667	25.226
4117	LEU507	CD1	64.283	72.984	25.124
4118	LEU507	CD2	66.222	71.883	23.998
4119	LEU507	C	68.878	74.882	25.017
4120	LEU507	O	68.574	76.005	25.44
4121	PRO508	N	69.789	74.669	24.08
4122	PRO508	CA	70.867	75.63	23.829
4123	PRO508	CB	71.738	74.992	22.792
4124	PRO508	CG	71.19	73.616	22.457
4125	PRO508	CD	69.977	73.414	23.349
4126	PRO508	C	70.347	76.976	23.349
4127	PRO508	O	70.467	77.97	24.076
4128	ARG509	N	69.544	76.932	22.299
4129	ARG509	CA	69.041	78.155	21.673
4130	ARG509	CB	68.834	77.895	20.185
4131	ARG509	CG	70.126	77.504	19.475
4132	ARG509	CD	71.213	78.563	19.64
4133	ARG509	NE	70.76	79.888	19.189
4134	ARG509	CZ	71.43	80.621	18.299
4135	ARG509	NH1	72.545	80.142	17.745
4136	ARG509	NH2	70.974	81.825	17.95
4137	ARG509	C	67.734	78.682	22.262
4138	ARG509	O	67.181	79.628	21.692
4139	LEU510	N	67.259	78.127	23.367
4140	LEU510	CA	65.961	78.558	23.9
4141	LEU510	CB	65.427	77.508	24.863
4142	LEU510	CG	64.004	77.848	25.288

Table 11

4143	LEU510	CD1	63.077	77.883	24.081
4144	LEU510	CD2	63.489	76.855	26.317
4145	LEU510	C	66.092	79.89	24.619
4146	LEU510	O	66.653	79.959	25.717
4147	GLN511	N	65.528	80.919	24.009
4148	GLN511	CA	65.633	82.285	24.512
4149	GLN511	CB	65.863	83.187	23.306
4150	GLN511	CG	66.983	82.638	22.434
4151	GLN511	CD	67.133	83.451	21.156
4152	GLN511	OE1	66.602	83.086	20.099
4153	GLN511	NE2	67.869	84.543	21.27
4154	GLN511	C	64.35	82.718	25.197
4155	GLN511	O	64.379	83.493	26.166
4156	GLU512	N	63.24	82.213	24.684
4157	GLU512	CA	61.92	82.567	25.219
4158	GLU512	CB	61.133	83.302	24.139
4159	GLU512	CG	61.832	84.579	23.687
4160	GLU512	CD	60.978	85.298	22.648
4161	GLU512	OE1	59.764	85.178	22.73
4162	GLU512	OE2	61.557	85.927	21.773
4163	GLU512	C	61.124	81.339	25.647
4164	GLU512	O	60.82	80.459	24.828
4165	LEU513	N	60.78	81.309	26.922
4166	LEU513	CA	59.912	80.259	27.46
4167	LEU513	CB	60.653	79.566	28.597
4168	LEU513	CG	59.894	78.356	29.126
4169	LEU513	CD1	59.528	77.399	28
4170	LEU513	CD2	60.704	77.635	30.195
4171	LEU513	C	58.598	80.873	27.952
4172	LEU513	O	58.562	81.621	28.942
4173	LEU514	N	57.536	80.58	27.22
4174	LEU514	CA	56.215	81.147	27.51
4175	LEU514	CB	55.621	81.625	26.192
4176	LEU514	CG	56.521	82.643	25.5
4177	LEU514	CD1	56.082	82.886	24.061
4178	LEU514	CD2	56.58	83.952	26.279
4179	LEU514	C	55.291	80.109	28.145
4180	LEU514	O	54.83	79.171	27.482
4181	LEU515	N	55.004	80.318	29.418
4182	LEU515	CA	54.173	79.41	30.216
4183	LEU515	CB	55.067	78.629	31.174
4184	LEU515	CG	56.082	77.739	30.469
4185	LEU515	CD1	57.131	77.248	31.456
4186	LEU515	CD2	55.401	76.57	29.772
4187	LEU515	C	53.178	80.19	31.073
4188	LEU515	O	53.331	80.243	32.3
4189	CYS516	N	52.222	80.833	30.427
4190	CYS516	CA	51.149	81.531	31.139
4191	CYS516	CB	50.745	82.777	30.368
4192	CYS516	SG	51.989	84.078	30.291
4193	CYS516	C	49.938	80.626	31.271
4194	CYS516	O	49.491	80.04	30.277
4195	ASN517	N	49.37	80.603	32.462
4196	ASN517	CA	48.242	79.724	32.794
4197	ASN517	CB	47.002	80.136	32.012
4198	ASN517	CG	46.592	81.54	32.448

Table 11

4199	ASN517	OD1	46.73	82.51	31.693
4200	ASN517	ND2	46.151	81.643	33.691
4201	ASN517	C	48.611	78.266	32.55
4202	ASN517	O	48.154	77.607	31.603
4203	ASN518	N	49.586	77.85	33.333
4204	ASN518	CA	50.064	76.47	33.374
4205	ASN518	CB	51.481	76.403	32.809
4206	ASN518	CG	51.508	76.636	31.298
4207	ASN518	OD1	51.33	77.758	30.805
4208	ASN518	ND2	51.838	75.577	30.584
4209	ASN518	C	50.051	76.009	34.828
4210	ASN518	O	50.002	76.838	35.745
4211	ARG519	N	50.239	74.72	35.048
4212	ARG519	CA	50.128	74.163	36.408
4213	ARG519	CB	49.533	72.764	36.339
4214	ARG519	CG	48.092	72.818	35.85
4215	ARG519	CD	47.424	71.453	35.94
4216	ARG519	NE	46.05	71.52	35.421
4217	ARG519	CZ	45.238	70.462	35.365
4218	ARG519	NH1	45.655	69.278	35.819
4219	ARG519	NH2	44.005	70.592	34.87
4220	ARG519	C	51.435	74.133	37.206
4221	ARG519	O	51.649	73.204	37.995
4222	LEU520	N	52.29	75.124	37.012
4223	LEU520	CA	53.525	75.223	37.805
4224	LEU520	CB	54.526	76.193	37.164
4225	LEU520	CG	55.264	75.657	35.931
4226	LEU520	CD1	55.652	74.197	36.11
4227	LEU520	CD2	54.496	75.833	34.625
4228	LEU520	C	53.167	75.721	39.205
4229	LEU520	O	52.919	76.918	39.402
4230	GLN521	N	53.133	74.803	40.157
4231	GLN521	CA	52.664	75.127	41.508
4232	GLN521	CB	51.992	73.889	42.088
4233	GLN521	CG	51.458	74.162	43.49
4234	GLN521	CD	51.43	72.869	44.296
4235	GLN521	OE1	52.179	71.928	44.002
4236	GLN521	NE2	50.653	72.88	45.364
4237	GLN521	C	53.789	75.528	42.451
4238	GLN521	O	53.612	76.421	43.286
4239	GLN522	N	54.937	74.891	42.302
4240	GLN522	CA	56.071	75.184	43.184
4241	GLN522	CB	56.408	73.917	43.964
4242	GLN522	CG	55.252	73.516	44.873
4243	GLN522	CD	55.566	72.209	45.588
4244	GLN522	OE1	56.605	72.077	46.244
4245	GLN522	NE2	54.658	71.258	45.452
4246	GLN522	C	57.284	75.65	42.388
4247	GLN522	O	57.639	75.035	41.375
4248	PRO523	N	57.988	76.636	42.926
4249	PRO523	CA	59.095	77.289	42.204
4250	PRO523	CB	59.418	78.507	43.017
4251	PRO523	CG	58.592	78.503	44.293
4252	PRO523	CD	57.696	77.28	44.212
4253	PRO523	C	60.354	76.43	42.01
4254	PRO523	O	61.154	76.728	41.114

Table 11

4255	ALA524	N	60.403	75.265	42.641
4256	ALA524	CA	61.561	74.374	42.512
4257	ALA524	CB	61.536	73.384	43.671
4258	ALA524	C	61.59	73.608	41.186
4259	ALA524	O	62.675	73.203	40.752
4260	VAL525	N	60.492	73.637	40.441
4261	VAL525	CA	60.462	72.988	39.123
4262	VAL525	CB	59.019	72.595	38.8
4263	VAL525	CG1	58.13	73.818	38.611
4264	VAL525	CG2	58.932	71.688	37.574
4265	VAL525	C	61.048	73.907	38.041
4266	VAL525	O	61.329	73.46	36.923
4267	LEU526	N	61.37	75.136	38.419
4268	LEU526	CA	62.025	76.054	37.492
4269	LEU526	CB	61.62	77.481	37.817
4270	LEU526	CG	60.111	77.685	37.785
4271	LEU526	CD1	59.794	79.115	38.174
4272	LEU526	CD2	59.519	77.381	36.413
4273	LEU526	C	63.539	75.946	37.611
4274	LEU526	O	64.263	76.413	36.723
4275	GLN527	N	64.01	75.219	38.611
4276	GLN527	CA	65.456	75.042	38.776
4277	GLN527	CB	65.743	74.292	40.07
4278	GLN527	CG	67.21	74.447	40.453
4279	GLN527	CD	67.511	75.927	40.674
4280	GLN527	OE1	66.909	76.559	41.55
4281	GLN527	NE2	68.394	76.469	39.851
4282	GLN527	C	66.178	74.348	37.594
4283	GLN527	O	67.216	74.898	37.198
4284	PRO528	N	65.669	73.289	36.954
4285	PRO528	CA	66.335	72.801	35.732
4286	PRO528	CB	65.693	71.483	35.426
4287	PRO528	CG	64.492	71.279	36.327
4288	PRO528	CD	64.489	72.462	37.274
4289	PRO528	C	66.252	73.717	34.499
4290	PRO528	O	66.911	73.417	33.497
4291	LEU529	N	65.597	74.867	34.591
4292	LEU529	CA	65.547	75.81	33.468
4293	LEU529	CB	64.289	76.664	33.556
4294	LEU529	CG	63.017	75.834	33.646
4295	LEU529	CD1	61.809	76.753	33.732
4296	LEU529	CD2	62.873	74.884	32.466
4297	LEU529	C	66.764	76.736	33.458
4298	LEU529	O	67.027	77.39	32.441
4299	ALA530	N	67.604	76.629	34.48
4300	ALA530	CA	68.863	77.389	34.53
4301	ALA530	CB	69.378	77.398	35.964
4302	ALA530	C	69.94	76.796	33.615
4303	ALA530	O	71.003	77.394	33.42
4304	SER531	N	69.634	75.65	33.026
4305	SER531	CA	70.508	75.019	32.037
4306	SER531	CB	70.387	73.514	32.183
4307	SER531	OG	69.087	73.16	31.741
4308	SER531	C	70.136	75.409	30.603
4309	SER531	O	70.537	74.707	29.668
4310	CYS532	N	69.224	76.354	30.437

Table 11

4311	CYS532	CA	68.935	76.873	29.096
4312	CYS532	CB	67.465	77.265	29.015
4313	CYS532	SG	66.289	75.98	29.486
4314	CYS532	C	69.791	78.111	28.841
4315	CYS532	O	69.453	79.207	29.302
4316	PRO533	N	70.832	77.951	28.037
4317	PRO533	CA	71.903	78.957	27.976
4318	PRO533	CB	73.04	78.269	27.283
4319	PRO533	CG	72.592	76.897	26.815
4320	PRO533	CD	71.167	76.727	27.307
4321	PRO533	C	71.533	80.243	27.232
4322	PRO533	O	72.247	81.244	27.354
4323	ARG534	N	70.419	80.241	26.519
4324	ARG534	CA	69.964	81.447	25.829
4325	ARG534	CB	69.591	81.054	24.409
4326	ARG534	CG	70.392	81.812	23.359
4327	ARG534	CD	71.884	81.554	23.509
4328	ARG534	NE	72.624	82.107	22.367
4329	ARG534	CZ	73.463	81.361	21.649
4330	ARG534	NH1	73.661	80.085	21.984
4331	ARG534	NH2	74.113	81.891	20.612
4332	ARG534	C	68.745	82.076	26.504
4333	ARG534	O	68.219	83.068	25.981
4334	LEU535	N	68.321	81.533	27.638
4335	LEU535	CA	67.025	81.908	28.222
4336	LEU535	CB	66.612	80.841	29.228
4337	LEU535	CG	65.157	81.004	29.655
4338	LEU535	CD1	64.234	80.871	28.45
4339	LEU535	CD2	64.784	79.983	30.724
4340	LEU535	C	67.054	83.266	28.908
4341	LEU535	O	67.527	83.415	30.041
4342	VAL536	N	66.46	84.232	28.232
4343	VAL536	CA	66.372	85.583	28.77
4344	VAL536	CB	66.791	86.567	27.681
4345	VAL536	CG1	66.667	88.01	28.154
4346	VAL536	CG2	68.212	86.283	27.206
4347	VAL536	C	64.946	85.87	29.211
4348	VAL536	O	64.742	86.556	30.221
4349	LEU537	N	63.993	85.238	28.544
4350	LEU537	CA	62.574	85.456	28.847
4351	LEU537	CB	61.856	85.784	27.538
4352	LEU537	CG	60.352	85.99	27.721
4353	LEU537	CD1	60.056	87.149	28.666
4354	LEU537	CD2	59.668	86.221	26.379
4355	LEU537	C	61.93	84.23	29.488
4356	LEU537	O	61.848	83.156	28.876
4357	LEU538	N	61.451	84.422	30.705
4358	LEU538	CA	60.688	83.39	31.411
4359	LEU538	CB	61.486	82.946	32.629
4360	LEU538	CG	60.822	81.78	33.345
4361	LEU538	CD1	60.629	80.599	32.402
4362	LEU538	CD2	61.635	81.365	34.564
4363	LEU538	C	59.342	83.972	31.84
4364	LEU538	O	59.24	84.672	32.855
4365	ASN539	N	58.323	83.69	31.052
4366	ASN539	CA	57.001	84.285	31.278

Table 11

4367	ASN539	CB	56.517	84.749	29.911
4368	ASN539	CG	55.225	85.551	29.979
4369	ASN539	OD1	54.413	85.485	29.05
4370	ASN539	ND2	55.071	86.332	31.035
4371	ASN539	C	56.046	83.26	31.897
4372	ASN539	O	55.503	82.403	31.196
4373	LEU540	N	55.793	83.418	33.187
4374	LEU540	CA	55.042	82.429	33.977
4375	LEU540	CB	55.913	82.009	35.153
4376	LEU540	CG	57.216	81.363	34.713
4377	LEU540	CD1	58.154	81.221	35.902
4378	LEU540	CD2	56.968	80.014	34.049
4379	LEU540	C	53.742	82.969	34.569
4380	LEU540	O	53.3	82.479	35.615
4381	GLN541	N	53.186	84.012	33.984
4382	GLN541	CA	52.046	84.681	34.62
4383	GLN541	CB	51.853	86.02	33.929
4384	GLN541	CG	53.138	86.811	34.118
4385	GLN541	CD	53.093	88.175	33.452
4386	GLN541	OE1	53.123	88.278	32.22
4387	GLN541	NE2	53.214	89.196	34.28
4388	GLN541	C	50.767	83.845	34.611
4389	GLN541	O	50.437	83.164	33.637
4390	GLY542	N	50.137	83.801	35.773
4391	GLY542	CA	48.872	83.077	35.93
4392	GLY542	C	49.081	81.672	36.486
4393	GLY542	O	48.182	80.827	36.396
4394	ASN543	N	50.275	81.42	36.998
4395	ASN543	CA	50.601	80.101	37.551
4396	ASN543	CB	51.981	79.679	37.047
4397	ASN543	CG	52.046	79.574	35.524
4398	ASN543	OD1	51.046	79.726	34.816
4399	ASN543	ND2	53.233	79.281	35.033
4400	ASN543	C	50.608	80.154	39.078
4401	ASN543	O	50.941	81.192	39.664
4402	PRO544	N	50.294	79.035	39.716
4403	PRO544	CA	50.159	79.004	41.185
4404	PRO544	CB	49.641	77.633	41.497
4405	PRO544	CG	49.501	76.832	40.21
4406	PRO544	CD	49.912	77.766	39.086
4407	PRO544	C	51.453	79.281	41.97
4408	PRO544	O	51.377	79.897	43.04
4409	LEU545	N	52.605	79.097	41.341
4410	LEU545	CA	53.893	79.392	41.991
4411	LEU545	CB	55.009	78.586	41.313
4412	LEU545	CG	55.737	79.221	40.122
4413	LEU545	CD1	56.836	78.281	39.66
4414	LEU545	CD2	54.853	79.549	38.925
4415	LEU545	C	54.247	80.885	42.028
4416	LEU545	O	55.162	81.275	42.764
4417	CYS546	N	53.418	81.72	41.417
4418	CYS546	CA	53.631	83.167	41.456
4419	CYS546	CB	52.957	83.782	40.239
4420	CYS546	SG	53.492	83.109	38.652
4421	CYS546	C	53.032	83.768	42.723
4422	CYS546	O	53.393	84.884	43.113

Table 11

4423	GLN547	N	52.306	82.94	43.461
4424	GLN547	CA	51.681	83.352	44.719
4425	GLN547	CB	50.408	82.533	44.926
4426	GLN547	CG	49.503	82.52	43.694
4427	GLN547	CD	49.084	83.929	43.276
4428	GLN547	OE1	49.358	84.352	42.147
4429	GLN547	NE2	48.407	84.623	44.175
4430	GLN547	C	52.599	83.171	45.935
4431	GLN547	O	52.102	83.137	47.068
4432	ALA548	N	53.891	82.981	45.702
4433	ALA548	CA	54.871	82.835	46.787
4434	ALA548	CB	56.191	82.349	46.201
4435	ALA548	C	55.096	84.144	47.545
4436	ALA548	O	54.192	84.98	47.664
4437	VAL549	N	56.285	84.299	48.101
4438	VAL549	CA	56.552	85.483	48.924
4439	VAL549	CB	57.62	85.132	49.959
4440	VAL549	CG1	57.695	86.193	51.056
4441	VAL549	CG2	57.324	83.774	50.585
4442	VAL549	C	57.021	86.625	48.026
4443	VAL549	O	56.219	87.441	47.553
4444	GLY550	N	58.295	86.588	47.688
4445	GLY550	CA	58.874	87.57	46.777
4446	GLY550	C	59.369	86.779	45.584
4447	GLY550	O	60.574	86.724	45.3
4448	ILEA551	N	58.414	86.324	44.79
4449	ILEA551	CA	58.697	85.317	43.762
4450	ILEA551	CB	57.356	84.768	43.272
4451	ILEA551	CG2	56.499	85.845	42.614
4452	ILEA551	CG1	57.548	83.584	42.336
4453	ILEA551	CD1	58.227	82.428	43.062
4454	ILEA551	C	59.561	85.84	42.607
4455	ILEA551	O	60.407	85.077	42.124
4456	LEU552	N	59.624	87.152	42.437
4457	LEU552	CA	60.486	87.731	41.407
4458	LEU552	CB	60.132	89.204	41.253
4459	LEU552	CG	58.727	89.386	40.693
4460	LEU552	CD1	58.28	90.839	40.788
4461	LEU552	CD2	58.645	88.888	39.256
4462	LEU552	C	61.956	87.596	41.787
4463	LEU552	O	62.713	86.961	41.042
4464	GLU553	N	62.293	87.92	43.027
4465	GLU553	CA	63.704	87.837	43.416
4466	GLU553	CB	64.09	88.895	44.461
4467	GLU553	CG	63.89	88.51	45.931
4468	GLU553	CD	62.455	88.723	46.401
4469	GLU553	OE1	61.698	89.338	45.658
4470	GLU553	OE2	62.11	88.175	47.438
4471	GLU553	C	64.075	86.434	43.886
4472	GLU553	O	65.247	86.066	43.762
4473	GLN554	N	63.092	85.594	44.17
4474	GLN554	CA	63.409	84.214	44.527
4475	GLN554	CB	62.222	83.59	45.254
4476	GLN554	CG	61.966	84.309	46.577
4477	GLN554	CD	60.8	83.682	47.341
4478	GLN554	OE1	59.625	84.018	47.13

Table 11

4479	GLN554	NE2	61.148	82.835	48.292
4480	GLN554	C	63.754	83.426	43.27
4481	GLN554	O	64.827	82.809	43.218
4482	LEU555	N	63.059	83.73	42.186
4483	LEU555	CA	63.372	83.068	40.919
4484	LEU555	CB	62.16	83.111	40.004
4485	LEU555	CG	61.027	82.277	40.578
4486	LEU555	CD1	59.804	82.344	39.673
4487	LEU555	CD2	61.471	80.833	40.789
4488	LEU555	C	64.566	83.701	40.223
4489	LEU555	O	65.324	82.973	39.577
4490	ALA556	N	64.891	84.935	40.568
4491	ALA556	CA	66.113	85.545	40.034
4492	ALA556	CB	66.033	87.056	40.227
4493	ALA556	C	67.367	85.009	40.727
4494	ALA556	O	68.398	84.832	40.067
4495	GLU557	N	67.206	84.527	41.951
4496	GLU557	CA	68.324	83.922	42.682
4497	GLU557	CB	68.039	84.044	44.174
4498	GLU557	CG	68.06	85.499	44.622
4499	GLU557	CD	67.376	85.643	45.978
4500	GLU557	OE1	66.545	84.801	46.292
4501	GLU557	OE2	67.612	86.652	46.628
4502	GLU557	C	68.512	82.45	42.327
4503	GLU557	O	69.584	81.888	42.577
4504	LEU558	N	67.506	81.849	41.713
4505	LEU558	CA	67.639	80.461	41.267
4506	LEU558	CB	66.294	79.765	41.445
4507	LEU558	CG	65.833	79.752	42.898
4508	LEU558	CD1	64.424	79.181	43.009
4509	LEU558	CD2	66.803	78.979	43.786
4510	LEU558	C	68.026	80.392	39.796
4511	LEU558	O	68.67	79.428	39.357
4512	LEU559	N	67.62	81.404	39.046
4513	LEU559	CA	67.883	81.457	37.601
4514	LEU559	CB	66.537	81.352	36.881
4515	LEU559	CG	65.673	80.196	37.381
4516	LEU559	CD1	64.234	80.329	36.9
4517	LEU559	CD2	66.249	78.843	36.99
4518	LEU559	C	68.505	82.796	37.192
4519	LEU559	O	67.874	83.526	36.417
4520	PRO560	N	69.796	82.973	37.449
4521	PRO560	CA	70.418	84.31	37.391
4522	PRO560	CB	71.682	84.176	38.183
4523	PRO560	CG	71.94	82.708	38.477
4524	PRO560	CD	70.727	81.957	37.96
4525	PRO560	C	70.742	84.829	35.98
4526	PRO560	O	71.278	85.933	35.844
4527	SER561	N	70.454	84.047	34.951
4528	SER561	CA	70.725	84.481	33.58
4529	SER561	CB	71.287	83.3	32.803
4530	SER561	OG	72.471	82.879	33.466
4531	SER561	C	69.459	84.993	32.898
4532	SER561	O	69.534	85.686	31.875
4533	VAL562	N	68.317	84.708	33.504
4534	VAL562	CA	67.046	85.165	32.947

Table 11

4535	VAL562	CB	65.933	84.265	33.467
4536	VAL562	CG1	64.601	84.631	32.828
4537	VAL562	CG2	66.256	82.8	33.2
4538	VAL562	C	66.817	86.608	33.373
4539	VAL562	O	66.612	86.906	34.556
4540	SER563	N	66.813	87.493	32.392
4541	SER563	CA	66.731	88.924	32.682
4542	SER563	CB	67.49	89.663	31.589
4543	SER563	OG	68.805	89.121	31.552
4544	SER563	C	65.286	89.405	32.732
4545	SER563	O	64.981	90.429	33.354
4546	SER564	N	64.397	88.61	32.167
4547	SER564	CA	62.974	88.925	32.211
4548	SER564	CB	62.488	89.148	30.786
4549	SER564	OG	61.107	89.467	30.852
4550	SER564	C	62.192	87.79	32.857
4551	SER564	O	61.62	86.937	32.162
4552	VAL565	N	62.215	87.762	34.179
4553	VAL565	CA	61.421	86.784	34.934
4554	VAL565	CB	62.125	86.463	36.251
4555	VAL565	CG1	61.412	85.333	36.987
4556	VAL565	CG2	63.586	86.092	36.026
4557	VAL565	C	60.043	87.376	35.222
4558	VAL565	O	59.812	87.998	36.266
4559	LEU566	N	59.122	87.141	34.308
4560	LEU566	CA	57.798	87.75	34.408
4561	LEU566	CB	57.323	88.157	33.021
4562	LEU566	CG	58.212	89.226	32.401
4563	LEU566	CD1	57.768	89.527	30.975
4564	LEU566	CD2	58.213	90.498	33.244
4565	LEU566	C	56.795	86.785	35.014
4566	LEU566	O	56.117	86.039	34.295
4567	THR567	N	56.687	86.837	36.329
4568	THR567	CA	55.709	86.012	37.045
4569	THR567	CB	56.393	85.328	38.222
4570	THR567	OG1	56.733	86.313	39.186
4571	THR567	CG2	57.661	84.604	37.791
4572	THR567	C	54.561	86.88	37.553
4573	THR567	O	53.882	86.441	38.47
4574	THR567	OXT	54.277	87.875	36.901

Table 12

Atom No.	Residue / Residue Position	Atom Type	X Coord.	Y Coord.	Z Coord.
1	MET1	N	25.639	32.902	36.49
2	MET1	CA	26.981	32.307	36.329
3	MET1	CB	27.631	32.812	35.043
4	MET1	CG	27.797	34.332	35.059
5	MET1	SD	28.559	35.081	33.602
6	MET1	CE	27.379	34.546	32.344
7	MET1	C	27.872	32.687	37.507
8	MET1	O	29.046	32.298	37.586
9	GLY2	N	27.289	33.443	38.422
10	GLY2	CA	28.052	34.024	39.53
11	GLY2	C	28.827	35.244	39.024
12	GLY2	O	28.333	36.377	39.024
13	THR3	N	30.035	34.979	38.567
14	THR3	CA	30.902	35.999	37.96
15	THR3	CB	31.984	36.436	38.95
16	THR3	OG1	32.457	35.292	39.638
17	THR3	CG2	31.428	37.396	39.999
18	THR3	C	31.522	35.604	36.595
19	THR3	O	31.389	36.424	35.673
20	PRO4	N	32.202	34.465	36.43
21	PRO4	CA	32.942	34.247	35.182
22	PRO4	CB	33.867	33.101	35.448
23	PRO4	CG	33.544	32.483	36.794
24	PRO4	CD	32.439	33.345	37.367
25	PRO4	C	32.047	33.916	33.997
26	PRO4	O	31.125	33.099	34.091
27	GLN5	N	32.347	34.573	32.891
28	GLN5	CA	31.735	34.265	31.6
29	GLN5	CB	31.439	35.59	30.908
30	GLN5	CG	30.341	35.538	29.846
31	GLN5	CD	30.807	36.449	28.72
32	GLN5	OE1	32.01	36.478	28.417
33	GLN5	NE2	29.886	37.203	28.15
34	GLN5	C	32.772	33.455	30.818
35	GLN5	O	33.19	32.381	31.264
36	LYS6	N	33.151	33.954	29.655
37	LYS6	CA	34.263	33.396	28.891
38	LYS6	CB	33.766	32.99	27.509
39	LYS6	CG	32.679	31.926	27.595
40	LYS6	CD	32.192	31.506	26.214
41	LYS6	CE	31.128	30.416	26.314
42	LYS6	NZ	30.67	30.005	24.975
43	LYS6	C	35.314	34.484	28.772
44	LYS6	O	36.507	34.266	29.012
45	ASP7	N	34.817	35.691	28.567
46	ASP7	CA	35.672	36.867	28.512
47	ASP7	CB	35.499	37.527	27.149
48	ASP7	CG	36.269	38.843	27.06
49	ASP7	OD1	37.47	38.802	26.825
50	ASP7	OD2	35.622	39.878	27.147
51	ASP7	C	35.315	37.833	29.633
52	ASP7	O	36.055	37.941	30.614
53	VAL8	N	34.128	38.409	29.58
54	VAL8	CA	33.82	39.486	30.528

Table 12

55	VAL8	CB	33.198	40.657	29.767
56	VAL8	CG1	32.082	40.208	28.833
57	VAL8	CG2	32.73	41.768	30.701
58	VAL8	C	32.943	39.027	31.689
59	VAL8	O	31.8	38.589	31.516
60	ILE9	N	33.55	39.055	32.863
61	ILE9	CA	32.847	38.788	34.123
62	ILE9	CB	33.9	38.825	35.231
63	ILE9	CG2	33.334	39.118	36.619
64	ILE9	CG1	34.691	37.53	35.248
65	ILE9	CD1	35.65	37.525	36.426
66	ILE9	C	31.754	39.821	34.383
67	ILE9	O	31.93	41.012	34.101
68	ILE10	N	30.595	39.347	34.81
69	ILE10	CA	29.527	40.263	35.21
70	ILE10	CB	28.201	39.512	35.158
71	ILE10	CG2	27.057	40.376	35.676
72	ILE10	CG1	27.914	39.042	33.738
73	ILE10	CD1	26.564	38.342	33.659
74	ILE10	C	29.798	40.793	36.619
75	ILE10	O	29.82	40.033	37.596
76	LYS11	N	30.081	42.083	36.701
77	LYS11	CA	30.324	42.717	38.001
78	LYS11	CB	30.964	44.083	37.781
79	LYS11	CG	31.214	44.785	39.113
80	LYS11	CD	31.653	46.231	38.918
81	LYS11	CE	31.783	46.946	40.258
82	LYS11	NZ	32.095	48.37	40.067
83	LYS11	C	29.023	42.892	38.782
84	LYS11	O	28.163	43.708	38.433
85	SER12	N	28.886	42.09	39.823
86	SER12	CA	27.739	42.194	40.727
87	SER12	CB	27.424	40.805	41.266
88	SER12	OG	27.184	39.959	40.148
89	SER12	C	28.059	43.148	41.874
90	SER12	O	29.087	43.836	41.853
91	ASP13	N	27.158	43.225	42.841
92	ASP13	CA	27.386	44.063	44.033
93	ASP13	CB	26.047	44.467	44.658
94	ASP13	CG	25.103	43.279	44.868
95	ASP13	OD1	24.338	42.997	43.956
96	ASP13	OD2	25.103	42.732	45.961
97	ASP13	C	28.3	43.365	45.048
98	ASP13	O	27.861	42.738	46.017
99	ALA14	N	29.588	43.499	44.795
100	ALA14	CA	30.628	42.871	45.611
101	ALA14	CB	31.578	42.199	44.623
102	ALA14	C	31.33	43.935	46.463
103	ALA14	O	30.992	45.117	46.327
104	PRO15	N	32.204	43.534	47.382
105	PRO15	CA	32.877	44.504	48.259
106	PRO15	CB	33.846	43.709	49.078
107	PRO15	CG	33.671	42.234	48.764
108	PRO15	CD	32.579	42.152	47.712
109	PRO15	C	33.585	45.613	47.486
110	PRO15	O	34.004	45.445	46.334

Table 12

111	ASP16	N	33.502	46.806	48.045
112	ASP16	CA	34.174	47.965	47.447
113	ASP16	CB	33.155	48.889	46.77
114	ASP16	CG	31.992	49.3	47.678
115	ASP16	OD1	30.888	49.394	47.163
116	ASP16	OD2	32.21	49.499	48.867
117	ASP16	C	35.017	48.712	48.477
118	ASP16	O	35.681	49.707	48.166
119	THR17	N	34.967	48.235	49.705
120	THR17	CA	35.724	48.867	50.782
121	THR17	CB	34.769	49.09	51.948
122	THR17	OG1	33.657	49.824	51.451
123	THR17	CG2	35.409	49.887	53.08
124	THR17	C	36.867	47.951	51.187
125	THR17	O	36.627	46.785	51.507
126	LEU18	N	38.082	48.474	51.107
127	LEU18	CA	39.308	47.718	51.418
128	LEU18	CB	40.471	48.709	51.364
129	LEU18	CG	41.82	48.074	51.697
130	LEU18	CD1	42.217	47.033	50.659
131	LEU18	CD2	42.904	49.139	51.812
132	LEU18	C	39.263	47.064	52.8
133	LEU18	O	39.369	47.739	53.833
134	LEU19	N	39.174	45.743	52.803
135	LEU19	CA	39.182	44.964	54.049
136	LEU19	CB	38.427	43.665	53.793
137	LEU19	CG	37.009	43.921	53.3
138	LEU19	CD1	36.368	42.634	52.8
139	LEU19	CD2	36.151	44.583	54.373
140	LEU19	C	40.605	44.622	54.476
141	LEU19	O	40.918	43.444	54.689
142	LEU20	N	41.37	45.643	54.827
143	LEU20	CA	42.814	45.489	55.054
144	LEU20	CB	43.401	46.886	55.227
145	LEU20	CG	44.913	46.889	55.046
146	LEU20	CD1	45.263	46.478	53.621
147	LEU20	CD2	45.497	48.263	55.354
148	LEU20	C	43.14	44.648	56.289
149	LEU20	O	44.006	43.765	56.215
150	GLU21	N	42.277	44.717	57.291
151	GLU21	CA	42.482	43.909	58.495
152	GLU21	CB	41.594	44.441	59.612
153	GLU21	CG	41.766	43.635	60.897
154	GLU21	CD	40.796	44.15	61.954
155	GLU21	OE1	40.278	45.239	61.746
156	GLU21	OE2	40.515	43.417	62.891
157	GLU21	C	42.135	42.448	58.242
158	GLU21	O	42.942	41.581	58.595
159	LYS22	N	41.187	42.211	57.351
160	LYS22	CA	40.761	40.843	57.074
161	LYS22	CB	39.388	40.881	56.418
162	LYS22	CG	38.319	41.477	57.323
163	LYS22	CD	36.963	41.438	56.628
164	LYS22	CE	35.864	42.038	57.495
165	LYS22	NZ	34.572	42.015	56.79
166	LYS22	C	41.738	40.149	56.135

Table 12

167	LYS22	O	41.974	38.943	56.286
168	HIS23	N	42.452	40.925	55.336
169	HIS23	CA	43.46	40.338	54.452
170	HIS23	CB	43.885	41.35	53.393
171	HIS23	CG	42.774	41.931	52.537
172	HIS23	ND1	41.683	41.303	52.059
173	HIS23	CE1	40.942	42.171	51.35
174	HIS23	NE2	41.58	43.362	51.366
175	HIS23	CD2	42.718	43.226	52.087
176	HIS23	C	44.684	39.943	55.263
177	HIS23	O	45.124	38.79	55.164
178	ALA24	N	45.005	40.754	56.261
179	ALA24	CA	46.152	40.463	57.125
180	ALA24	CB	46.493	41.723	57.905
181	ALA24	C	45.859	39.325	58.095
182	ALA24	O	46.68	38.403	58.22
183	ASP25	N	44.609	39.246	58.528
184	ASP25	CA	44.166	38.149	59.391
185	ASP25	CB	42.719	38.383	59.824
186	ASP25	CG	42.57	39.629	60.696
187	ASP25	OD1	43.493	39.926	61.442
188	ASP25	OD2	41.501	40.226	60.65
189	ASP25	C	44.232	36.824	58.647
190	ASP25	O	44.936	35.918	59.11
191	TYR26	N	43.786	36.827	57.4
192	TYR26	CA	43.784	35.606	56.592
193	TYR26	CB	43.004	35.88	55.308
194	TYR26	CG	43.125	34.783	54.252
195	TYR26	CD1	42.393	33.61	54.377
196	TYR26	CE1	42.521	32.608	53.423
197	TYR26	CZ	43.378	32.786	52.346
198	TYR26	OH	43.577	31.757	51.453
199	TYR26	CE2	44.098	33.964	52.208
200	TYR26	CD2	43.969	34.964	53.162
201	TYR26	C	45.189	35.13	56.236
202	TYR26	O	45.471	33.939	56.398
203	ILE27	N	46.108	36.049	55.988
204	ILE27	CA	47.455	35.628	55.591
205	ILE27	CB	48.165	36.79	54.905
206	ILE27	CG2	49.602	36.408	54.568
207	ILE27	CG1	47.432	37.204	53.636
208	ILE27	CD1	47.451	36.085	52.601
209	ILE27	C	48.282	35.137	56.777
210	ILE27	O	48.914	34.077	56.667
211	ALA28	N	48.064	35.71	57.95
212	ALA28	CA	48.816	35.25	59.123
213	ALA28	CB	48.823	36.354	60.171
214	ALA28	C	48.21	33.976	59.709
215	ALA28	O	48.942	33.08	60.15
216	SER29	N	46.918	33.799	59.487
217	SER29	CA	46.236	32.583	59.93
218	SER29	CB	44.776	32.899	60.225
219	SER29	OG	44.145	33.2	58.988
220	SER29	C	46.284	31.469	58.889
221	SER29	O	45.878	30.347	59.206
222	TYR30	N	46.922	31.697	57.75

Table 12

223	TYR30	CA	46.937	30.681	56.693
224	TYR30	CB	47.36	31.343	55.386
225	TYR30	CG	47.285	30.42	54.174
226	TYR30	CD1	46.057	30.175	53.572
227	TYR30	CE1	45.98	29.33	52.472
228	TYR30	CZ	47.133	28.734	51.98
229	TYR30	OH	47.06	27.902	50.885
230	TYR30	CE2	48.361	28.977	52.578
231	TYR30	CD2	48.436	29.823	53.678
232	TYR30	C	47.877	29.528	57.031
233	TYR30	O	47.524	28.367	56.788
234	GLY31	N	48.872	29.813	57.856
235	GLY31	CA	49.777	28.765	58.34
236	GLY31	C	49.276	28.164	59.654
237	GLY31	O	49.84	27.189	60.161
238	SER32	N	48.206	28.741	60.176
239	SER32	CA	47.602	28.29	61.426
240	SER32	CB	47.293	29.527	62.261
241	SER32	OG	48.479	30.309	62.323
242	SER32	C	46.309	27.514	61.171
243	SER32	O	45.659	27.072	62.127
244	LYS33	N	45.923	27.397	59.909
245	LYS33	CA	44.703	26.669	59.544
246	LYS33	CB	44.376	26.939	58.078
247	LYS33	CG	43.771	28.319	57.858
248	LYS33	CD	43.464	28.547	56.382
249	LYS33	CE	42.648	29.817	56.167
250	LYS33	NZ	43.346	30.996	56.697
251	LYS33	C	44.854	25.167	59.739
252	LYS33	O	44.734	24.647	60.855
253	LYS34	N	44.978	24.471	58.624
254	LYS34	CA	45.114	23.015	58.66
255	LYS34	CB	44.185	22.392	57.628
256	LYS34	CG	42.726	22.508	58.048
257	LYS34	CD	41.807	21.82	57.046
258	LYS34	CE	42.171	20.348	56.869
259	LYS34	NZ	42.041	19.601	58.131
260	LYS34	C	46.54	22.574	58.383
261	LYS34	O	47.288	23.228	57.651
262	ASP35	N	46.871	21.413	58.923
263	ASP35	CA	48.185	20.803	58.688
264	ASP35	CB	48.464	19.864	59.862
265	ASP35	CG	49.801	19.141	59.705
266	ASP35	OD1	49.784	18.021	59.214
267	ASP35	OD2	50.8	19.695	60.138
268	ASP35	C	48.208	20.019	57.373
269	ASP35	O	49.267	19.817	56.772
270	ASP36	N	47.031	19.689	56.869
271	ASP36	CA	46.935	18.925	55.624
272	ASP36	CB	45.951	17.772	55.812
273	ASP36	CG	46.412	16.824	56.919
274	ASP36	OD1	46.944	15.775	56.587
275	ASP36	OD2	46.1	17.11	58.07
276	ASP36	C	46.454	19.827	54.497
277	ASP36	O	47.258	20.556	53.896
278	TYR37	N	45.136	19.855	54.334

Table 12

279	TYR37	CA	44.437	20.613	53.276
280	TYR37	CB	44.204	22.028	53.813
281	TYR37	CG	42.966	22.75	53.276
282	TYR37	CD1	41.867	22.018	52.844
283	TYR37	CE1	40.747	22.674	52.35
284	TYR37	CZ	40.731	24.061	52.291
285	TYR37	OH	39.63	24.711	51.778
286	TYR37	CE2	41.826	24.796	52.725
287	TYR37	CD2	42.946	24.138	53.219
288	TYR37	C	45.252	20.626	51.978
289	TYR37	O	45.886	19.627	51.618
290	GLU38	N	45.291	21.767	51.315
291	GLU38	CA	46.163	21.911	50.151
292	GLU38	CB	45.486	22.723	49.04
293	GLU38	CG	44.802	24.021	49.477
294	GLU38	CD	45.791	25.093	49.927
295	GLU38	OE1	46.327	25.787	49.078
296	GLU38	OE2	45.998	25.17	51.132
297	GLU38	C	47.53	22.48	50.53
298	GLU38	O	48.36	22.669	49.64
299	TYR39	N	47.822	22.588	51.817
300	TYR39	CA	49.075	23.206	52.252
301	TYR39	CB	48.932	23.577	53.726
302	TYR39	CG	50.053	24.449	54.287
303	TYR39	CD1	49.914	25.831	54.281
304	TYR39	CE1	50.927	26.634	54.788
305	TYR39	CZ	52.075	26.051	55.305
306	TYR39	OH	53.087	26.847	55.795
307	TYR39	CE2	52.214	24.669	55.321
308	TYR39	CD2	51.2	23.868	54.815
309	TYR39	C	50.216	22.213	52.064
310	TYR39	O	51.216	22.548	51.42
311	CYS40	N	49.895	20.947	52.274
312	CYS40	CA	50.872	19.881	52.031
313	CYS40	CB	50.383	18.629	52.751
314	CYS40	SG	51.432	17.165	52.592
315	CYS40	C	51.036	19.587	50.536
316	CYS40	O	52.134	19.226	50.095
317	MET41	N	50.052	19.992	49.748
318	MET41	CA	50.1	19.771	48.303
319	MET41	CB	48.665	19.663	47.806
320	MET41	CG	47.902	18.589	48.571
321	MET41	SD	46.164	18.402	48.116
322	MET41	CE	46.376	18.033	46.359
323	MET41	C	50.798	20.93	47.598
324	MET41	O	51.459	20.729	46.575
325	SER42	N	50.81	22.078	48.255
326	SER42	CA	51.479	23.272	47.74
327	SER42	CB	50.635	24.494	48.076
328	SER42	OG	49.349	24.311	47.497
329	SER42	C	52.884	23.421	48.317
330	SER42	O	53.572	24.41	48.039
331	GLU43	N	53.375	22.364	48.946
332	GLU43	CA	54.723	22.368	49.52
333	GLU43	CB	54.838	21.152	50.436
334	GLU43	CG	56.117	21.155	51.266

Table 12

335	GLU43	CD	56.092	22.287	52.293
336	GLU43	OE1	57.164	22.666	52.744
337	GLU43	OE2	55.002	22.604	52.747
338	GLU43	C	55.817	22.318	48.444
339	GLU43	O	56.936	22.767	48.708
340	TYR44	N	55.443	22.024	47.205
341	TYR44	CA	56.393	22.079	46.084
342	TYR44	CB	55.927	21.153	44.957
343	TYR44	CG	54.778	21.667	44.085
344	TYR44	CD1	55.054	22.248	42.852
345	TYR44	CE1	54.018	22.717	42.055
346	TYR44	CZ	52.705	22.594	42.488
347	TYR44	OH	51.679	23.093	41.717
348	TYR44	CE2	52.423	21.999	43.709
349	TYR44	CD2	53.461	21.53	44.504
350	TYR44	C	56.566	23.504	45.543
351	TYR44	O	57.341	23.715	44.603
352	LEU45	N	55.823	24.453	46.09
353	LEU45	CA	56.012	25.861	45.762
354	LEU45	CB	54.913	26.321	44.796
355	LEU45	CG	53.481	26.016	45.245
356	LEU45	CD1	52.931	27.067	46.208
357	LEU45	CD2	52.562	25.948	44.032
358	LEU45	C	56.047	26.695	47.037
359	LEU45	O	55.905	27.924	46.97
360	ARG46	N	56.44	26.071	48.139
361	ARG46	CA	56.299	26.696	49.46
362	ARG46	CB	56.501	25.607	50.512
363	ARG46	CG	56.421	26.122	51.948
364	ARG46	CD	55.11	26.844	52.248
365	ARG46	NE	53.936	25.991	52.018
366	ARG46	CZ	52.882	26.412	51.316
367	ARG46	NH1	52.9	27.618	50.744
368	ARG46	NH2	51.828	25.615	51.156
369	ARG46	C	57.258	27.862	49.697
370	ARG46	O	56.849	28.838	50.336
371	MET47	N	58.357	27.913	48.965
372	MET47	CA	59.238	29.082	49.052
373	MET47	CB	60.536	28.757	48.322
374	MET47	CG	61.517	29.916	48.426
375	MET47	SD	61.957	30.378	50.115
376	MET47	CE	62.791	28.852	50.601
377	MET47	C	58.601	30.334	48.436
378	MET47	O	58.631	31.402	49.059
379	SER48	N	57.803	30.148	47.396
380	SER48	CA	57.133	31.289	46.774
381	SER48	CB	56.86	30.972	45.311
382	SER48	OG	58.116	30.786	44.673
383	SER48	C	55.83	31.59	47.505
384	SER48	O	55.477	32.762	47.664
385	GLY49	N	55.289	30.572	48.156
386	GLY49	CA	54.122	30.729	49.03
387	GLY49	C	54.44	31.642	50.209
388	GLY49	O	53.755	32.654	50.421
389	ILE50	N	55.581	31.391	50.832
390	ILE50	CA	56.039	32.211	51.955

Table 12

391	ILE50	CB	57.212	31.491	52.62
392	ILE50	CG2	57.839	32.354	53.706
393	ILE50	CG1	56.775	30.156	53.211
394	ILE50	CD1	55.746	30.343	54.322
395	ILE50	C	56.467	33.607	51.499
396	ILE50	O	56.145	34.583	52.187
397	TYR51	N	56.915	33.728	50.258
398	TYR51	CA	57.238	35.047	49.708
399	TYR51	CB	57.986	34.871	48.389
400	TYR51	CG	58.101	36.166	47.589
401	TYR51	CD1	58.85	37.227	48.082
402	TYR51	CE1	58.928	38.413	47.364
403	TYR51	CZ	58.257	38.532	46.155
404	TYR51	OH	58.276	39.731	45.477
405	TYR51	CE2	57.518	37.47	45.653
406	TYR51	CD2	57.44	36.285	46.373
407	TYR51	C	55.988	35.895	49.472
408	TYR51	O	55.978	37.062	49.884
409	TRP52	N	54.895	35.273	49.054
410	TRP52	CA	53.652	36.023	48.834
411	TRP52	CB	52.609	35.138	48.154
412	TRP52	CG	53.042	34.527	46.837
413	TRP52	CD1	53.845	35.097	45.873
414	TRP52	NE1	54.022	34.197	44.874
415	TRP52	CE2	53.354	33.054	45.124
416	TRP52	CZ2	53.269	31.845	44.45
417	TRP52	CH2	52.477	30.824	44.96
418	TRP52	CZ3	51.777	31.006	46.15
419	TRP52	CE3	51.874	32.206	46.843
420	TRP52	CD2	52.668	33.224	46.339
421	TRP52	C	53.096	36.487	50.17
422	TRP52	O	52.905	37.696	50.362
423	GLY53	N	53.145	35.584	51.138
424	GLY53	CA	52.709	35.871	52.509
425	GLY53	C	53.46	37.048	53.128
426	GLY53	O	52.844	38.072	53.451
427	LEU54	N	54.78	36.988	53.09
428	LEU54	CA	55.6	38.034	53.71
429	LEU54	CB	57.049	37.572	53.706
430	LEU54	CG	57.232	36.334	54.565
431	LEU54	CD1	58.663	35.833	54.479
432	LEU54	CD2	56.854	36.625	56.007
433	LEU54	C	55.536	39.369	52.979
434	LEU54	O	55.445	40.412	53.64
435	THR55	N	55.363	39.342	51.67
436	THR55	CA	55.323	40.601	50.935
437	THR55	CB	55.593	40.341	49.459
438	THR55	OG1	56.87	39.73	49.354
439	THR55	CG2	55.634	41.644	48.67
440	THR55	C	53.982	41.299	51.11
441	THR55	O	53.987	42.498	51.413
442	VAL56	N	52.906	40.539	51.253
443	VAL56	CA	51.608	41.19	51.44
444	VAL56	CB	50.467	40.277	50.972
445	VAL56	CG1	50.403	38.939	51.695
446	VAL56	CG2	49.121	40.977	51.078

Table 12

447	VAL56	C	51.427	41.652	52.887
448	VAL56	O	50.965	42.784	53.085
449	MET57	N	52.091	40.987	53.822
450	MET57	CA	52.038	41.442	55.212
451	MET57	CB	52.523	40.335	56.139
452	MET57	CG	51.568	39.149	56.13
453	MET57	SD	49.899	39.469	56.745
454	MET57	CE	50.262	39.707	58.497
455	MET57	C	52.899	42.679	55.401
456	MET57	O	52.426	43.65	56.003
457	ASP58	N	53.989	42.772	54.655
458	ASP58	CA	54.839	43.956	54.766
459	ASP58	CB	56.218	43.653	54.202
460	ASP58	CG	57.167	44.759	54.65
461	ASP58	OD1	56.97	45.248	55.753
462	ASP58	OD2	58.092	45.063	53.912
463	ASP58	C	54.246	45.156	54.031
464	ASP58	O	54.287	46.257	54.589
465	LEU59	N	53.452	44.91	53
466	LEU59	CA	52.771	46.009	52.302
467	LEU59	CB	52.25	45.506	50.959
468	LEU59	CG	53.369	45.239	49.96
469	LEU59	CD1	52.825	44.57	48.703
470	LEU59	CD2	54.102	46.526	49.607
471	LEU59	C	51.594	46.553	53.108
472	LEU59	O	51.255	47.736	52.983
473	MET60	N	51.069	45.742	54.012
474	MET60	CA	50.021	46.2	54.925
475	MET60	CB	49.055	45.044	55.153
476	MET60	CG	48.399	44.625	53.843
477	MET60	SD	47.168	43.309	53.965
478	MET60	CE	48.227	41.986	54.584
479	MET60	C	50.572	46.705	56.264
480	MET60	O	49.784	46.979	57.179
481	GLY61	N	51.891	46.703	56.42
482	GLY61	CA	52.545	47.214	57.638
483	GLY61	C	52.737	46.155	58.726
484	GLY61	O	53.5	46.35	59.68
485	GLN62	N	52.182	44.983	58.481
486	GLN62	CA	52.059	43.944	59.499
487	GLN62	CB	50.598	43.525	59.517
488	GLN62	CG	49.755	44.728	59.924
489	GLN62	CD	48.289	44.513	59.582
490	GLN62	OE1	47.583	43.74	60.239
491	GLN62	NE2	47.83	45.26	58.593
492	GLN62	C	52.983	42.762	59.24
493	GLN62	O	52.645	41.609	59.536
494	LEU63	N	54.229	43.079	58.919
495	LEU63	CA	55.242	42.036	58.699
496	LEU63	CB	56.409	42.643	57.928
497	LEU63	CG	57.451	41.593	57.556
498	LEU63	CD1	56.839	40.503	56.683
499	LEU63	CD2	58.651	42.226	56.86
500	LEU63	C	55.748	41.478	60.033
501	LEU63	O	56.136	40.305	60.106
502	HIS64	N	55.418	42.196	61.097

Table 12

503	HIS64	CA	55.759	41.82	62.472
504	HIS64	CB	55.662	43.082	63.332
505	HIS64	CG	54.331	43.818	63.248
506	HIS64	ND1	54.087	44.973	62.597
507	HIS64	CE1	52.789	45.306	62.751
508	HIS64	NE2	52.211	44.358	63.523
509	HIS64	CD2	53.151	43.443	63.847
510	HIS64	C	54.848	40.729	63.052
511	HIS64	O	55.036	40.327	64.205
512	ARG65	N	53.862	40.283	62.286
513	ARG65	CA	53.015	39.171	62.716
514	ARG65	CB	51.613	39.387	62.159
515	ARG65	CG	50.974	40.658	62.703
516	ARG65	CD	49.588	40.867	62.105
517	ARG65	NE	48.736	39.69	62.339
518	ARG65	CZ	47.448	39.639	61.992
519	ARG65	NH1	46.868	40.699	61.427
520	ARG65	NH2	46.734	38.536	62.23
521	ARG65	C	53.545	37.831	62.207
522	ARG65	O	53.041	36.775	62.606
523	MET66	N	54.553	37.873	61.351
524	MET66	CA	55.078	36.644	60.75
525	MET66	CB	55.528	36.967	59.334
526	MET66	CG	54.366	37.52	58.515
527	MET66	SD	52.934	36.427	58.341
528	MET66	CE	53.706	35.061	57.443
529	MET66	C	56.223	36.029	61.553
530	MET66	O	56.938	36.709	62.301
531	ASN67	N	56.396	34.731	61.363
532	ASN67	CA	57.419	33.95	62.078
533	ASN67	CB	56.968	32.491	62.088
534	ASN67	CG	55.602	32.344	62.76
535	ASN67	OD1	54.558	32.415	62.102
536	ASN67	ND2	55.637	32.042	64.045
537	ASN67	C	58.79	34.037	61.406
538	ASN67	O	59.329	33.013	60.961
539	ARG68	N	59.44	35.178	61.58
540	ARG68	CA	60.693	35.5	60.876
541	ARG68	CB	61.153	36.87	61.353
542	ARG68	CG	62.48	37.255	60.71
543	ARG68	CD	63.122	38.42	61.448
544	ARG68	NE	63.297	38.068	62.867
545	ARG68	CZ	64.426	37.568	63.379
546	ARG68	NH1	64.456	37.166	64.651
547	ARG68	NH2	65.493	37.383	62.598
548	ARG68	C	61.835	34.516	61.117
549	ARG68	O	62.373	33.979	60.143
550	GLU69	N	62.01	34.073	62.353
551	GLU69	CA	63.126	33.17	62.662
552	GLU69	CB	63.289	33.126	64.177
553	GLU69	CG	64.43	32.206	64.599
554	GLU69	CD	64.48	32.111	66.121
555	GLU69	OE1	65.118	32.963	66.721
556	GLU69	OE2	63.754	31.283	66.654
557	GLU69	C	62.904	31.748	62.138
558	GLU69	O	63.856	31.121	61.657

Table 12

559	GLU70	N	61.649	31.372	61.96
560	GLU70	CA	61.345	30.023	61.485
561	GLU70	CB	59.984	29.637	62.044
562	GLU70	CG	60.063	29.553	63.564
563	GLU70	CD	58.671	29.616	64.179
564	GLU70	OE1	58.02	28.586	64.258
565	GLU70	OE2	58.276	30.718	64.545
566	GLU70	C	61.347	29.991	59.963
567	GLU70	O	61.813	29.012	59.366
568	ILE71	N	61.122	31.154	59.376
569	ILE71	CA	61.21	31.298	57.926
570	ILE71	CB	60.431	32.55	57.542
571	ILE71	CG2	60.629	32.888	56.069
572	ILE71	CG1	58.954	32.362	57.862
573	ILE71	CD1	58.158	33.637	57.617
574	ILE71	C	62.665	31.422	57.49
575	ILE71	O	63.06	30.787	56.506
576	LEU72	N	63.491	31.955	58.375
577	LEU72	CA	64.928	32.059	58.103
578	LEU72	CB	65.554	32.999	59.131
579	LEU72	CG	65.957	34.352	58.546
580	LEU72	CD1	64.79	35.083	57.889
581	LEU72	CD2	66.588	35.228	59.622
582	LEU72	C	65.598	30.693	58.195
583	LEU72	O	66.353	30.324	57.285
584	ALA73	N	65.113	29.864	59.108
585	ALA73	CA	65.634	28.5	59.226
586	ALA73	CB	65.173	27.918	60.557
587	ALA73	C	65.149	27.611	58.083
588	ALA73	O	65.958	26.872	57.505
589	PHE74	N	63.949	27.887	57.594
590	PHE74	CA	63.408	27.149	56.451
591	PHE74	CB	61.937	27.527	56.291
592	PHE74	CG	61.237	26.906	55.084
593	PHE74	CD1	61.015	25.536	55.034
594	PHE74	CE1	60.377	24.975	53.935
595	PHE74	CZ	59.959	25.784	52.886
596	PHE74	CE2	60.178	27.155	52.937
597	PHE74	CD2	60.817	27.715	54.035
598	PHE74	C	64.165	27.476	55.168
599	PHE74	O	64.663	26.549	54.521
600	ILE75	N	64.508	28.741	54.982
601	ILE75	CA	65.232	29.158	53.775
602	ILE75	CB	65.159	30.676	53.689
603	ILE75	CG2	66.016	31.212	52.551
604	ILE75	CG1	63.722	31.135	53.515
605	ILE75	CD1	63.658	32.651	53.45
606	ILE75	C	66.694	28.721	53.789
607	ILE75	O	67.193	28.237	52.763
608	LYS76	N	67.263	28.61	54.979
609	LYS76	CA	68.647	28.15	55.095
610	LYS76	CB	69.14	28.518	56.489
611	LYS76	CG	70.616	28.191	56.67
612	LYS76	CD	71.106	28.629	58.044
613	LYS76	CE	72.593	28.343	58.213
614	LYS76	NZ	73.067	28.789	59.533

Table 12

615	LYS76	C	68.747	26.639	54.881
616	LYS76	O	69.69	26.176	54.23
617	SER77	N	67.661	25.939	55.168
618	SER77	CA	67.589	24.495	54.929
619	SER77	CB	66.669	23.893	55.981
620	SER77	OG	67.19	24.24	57.256
621	SER77	C	67.064	24.157	53.53
622	SER77	O	66.946	22.976	53.178
623	CYS78	N	66.704	25.174	52.763
624	CYS78	CA	66.282	24.96	51.383
625	CYS78	CB	65.125	25.89	51.046
626	CYS78	SG	63.546	25.496	51.825
627	CYS78	C	67.413	25.203	50.395
628	CYS78	O	67.296	24.783	49.238
629	GLN79	N	68.482	25.863	50.812
630	GLN79	CA	69.61	26.021	49.888
631	GLN79	CB	70.543	27.143	50.334
632	GLN79	CG	71.732	27.223	49.377
633	GLN79	CD	72.624	28.427	49.635
634	GLN79	OE1	73.014	28.723	50.774
635	GLN79	NE2	72.908	29.13	48.555
636	GLN79	C	70.395	24.72	49.779
637	GLN79	O	70.88	24.178	50.777
638	HIS80	N	70.483	24.21	48.565
639	HIS80	CA	71.26	22.997	48.324
640	HIS80	CB	70.639	22.196	47.183
641	HIS80	CG	69.405	21.404	47.59
642	HIS80	ND1	69.162	20.112	47.303
643	HIS80	CE1	67.982	19.747	47.841
644	HIS80	NE2	67.467	20.825	48.474
645	HIS80	CD2	68.332	21.854	48.325
646	HIS80	C	72.713	23.351	48.04
647	HIS80	O	73.042	24.509	47.757
648	GLU81	N	73.548	22.326	47.956
649	GLU81	CA	75.004	22.519	47.798
650	GLU81	CB	75.712	21.209	48.129
651	GLU81	CG	75.549	20.82	49.595
652	GLU81	CD	76.197	21.864	50.505
653	GLU81	OE1	75.453	22.659	51.062
654	GLU81	OE2	77.393	21.756	50.732
655	GLU81	C	75.453	22.983	46.406
656	GLU81	O	76.638	23.27	46.213
657	CYS82	N	74.526	23.093	45.468
658	CYS82	CA	74.834	23.662	44.155
659	CYS82	CB	74.071	22.89	43.087
660	CYS82	SG	72.273	22.938	43.24
661	CYS82	C	74.455	25.144	44.092
662	CYS82	O	74.459	25.739	43.008
663	GLY83	N	73.977	25.683	45.203
664	GLY83	CA	73.634	27.104	45.265
665	GLY83	C	72.135	27.333	45.248
666	GLY83	O	71.602	28.124	46.041
667	GLY84	N	71.498	26.683	44.289
668	GLY84	CA	70.053	26.769	44.085
669	GLY84	C	69.241	26.441	45.322
670	GLY84	O	69.542	25.515	46.088

Table 12

671	ILE85	N	68.202	27.232	45.497
672	ILE85	CA	67.308	27.072	46.629
673	ILE85	CB	66.971	28.473	47.123
674	ILE85	CG2	66.144	28.43	48.403
675	ILE85	CG1	68.274	29.233	47.357
676	ILE85	CD1	68.041	30.711	47.635
677	ILE85	C	66.077	26.306	46.165
678	ILE85	O	65.594	26.501	45.04
679	SER86	N	65.767	25.27	46.919
680	SER86	CA	64.601	24.433	46.656
681	SER86	CB	64.751	23.131	47.425
682	SER86	OG	64.727	23.429	48.813
683	SER86	C	63.322	25.123	47.103
684	SER86	O	63.343	26.102	47.857
685	ALA87	N	62.208	24.567	46.659
686	ALA87	CA	60.884	25.1	47.009
687	ALA87	CB	59.902	24.587	45.976
688	ALA87	C	60.403	24.641	48.38
689	ALA87	O	59.413	25.159	48.912
690	SER88	N	61.093	23.642	48.898
691	SER88	CA	60.869	23.084	50.228
692	SER88	CB	59.593	22.255	50.214
693	SER88	OG	59.457	21.603	51.467
694	SER88	C	62.07	22.204	50.522
695	SER88	O	62.657	21.673	49.574
696	ILE89	N	62.447	22.078	51.784
697	ILE89	CA	63.637	21.303	52.175
698	ILE89	CB	63.595	21.164	53.694
699	ILE89	CG2	64.839	20.455	54.22
700	ILE89	CG1	63.454	22.535	54.346
701	ILE89	CD1	63.31	22.421	55.86
702	ILE89	C	63.661	19.916	51.523
703	ILE89	O	62.649	19.204	51.525
704	GLY90	N	64.719	19.663	50.765
705	GLY90	CA	64.898	18.359	50.11
706	GLY90	C	64.479	18.336	48.635
707	GLY90	O	64.821	17.395	47.909
708	HIS91	N	63.726	19.338	48.213
709	HIS91	CA	63.198	19.393	46.841
710	HIS91	CB	61.998	20.342	46.779
711	HIS91	CG	60.687	19.876	47.404
712	HIS91	ND1	60.497	19.209	48.563
713	HIS91	CE1	59.179	18.995	48.748
714	HIS91	NE2	58.526	19.544	47.701
715	HIS91	CD2	59.439	20.093	46.869
716	HIS91	C	64.267	19.88	45.871
717	HIS91	O	65.34	20.322	46.291
718	ASP92	N	63.974	19.799	44.585
719	ASP92	CA	64.925	20.278	43.567
720	ASP92	CB	64.394	19.995	42.159
721	ASP92	CG	64.699	18.567	41.702
722	ASP92	OD1	64.601	17.666	42.524
723	ASP92	OD2	64.959	18.397	40.517
724	ASP92	C	65.189	21.775	43.704
725	ASP92	O	64.275	22.564	43.98
726	PRO93	N	66.465	22.115	43.641

Table 12

727	PRO93	CA	66.889	23.507	43.494
728	PRO93	CB	68.384	23.466	43.524
729	PRO93	CG	68.846	22.019	43.568
730	PRO93	CD	67.586	21.175	43.579
731	PRO93	C	66.371	24.097	42.186
732	PRO93	O	66.435	23.466	41.122
733	HIS94	N	65.828	25.295	42.293
734	HIS94	CA	65.232	25.945	41.128
735	HIS94	CB	63.742	25.638	41.179
736	HIS94	CG	63.023	25.69	39.85
737	HIS94	ND1	62.769	24.639	39.052
738	HIS94	CE1	62.107	25.06	37.957
739	HIS94	NE2	61.937	26.396	38.069
740	HIS94	CD2	62.491	26.797	39.235
741	HIS94	C	65.467	27.449	41.193
742	HIS94	O	65.287	28.058	42.252
743	LEU95	N	65.691	28.067	40.045
744	LEU95	CA	65.985	29.507	39.993
745	LEU95	CB	66.46	29.808	38.576
746	LEU95	CG	67.029	31.211	38.422
747	LEU95	CD1	68.116	31.481	39.457
748	LEU95	CD2	67.575	31.402	37.013
749	LEU95	C	64.789	30.401	40.352
750	LEU95	O	64.993	31.47	40.936
751	LEU96	N	63.582	29.863	40.274
752	LEU96	CA	62.395	30.616	40.696
753	LEU96	CB	61.168	29.902	40.139
754	LEU96	CG	59.862	30.546	40.589
755	LEU96	CD1	59.724	31.958	40.03
756	LEU96	CD2	58.672	29.689	40.174
757	LEU96	C	62.284	30.678	42.22
758	LEU96	O	62.025	31.751	42.78
759	TYR97	N	62.747	29.629	42.88
760	TYR97	CA	62.669	29.577	44.339
761	TYR97	CB	62.431	28.135	44.759
762	TYR97	CG	61.13	27.578	44.188
763	TYR97	CD1	61.161	26.567	43.235
764	TYR97	CE1	59.976	26.067	42.712
765	TYR97	CZ	58.762	26.579	43.146
766	TYR97	OH	57.586	26.021	42.696
767	TYR97	CE2	58.726	27.593	44.094
768	TYR97	CD2	59.913	28.093	44.615
769	TYR97	C	63.943	30.141	44.95
770	TYR97	O	63.916	30.697	46.055
771	THR98	N	64.964	30.233	44.116
772	THR98	CA	66.181	30.952	44.481
773	THR98	CB	67.272	30.614	43.468
774	THR98	OG1	67.564	29.227	43.573
775	THR98	CG2	68.558	31.379	43.746
776	THR98	C	65.901	32.45	44.478
777	THR98	O	66.176	33.118	45.483
778	LEU99	N	65.101	32.889	43.517
779	LEU99	CA	64.678	34.289	43.466
780	LEU99	CB	63.958	34.543	42.146
781	LEU99	CG	63.39	35.957	42.095
782	LEU99	CD1	64.49	37.003	42.215

Table 12

783	LEU99	CD2	62.563	36.189	40.836
784	LEU99	C	63.738	34.622	44.618
785	LEU99	O	64.053	35.543	45.381
786	SER100	N	62.825	33.714	44.925
787	SER100	CA	61.867	33.947	46.013
788	SER100	CB	60.834	32.826	46.006
789	SER100	OG	60.151	32.859	44.76
790	SER100	C	62.542	34.001	47.382
791	SER100	O	62.311	34.963	48.125
792	ALA101	N	63.558	33.177	47.588
793	ALA101	CA	64.267	33.192	48.869
794	ALA101	CB	65.054	31.9	49.01
795	ALA101	C	65.217	34.377	48.999
796	ALA101	O	65.276	34.976	50.079
797	VAL102	N	65.722	34.871	47.88
798	VAL102	CA	66.559	36.074	47.913
799	VAL102	CB	67.356	36.16	46.614
800	VAL102	CG1	68.001	37.529	46.427
801	VAL102	CG2	68.409	35.059	46.548
802	VAL102	C	65.708	37.328	48.103
803	VAL102	O	66.104	38.212	48.872
804	GLN103	N	64.458	37.273	47.675
805	GLN103	CA	63.549	38.394	47.906
806	GLN103	CB	62.376	38.267	46.948
807	GLN103	CG	62.841	38.34	45.502
808	GLN103	CD	61.654	38.188	44.562
809	GLN103	OE1	61.201	37.072	44.272
810	GLN103	NE2	61.181	39.323	44.08
811	GLN103	C	63.037	38.409	49.342
812	GLN103	O	62.981	39.486	49.948
813	ILE104	N	62.94	37.239	49.954
814	ILE104	CA	62.553	37.173	51.366
815	ILE104	CB	62.145	35.746	51.702
816	ILE104	CG2	61.878	35.616	53.195
817	ILE104	CG1	60.923	35.313	50.907
818	ILE104	CD1	60.579	33.855	51.189
819	ILE104	C	63.707	37.577	52.279
820	ILE104	O	63.497	38.348	53.224
821	LEU105	N	64.926	37.287	51.855
822	LEU105	CA	66.092	37.695	52.639
823	LEU105	CB	67.258	36.773	52.317
824	LEU105	CG	66.981	35.337	52.746
825	LEU105	CD1	68.155	34.439	52.383
826	LEU105	CD2	66.68	35.242	54.239
827	LEU105	C	66.48	39.149	52.38
828	LEU105	O	67.214	39.741	53.178
829	THR106	N	65.918	39.757	51.351
830	THR106	CA	66.075	41.198	51.177
831	THR106	CB	65.913	41.527	49.696
832	THR106	OG1	66.984	40.913	48.992
833	THR106	CG2	65.982	43.026	49.433
834	THR106	C	65.017	41.928	51.999
835	THR106	O	65.346	42.876	52.723
836	LEU107	N	63.865	41.287	52.128
837	LEU107	CA	62.733	41.856	52.867
838	LEU107	CB	61.511	41.017	52.506

Table 12

839	LEU107	CG	60.217	41.625	53.024
840	LEU107	CD1	60	42.995	52.401
841	LEU107	CD2	59.037	40.711	52.719
842	LEU107	C	62.949	41.81	54.381
843	LEU107	O	62.571	42.746	55.094
844	TYR108	N	63.632	40.778	54.846
845	TYR108	CA	64.003	40.685	56.263
846	TYR108	CB	63.937	39.224	56.692
847	TYR108	CG	62.548	38.729	57.086
848	TYR108	CD1	62.162	37.427	56.793
849	TYR108	CE1	60.907	36.971	57.177
850	TYR108	CZ	60.041	37.822	57.852
851	TYR108	OH	58.87	37.325	58.382
852	TYR108	CE2	60.417	39.128	58.129
853	TYR108	CD2	61.672	39.582	57.746
854	TYR108	C	65.4	41.226	56.565
855	TYR108	O	65.791	41.261	57.738
856	ASP109	N	66.091	41.717	55.543
857	ASP109	CA	67.51	42.101	55.642
858	ASP109	CB	67.635	43.436	56.369
859	ASP109	CG	69.061	43.959	56.234
860	ASP109	OD1	69.698	43.612	55.249
861	ASP109	OD2	69.506	44.65	57.139
862	ASP109	C	68.305	41.002	56.352
863	ASP109	O	68.882	41.186	57.431
864	SER110	N	68.314	39.848	55.712
865	SER110	CA	68.906	38.639	56.276
866	SER110	CB	67.822	37.86	57.011
867	SER110	OG	67.286	38.693	58.032
868	SER110	C	69.486	37.772	55.168
869	SER110	O	69.478	36.538	55.266
870	ILE111	N	70.163	38.414	54.227
871	ILE111	CA	70.766	37.686	53.099
872	ILE111	CB	71.137	38.684	52.001
873	ILE111	CG2	69.905	39.172	51.249
874	ILE111	CG1	71.921	39.865	52.566
875	ILE111	CD1	72.294	40.859	51.474
876	ILE111	C	72.004	36.881	53.507
877	ILE111	O	72.225	35.809	52.933
878	ASN112	N	72.515	37.178	54.695
879	ASN112	CA	73.7	36.531	55.268
880	ASN112	CB	74.252	37.463	56.345
881	ASN112	CG	74.176	38.93	55.915
882	ASN112	OD1	74.607	39.307	54.818
883	ASN112	ND2	73.6	39.743	56.787
884	ASN112	C	73.374	35.185	55.927
885	ASN112	O	74.259	34.549	56.511
886	VAL113	N	72.109	34.789	55.888
887	VAL113	CA	71.699	33.489	56.425
888	VAL113	CB	70.24	33.614	56.865
889	VAL113	CG1	69.665	32.297	57.378
890	VAL113	CG2	70.095	34.697	57.927
891	VAL113	C	71.859	32.405	55.357
892	VAL113	O	71.957	31.212	55.671
893	ILE114	N	72.005	32.836	54.115
894	ILE114	CA	72.216	31.892	53.021

Table 12

895	ILE114	CB	70.98	31.96	52.127
896	ILE114	CG2	71.214	32.787	50.863
897	ILE114	CG1	70.51	30.556	51.777
898	ILE114	CD1	69.216	30.587	50.981
899	ILE114	C	73.518	32.233	52.289
900	ILE114	O	74.014	33.362	52.387
901	ASP115	N	74.135	31.239	51.672
902	ASP115	CA	75.386	31.489	50.952
903	ASP115	CB	76.126	30.165	50.768
904	ASP115	CG	77.567	30.411	50.329
905	ASP115	OD1	78.464	30.038	51.068
906	ASP115	OD2	77.743	31.011	49.274
907	ASP115	C	75.088	32.152	49.606
908	ASP115	O	74.808	31.484	48.599
909	VAL116	N	75.373	33.444	49.562
910	VAL116	CA	75.068	34.274	48.392
911	VAL116	CB	75.13	35.733	48.848
912	VAL116	CG1	76.289	35.988	49.807
913	VAL116	CG2	75.168	36.708	47.676
914	VAL116	C	76.003	34.044	47.203
915	VAL116	O	75.519	34.038	46.064
916	ASN117	N	77.187	33.513	47.457
917	ASN117	CA	78.139	33.274	46.369
918	ASN117	CB	79.538	33.235	46.968
919	ASN117	CG	79.834	34.579	47.627
920	ASN117	OD1	79.688	34.745	48.845
921	ASN117	ND2	80.167	35.549	46.793
922	ASN117	C	77.83	31.965	45.658
923	ASN117	O	77.951	31.886	44.429
924	LYS118	N	77.129	31.1	46.371
925	LYS118	CA	76.681	29.834	45.806
926	LYS118	CB	76.4	28.895	46.974
927	LYS118	CG	76.771	27.451	46.66
928	LYS118	CD	78.277	27.271	46.519
929	LYS118	CE	78.997	27.572	47.83
930	LYS118	NZ	78.563	26.65	48.892
931	LYS118	C	75.412	30.063	44.988
932	LYS118	O	75.271	29.492	43.899
933	VAL119	N	74.662	31.09	45.363
934	VAL119	CA	73.474	31.483	44.596
935	VAL119	CB	72.665	32.485	45.415
936	VAL119	CG1	71.565	33.126	44.582
937	VAL119	CG2	72.081	31.859	46.671
938	VAL119	C	73.883	32.145	43.284
939	VAL119	O	73.381	31.756	42.22
940	VAL120	N	74.981	32.885	43.333
941	VAL120	CA	75.52	33.525	42.13
942	VAL120	CB	76.6	34.514	42.562
943	VAL120	CG1	77.342	35.091	41.364
944	VAL120	CG2	76.019	35.629	43.422
945	VAL120	C	76.123	32.505	41.166
946	VAL120	O	75.879	32.597	39.956
947	GLU121	N	76.634	31.409	41.705
948	GLU121	CA	77.197	30.354	40.86
949	GLU121	CB	78.138	29.524	41.719
950	GLU121	CG	79.338	30.365	42.136

Table 12

951	GLU121	CD	80.1	29.68	43.263
952	GLU121	OE1	79.445	29.111	44.125
953	GLU121	OE2	81.312	29.836	43.308
954	GLU121	C	76.117	29.47	40.24
955	GLU121	O	76.265	29.077	39.075
956	TYR122	N	74.957	29.404	40.875
957	TYR122	CA	73.83	28.679	40.286
958	TYR122	CB	72.786	28.458	41.372
959	TYR122	CG	71.555	27.664	40.941
960	TYR122	CD1	71.688	26.35	40.507
961	TYR122	CE1	70.563	25.625	40.132
962	TYR122	CZ	69.308	26.214	40.198
963	TYR122	OH	68.2	25.524	39.752
964	TYR122	CE2	69.172	27.524	40.64
965	TYR122	CD2	70.297	28.25	41.011
966	TYR122	C	73.215	29.483	39.146
967	TYR122	O	73.021	28.936	38.053
968	VAL123	N	73.202	30.798	39.303
969	VAL123	CA	72.686	31.678	38.249
970	VAL123	CB	72.539	33.078	38.836
971	VAL123	CG1	72.183	34.096	37.763
972	VAL123	CG2	71.514	33.102	39.963
973	VAL123	C	73.631	31.719	37.047
974	VAL123	O	73.186	31.509	35.91
975	LYS124	N	74.922	31.659	37.334
976	LYS124	CA	75.947	31.652	36.285
977	LYS124	CB	77.296	31.814	36.985
978	LYS124	CG	78.472	31.835	36.014
979	LYS124	CD	78.441	33.071	35.126
980	LYS124	CE	79.599	33.084	34.134
981	LYS124	NZ	79.54	34.272	33.267
982	LYS124	C	75.946	30.348	35.485
983	LYS124	O	76.015	30.403	34.25
984	GLY125	N	75.588	29.255	36.144
985	GLY125	CA	75.568	27.929	35.513
986	GLY125	C	74.278	27.623	34.75
987	GLY125	O	74.262	26.719	33.907
988	LEU126	N	73.213	28.354	35.041
989	LEU126	CA	71.959	28.181	34.297
990	LEU126	CB	70.798	28.594	35.186
991	LEU126	CG	70.643	27.665	36.378
992	LEU126	CD1	69.62	28.234	37.345
993	LEU126	CD2	70.258	26.255	35.943
994	LEU126	C	71.92	29.033	33.034
995	LEU126	O	70.995	28.902	32.223
996	GLN127	N	72.896	29.913	32.9
997	GLN127	CA	73.019	30.775	31.726
998	GLN127	CB	74.011	31.846	32.13
999	GLN127	CG	74.282	32.885	31.059
1000	GLN127	CD	75.405	33.739	31.617
1001	GLN127	OE1	75.555	34.921	31.292
1002	GLN127	NE2	76.157	33.127	32.514
1003	GLN127	C	73.565	30.008	30.528
1004	GLN127	O	74.714	29.552	30.537
1005	LYS128	N	72.753	29.908	29.493
1006	LYS128	CA	73.155	29.176	28.29

Table 12

1007	LYS128	CB	71.918	28.602	27.62
1008	LYS128	CG	71.157	27.714	28.593
1009	LYS128	CD	71.968	26.515	29.07
1010	LYS128	CE	71.18	25.72	30.106
1011	LYS128	NZ	71.954	24.571	30.598
1012	LYS128	C	73.903	30.069	27.313
1013	LYS128	O	73.984	31.291	27.487
1014	GLU129	N	74.282	29.473	26.194
1015	GLU129	CA	75.105	30.16	25.184
1016	GLU129	CB	75.707	29.129	24.225
1017	GLU129	CG	76.667	28.148	24.899
1018	GLU129	CD	76.027	26.768	25.051
1019	GLU129	OE1	74.834	26.729	25.333
1020	GLU129	OE2	76.744	25.786	24.937
1021	GLU129	C	74.322	31.181	24.354
1022	GLU129	O	74.92	31.99	23.639
1023	ASP130	N	73.005	31.165	24.473
1024	ASP130	CA	72.171	32.153	23.789
1025	ASP130	CB	70.988	31.448	23.128
1026	ASP130	CG	70.045	30.863	24.174
1027	ASP130	OD1	69.159	31.593	24.596
1028	ASP130	OD2	70.285	29.745	24.609
1029	ASP130	C	71.678	33.239	24.75
1030	ASP130	O	70.8	34.029	24.386
1031	GLY131	N	72.13	33.195	25.995
1032	GLY131	CA	71.702	34.194	26.98
1033	GLY131	C	70.707	33.639	27.996
1034	GLY131	O	70.881	33.824	29.207
1035	SER132	N	69.681	32.974	27.483
1036	SER132	CA	68.594	32.403	28.296
1037	SER132	CB	67.827	31.415	27.436
1038	SER132	OG	68.718	30.364	27.084
1039	SER132	C	69.058	31.638	29.523
1040	SER132	O	70.073	30.932	29.509
1041	PHE133	N	68.308	31.82	30.594
1042	PHE133	CA	68.565	31.067	31.815
1043	PHE133	CB	68.489	31.997	33.02
1044	PHE133	CG	69.614	33.025	33.105
1045	PHE133	CD1	69.51	34.246	32.45
1046	PHE133	CE1	70.539	35.173	32.533
1047	PHE133	CZ	71.671	34.882	33.278
1048	PHE133	CE2	71.772	33.668	33.944
1049	PHE133	CD2	70.744	32.74	33.858
1050	PHE133	C	67.566	29.931	31.966
1051	PHE133	O	66.417	30.012	31.504
1052	ALA134	N	68.096	28.813	32.425
1053	ALA134	CA	67.276	27.655	32.771
1054	ALA134	CB	68.122	26.395	32.631
1055	ALA134	C	66.767	27.78	34.203
1056	ALA134	O	67.438	28.355	35.065
1057	GLY135	N	65.55	27.319	34.423
1058	GLY135	CA	64.985	27.309	35.777
1059	GLY135	C	65.741	26.306	36.633
1060	GLY135	O	66.395	26.661	37.62
1061	ASP136	N	65.503	25.045	36.341
1062	ASP136	CA	66.294	23.968	36.927

Table 12

1063	ASP136	CB	65.384	22.791	37.279
1064	ASP136	CG	64.51	22.357	36.1
1065	ASP136	OD1	65.055	22.194	35.012
1066	ASP136	OD2	63.361	22.029	36.349
1067	ASP136	C	67.409	23.546	35.975
1068	ASP136	O	67.361	23.826	34.765
1069	ILE137	N	68.26	22.671	36.488
1070	ILE137	CA	69.451	22.173	35.768
1071	ILE137	CB	70.447	21.562	36.764
1072	ILE137	CG2	70.653	22.509	37.942
1073	ILE137	CG1	70.054	20.167	37.273
1074	ILE137	CD1	69.09	20.17	38.459
1075	ILE137	C	69.173	21.138	34.667
1076	ILE137	O	70.12	20.638	34.051
1077	TRP138	N	67.908	20.886	34.36
1078	TRP138	CA	67.547	19.932	33.313
1079	TRP138	CB	66.201	19.314	33.679
1080	TRP138	CG	66.215	18.583	35.01
1081	TRP138	CD1	65.637	18.992	36.193
1082	TRP138	NE1	65.888	18.055	37.143
1083	TRP138	CE2	66.607	17.034	36.639
1084	TRP138	CZ2	67.107	15.868	37.199
1085	TRP138	CH2	67.829	14.979	36.411
1086	TRP138	CZ3	68.055	15.253	35.067
1087	TRP138	CE3	67.56	16.42	34.498
1088	TRP138	CD2	66.84	17.31	35.279
1089	TRP138	C	67.473	20.603	31.939
1090	TRP138	O	67.276	19.923	30.925
1091	GLY139	N	67.644	21.916	31.908
1092	GLY139	CA	67.69	22.639	30.633
1093	GLY139	C	66.352	23.299	30.342
1094	GLY139	O	65.906	23.383	29.19
1095	GLU140	N	65.754	23.826	31.395
1096	GLU140	CA	64.424	24.442	31.31
1097	GLU140	CB	63.816	24.274	32.693
1098	GLU140	CG	62.367	24.724	32.806
1099	GLU140	CD	62.053	24.741	34.292
1100	GLU140	OE1	63.021	24.737	35.041
1101	GLU140	OE2	60.89	24.746	34.66
1102	GLU140	C	64.52	25.927	30.944
1103	GLU140	O	64.366	26.798	31.809
1104	ILE141	N	64.755	26.186	29.668
1105	ILE141	CA	65.003	27.543	29.15
1106	ILE141	CB	65.631	27.358	27.769
1107	ILE141	CG2	65.662	28.645	26.953
1108	ILE141	CG1	67.032	26.793	27.931
1109	ILE141	CD1	67.837	27.695	28.854
1110	ILE141	C	63.744	28.396	29.044
1111	ILE141	O	62.747	27.967	28.451
1112	ASP142	N	63.791	29.588	29.625
1113	ASP142	CA	62.645	30.501	29.515
1114	ASP142	CB	61.535	29.924	30.394
1115	ASP142	CG	60.164	30.46	30.003
1116	ASP142	OD1	59.82	31.521	30.513
1117	ASP142	OD2	59.499	29.829	29.198
1118	ASP142	C	63.008	31.929	29.953

Table 12

1119	ASP142	O	63.785	32.125	30.898
1120	THR143	N	62.321	32.912	29.383
1121	THR143	CA	62.517	34.321	29.784
1122	THR143	CB	61.731	35.245	28.858
1123	THR143	OG1	60.354	34.891	28.903
1124	THR143	CG2	62.199	35.159	27.418
1125	THR143	C	62.066	34.637	31.212
1126	THR143	O	62.637	35.541	31.827
1127	ARG144	N	61.245	33.786	31.809
1128	ARG144	CA	60.841	33.994	33.199
1129	ARG144	CB	59.636	33.109	33.485
1130	ARG144	CG	59.134	33.291	34.911
1131	ARG144	CD	57.901	32.438	35.171
1132	ARG144	NE	57.345	32.714	36.504
1133	ARG144	CZ	56.78	31.775	37.265
1134	ARG144	NH1	56.761	30.506	36.852
1135	ARG144	NH2	56.272	32.098	38.456
1136	ARG144	C	61.967	33.621	34.155
1137	ARG144	O	62.222	34.359	35.111
1138	PHE145	N	62.816	32.706	33.72
1139	PHE145	CA	63.935	32.277	34.555
1140	PHE145	CB	64.195	30.805	34.281
1141	PHE145	CG	62.971	29.947	34.584
1142	PHE145	CD1	62.477	29.074	33.624
1143	PHE145	CE1	61.355	28.303	33.898
1144	PHE145	CZ	60.726	28.406	35.132
1145	PHE145	CE2	61.22	29.278	36.093
1146	PHE145	CD2	62.342	30.048	35.82
1147	PHE145	C	65.156	33.134	34.259
1148	PHE145	O	65.986	33.369	35.144
1149	SER146	N	65.095	33.825	33.134
1150	SER146	CA	66.104	34.834	32.831
1151	SER146	CB	66.066	35.125	31.334
1152	SER146	OG	66.328	33.901	30.651
1153	SER146	C	65.823	36.095	33.65
1154	SER146	O	66.753	36.671	34.233
1155	PHE147	N	64.548	36.328	33.922
1156	PHE147	CA	64.134	37.407	34.824
1157	PHE147	CB	62.643	37.65	34.619
1158	PHE147	CG	61.99	38.534	35.677
1159	PHE147	CD1	62.496	39.799	35.949
1160	PHE147	CE1	61.897	40.593	36.917
1161	PHE147	CZ	60.79	40.124	37.612
1162	PHE147	CE2	60.282	38.861	37.34
1163	PHE147	CD2	60.883	38.066	36.373
1164	PHE147	C	64.399	37.052	36.286
1165	PHE147	O	64.882	37.908	37.038
1166	CYS148	N	64.312	35.775	36.62
1167	CYS148	CA	64.647	35.343	37.979
1168	CYS148	CB	64.276	33.875	38.157
1169	CYS148	SG	62.513	33.488	38.089
1170	CYS148	C	66.132	35.521	38.258
1171	CYS148	O	66.481	36.178	39.245
1172	ALA149	N	66.952	35.245	37.259
1173	ALA149	CA	68.397	35.398	37.413
1174	ALA149	CB	69.058	34.739	36.217

Table 12

1175	ALA149	C	68.842	36.856	37.481
1176	ALA149	O	69.6	37.21	38.395
1177	VAL150	N	68.197	37.721	36.712
1178	VAL150	CA	68.599	39.132	36.723
1179	VAL150	CB	68.159	39.802	35.415
1180	VAL150	CG1	66.648	39.961	35.306
1181	VAL150	CG2	68.816	41.163	35.232
1182	VAL150	C	68.047	39.869	37.948
1183	VAL150	O	68.749	40.732	38.488
1184	ALA151	N	66.984	39.351	38.546
1185	ALA151	CA	66.448	39.971	39.754
1186	ALA151	CB	64.958	39.666	39.842
1187	ALA151	C	67.169	39.454	40.992
1188	ALA151	O	67.467	40.243	41.897
1189	THR152	N	67.693	38.243	40.893
1190	THR152	CA	68.463	37.669	41.996
1191	THR152	CB	68.65	36.174	41.752
1192	THR152	OG1	67.378	35.548	41.833
1193	THR152	CG2	69.535	35.54	42.815
1194	THR152	C	69.82	38.346	42.101
1195	THR152	O	70.14	38.886	43.167
1196	LEU153	N	70.448	38.595	40.962
1197	LEU153	CA	71.746	39.27	40.993
1198	LEU153	CB	72.504	38.977	39.71
1199	LEU153	CG	72.987	37.535	39.663
1200	LEU153	CD1	73.843	37.316	38.425
1201	LEU153	CD2	73.79	37.195	40.914
1202	LEU153	C	71.619	40.777	41.192
1203	LEU153	O	72.527	41.387	41.772
1204	ALA154	N	70.444	41.328	40.937
1205	ALA154	CA	70.215	42.735	41.258
1206	ALA154	CB	68.956	43.207	40.545
1207	ALA154	C	70.05	42.926	42.763
1208	ALA154	O	70.762	43.757	43.34
1209	LEU155	N	69.379	41.983	43.41
1210	LEU155	CA	69.156	42.067	44.862
1211	LEU155	CB	67.967	41.186	45.223
1212	LEU155	CG	66.673	41.709	44.616
1213	LEU155	CD1	65.531	40.726	44.838
1214	LEU155	CD2	66.325	43.08	45.179
1215	LEU155	C	70.361	41.617	45.685
1216	LEU155	O	70.443	41.931	46.877
1217	LEU156	N	71.291	40.914	45.058
1218	LEU156	CA	72.538	40.558	45.742
1219	LEU156	CB	73.006	39.195	45.243
1220	LEU156	CG	72.003	38.095	45.568
1221	LEU156	CD1	72.443	36.77	44.959
1222	LEU156	CD2	71.789	37.956	47.072
1223	LEU156	C	73.642	41.586	45.497
1224	LEU156	O	74.688	41.536	46.155
1225	GLY157	N	73.406	42.508	44.576
1226	GLY157	CA	74.401	43.533	44.247
1227	GLY157	C	75.536	42.957	43.405
1228	GLY157	O	76.683	43.412	43.487
1229	LYS158	N	75.197	42.005	42.553
1230	LYS158	CA	76.21	41.326	41.749

Table 12

1231	LYS158	CB	76.675	40.088	42.508
1232	LYS158	CG	78.072	39.657	42.076
1233	LYS158	CD	78.556	38.466	42.893
1234	LYS158	CE	80.015	38.142	42.596
1235	LYS158	NZ	80.219	37.876	41.164
1236	LYS158	C	75.618	40.945	40.397
1237	LYS158	O	75.796	39.824	39.9
1238	LEU159	N	75.093	41.952	39.718
1239	LEU159	CA	74.424	41.733	38.428
1240	LEU159	CB	73.543	42.946	38.148
1241	LEU159	CG	72.69	42.746	36.902
1242	LEU159	CD1	71.834	41.493	37.037
1243	LEU159	CD2	71.821	43.968	36.63
1244	LEU159	C	75.42	41.531	37.283
1245	LEU159	O	75.125	40.8	36.33
1246	ASP160	N	76.668	41.886	37.547
1247	ASP160	CA	77.757	41.757	36.571
1248	ASP160	CB	78.823	42.8	36.892
1249	ASP160	CG	78.221	44.203	36.873
1250	ASP160	OD1	78.047	44.733	35.786
1251	ASP160	OD2	77.842	44.67	37.94
1252	ASP160	C	78.404	40.368	36.573
1253	ASP160	O	79.493	40.199	36.014
1254	ALA161	N	77.787	39.411	37.252
1255	ALA161	CA	78.308	38.044	37.271
1256	ALA161	CB	77.81	37.358	38.535
1257	ALA161	C	77.835	37.248	36.058
1258	ALA161	O	78.38	36.179	35.764
1259	ILE162	N	76.823	37.758	35.375
1260	ILE162	CA	76.36	37.14	34.131
1261	ILE162	CB	74.865	36.878	34.241
1262	ILE162	CG2	74.595	35.761	35.243
1263	ILE162	CG1	74.131	38.16	34.626
1264	ILE162	CD1	72.626	37.949	34.743
1265	ILE162	C	76.636	38.061	32.949
1266	ILE162	O	76.975	39.238	33.124
1267	ASN163	N	76.533	37.51	31.753
1268	ASN163	CA	76.664	38.33	30.556
1269	ASN163	CB	77.185	37.504	29.387
1270	ASN163	CG	77.52	38.44	28.227
1271	ASN163	OD1	76.636	39.092	27.656
1272	ASN163	ND2	78.804	38.569	27.95
1273	ASN163	C	75.295	38.909	30.235
1274	ASN163	O	74.505	38.347	29.462
1275	VAL164	N	75.138	40.152	30.651
1276	VAL164	CA	73.85	40.831	30.551
1277	VAL164	CB	73.94	42.094	31.404
1278	VAL164	CG1	72.615	42.845	31.43
1279	VAL164	CG2	74.381	41.757	32.825
1280	VAL164	C	73.486	41.185	29.109
1281	VAL164	O	72.321	40.999	28.746
1282	GLU165	N	74.481	41.284	28.241
1283	GLU165	CA	74.223	41.656	26.848
1284	GLU165	CB	75.555	42.062	26.228
1285	GLU165	CG	75.417	42.42	24.753
1286	GLU165	CD	76.8	42.695	24.171

Table 12

1287	GLU165	OE1	77.755	42.154	24.714
1288	GLU165	OE2	76.885	43.473	23.232
1289	GLU165	C	73.636	40.492	26.051
1290	GLU165	O	72.663	40.686	25.312
1291	LYS166	N	74.033	39.282	26.408
1292	LYS166	CA	73.547	38.102	25.699
1293	LYS166	CB	74.549	36.975	25.919
1294	LYS166	CG	74.45	35.928	24.818
1295	LYS166	CD	74.854	36.531	23.478
1296	LYS166	CE	74.732	35.522	22.343
1297	LYS166	NZ	73.333	35.112	22.156
1298	LYS166	C	72.179	37.688	26.229
1299	LYS166	O	71.309	37.285	25.447
1300	ALA167	N	71.914	38.042	27.477
1301	ALA167	CA	70.606	37.754	28.066
1302	ALA167	CB	70.746	37.784	29.582
1303	ALA167	C	69.564	38.772	27.603
1304	ALA167	O	68.433	38.385	27.278
1305	ILE168	N	70.023	39.978	27.304
1306	ILE168	CA	69.148	40.998	26.72
1307	ILE168	CB	69.83	42.358	26.837
1308	ILE168	CG2	69.078	43.419	26.046
1309	ILE168	CG1	69.956	42.793	28.29
1310	ILE168	CD1	70.807	44.052	28.402
1311	ILE168	C	68.877	40.691	25.252
1312	ILE168	O	67.725	40.801	24.819
1313	GLU169	N	69.822	40.029	24.603
1314	GLU169	CA	69.627	39.609	23.214
1315	GLU169	CB	70.976	39.156	22.673
1316	GLU169	CG	70.889	38.711	21.219
1317	GLU169	CD	72.274	38.297	20.739
1318	GLU169	OE1	73.239	38.76	21.333
1319	GLU169	OE2	72.347	37.508	19.807
1320	GLU169	C	68.614	38.468	23.107
1321	GLU169	O	67.734	38.523	22.237
1322	PHE170	N	68.572	37.61	24.114
1323	PHE170	CA	67.557	36.557	24.134
1324	PHE170	CB	67.912	35.534	25.204
1325	PHE170	CG	66.845	34.457	25.376
1326	PHE170	CD1	66.655	33.505	24.383
1327	PHE170	CE1	65.681	32.527	24.535
1328	PHE170	CZ	64.891	32.504	25.676
1329	PHE170	CE2	65.075	33.46	26.666
1330	PHE170	CD2	66.05	34.438	26.516
1331	PHE170	C	66.171	37.122	24.427
1332	PHE170	O	65.223	36.796	23.706
1333	VAL171	N	66.095	38.125	25.285
1334	VAL171	CA	64.789	38.709	25.6
1335	VAL171	CB	64.921	39.516	26.887
1336	VAL171	CG1	63.66	40.321	27.181
1337	VAL171	CG2	65.25	38.594	28.054
1338	VAL171	C	64.256	39.581	24.463
1339	VAL171	O	63.072	39.459	24.121
1340	LEU172	N	65.15	40.184	23.695
1341	LEU172	CA	64.711	41	22.558
1342	LEU172	CB	65.819	41.97	22.173

Table 12

1343	LEU172	CG	66.098	42.971	23.286
1344	LEU172	CD1	67.26	43.881	22.907
1345	LEU172	CD2	64.854	43.785	23.623
1346	LEU172	C	64.339	40.151	21.347
1347	LEU172	O	63.425	40.532	20.605
1348	SER173	N	64.838	38.925	21.293
1349	SER173	CA	64.444	38.006	20.218
1350	SER173	CB	65.569	37.016	19.936
1351	SER173	OG	65.713	36.164	21.062
1352	SER173	C	63.156	37.249	20.559
1353	SER173	O	62.683	36.438	19.755
1354	CYS174	N	62.611	37.493	21.741
1355	CYS174	CA	61.299	36.955	22.098
1356	CYS174	CB	61.309	36.569	23.569
1357	CYS174	SG	62.54	35.332	24.02
1358	CYS174	C	60.183	37.971	21.86
1359	CYS174	O	59.009	37.626	22.047
1360	MET175	N	60.534	39.18	21.442
1361	MET175	CA	59.533	40.231	21.211
1362	MET175	CB	60.266	41.546	20.948
1363	MET175	CG	59.313	42.736	20.87
1364	MET175	SD	60.063	44.323	20.436
1365	MET175	CE	61.269	44.459	21.774
1366	MET175	C	58.637	39.897	20.019
1367	MET175	O	59.108	39.523	18.939
1368	ASN176	N	57.34	39.993	20.247
1369	ASN176	CA	56.355	39.748	19.197
1370	ASN176	CB	55.116	39.118	19.814
1371	ASN176	CG	55.467	37.787	20.466
1372	ASN176	OD1	55.577	37.69	21.691
1373	ASN176	ND2	55.604	36.767	19.641
1374	ASN176	C	55.968	41.045	18.503
1375	ASN176	O	56.294	42.148	18.959
1376	PHE177	N	55.075	40.902	17.537
1377	PHE177	CA	54.623	42.033	16.707
1378	PHE177	CB	54.004	41.477	15.42
1379	PHE177	CG	52.796	40.55	15.594
1380	PHE177	CD1	51.516	41.084	15.682
1381	PHE177	CE1	50.42	40.246	15.84
1382	PHE177	CZ	50.6	38.871	15.9
1383	PHE177	CE2	51.876	38.333	15.794
1384	PHE177	CD2	52.972	39.171	15.636
1385	PHE177	C	53.619	42.956	17.41
1386	PHE177	O	53.224	43.985	16.856
1387	ASP178	N	53.227	42.597	18.622
1388	ASP178	CA	52.327	43.431	19.418
1389	ASP178	CB	51.263	42.542	20.058
1390	ASP178	CG	51.885	41.492	20.978
1391	ASP178	OD1	52.14	41.822	22.128
1392	ASP178	OD2	52.139	40.394	20.5
1393	ASP178	C	53.082	44.215	20.495
1394	ASP178	O	52.456	44.865	21.339
1395	GLY179	N	54.4	44.084	20.535
1396	GLY179	CA	55.183	44.806	21.545
1397	GLY179	C	55.624	43.891	22.687
1398	GLY179	O	56.785	43.926	23.112

Table 12

1399	GLY180	N	54.685	43.104	23.187
1400	GLY180	CA	54.954	42.16	24.276
1401	GLY180	C	55.894	41.035	23.866
1402	GLY180	O	56.266	40.899	22.695
1403	PHE181	N	56.258	40.23	24.847
1404	PHE181	CA	57.252	39.176	24.641
1405	PHE181	CB	58.408	39.422	25.609
1406	PHE181	CG	59.151	40.756	25.478
1407	PHE181	CD1	58.71	41.886	26.16
1408	PHE181	CE1	59.397	43.086	26.04
1409	PHE181	CZ	60.536	43.157	25.249
1410	PHE181	CE2	60.987	42.026	24.581
1411	PHE181	CD2	60.297	40.826	24.7
1412	PHE181	C	56.675	37.789	24.918
1413	PHE181	O	55.765	37.633	25.747
1414	GLY182	N	57.208	36.805	24.213
1415	GLY182	CA	56.882	35.4	24.477
1416	GLY182	C	57.832	34.795	25.512
1417	GLY182	O	58.746	35.461	26.017
1418	CYS183	N	57.596	33.535	25.843
1419	CYS183	CA	58.412	32.872	26.873
1420	CYS183	CB	57.593	31.755	27.521
1421	CYS183	SG	56.923	30.465	26.445
1422	CYS183	C	59.721	32.336	26.303
1423	CYS183	O	60.746	32.285	26.999
1424	ARG184	N	59.661	31.987	25.029
1425	ARG184	CA	60.821	31.649	24.203
1426	ARG184	CB	60.893	30.131	24.047
1427	ARG184	CG	61.178	29.422	25.366
1428	ARG184	CD	61.162	27.911	25.182
1429	ARG184	NE	59.858	27.476	24.657
1430	ARG184	CZ	59.717	26.79	23.52
1431	ARG184	NH1	60.792	26.458	22.802
1432	ARG184	NH2	58.499	26.439	23.1
1433	ARG184	C	60.573	32.309	22.851
1434	ARG184	O	59.416	32.655	22.578
1435	PRO185	N	61.602	32.503	22.037
1436	PRO185	CA	61.419	33.187	20.751
1437	PRO185	CB	62.78	33.235	20.127
1438	PRO185	CG	63.788	32.59	21.064
1439	PRO185	CD	62.999	32.133	22.28
1440	PRO185	C	60.422	32.446	19.868
1441	PRO185	O	60.53	31.231	19.667
1442	GLY186	N	59.375	33.156	19.482
1443	GLY186	CA	58.321	32.557	18.66
1444	GLY186	C	57.001	32.432	19.422
1445	GLY186	O	55.924	32.504	18.818
1446	SER187	N	57.092	32.285	20.736
1447	SER187	CA	55.898	32.139	21.582
1448	SER187	CB	56.326	31.784	22.998
1449	SER187	OG	57.157	30.632	22.943
1450	SER187	C	55.118	33.445	21.608
1451	SER187	O	55.683	34.502	21.314
1452	GLU188	N	53.83	33.358	21.888
1453	GLU188	CA	52.959	34.543	21.886
1454	GLU188	CB	51.515	34.073	21.752

Table 12

1455	GLU188	CG	51.31	33.256	20.481
1456	GLU188	CD	49.86	32.788	20.388
1457	GLU188	OE1	49	33.514	20.867
1458	GLU188	OE2	49.646	31.7	19.874
1459	GLU188	C	53.099	35.377	23.159
1460	GLU188	O	53.511	34.866	24.207
1461	SER189	N	52.781	36.656	23.031
1462	SER189	CA	52.765	37.579	24.175
1463	SER189	CB	52.602	39.008	23.67
1464	SER189	OG	53.678	39.334	22.807
1465	SER189	C	51.591	37.318	25.108
1466	SER189	O	50.468	37.041	24.667
1467	HIS190	N	51.866	37.434	26.395
1468	HIS190	CA	50.805	37.41	27.413
1469	HIS190	CB	50.353	35.98	27.709
1470	HIS190	CG	51.355	35.073	28.396
1471	HIS190	ND1	51.303	34.665	29.679
1472	HIS190	CE1	52.36	33.866	29.929
1473	HIS190	NE2	53.068	33.745	28.784
1474	HIS190	CD2	52.453	34.473	27.826
1475	HIS190	C	51.286	38.116	28.677
1476	HIS190	O	52.497	38.204	28.914
1477	ALA191	N	50.343	38.517	29.516
1478	ALA191	CA	50.613	39.311	30.735
1479	ALA191	CB	49.337	39.332	31.565
1480	ALA191	C	51.748	38.813	31.631
1481	ALA191	O	52.654	39.592	31.948
1482	GLY192	N	51.797	37.512	31.876
1483	GLY192	CA	52.849	36.921	32.714
1484	GLY192	C	54.245	37.158	32.145
1485	GLY192	O	55.092	37.772	32.806
1486	GLN193	N	54.386	36.907	30.855
1487	GLN193	CA	55.689	37.027	30.208
1488	GLN193	CB	55.622	36.276	28.895
1489	GLN193	CG	56.84	35.387	28.781
1490	GLN193	CD	56.857	34.42	29.956
1491	GLN193	OE1	55.811	33.94	30.408
1492	GLN193	NE2	58.058	34.043	30.347
1493	GLN193	C	56.074	38.466	29.92
1494	GLN193	O	57.258	38.814	30.005
1495	ILE194	N	55.079	39.327	29.816
1496	ILE194	CA	55.361	40.743	29.636
1497	ILE194	CB	54.12	41.417	29.075
1498	ILE194	CG2	54.309	42.927	28.988
1499	ILE194	CG1	53.811	40.838	27.703
1500	ILE194	CD1	52.583	41.491	27.091
1501	ILE194	C	55.788	41.367	30.957
1502	ILE194	O	56.769	42.116	30.954
1503	TYR195	N	55.318	40.815	32.064
1504	TYR195	CA	55.789	41.27	33.372
1505	TYR195	CB	54.917	40.672	34.47
1506	TYR195	CG	55.355	41.078	35.875
1507	TYR195	CD1	54.944	42.3	36.389
1508	TYR195	CE1	55.35	42.688	37.658
1509	TYR195	CZ	56.166	41.856	38.411
1510	TYR195	OH	56.679	42.313	39.607

Table 12

1511	TYR195	CE2	56.563	40.625	37.909
1512	TYR195	CD2	56.154	40.235	36.64
1513	TYR195	C	57.23	40.842	33.598
1514	TYR195	O	58.074	41.695	33.904
1515	CYS196	N	57.545	39.625	33.188
1516	CYS196	CA	58.899	39.102	33.375
1517	CYS196	CB	58.895	37.619	33.025
1518	CYS196	SG	57.805	36.595	34.037
1519	CYS196	C	59.924	39.822	32.506
1520	CYS196	O	60.941	40.29	33.032
1521	CYS197	N	59.558	40.132	31.275
1522	CYS197	CA	60.518	40.777	30.382
1523	CYS197	CB	60.163	40.402	28.955
1524	CYS197	SG	60.243	38.631	28.604
1525	CYS197	C	60.584	42.295	30.547
1526	CYS197	O	61.663	42.864	30.343
1527	THR198	N	59.554	42.909	31.11
1528	THR198	CA	59.662	44.339	31.428
1529	THR198	CB	58.291	45.012	31.494
1530	THR198	OG1	57.483	44.352	32.463
1531	THR198	CG2	57.573	44.989	30.149
1532	THR198	C	60.393	44.525	32.751
1533	THR198	O	61.157	45.486	32.895
1534	GLY199	N	60.334	43.512	33.601
1535	GLY199	CA	61.138	43.491	34.818
1536	GLY199	C	62.611	43.372	34.452
1537	GLY199	O	63.409	44.254	34.795
1538	PHE200	N	62.901	42.417	33.581
1539	PHE200	CA	64.263	42.179	33.092
1540	PHE200	CB	64.189	41.043	32.071
1541	PHE200	CG	65.533	40.527	31.557
1542	PHE200	CD1	66.034	39.326	32.039
1543	PHE200	CE1	67.257	38.85	31.587
1544	PHE200	CZ	67.973	39.569	30.641
1545	PHE200	CE2	67.462	40.757	30.138
1546	PHE200	CD2	66.239	41.231	30.59
1547	PHE200	C	64.849	43.42	32.421
1548	PHE200	O	65.894	43.915	32.863
1549	LEU201	N	64.072	44.05	31.554
1550	LEU201	CA	64.576	45.213	30.82
1551	LEU201	CB	63.682	45.451	29.605
1552	LEU201	CG	64.394	45.125	28.29
1553	LEU201	CD1	65.075	43.762	28.297
1554	LEU201	CD2	63.449	45.237	27.101
1555	LEU201	C	64.661	46.473	31.681
1556	LEU201	O	65.585	47.266	31.465
1557	ALA202	N	63.933	46.52	32.785
1558	ALA202	CA	64.053	47.656	33.702
1559	ALA202	CB	62.767	47.785	34.508
1560	ALA202	C	65.242	47.516	34.648
1561	ALA202	O	65.863	48.526	35.006
1562	ILE203	N	65.669	46.286	34.887
1563	ILE203	CA	66.85	46.049	35.726
1564	ILE203	CB	66.762	44.63	36.281
1565	ILE203	CG2	67.979	44.3	37.136
1566	ILE203	CG1	65.493	44.438	37.097

Table 12

1567	ILE203	CD1	65.345	42.987	37.536
1568	ILE203	C	68.131	46.187	34.908
1569	ILE203	O	69.156	46.662	35.411
1570	THR204	N	68.017	45.915	33.619
1571	THR204	CA	69.161	46.061	32.708
1572	THR204	CB	69.03	45.034	31.592
1573	THR204	OG1	67.834	45.31	30.873
1574	THR204	CG2	68.96	43.614	32.139
1575	THR204	C	69.258	47.449	32.076
1576	THR204	O	70.16	47.681	31.263
1577	SER205	N	68.301	48.315	32.386
1578	SER205	CA	68.222	49.684	31.845
1579	SER205	CB	69.455	50.464	32.281
1580	SER205	OG	69.513	50.396	33.699
1581	SER205	C	68.081	49.72	30.321
1582	SER205	O	68.427	50.718	29.677
1583	GLN206	N	67.332	48.758	29.809
1584	GLN206	CA	67.07	48.622	28.374
1585	GLN206	CB	67.266	47.17	27.965
1586	GLN206	CG	68.734	46.823	27.777
1587	GLN206	CD	69.254	47.459	26.491
1588	GLN206	OE1	70.358	48.013	26.459
1589	GLN206	NE2	68.47	47.32	25.434
1590	GLN206	C	65.651	49.046	28.045
1591	GLN206	O	65.029	48.528	27.107
1592	LEU207	N	65.228	50.118	28.694
1593	LEU207	CA	63.839	50.588	28.601
1594	LEU207	CB	63.534	51.554	29.748
1595	LEU207	CG	63.26	50.884	31.096
1596	LEU207	CD1	62.333	49.683	30.931
1597	LEU207	CD2	64.533	50.49	31.839
1598	LEU207	C	63.575	51.304	27.282
1599	LEU207	O	62.455	51.248	26.765
1600	HIS208	N	64.659	51.681	26.624
1601	HIS208	CA	64.615	52.335	25.316
1602	HIS208	CB	65.927	53.101	25.145
1603	HIS208	CG	67.18	52.29	25.439
1604	HIS208	ND1	67.955	52.373	26.54
1605	HIS208	CE1	68.969	51.489	26.437
1606	HIS208	NE2	68.845	50.859	25.248
1607	HIS208	CD2	67.756	51.348	24.617
1608	HIS208	C	64.434	51.341	24.163
1609	HIS208	O	64.251	51.753	23.013
1610	GLN209	N	64.453	50.052	24.473
1611	GLN209	CA	64.23	49.034	23.452
1612	GLN209	CB	65.088	47.824	23.796
1613	GLN209	CG	65.65	47.163	22.544
1614	GLN209	CD	66.873	47.937	22.066
1615	GLN209	OE1	67.452	48.721	22.829
1616	GLN209	NE2	67.355	47.574	20.89
1617	GLN209	C	62.763	48.605	23.435
1618	GLN209	O	62.319	47.918	22.506
1619	VAL210	N	62.021	49.022	24.45
1620	VAL210	CA	60.607	48.656	24.557
1621	VAL210	CB	60.213	48.716	26.031
1622	VAL210	CG1	58.783	48.233	26.249

Table 12

1623	VAL210	CG2	61.174	47.912	26.894
1624	VAL210	C	59.73	49.633	23.781
1625	VAL210	O	59.797	50.848	24.002
1626	ASN211	N	58.915	49.109	22.879
1627	ASN211	CA	57.911	49.961	22.237
1628	ASN211	CB	57.444	49.342	20.922
1629	ASN211	CG	56.58	50.333	20.136
1630	ASN211	OD1	55.705	51.015	20.689
1631	ASN211	ND2	56.819	50.378	18.839
1632	ASN211	C	56.735	50.119	23.194
1633	ASN211	O	55.725	49.409	23.091
1634	SER212	N	56.769	51.223	23.922
1635	SER212	CA	55.784	51.476	24.972
1636	SER212	CB	56.35	52.544	25.898
1637	SER212	OG	57.55	52.041	26.472
1638	SER212	C	54.434	51.936	24.433
1639	SER212	O	53.422	51.724	25.103
1640	ASP213	N	54.369	52.304	23.167
1641	ASP213	CA	53.09	52.729	22.603
1642	ASP213	CB	53.356	53.63	21.401
1643	ASP213	CG	54.158	54.857	21.825
1644	ASP213	OD1	53.543	55.798	22.305
1645	ASP213	OD2	55.376	54.818	21.7
1646	ASP213	C	52.282	51.516	22.159
1647	ASP213	O	51.122	51.364	22.564
1648	LEU214	N	52.973	50.544	21.586
1649	LEU214	CA	52.295	49.353	21.072
1650	LEU214	CB	53.175	48.751	19.985
1651	LEU214	CG	52.498	47.59	19.269
1652	LEU214	CD1	51.138	48.001	18.715
1653	LEU214	CD2	53.394	47.056	18.158
1654	LEU214	C	52.052	48.339	22.184
1655	LEU214	O	50.924	47.847	22.324
1656	LEU215	N	52.984	48.277	23.122
1657	LEU215	CA	52.814	47.389	24.273
1658	LEU215	CB	54.181	47.158	24.908
1659	LEU215	CG	54.103	46.281	26.152
1660	LEU215	CD1	53.349	44.985	25.879
1661	LEU215	CD2	55.494	45.992	26.704
1662	LEU215	C	51.847	48.005	25.28
1663	LEU215	O	50.996	47.288	25.819
1664	GLY216	N	51.79	49.326	25.301
1665	GLY216	CA	50.839	50.045	26.145
1666	GLY216	C	49.421	49.817	25.654
1667	GLY216	O	48.555	49.41	26.438
1668	TRP217	N	49.24	49.9	24.346
1669	TRP217	CA	47.928	49.645	23.754
1670	TRP217	CB	47.987	49.982	22.27
1671	TRP217	CG	46.688	49.691	21.55
1672	TRP217	CD1	45.524	50.424	21.625
1673	TRP217	NE1	44.588	49.823	20.849
1674	TRP217	CE2	45.081	48.719	20.257
1675	TRP217	CZ2	44.525	47.781	19.399
1676	TRP217	CH2	45.298	46.719	18.944
1677	TRP217	CZ3	46.624	46.591	19.346
1678	TRP217	CE3	47.189	47.524	20.205

Table 12

1679	TRP217	CD2	46.421	48.586	20.661
1680	TRP217	C	47.487	48.193	23.933
1681	TRP217	O	46.36	47.973	24.392
1682	TRP218	N	48.418	47.255	23.846
1683	TRP218	CA	48.065	45.847	24.044
1684	TRP218	CB	49.276	44.988	23.689
1685	TRP218	CG	48.974	43.51	23.524
1686	TRP218	CD1	48.616	42.882	22.352
1687	TRP218	NE1	48.432	41.563	22.604
1688	TRP218	CE2	48.65	41.282	23.904
1689	TRP218	CZ2	48.585	40.105	24.633
1690	TRP218	CH2	48.857	40.124	25.995
1691	TRP218	CZ3	49.196	41.314	26.628
1692	TRP218	CE3	49.27	42.498	25.901
1693	TRP218	CD2	48.997	42.485	24.544
1694	TRP218	C	47.658	45.589	25.495
1695	TRP218	O	46.551	45.086	25.727
1696	LEU219	N	48.369	46.205	26.426
1697	LEU219	CA	48.072	46.021	27.85
1698	LEU219	CB	49.247	46.554	28.665
1699	LEU219	CG	50.52	45.735	28.469
1700	LEU219	CD1	51.69	46.373	29.208
1701	LEU219	CD2	50.337	44.289	28.914
1702	LEU219	C	46.795	46.736	28.299
1703	LEU219	O	46.024	46.154	29.074
1704	CYS220	N	46.444	47.845	27.666
1705	CYS220	CA	45.202	48.525	28.052
1706	CYS220	CB	45.288	50.023	27.767
1707	CYS220	SG	45.291	50.544	26.037
1708	CYS220	C	43.982	47.91	27.364
1709	CYS220	O	42.879	47.992	27.916
1710	GLU221	N	44.214	47.072	26.361
1711	GLU221	CA	43.119	46.313	25.745
1712	GLU221	CB	43.508	45.882	24.335
1713	GLU221	CG	43.683	47.065	23.393
1714	GLU221	CD	42.379	47.84	23.23
1715	GLU221	OE1	41.388	47.21	22.895
1716	GLU221	OE2	42.458	49.061	23.216
1717	GLU221	C	42.772	45.064	26.554
1718	GLU221	O	41.756	44.418	26.274
1719	ARG222	N	43.548	44.777	27.59
1720	ARG222	CA	43.252	43.633	28.452
1721	ARG222	CB	44.541	43.198	29.146
1722	ARG222	CG	45.646	42.904	28.136
1723	ARG222	CD	45.292	41.729	27.232
1724	ARG222	NE	45.617	42.034	25.834
1725	ARG222	CZ	44.688	42.163	24.886
1726	ARG222	NH1	43.414	41.876	25.159
1727	ARG222	NH2	45.044	42.487	23.642
1728	ARG222	C	42.201	43.99	29.5
1729	ARG222	O	41.588	43.08	30.076
1730	GLN223	N	41.925	45.275	29.674
1731	GLN223	CA	40.9	45.693	30.633
1732	GLN223	CB	41.158	47.128	31.077
1733	GLN223	CG	40.121	47.56	32.111
1734	GLN223	CD	40.563	48.832	32.823

Table 12

1735	GLN223	OE1	41.053	49.784	32.2
1736	GLN223	NE2	40.456	48.795	34.138
1737	GLN223	C	39.502	45.573	30.04
1738	GLN223	O	39.087	46.335	29.16
1739	LEU224	N	38.775	44.612	30.574
1740	LEU224	CA	37.399	44.356	30.158
1741	LEU224	CB	37.096	42.908	30.517
1742	LEU224	CG	37.949	41.984	29.664
1743	LEU224	CD1	37.705	40.538	30.048
1744	LEU224	CD2	37.67	42.202	28.18
1745	LEU224	C	36.443	45.309	30.864
1746	LEU224	O	36.812	45.898	31.887
1747	PRO225	N	35.209	45.406	30.378
1748	PRO225	CA	34.2	46.305	30.977
1749	PRO225	CB	33.043	46.286	30.025
1750	PRO225	CG	33.308	45.279	28.919
1751	PRO225	CD	34.695	44.722	29.183
1752	PRO225	C	33.723	45.934	32.396
1753	PRO225	O	32.934	46.678	32.985
1754	SER226	N	34.218	44.835	32.949
1755	SER226	CA	33.978	44.497	34.356
1756	SER226	CB	34.204	43.004	34.54
1757	SER226	OG	35.609	42.78	34.473
1758	SER226	C	34.983	45.195	35.271
1759	SER226	O	34.911	45.044	36.494
1760	GLY227	N	35.986	45.824	34.677
1761	GLY227	CA	37.024	46.493	35.447
1762	GLY227	C	38.35	45.743	35.398
1763	GLY227	O	39.418	46.372	35.4
1764	GLY228	N	38.281	44.429	35.25
1765	GLY228	CA	39.478	43.6	35.389
1766	GLY228	C	40.235	43.358	34.095
1767	GLY228	O	39.674	43.334	32.994
1768	LEU229	N	41.518	43.12	34.281
1769	LEU229	CA	42.45	42.888	33.18
1770	LEU229	CB	43.805	43.518	33.535
1771	LEU229	CG	43.984	45.025	33.28
1772	LEU229	CD1	42.942	45.936	33.919
1773	LEU229	CD2	45.352	45.471	33.769
1774	LEU229	C	42.632	41.384	32.987
1775	LEU229	O	42.696	40.636	33.974
1776	ASN230	N	42.547	40.939	31.745
1777	ASN230	CA	42.849	39.541	31.428
1778	ASN230	CB	41.954	39.013	30.306
1779	ASN230	CG	42.032	39.815	29.01
1780	ASN230	OD1	43.113	40.026	28.45
1781	ASN230	ND2	40.866	40.022	28.429
1782	ASN230	C	44.325	39.382	31.081
1783	ASN230	O	45.112	40.33	31.19
1784	GLY231	N	44.7	38.164	30.732
1785	GLY231	CA	46.107	37.867	30.443
1786	GLY231	C	46.447	38.093	28.978
1787	GLY231	O	47.574	38.476	28.641
1788	ARG232	N	45.506	37.714	28.133
1789	ARG232	CA	45.63	37.864	26.685
1790	ARG232	CB	46.574	36.776	26.164

Table 12

1791	ARG232	CG	46.11	35.38	26.535
1792	ARG232	CD	47.139	34.331	26.134
1793	ARG232	NE	46.706	32.995	26.569
1794	ARG232	CZ	47.18	32.388	27.659
1795	ARG232	NH1	48.123	32.976	28.399
1796	ARG232	NH2	46.724	31.181	27.999
1797	ARG232	C	44.219	37.785	26.093
1798	ARG232	O	43.295	37.358	26.802
1799	PRO233	N	44.05	38.191	24.84
1800	PRO233	CA	42.715	38.497	24.304
1801	PRO233	CB	42.932	38.832	22.86
1802	PRO233	CG	44.423	38.917	22.585
1803	PRO233	CD	45.105	38.606	23.905
1804	PRO233	C	41.69	37.376	24.456
1805	PRO233	O	42.009	36.184	24.392
1806	GLU234	N	40.484	37.817	24.789
1807	GLU234	CA	39.278	36.977	24.919
1808	GLU234	CB	39.106	36.09	23.687
1809	GLU234	CG	38.852	36.909	22.426
1810	GLU234	CD	38.719	35.987	21.217
1811	GLU234	OE1	39.514	35.064	21.113
1812	GLU234	OE2	37.901	36.298	20.363
1813	GLU234	C	39.259	36.107	26.175
1814	GLU234	O	38.518	35.118	26.213
1815	LYS235	N	39.999	36.501	27.197
1816	LYS235	CA	39.978	35.76	28.459
1817	LYS235	CB	41.407	35.456	28.878
1818	LYS235	CG	42.028	34.359	28.028
1819	LYS235	CD	43.49	34.184	28.404
1820	LYS235	CE	43.668	34.018	29.907
1821	LYS235	NZ	45.096	33.997	30.255
1822	LYS235	C	39.299	36.532	29.579
1823	LYS235	O	39.113	37.754	29.504
1824	LEU236	N	38.936	35.779	30.602
1825	LEU236	CA	38.415	36.328	31.857
1826	LEU236	CB	38.096	35.155	32.777
1827	LEU236	CG	36.878	34.399	32.275
1828	LEU236	CD1	36.694	33.077	33.007
1829	LEU236	CD2	35.642	35.273	32.399
1830	LEU236	C	39.419	37.245	32.543
1831	LEU236	O	40.636	37.032	32.474
1832	PRO237	N	38.892	38.299	33.143
1833	PRO237	CA	39.686	39.157	34.015
1834	PRO237	CB	38.79	40.307	34.339
1835	PRO237	CG	37.388	40.016	33.837
1836	PRO237	CD	37.479	38.673	33.14
1837	PRO237	C	40.077	38.404	35.277
1838	PRO237	O	39.273	37.652	35.835
1839	ASP238	N	41.308	38.598	35.708
1840	ASP238	CA	41.799	37.909	36.908
1841	ASP238	CB	42.324	36.544	36.465
1842	ASP238	CG	42.739	35.677	37.649
1843	ASP238	OD1	43.81	35.932	38.187
1844	ASP238	OD2	42.022	34.735	37.955
1845	ASP238	C	42.903	38.747	37.545
1846	ASP238	O	43.809	39.188	36.83

Table 12

1847	VAL239	N	42.946	38.816	38.868
1848	VAL239	CA	43.89	39.735	39.531
1849	VAL239	CB	43.523	39.876	41.003
1850	VAL239	CG1	42.254	40.697	41.176
1851	VAL239	CG2	43.398	38.525	41.69
1852	VAL239	C	45.386	39.401	39.409
1853	VAL239	O	46.179	40.347	39.48
1854	CYS240	N	45.776	38.204	38.991
1855	CYS240	CA	47.214	37.99	38.77
1856	CYS240	CB	47.572	36.506	38.842
1857	CYS240	SG	46.878	35.394	37.595
1858	CYS240	C	47.644	38.581	37.428
1859	CYS240	O	48.65	39.299	37.381
1860	TYR241	N	46.71	38.609	36.49
1861	TYR241	CA	46.979	39.173	35.169
1862	TYR241	CB	46.015	38.553	34.168
1863	TYR241	CG	46.153	37.044	33.993
1864	TYR241	CD1	45.052	36.221	34.196
1865	TYR241	CE1	45.174	34.847	34.037
1866	TYR241	CZ	46.397	34.302	33.668
1867	TYR241	OH	46.523	32.937	33.523
1868	TYR241	CE2	47.495	35.123	33.452
1869	TYR241	CD2	47.371	36.496	33.613
1870	TYR241	C	46.755	40.673	35.212
1871	TYR241	O	47.52	41.434	34.607
1872	SER242	N	45.921	41.076	36.155
1873	SER242	CA	45.677	42.492	36.405
1874	SER242	CB	44.526	42.639	37.393
1875	SER242	OG	43.373	42.029	36.826
1876	SER242	C	46.927	43.147	36.971
1877	SER242	O	47.392	44.127	36.379
1878	TRP243	N	47.607	42.472	37.885
1879	TRP243	CA	48.855	43.027	38.414
1880	TRP243	CB	49.265	42.296	39.687
1881	TRP243	CG	50.708	42.579	40.072
1882	TRP243	CD1	51.751	41.68	40.048
1883	TRP243	NE1	52.884	42.322	40.424
1884	TRP243	CE2	52.641	43.616	40.699
1885	TRP243	CZ2	53.461	44.664	41.091
1886	TRP243	CH2	52.917	45.926	41.293
1887	TRP243	CZ3	51.557	46.143	41.103
1888	TRP243	CE3	50.727	45.1	40.71
1889	TRP243	CD2	51.265	43.839	40.506
1890	TRP243	C	50.004	42.943	37.416
1891	TRP243	O	50.725	43.936	37.265
1892	TRP244	N	50.044	41.908	36.594
1893	TRP244	CA	51.157	41.792	35.645
1894	TRP244	CB	51.203	40.369	35.102
1895	TRP244	CG	51.608	39.348	36.148
1896	TRP244	CD1	52.419	39.57	37.238
1897	TRP244	NE1	52.536	38.413	37.934
1898	TRP244	CE2	51.837	37.422	37.35
1899	TRP244	CZ2	51.646	36.088	37.676
1900	TRP244	CH2	50.853	35.286	36.863
1901	TRP244	CZ3	50.252	35.817	35.727
1902	TRP244	CE3	50.436	37.153	35.394

Table 12

1903	TRP244	CD2	51.227	37.955	36.201
1904	TRP244	C	51.053	42.804	34.507
1905	TRP244	O	52.042	43.492	34.221
1906	VAL245	N	49.834	43.103	34.089
1907	VAL245	CA	49.639	44.115	33.051
1908	VAL245	CB	48.261	43.918	32.429
1909	VAL245	CG1	47.894	45.083	31.523
1910	VAL245	CG2	48.162	42.604	31.669
1911	VAL245	C	49.742	45.526	33.622
1912	VAL245	O	50.425	46.364	33.022
1913	LEU246	N	49.348	45.688	34.876
1914	LEU246	CA	49.403	46.996	35.537
1915	LEU246	CB	48.655	46.866	36.86
1916	LEU246	CG	48.499	48.193	37.587
1917	LEU246	CD1	47.577	49.118	36.803
1918	LEU246	CD2	47.946	47.966	38.989
1919	LEU246	C	50.841	47.405	35.833
1920	LEU246	O	51.265	48.507	35.46
1921	ALA247	N	51.635	46.438	36.256
1922	ALA247	CA	53.027	46.712	36.587
1923	ALA247	CB	53.55	45.571	37.442
1924	ALA247	C	53.889	46.871	35.344
1925	ALA247	O	54.648	47.843	35.288
1926	SER248	N	53.549	46.174	34.27
1927	SER248	CA	54.3	46.342	33.019
1928	SER248	CB	54.031	45.151	32.112
1929	SER248	OG	54.539	43.996	32.76
1930	SER248	C	53.908	47.624	32.29
1931	SER248	O	54.78	48.288	31.717
1932	LEU249	N	52.706	48.101	32.565
1933	LEU249	CA	52.229	49.354	31.989
1934	LEU249	CB	50.715	49.36	32.161
1935	LEU249	CG	50.019	50.297	31.19
1936	LEU249	CD1	50.396	49.964	29.754
1937	LEU249	CD2	48.508	50.232	31.369
1938	LEU249	C	52.865	50.536	32.719
1939	LEU249	O	53.298	51.5	32.073
1940	LYS250	N	53.184	50.324	33.986
1941	LYS250	CA	53.925	51.322	34.759
1942	LYS250	CB	53.729	51.002	36.237
1943	LYS250	CG	54.551	51.917	37.138
1944	LYS250	CD	54.169	53.383	36.975
1945	LYS250	CE	55.018	54.266	37.88
1946	LYS250	NZ	54.875	53.855	39.285
1947	LYS250	C	55.416	51.308	34.419
1948	LYS250	O	55.999	52.383	34.231
1949	ILE251	N	55.937	50.144	34.059
1950	ILE251	CA	57.351	50.027	33.678
1951	ILE251	CB	57.722	48.542	33.671
1952	ILE251	CG2	59.112	48.315	33.084
1953	ILE251	CG1	57.649	47.952	35.073
1954	ILE251	CD1	57.92	46.453	35.062
1955	ILE251	C	57.637	50.636	32.305
1956	ILE251	O	58.722	51.194	32.092
1957	ILE252	N	56.634	50.665	31.442
1958	ILE252	CA	56.806	51.297	30.134

Table 12

1959	ILE252	CB	56.091	50.466	29.076
1960	ILE252	CG2	56.634	49.043	29.069
1961	ILE252	CG1	54.587	50.449	29.292
1962	ILE252	CD1	53.904	49.556	28.268
1963	ILE252	C	56.322	52.75	30.099
1964	ILE252	O	56.389	53.383	29.039
1965	GLY253	N	55.821	53.259	31.217
1966	GLY253	CA	55.406	54.668	31.309
1967	GLY253	C	53.93	54.91	30.992
1968	GLY253	O	53.345	55.905	31.441
1969	ARG254	N	53.295	53.919	30.389
1970	ARG254	CA	51.939	54.061	29.845
1971	ARG254	CB	51.82	53.177	28.614
1972	ARG254	CG	52.849	53.56	27.564
1973	ARG254	CD	52.656	54.994	27.085
1974	ARG254	NE	53.692	55.354	26.108
1975	ARG254	CZ	54.796	56.032	26.431
1976	ARG254	NH1	54.983	56.449	27.686
1977	ARG254	NH2	55.701	56.314	25.493
1978	ARG254	C	50.841	53.683	30.83
1979	ARG254	O	49.722	53.365	30.405
1980	LEU255	N	51.079	53.903	32.115
1981	LEU255	CA	50.122	53.489	33.152
1982	LEU255	CB	50.802	53.587	34.513
1983	LEU255	CG	49.936	52.955	35.595
1984	LEU255	CD1	49.734	51.475	35.306
1985	LEU255	CD2	50.531	53.15	36.985
1986	LEU255	C	48.867	54.366	33.154
1987	LEU255	O	47.778	53.872	33.466
1988	HIS256	N	48.975	55.508	32.495
1989	HIS256	CA	47.874	56.46	32.333
1990	HIS256	CB	48.494	57.805	31.953
1991	HIS256	CG	49.486	57.746	30.8
1992	HIS256	ND1	50.829	57.847	30.882
1993	HIS256	CE1	51.362	57.745	29.648
1994	HIS256	NE2	50.343	57.592	28.773
1995	HIS256	CD2	49.183	57.603	29.466
1996	HIS256	C	46.842	56.041	31.275
1997	HIS256	O	45.869	56.77	31.054
1998	TRP257	N	47.066	54.919	30.604
1999	TRP257	CA	46.067	54.392	29.674
2000	TRP257	CB	46.761	53.764	28.469
2001	TRP257	CG	47.306	54.766	27.47
2002	TRP257	CD1	46.924	56.082	27.333
2003	TRP257	NE1	47.642	56.637	26.324
2004	TRP257	CE2	48.48	55.74	25.772
2005	TRP257	CZ2	49.39	55.819	24.728
2006	TRP257	CH2	50.126	54.697	24.367
2007	TRP257	CZ3	49.955	53.496	25.049
2008	TRP257	CE3	49.048	53.408	26.099
2009	TRP257	CD2	48.312	54.525	26.462
2010	TRP257	C	45.151	53.359	30.331
2011	TRP257	O	44.166	52.939	29.711
2012	ILE258	N	45.453	52.953	31.554
2013	ILE258	CA	44.57	51.994	32.227
2014	ILE258	CB	45.409	51.032	33.077

Table 12

2015	ILE258	CG2	45.788	51.633	34.426
2016	ILE258	CG1	44.685	49.707	33.293
2017	ILE258	CD1	44.452	48.992	31.966
2018	ILE258	C	43.54	52.751	33.07
2019	ILE258	O	43.832	53.818	33.626
2020	ASP259	N	42.31	52.269	33.073
2021	ASP259	CA	41.296	52.89	33.924
2022	ASP259	CB	39.902	52.613	33.369
2023	ASP259	CG	38.872	53.465	34.104
2024	ASP259	OD1	38.67	53.204	35.286
2025	ASP259	OD2	38.451	54.462	33.54
2026	ASP259	C	41.443	52.338	35.338
2027	ASP259	O	40.881	51.287	35.69
2028	ARG260	N	42.021	53.168	36.19
2029	ARG260	CA	42.351	52.748	37.552
2030	ARG260	CB	43.276	53.793	38.159
2031	ARG260	CG	44.569	53.928	37.366
2032	ARG260	CD	45.47	54.977	38.003
2033	ARG260	NE	46.75	55.115	37.29
2034	ARG260	CZ	47.088	56.219	36.619
2035	ARG260	NH1	46.202	57.205	36.465
2036	ARG260	NH2	48.289	56.31	36.047
2037	ARG260	C	41.142	52.58	38.465
2038	ARG260	O	41.143	51.627	39.247
2039	GLU261	N	40.031	53.234	38.159
2040	GLU261	CA	38.859	53.123	39.035
2041	GLU261	CB	37.947	54.322	38.809
2042	GLU261	CG	38.639	55.636	39.157
2043	GLU261	CD	39.093	55.636	40.615
2044	GLU261	OE1	38.24	55.783	41.478
2045	GLU261	OE2	40.292	55.525	40.828
2046	GLU261	C	38.077	51.84	38.776
2047	GLU261	O	37.568	51.229	39.725
2048	LYS262	N	38.165	51.33	37.56
2049	LYS262	CA	37.495	50.07	37.25
2050	LYS262	CB	37.232	49.999	35.753
2051	LYS262	CG	36.219	51.042	35.306
2052	LYS262	CD	35.952	50.925	33.811
2053	LYS262	CE	34.942	51.964	33.342
2054	LYS262	NZ	34.685	51.829	31.899
2055	LYS262	C	38.345	48.882	37.675
2056	LYS262	O	37.803	47.93	38.248
2057	LEU263	N	39.657	49.056	37.657
2058	LEU263	CA	40.531	47.962	38.078
2059	LEU263	CB	41.932	48.188	37.524
2060	LEU263	CG	42.86	47.037	37.897
2061	LEU263	CD1	42.278	45.694	37.466
2062	LEU263	CD2	44.25	47.24	37.308
2063	LEU263	C	40.569	47.888	39.597
2064	LEU263	O	40.441	46.793	40.158
2065	ARG264	N	40.405	49.04	40.224
2066	ARG264	CA	40.317	49.093	41.677
2067	ARG264	CB	40.356	50.545	42.134
2068	ARG264	CG	40.062	50.619	43.623
2069	ARG264	CD	40.165	52.03	44.185
2070	ARG264	NE	39.734	52.023	45.593

Table 12

2071	ARG264	CZ	40.534	51.731	46.622
2072	ARG264	NH1	41.846	51.572	46.43
2073	ARG264	NH2	40.033	51.697	47.859
2074	ARG264	C	39.038	48.438	42.173
2075	ARG264	O	39.139	47.511	42.982
2076	ASN265	N	37.93	48.661	41.482
2077	ASN265	CA	36.668	48.048	41.908
2078	ASN265	CB	35.492	48.829	41.333
2079	ASN265	CG	35.129	49.997	42.251
2080	ASN265	OD1	34.476	49.808	43.284
2081	ASN265	ND2	35.572	51.187	41.881
2082	ASN265	C	36.563	46.569	41.541
2083	ASN265	O	35.943	45.818	42.304
2084	PHE266	N	37.365	46.109	40.595
2085	PHE266	CA	37.423	44.671	40.328
2086	PHE266	CB	38.068	44.45	38.968
2087	PHE266	CG	38.268	42.98	38.61
2088	PHE266	CD1	37.201	42.234	38.127
2089	PHE266	CE1	37.381	40.897	37.8
2090	PHE266	CZ	38.628	40.306	37.956
2091	PHE266	CE2	39.697	41.052	38.434
2092	PHE266	CD2	39.517	42.39	38.76
2093	PHE266	C	38.242	43.951	41.396
2094	PHE266	O	37.817	42.898	41.886
2095	ILE267	N	39.251	44.628	41.918
2096	ILE267	CA	40.071	44.044	42.98
2097	ILE267	CB	41.414	44.766	42.98
2098	ILE267	CG2	42.315	44.234	44.081
2099	ILE267	CG1	42.111	44.612	41.634
2100	ILE267	CD1	43.459	45.326	41.627
2101	ILE267	C	39.382	44.166	44.343
2102	ILE267	O	39.485	43.249	45.169
2103	LEU268	N	38.482	45.13	44.461
2104	LEU268	CA	37.645	45.245	45.66
2105	LEU268	CB	36.966	46.612	45.659
2106	LEU268	CG	37.939	47.78	45.775
2107	LEU268	CD1	37.249	49.097	45.444
2108	LEU268	CD2	38.594	47.851	47.148
2109	LEU268	C	36.57	44.159	45.664
2110	LEU268	O	36.359	43.513	46.698
2111	ALA269	N	36.14	43.775	44.471
2112	ALA269	CA	35.165	42.694	44.301
2113	ALA269	CB	34.566	42.827	42.904
2114	ALA269	C	35.763	41.294	44.457
2115	ALA269	O	35.019	40.313	44.579
2116	CYS270	N	37.082	41.206	44.522
2117	CYS270	CA	37.739	39.927	44.785
2118	CYS270	CB	39.056	39.868	44.02
2119	CYS270	SG	38.912	39.869	42.22
2120	CYS270	C	38.009	39.71	46.273
2121	CYS270	O	38.47	38.622	46.642
2122	GLN271	N	37.717	40.696	47.108
2123	GLN271	CA	37.932	40.538	48.552
2124	GLN271	CB	37.871	41.908	49.217
2125	GLN271	CG	38.867	42.853	48.569
2126	GLN271	CD	38.911	44.207	49.266

Table 12

2127	GLN271	OE1	38.288	44.432	50.309
2128	GLN271	NE2	39.785	45.05	48.748
2129	GLN271	C	36.856	39.657	49.168
2130	GLN271	O	35.669	39.793	48.851
2131	ASP272	N	37.265	38.715	49.995
2132	ASP272	CA	36.256	37.952	50.724
2133	ASP272	CB	36.746	36.522	50.939
2134	ASP272	CG	35.623	35.521	51.191
2135	ASP272	OD1	34.541	35.956	51.577
2136	ASP272	OD2	35.795	34.375	50.796
2137	ASP272	C	36.002	38.671	52.044
2138	ASP272	O	36.919	39.144	52.725
2139	GLU273	N	34.728	38.834	52.355
2140	GLU273	CA	34.356	39.462	53.622
2141	GLU273	CB	32.971	40.076	53.462
2142	GLU273	CG	33.01	41.15	52.379
2143	GLU273	CD	31.612	41.669	52.066
2144	GLU273	OE1	30.702	40.852	52.075
2145	GLU273	OE2	31.509	42.82	51.666
2146	GLU273	C	34.394	38.415	54.729
2147	GLU273	O	34.71	38.717	55.885
2148	GLU274	N	34.236	37.167	54.323
2149	GLU274	CA	34.507	36.046	55.219
2150	GLU274	CB	33.689	34.837	54.776
2151	GLU274	CG	32.196	35.146	54.719
2152	GLU274	CD	31.661	35.505	56.103
2153	GLU274	OE1	32.124	34.911	57.067
2154	GLU274	OE2	30.793	36.364	56.165
2155	GLU274	C	35.992	35.729	55.111
2156	GLU274	O	36.461	35.35	54.032
2157	THR275	N	36.687	35.867	56.231
2158	THR275	CA	38.156	35.712	56.348
2159	THR275	CB	38.529	34.268	56.721
2160	THR275	OG1	39.945	34.189	56.84
2161	THR275	CG2	38.069	33.195	55.735
2162	THR275	C	38.951	36.227	55.137
2163	THR275	O	39.538	35.458	54.366
2164	GLY276	N	38.914	37.546	54.999
2165	GLY276	CA	39.692	38.336	54.025
2166	GLY276	C	40.156	37.662	52.742
2167	GLY276	O	39.373	37.067	51.998
2168	GLY277	N	41.436	37.839	52.464
2169	GLY277	CA	42.047	37.342	51.224
2170	GLY277	C	41.424	37.88	49.931
2171	GLY277	O	40.34	38.48	49.91
2172	PHE278	N	42.177	37.697	48.861
2173	PHE278	CA	41.684	37.991	47.511
2174	PHE278	CB	42.632	38.924	46.773
2175	PHE278	CG	42.68	40.37	47.25
2176	PHE278	CD1	43.555	40.752	48.257
2177	PHE278	CE1	43.605	42.074	48.671
2178	PHE278	CZ	42.784	43.019	48.074
2179	PHE278	CE2	41.911	42.638	47.066
2180	PHE278	CD2	41.858	41.314	46.652
2181	PHE278	C	41.549	36.711	46.696
2182	PHE278	O	42.362	35.781	46.812

Table 12

2183	ALA279	N	40.448	36.649	45.972
2184	ALA279	CA	40.16	35.56	45.04
2185	ALA279	CB	38.649	35.45	44.917
2186	ALA279	C	40.757	35.863	43.672
2187	ALA279	O	41.172	36.997	43.409
2188	ASP280	N	40.806	34.858	42.814
2189	ASP280	CA	41.357	35.064	41.465
2190	ASP280	CB	41.688	33.711	40.811
2191	ASP280	CG	40.527	32.72	40.702
2192	ASP280	OD1	40.202	32.1	41.707
2193	ASP280	OD2	39.935	32.652	39.636
2194	ASP280	C	40.414	35.918	40.612
2195	ASP280	O	40.849	36.882	39.961
2196	ARG281	N	39.133	35.599	40.695
2197	ARG281	CA	38.051	36.411	40.148
2198	ARG281	CB	37.463	35.679	38.942
2199	ARG281	CG	38.52	35.426	37.875
2200	ARG281	CD	37.938	34.729	36.654
2201	ARG281	NE	37.351	33.434	37.02
2202	ARG281	CZ	37.887	32.27	36.655
2203	ARG281	NH1	39.006	32.249	35.925
2204	ARG281	NH2	37.305	31.124	37.016
2205	ARG281	C	37.013	36.544	41.261
2206	ARG281	O	37.01	35.706	42.175
2207	PRO282	N	36.16	37.557	41.196
2208	PRO282	CA	35.226	37.842	42.294
2209	PRO282	CB	34.381	38.98	41.808
2210	PRO282	CG	34.908	39.464	40.468
2211	PRO282	CD	36.076	38.556	40.128
2212	PRO282	C	34.373	36.63	42.651
2213	PRO282	O	34.098	35.785	41.793
2214	GLY283	N	34.206	36.415	43.945
2215	GLY283	CA	33.38	35.295	44.423
2216	GLY283	C	34.154	34	44.702
2217	GLY283	O	33.731	33.201	45.546
2218	ASP284	N	35.241	33.777	43.976
2219	ASP284	CA	36.042	32.554	44.128
2220	ASP284	CB	37.148	32.535	43.081
2221	ASP284	CG	36.594	32.578	41.663
2222	ASP284	OD1	35.6	31.912	41.415
2223	ASP284	OD2	37.296	33.125	40.824
2224	ASP284	C	36.71	32.456	45.493
2225	ASP284	O	36.668	33.383	46.312
2226	MET285	N	37.282	31.289	45.735
2227	MET285	CA	38.07	31.065	46.947
2228	MET285	CB	38.543	29.617	46.972
2229	MET285	CG	37.371	28.643	46.987
2230	MET285	SD	37.825	26.894	47.02
2231	MET285	CE	38.777	26.876	48.557
2232	MET285	C	39.279	31.991	46.965
2233	MET285	O	39.856	32.312	45.919
2234	VAL286	N	39.565	32.506	48.146
2235	VAL286	CA	40.704	33.405	48.327
2236	VAL286	CB	40.371	34.354	49.467
2237	VAL286	CG1	39.192	35.22	49.058
2238	VAL286	CG2	40.054	33.601	50.754

Table 12

2239	VAL286	C	41.993	32.639	48.597
2240	VAL286	O	41.972	31.514	49.111
2241	ASP287	N	43.099	33.213	48.155
2242	ASP287	CA	44.407	32.565	48.34
2243	ASP287	CB	44.591	31.524	47.23
2244	ASP287	CG	44.683	32.182	45.858
2245	ASP287	OD1	43.695	32.19	45.14
2246	ASP287	OD2	45.759	32.684	45.55
2247	ASP287	C	45.538	33.598	48.324
2248	ASP287	O	45.434	34.605	47.616
2249	PRO288	N	46.658	33.292	48.968
2250	PRO288	CA	47.727	34.292	49.169
2251	PRO288	CB	48.708	33.634	50.091
2252	PRO288	CG	48.253	32.217	50.394
2253	PRO288	CD	46.928	32.036	49.676
2254	PRO288	C	48.45	34.773	47.899
2255	PRO288	O	48.891	35.927	47.875
2256	PHE289	N	48.353	34.028	46.808
2257	PHE289	CA	48.962	34.433	45.535
2258	PHE289	CB	48.838	33.229	44.603
2259	PHE289	CG	49.372	33.374	43.18
2260	PHE289	CD1	50.734	33.506	42.951
2261	PHE289	CE1	51.216	33.612	41.653
2262	PHE289	CZ	50.334	33.586	40.581
2263	PHE289	CE2	48.971	33.455	40.808
2264	PHE289	CD2	48.491	33.347	42.107
2265	PHE289	C	48.213	35.631	44.958
2266	PHE289	O	48.783	36.722	44.821
2267	HIS290	N	46.896	35.508	44.968
2268	HIS290	CA	46.032	36.582	44.483
2269	HIS290	CB	44.721	35.971	44.008
2270	HIS290	CG	44.899	35.089	42.79
2271	HIS290	ND1	44.744	33.754	42.729
2272	HIS290	CE1	44.997	33.33	41.475
2273	HIS290	NE2	45.304	34.417	40.733
2274	HIS290	CD2	45.248	35.508	41.529
2275	HIS290	C	45.769	37.636	45.552
2276	HIS290	O	45.434	38.774	45.213
2277	THR291	N	46.122	37.341	46.791
2278	THR291	CA	46.007	38.343	47.849
2279	THR291	CB	45.971	37.653	49.206
2280	THR291	OG1	44.836	36.799	49.22
2281	THR291	CG2	45.816	38.659	50.342
2282	THR291	C	47.175	39.316	47.782
2283	THR291	O	46.955	40.533	47.85
2284	LEU292	N	48.32	38.814	47.348
2285	LEU292	CA	49.477	39.68	47.138
2286	LEU292	CB	50.719	38.808	46.976
2287	LEU292	CG	51.947	39.635	46.603
2288	LEU292	CD1	52.224	40.72	47.635
2289	LEU292	CD2	53.174	38.751	46.412
2290	LEU292	C	49.282	40.532	45.891
2291	LEU292	O	49.485	41.751	45.959
2292	PHE293	N	48.634	39.974	44.882
2293	PHE293	CA	48.42	40.743	43.652
2294	PHE293	CB	48.223	39.776	42.494

Table 12

2295	PHE293	CG	49.469	38.952	42.185
2296	PHE293	CD1	49.341	37.654	41.715
2297	PHE293	CE1	50.475	36.906	41.432
2298	PHE293	CZ	51.737	37.45	41.623
2299	PHE293	CE2	51.867	38.748	42.096
2300	PHE293	CD2	50.733	39.498	42.375
2301	PHE293	C	47.239	41.705	43.76
2302	PHE293	O	47.279	42.781	43.154
2303	GLY294	N	46.34	41.442	44.692
2304	GLY294	CA	45.253	42.374	44.981
2305	GLY294	C	45.783	43.59	45.73
2306	GLY294	O	45.597	44.73	45.283
2307	ILE295	N	46.596	43.329	46.741
2308	ILE295	CA	47.18	44.399	47.558
2309	ILE295	CB	47.809	43.728	48.777
2310	ILE295	CG2	48.766	44.652	49.516
2311	ILE295	CG1	46.732	43.22	49.727
2312	ILE295	CD1	45.906	44.365	50.302
2313	ILE295	C	48.216	45.228	46.793
2314	ILE295	O	48.145	46.465	46.831
2315	ALA296	N	48.97	44.586	45.915
2316	ALA296	CA	49.948	45.312	45.1
2317	ALA296	CB	50.926	44.304	44.509
2318	ALA296	C	49.266	46.088	43.977
2319	ALA296	O	49.598	47.259	43.747
2320	GLY297	N	48.18	45.526	43.471
2321	GLY297	CA	47.353	46.187	42.462
2322	GLY297	C	46.775	47.481	43.011
2323	GLY297	O	47.107	48.557	42.5
2324	LEU298	N	46.138	47.395	44.169
2325	LEU298	CA	45.531	48.579	44.788
2326	LEU298	CB	44.743	48.153	46.02
2327	LEU298	CG	43.52	47.325	45.651
2328	LEU298	CD1	42.813	46.814	46.9
2329	LEU298	CD2	42.56	48.126	44.78
2330	LEU298	C	46.561	49.624	45.204
2331	LEU298	O	46.345	50.808	44.907
2332	SER299	N	47.742	49.205	45.629
2333	SER299	CA	48.766	50.182	46.009
2334	SER299	CB	49.912	49.465	46.705
2335	SER299	OG	50.832	50.461	47.127
2336	SER299	C	49.321	50.932	44.801
2337	SER299	O	49.404	52.165	44.859
2338	LEU300	N	49.395	50.264	43.658
2339	LEU300	CA	49.879	50.912	42.431
2340	LEU300	CB	50.432	49.827	41.507
2341	LEU300	CG	51.271	50.412	40.372
2342	LEU300	CD1	52.473	51.167	40.927
2343	LEU300	CD2	51.731	49.328	39.405
2344	LEU300	C	48.765	51.696	41.719
2345	LEU300	O	49.046	52.546	40.865
2346	LEU301	N	47.525	51.479	42.134
2347	LEU301	CA	46.394	52.268	41.63
2348	LEU301	CB	45.132	51.411	41.668
2349	LEU301	CG	45.205	50.246	40.691
2350	LEU301	CD1	44.053	49.275	40.911

Table 12

2351	LEU301	CD2	45.24	50.733	39.249
2352	LEU301	C	46.152	53.53	42.459
2353	LEU301	O	45.396	54.41	42.03
2354	GLY302	N	46.785	53.624	43.618
2355	GLY302	CA	46.681	54.846	44.422
2356	GLY302	C	46.209	54.599	45.854
2357	GLY302	O	45.822	55.543	46.557
2358	GLU303	N	46.208	53.348	46.281
2359	GLU303	CA	45.812	53.052	47.661
2360	GLU303	CB	45.241	51.636	47.745
2361	GLU303	CG	44.821	51.216	49.155
2362	GLU303	CD	43.859	52.219	49.782
2363	GLU303	OE1	42.661	51.998	49.714
2364	GLU303	OE2	44.356	53.158	50.394
2365	GLU303	C	46.999	53.24	48.603
2366	GLU303	O	47.681	52.273	48.962
2367	GLU304	N	46.991	54.409	49.227
2368	GLU304	CA	48.064	54.869	50.124
2369	GLU304	CB	47.977	56.388	50.206
2370	GLU304	CG	46.613	56.843	50.713
2371	GLU304	CD	46.537	58.367	50.721
2372	GLU304	OE1	45.729	58.888	51.476
2373	GLU304	OE2	47.203	58.968	49.891
2374	GLU304	C	48.035	54.281	51.541
2375	GLU304	O	48.833	54.698	52.386
2376	GLN305	N	47.101	53.384	51.819
2377	GLN305	CA	47.142	52.624	53.073
2378	GLN305	CB	45.746	52.098	53.385
2379	GLN305	CG	44.735	53.217	53.596
2380	GLN305	CD	43.349	52.609	53.788
2381	GLN305	OE1	43.183	51.628	54.52
2382	GLN305	NE2	42.386	53.146	53.06
2383	GLN305	C	48.084	51.431	52.921
2384	GLN305	O	48.559	50.864	53.911
2385	ILE306	N	48.364	51.083	51.676
2386	ILE306	CA	49.302	50.013	51.367
2387	ILE306	CB	48.686	49.172	50.254
2388	ILE306	CG2	49.573	47.983	49.912
2389	ILE306	CG1	47.295	48.69	50.648
2390	ILE306	CD1	46.632	47.932	49.505
2391	ILE306	C	50.613	50.629	50.892
2392	ILE306	O	50.611	51.5	50.013
2393	LYS307	N	51.713	50.165	51.464
2394	LYS307	CA	53.043	50.639	51.069
2395	LYS307	CB	54.093	49.846	51.84
2396	LYS307	CG	53.949	50.058	53.341
2397	LYS307	CD	55.022	49.301	54.111
2398	LYS307	CE	54.863	49.495	55.614
2399	LYS307	NZ	55.865	48.715	56.357
2400	LYS307	C	53.25	50.45	49.571
2401	LYS307	O	52.791	49.458	48.991
2402	PRO308	N	53.893	51.429	48.953
2403	PRO308	CA	54.059	51.432	47.498
2404	PRO308	CB	54.815	52.685	47.183
2405	PRO308	CG	55.073	53.451	48.472
2406	PRO308	CD	54.442	52.631	49.585

Table 12

2407	PRO308	C	54.81	50.192	47.042
2408	PRO308	O	55.782	49.77	47.681
2409	VAL309	N	54.282	49.559	46.012
2410	VAL309	CA	54.893	48.337	45.496
2411	VAL309	CB	53.782	47.31	45.292
2412	VAL309	CG1	52.667	47.871	44.419
2413	VAL309	CG2	54.304	45.985	44.746
2414	VAL309	C	55.665	48.611	44.206
2415	VAL309	O	55.172	49.255	43.272
2416	ASN310	N	56.909	48.172	44.214
2417	ASN310	CA	57.79	48.283	43.055
2418	ASN310	CB	59.194	47.942	43.547
2419	ASN310	CG	60.216	47.897	42.416
2420	ASN310	OD1	60.203	46.971	41.591
2421	ASN310	ND2	61.119	48.86	42.422
2422	ASN310	C	57.346	47.311	41.971
2423	ASN310	O	57.44	46.09	42.155
2424	PRO311	N	57.077	47.85	40.791
2425	PRO311	CA	56.422	47.09	39.715
2426	PRO311	CB	55.968	48.131	38.738
2427	PRO311	CG	56.518	49.487	39.146
2428	PRO311	CD	57.241	49.269	40.462
2429	PRO311	C	57.309	46.056	39.004
2430	PRO311	O	56.789	45.237	38.241
2431	VAL312	N	58.594	46.018	39.316
2432	VAL312	CA	59.491	45.052	38.691
2433	VAL312	CB	60.82	45.762	38.461
2434	VAL312	CG1	61.908	44.807	37.99
2435	VAL312	CG2	60.654	46.924	37.492
2436	VAL312	C	59.706	43.835	39.586
2437	VAL312	O	59.618	42.693	39.12
2438	PHE313	N	59.864	44.081	40.877
2439	PHE313	CA	60.187	42.992	41.809
2440	PHE313	CB	61.265	43.476	42.774
2441	PHE313	CG	62.615	43.798	42.139
2442	PHE313	CD1	62.982	45.117	41.902
2443	PHE313	CE1	64.213	45.403	41.327
2444	PHE313	CZ	65.081	44.37	40.998
2445	PHE313	CE2	64.72	43.053	41.247
2446	PHE313	CD2	63.488	42.767	41.82
2447	PHE313	C	58.995	42.51	42.631
2448	PHE313	O	59.098	41.472	43.297
2449	CYS314	N	57.912	43.273	42.599
2450	CYS314	CA	56.711	43.024	43.418
2451	CYS314	CB	56.06	41.705	43.004
2452	CYS314	SG	54.437	41.355	43.723
2453	CYS314	C	57.073	43.027	44.906
2454	CYS314	O	56.716	42.124	45.668
2455	MET315	N	57.829	44.043	45.29
2456	MET315	CA	58.271	44.201	46.681
2457	MET315	CB	59.775	43.939	46.766
2458	MET315	CG	60.14	42.489	46.474
2459	MET315	SD	61.893	42.094	46.663
2460	MET315	CE	62.08	42.498	48.415
2461	MET315	C	57.978	45.62	47.146
2462	MET315	O	57.768	46.501	46.306

Table 12

2463	PRO316	N	57.888	45.833	48.449
2464	PRO316	CA	57.776	47.198	48.967
2465	PRO316	CB	57.767	47.065	50.457
2466	PRO316	CG	57.833	45.59	50.822
2467	PRO316	CD	57.939	44.827	49.513
2468	PRO316	C	58.921	48.081	48.478
2469	PRO316	O	60.109	47.752	48.616
2470	GLU317	N	58.537	49.273	48.054
2471	GLU317	CA	59.458	50.231	47.437
2472	GLU317	CB	58.656	51.47	47.055
2473	GLU317	CG	59.399	52.336	46.045
2474	GLU317	CD	59.31	51.675	44.678
2475	GLU317	OE1	58.257	51.118	44.404
2476	GLU317	OE2	60.271	51.741	43.921
2477	GLU317	C	60.562	50.662	48.391
2478	GLU317	O	61.735	50.555	48.021
2479	GLU318	N	60.232	50.779	49.669
2480	GLU318	CA	61.221	51.22	50.659
2481	GLU318	CB	60.482	51.685	51.911
2482	GLU318	CG	59.622	50.584	52.522
2483	GLU318	CD	58.833	51.135	53.706
2484	GLU318	OE1	58.506	50.346	54.58
2485	GLU318	OE2	58.427	52.284	53.618
2486	GLU318	C	62.265	50.155	51.021
2487	GLU318	O	63.376	50.528	51.412
2488	VAL319	N	62.031	48.904	50.652
2489	VAL319	CA	63.021	47.866	50.927
2490	VAL319	CB	62.3	46.53	51.068
2491	VAL319	CG1	63.288	45.382	51.243
2492	VAL319	CG2	61.314	46.574	52.228
2493	VAL319	C	64.019	47.81	49.78
2494	VAL319	O	65.232	47.726	50.015
2495	LEU320	N	63.543	48.196	48.607
2496	LEU320	CA	64.409	48.232	47.431
2497	LEU320	CB	63.552	48.006	46.197
2498	LEU320	CG	62.901	46.633	46.277
2499	LEU320	CD1	61.914	46.423	45.144
2500	LEU320	CD2	63.951	45.529	46.28
2501	LEU320	C	65.161	49.554	47.358
2502	LEU320	O	66.308	49.585	46.895
2503	GLN321	N	64.645	50.546	48.062
2504	GLN321	CA	65.392	51.787	48.265
2505	GLN321	CB	64.432	52.844	48.791
2506	GLN321	CG	63.324	53.166	47.799
2507	GLN321	CD	62.241	53.956	48.524
2508	GLN321	OE1	61.048	53.849	48.211
2509	GLN321	NE2	62.662	54.652	49.565
2510	GLN321	C	66.498	51.591	49.299
2511	GLN321	O	67.619	52.064	49.084
2512	ARG322	N	66.259	50.719	50.266
2513	ARG322	CA	67.257	50.455	51.309
2514	ARG322	CB	66.561	49.715	52.446
2515	ARG322	CG	67.543	49.308	53.538
2516	ARG322	CD	66.855	48.523	54.649
2517	ARG322	NE	67.832	48.089	55.66
2518	ARG322	CZ	67.913	48.623	56.881

Table 12

2519	ARG322	NH1	67.07	49.591	57.245
2520	ARG322	NH2	68.831	48.179	57.742
2521	ARG322	C	68.423	49.612	50.793
2522	ARG322	O	69.581	49.875	51.139
2523	VAL323	N	68.141	48.714	49.861
2524	VAL323	CA	69.218	47.926	49.251
2525	VAL323	CB	68.723	46.508	48.984
2526	VAL323	CG1	68.421	45.787	50.293
2527	VAL323	CG2	67.505	46.492	48.07
2528	VAL323	C	69.771	48.564	47.973
2529	VAL323	O	70.749	48.053	47.413
2530	ASN324	N	69.228	49.717	47.604
2531	ASN324	CA	69.642	50.478	46.413
2532	ASN324	CB	71.082	50.964	46.579
2533	ASN324	CG	71.19	51.955	47.736
2534	ASN324	OD1	70.782	53.116	47.613
2535	ASN324	ND2	71.809	51.509	48.818
2536	ASN324	C	69.498	49.667	45.13
2537	ASN324	O	70.41	49.614	44.296
2538	VAL325	N	68.321	49.093	44.951
2539	VAL325	CA	68.017	48.324	43.742
2540	VAL325	CB	67.85	46.841	44.078
2541	VAL325	CG1	67.643	46.023	42.809
2542	VAL325	CG2	69.065	46.3	44.823
2543	VAL325	C	66.752	48.894	43.107
2544	VAL325	O	65.658	48.32	43.17
2545	GLN326	N	66.921	50.071	42.53
2546	GLN326	CA	65.801	50.776	41.899
2547	GLN326	CB	65.739	52.189	42.474
2548	GLN326	CG	65.343	52.191	43.948
2549	GLN326	CD	63.876	51.794	44.104
2550	GLN326	OE1	63.514	51.013	44.992
2551	GLN326	NE2	63.04	52.375	43.261
2552	GLN326	C	65.941	50.843	40.381
2553	GLN326	O	66.745	51.617	39.85
2554	PRO327	N	65.116	50.063	39.702
2555	PRO327	CA	65.046	50.094	38.238
2556	PRO327	CB	64.162	48.944	37.87
2557	PRO327	CG	63.557	48.354	39.133
2558	PRO327	CD	64.142	49.142	40.289
2559	PRO327	C	64.466	51.413	37.732
2560	PRO327	O	63.543	51.978	38.334
2561	GLU328	N	65.004	51.89	36.624
2562	GLU328	CA	64.529	53.157	36.052
2563	GLU328	CB	65.71	53.912	35.454
2564	GLU328	CG	65.288	55.275	34.91
2565	GLU328	CD	66.489	55.969	34.28
2566	GLU328	OE1	67.6	55.584	34.621
2567	GLU328	OE2	66.282	56.888	33.5
2568	GLU328	C	63.491	52.908	34.966
2569	GLU328	O	63.842	52.713	33.8
2570	LEU329	N	62.228	53.029	35.338
2571	LEU329	CA	61.119	52.793	34.399
2572	LEU329	CB	59.807	52.832	35.175
2573	LEU329	CG	59.845	51.956	36.426
2574	LEU329	CD1	58.562	52.115	37.232

Table 12

2575	LEU329	CD2	60.092	50.487	36.099
2576	LEU329	C	61.092	53.866	33.31
2577	LEU329	O	61.756	54.903	33.446
2578	VAL330	N	60.407	53.582	32.214
2579	VAL330	CA	60.291	54.567	31.129
2580	VAL330	CB	59.554	53.943	29.945
2581	VAL330	CG1	59.371	54.932	28.796
2582	VAL330	CG2	60.245	52.685	29.442
2583	VAL330	C	59.51	55.78	31.621
2584	VAL330	O	58.394	55.649	32.139
2585	SER331	N	60.135	56.939	31.528
2586	SER331	CA	59.479	58.179	31.939
2587	SER331	CB	60.269	58.798	33.082
2588	SER331	OG	59.633	60.024	33.412
2589	SER331	C	59.404	59.166	30.781
2590	SER331	O	60.341	59.197	29.998
2591	SER331	OXT	58.428	59.902	30.728

CLAIMS

What is claimed is:

1. A method of inducing apoptosis in a eukaryotic cell, the method comprising contacting the cell with an agent that is a RabGGT inhibitor.

2. The method of claim 1, wherein the RabGGT inhibitor reduces the level of RabGGT mRNA in the cell.

3. The method of claim 1, wherein the RabGGT inhibitor is an interfering RNA.

4. The method of claim 1, wherein the RabGGT inhibitor reduces the level of RabGGT protein in the cell.

5. The method of claim 1, wherein the RabGGT inhibitor inhibits RabGGT enzymatic activity.

6. The method of claim 5, wherein the RabGGT inhibitor is a benzodiazapine compound.

7. The method of claim 5, wherein the RabGGT inhibitor is a tetrahydroquinoline compound.

8. The method of claim 1, wherein the agent does not substantially inhibit farnesyl transferase activity.

9. A method of inhibiting tumor growth in an individual having a tumor, the method comprising:

identifying a compound that is a RabGGT inhibitor;

testing the ability of the compound to modulate farnesyl transferase (FT) activity;

modifying the compound, wherein the modified compound exhibits reduced modulation of FT activity compared to the unmodified compound, wherein inhibition of RabGGT is retained; and

administering to the individual an effective amount of an agent that is a RabGGT inhibitor.

10. The method of claim 9, wherein the RabGGT inhibitor reduces the level of RabGGT mRNA in the tumor.

11. The method of claim 9, wherein the RabGGT inhibitor is an interfering RNA.

12. The method of claim 9, wherein the RabGGT inhibitor reduces the level of RabGGT protein in the tumor.

13. The method of claim 9, wherein the RabGGT inhibitor inhibits RabGGT enzymatic activity.

14. The method of claim 13, wherein the RabGGT inhibitor is a benzodiazapine compound.

15. The method of claim 13, wherein the RabGGT inhibitor is a tetrahydroquinoline compound.

16. The method of claim 9, wherein the agent does not substantially inhibit farnesyl transferase activity.

17. A method of determining the susceptibility of a tumor to treatment with a RabGGT inhibitor, the method comprising detecting a level of RabGGT in the tumor, wherein a level of RabGGT that is elevated compared to a normal cell of the same tissue type indicates that the tumor is susceptible to treatment with a RabGGT inhibitor.

18. A method of identifying an agent that selectively modulates RabGGT enzymatic activity, the method comprising;

determining the effect, if any, of the agent on enzymatic activity of RabGGT; and

determining the effect, if any, of the agent on enzymatic activity of farnesyl transferase.

wherein an increase or decrease of enzymatic activity of RabGGT of at least about 15% compared to the enzymatic activity of RabGGT in the absence of the agent, and a reduction of enzymatic activity of farnesyl transferase of less than about 10% compared to the enzymatic activity of farnesyl transferase in the absence of the agent, indicates that the agent is a selective modulator of RabGGT enzymatic activity.

19. An agent identified by the method of claim 18.

20. A method of identifying an agent that modulates RabGGT enzymatic activity and modulates apoptosis, the method comprising:

determining the effect, if any, of the agent on RabGGT enzymatic activity; and

determining the effect, if any, of the agent on apoptosis in a eukaryotic cell,

wherein an increase or decrease of enzymatic activity of RabGGT of at least about 15% compared to the enzymatic activity of RabGGT in the absence of the agent, and wherein an increase or decrease in apoptosis of at least about 15% compared to the level of apoptosis in the absence of the agent indicates that the agent modulates RabGGT enzymatic activity and apoptosis.

21. A database comprising:

a machine-readable data storage medium comprising a data storage material encoded with machine-readable data, wherein said data comprises the three-dimensional coordinates of a subset of the atoms in a RabGGT polypeptide.

22. A computer for producing a three-dimensional representation of a RabGGT protein, wherein said computer comprises:

a machine-readable data storage medium comprising a data storage material encoded with machine-readable data, wherein said data comprises the three-dimensional coordinates of a subset of the atoms in RabGGT polypeptide;

a working memory for storing instructions for processing said machine-readable data;

a central-processing unit coupled to said working memory and to said machine-readable data storage medium for processing said machine readable data into said three-dimensional representation; and

a display coupled to said central-processing unit for displaying said three-dimensional representation.

23. The computer of claim 22, wherein said RabGGT polypeptide is complexed with a Rab protein.

24. The computer of claim 22, wherein said RabGGT polypeptide is bound to an agent.

25. The computer of claim 24, wherein said agent is an inhibitor of RabGGT enzymatic activity.

26. A computer-assisted method for identifying potential modulators of apoptosis, using a programmed computer comprising a processor, a data storage system, an input device, and an output device, comprising the steps of:

(a) inputting into the programmed computer through said input device data comprising the three-dimensional coordinates of a subset of the atoms in a RabGGT enzyme, thereby generating a criteria data set;

(b) comparing, using said processor, said criteria data set to a computer database of chemical structures stored in said computer data storage system;

(c) selecting from said database, using computer methods, chemical structures having a portion that is structurally similar to said criteria data set;

(d) outputting to said output device the selected chemical structures having a portion similar to said criteria data set.

27. A compound having a chemical structure selected using the method of claim 26.

28. A method of identifying an agent that modulates a binding event between a RabGGT polypeptide and a second polypeptide or polypeptide complex, the method comprising:

contacting the agent with a sample comprising a RabGGT polypeptide and a second polypeptide; and

determining the effect, if any, of the test agent on the binding between the RabGGT polyeptide and the second polypeptide or polypeptide complex.

29. The method of claim 28, wherein the second polypeptide is a Rab polypeptide.

30. The method of claim 28, wherein the polypeptide complex is a Rab/REP complex.

31. The method of claim 28, wherein said determining is performed using a method selected from a FRET assay, a BRET assay, a fluorescence quenching assay; a fluorescence anisotropy assay; an immunological assay; and an assay involving binding of a detectably labeled protein to an immobilized protein.

32. A method of identifying an agent that induces apoptosis and/or inhibits cell proliferation comprising:

a) screening a test agent in an assay system that detects changes in RabGGT level or activity,

b) identifying a test agent that reduces RabGGT levels or activity in said assay system, and

c) determining whether the test agent identified in (b) induces apoptosis in a cell and/or inhibits cell proliferation.

33. The method of claim 32 wherein the assay system is a high-throughput screening (HTS) system that detects changes in RabGGT enzymatic activity.

34. A method of identifying a clinical compound for treatment of disorders associated with undesired or uncontrolled cell proliferation comprising:

a) performing the method of claim 32 to identify an agent that induces apoptosis and/or inhibits cell proliferation,

b) using said agent as a lead compound to design and synthesize analog compounds, and

c) selecting an analog compound having favorable properties for use as a clinical compound.

35. A kit comprising a clinical compound identified according to the method of claim 34 and instructions for administering the clinical compound to a patient afflicted with a disorder associated with undesired or uncontrolled cell proliferation .

36. A method of inducing apoptosis in a cell comprising contacting the cell with the clinical compound identified by the method of claim 34.

37. The method of claim 1, wherein the RabGGT inhibitor is an antibody.

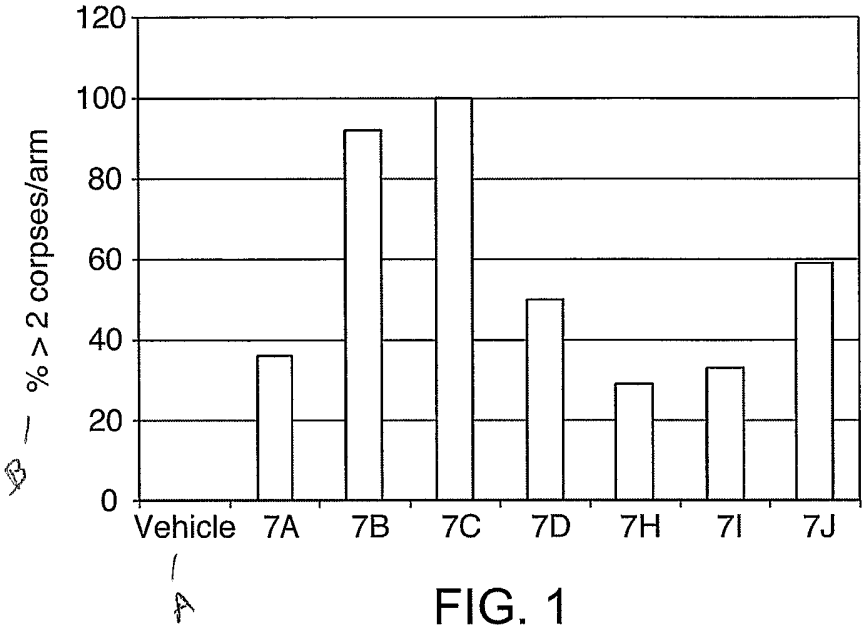

120
100
80
60
40
20
0
% > 2 corpses/arm
Vehicle
7A
7B
7C
7D
7H
7I
7J

FIG. 1

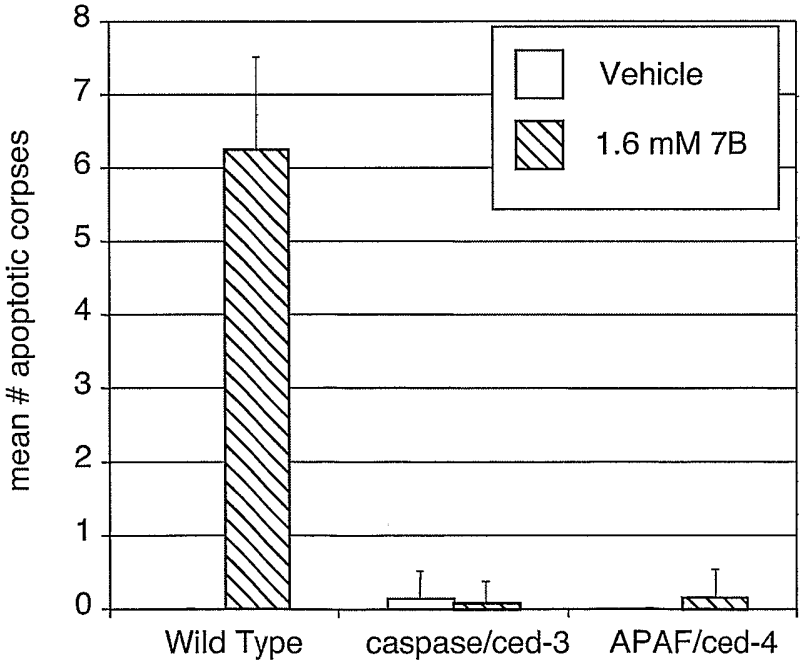

8
7
6
5
4
3
2
1
0
mean # apoptotic corpses
Vehicle
1.6 mM 7B
Wild Type
caspase/ced-3
APAF/ced-4

FIG. 2

FIG. 3

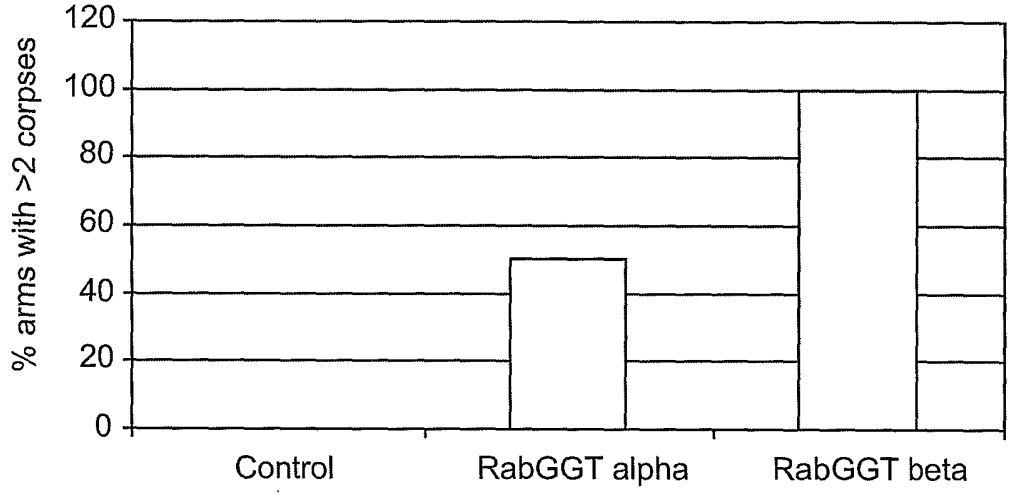
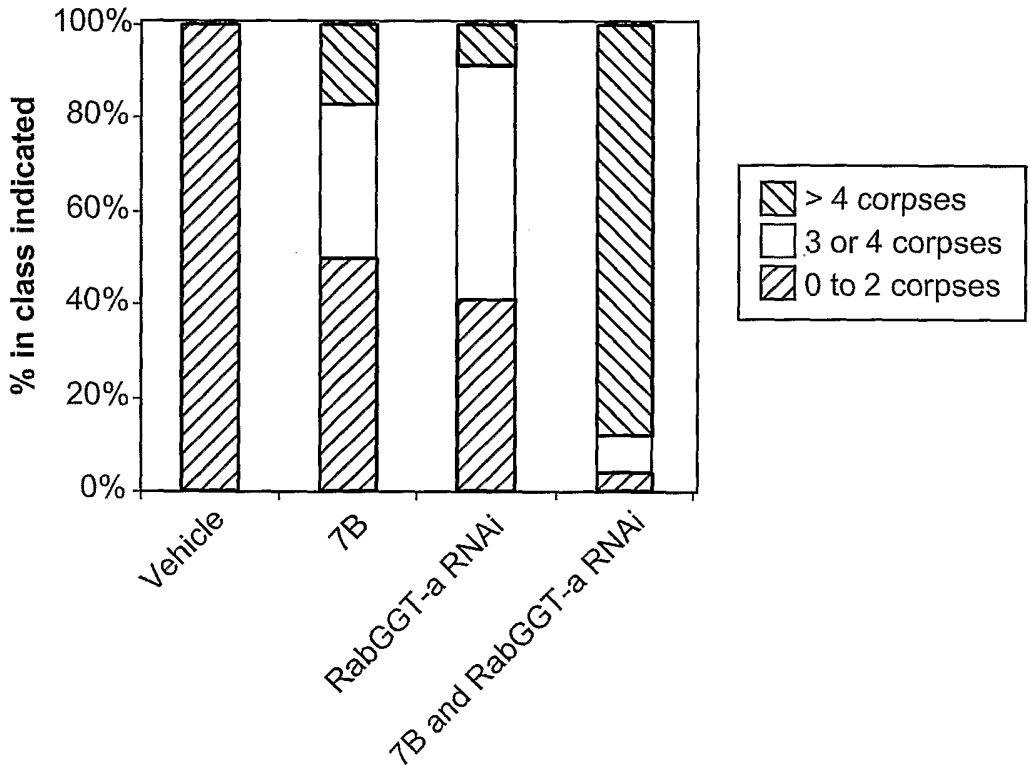

120
100
80
60
40
20
0
% arms with >2 corpses
Control
RabGGT alpha
RabGGT beta

FIG. 4


100%
80%
60%
40%
20%
0%
% in class indicated
Vehicle
7B
RabGGT-a RNAi
7B and RabGGT-a RNAi
> 4 corpses
3 or 4 corpses
0 to 2 corpses

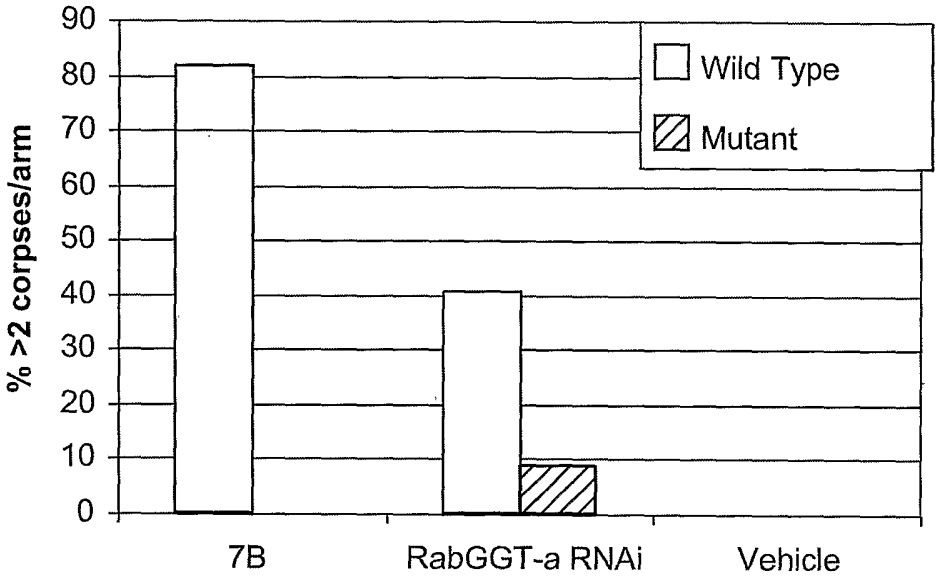

90
80
70
60
50
40
30
20
10
0
% >2 corpses/arm
Wild Type
Mutant
7B
RabGGT-a RNAi
Vehicle

FIG. 5

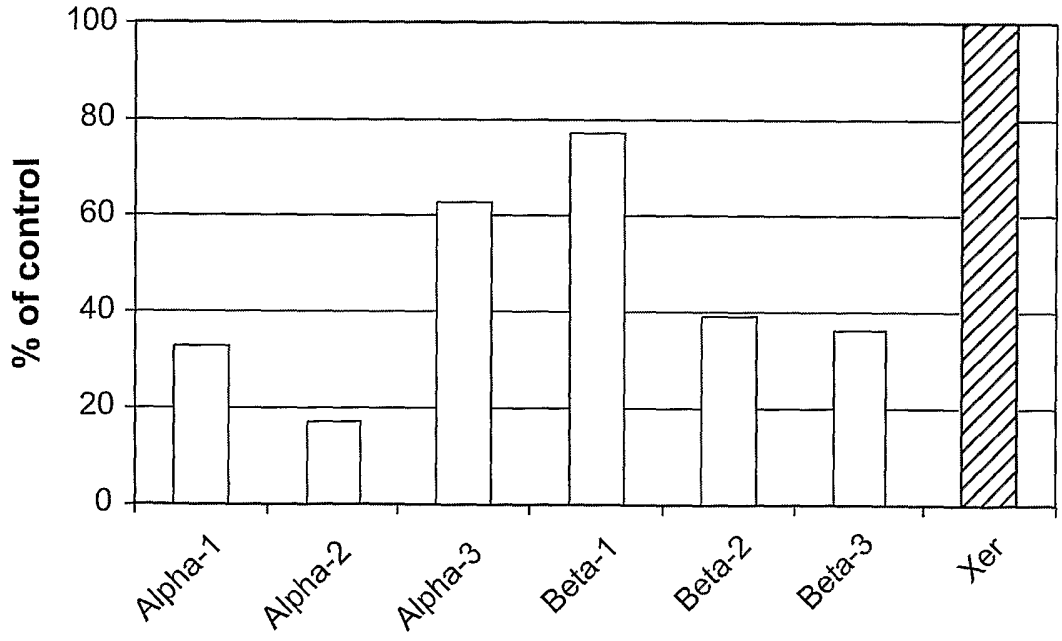

100
80
60
40
20
0
% of control
Alpha-1
Alpha-2
Alpha-3
Beta-1
Beta-2
Beta-3
Xer

FIG. 6

FIG. 7

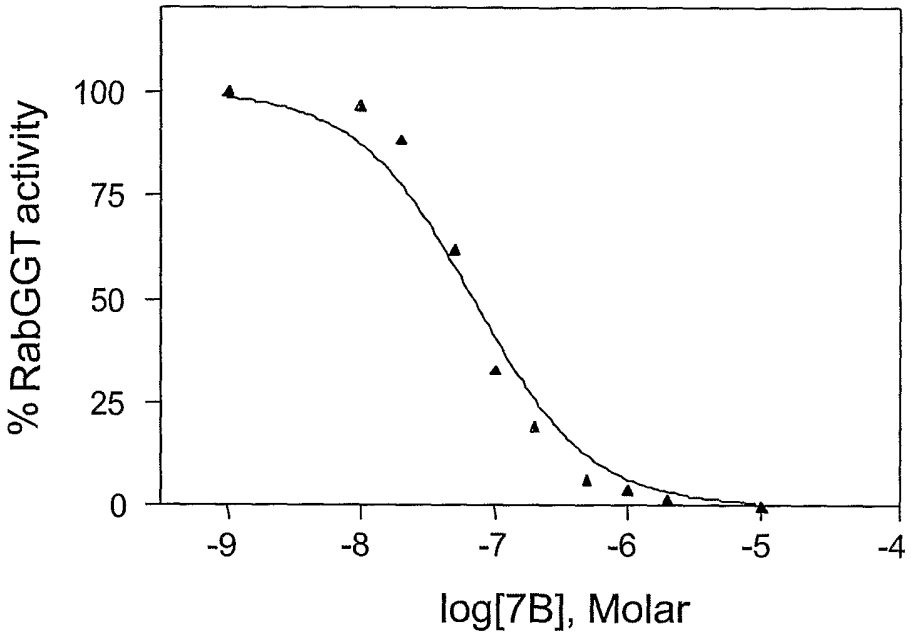

% RabGGT activity
100
75
50
25
0
-9
-8
-7
-6
-5
-4
log[7B], Molar

FIG. 8A

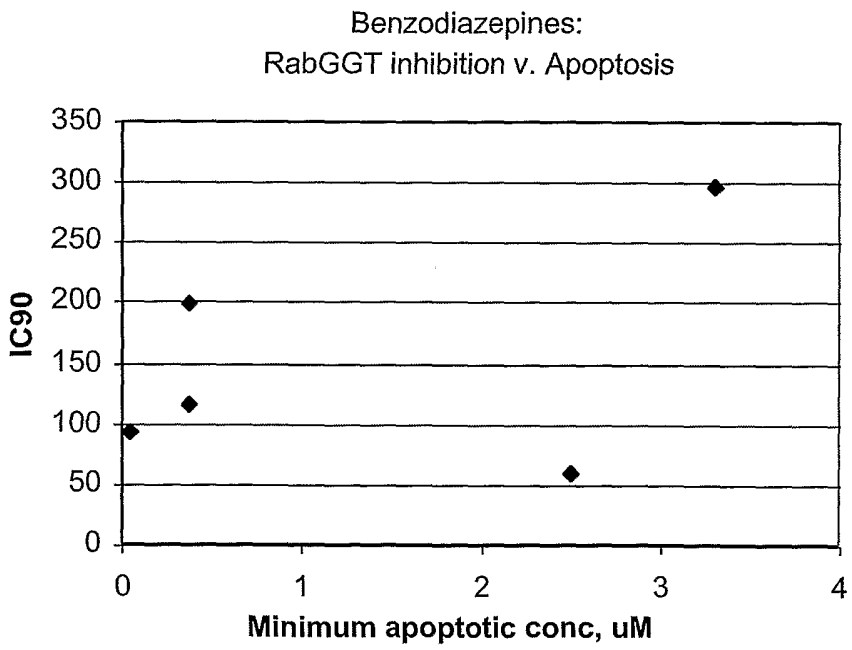

Benzodiazepines:
RabGGT inhibition v. Apoptosis
IC90
350
300
250
200
150
100
50
0
0
1
2
3
4
Minimum apoptotic conc, uM

FIG. 8B

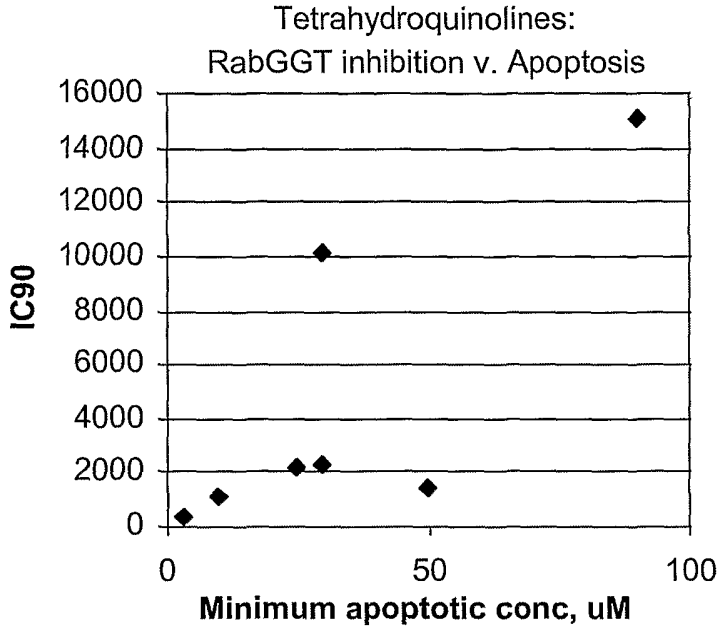

Tetrahydroquinolines:
RabGGT inhibition v. Apoptosis
16000
14000
12000
10000
8000
6000
4000
2000
0
IC90
0
50
100
Minimum apoptotic conc, uM

FIG. 8C

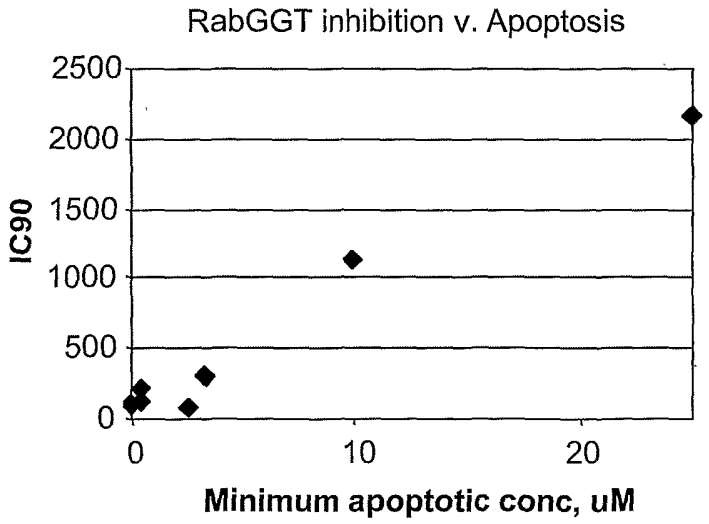

RabGGT inhibition v. Apoptosis
2500
2000
1500
1000
500
0
IC90
0
10
20
Minimum apoptotic conc, uM

FIG. 9

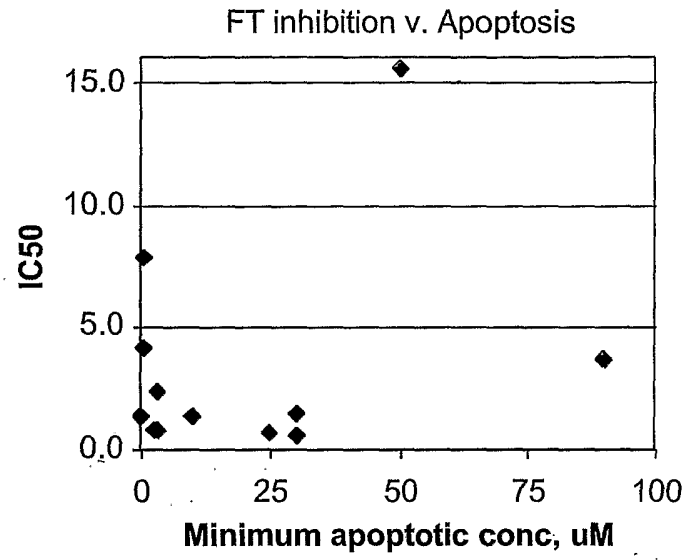

FT inhibition v. Apoptosis
15.0
10.0
5.0
0.0
IC50
0
25
50
75
100
Minimum apoptotic conc, uM

FIG. 10

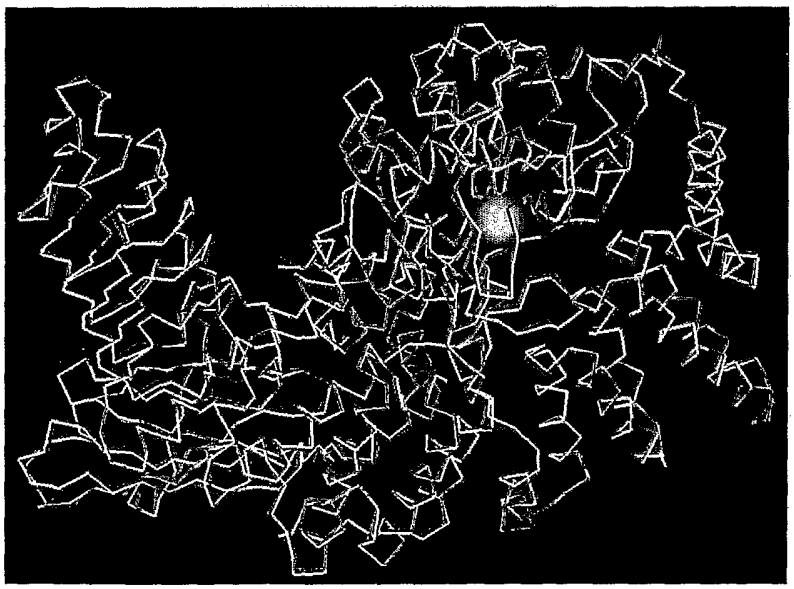


FIG. 11A

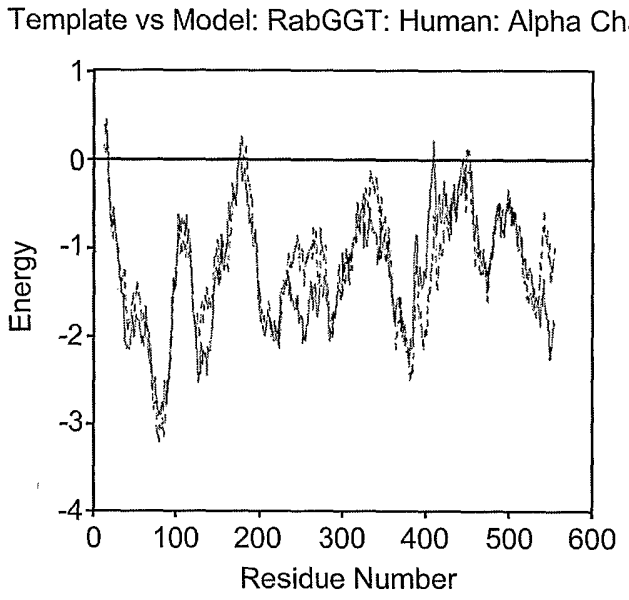


FIG. 11B

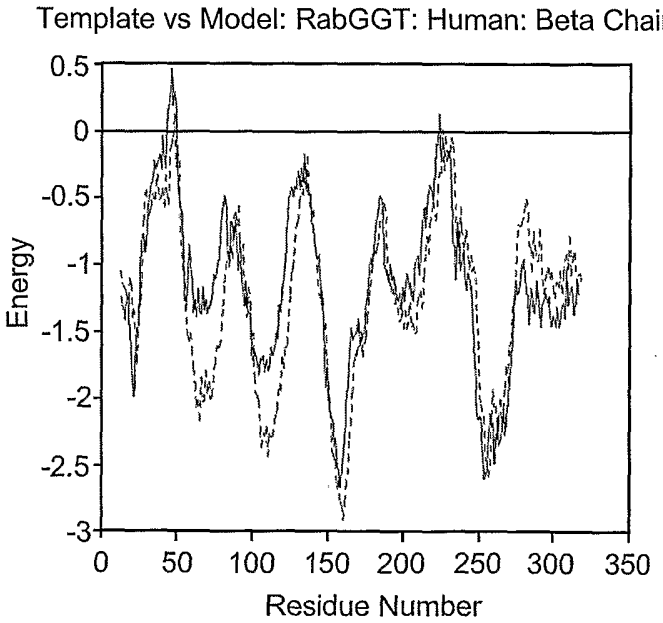


FIG. 12

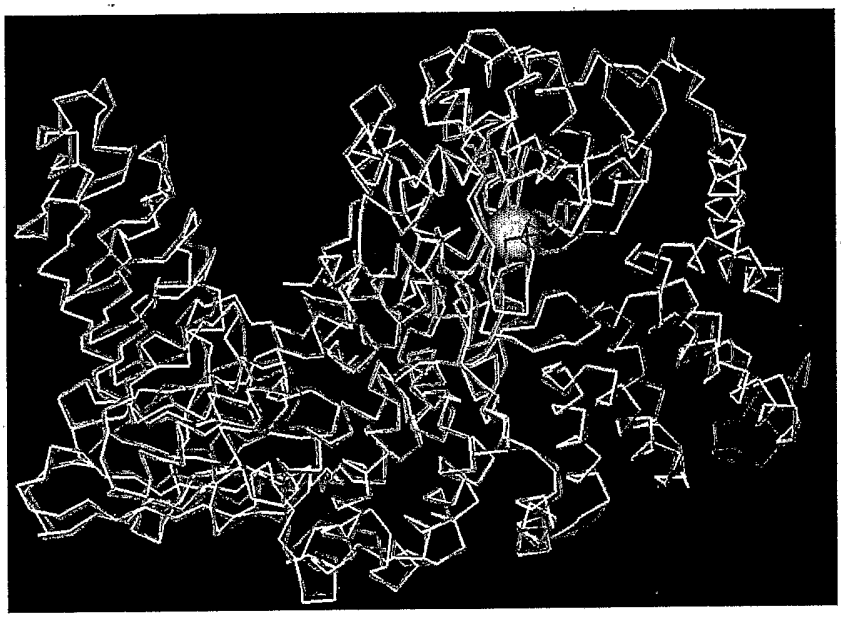


FIG. 13A

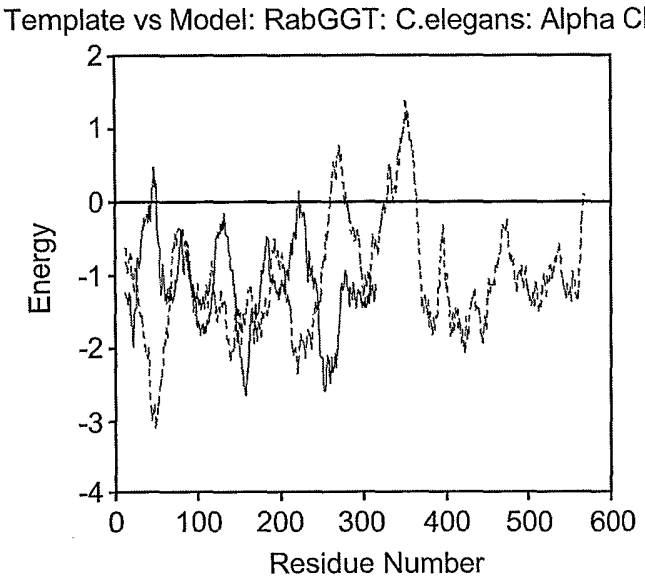


FIG. 13B

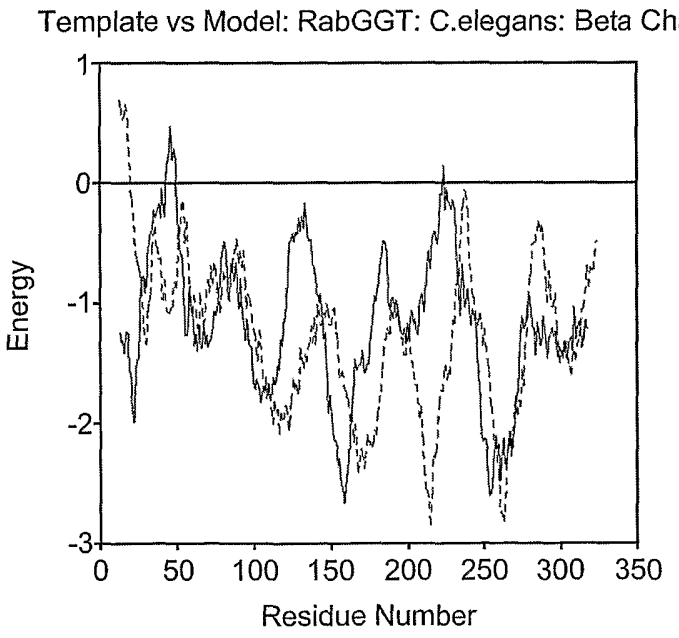


FIG. 14A

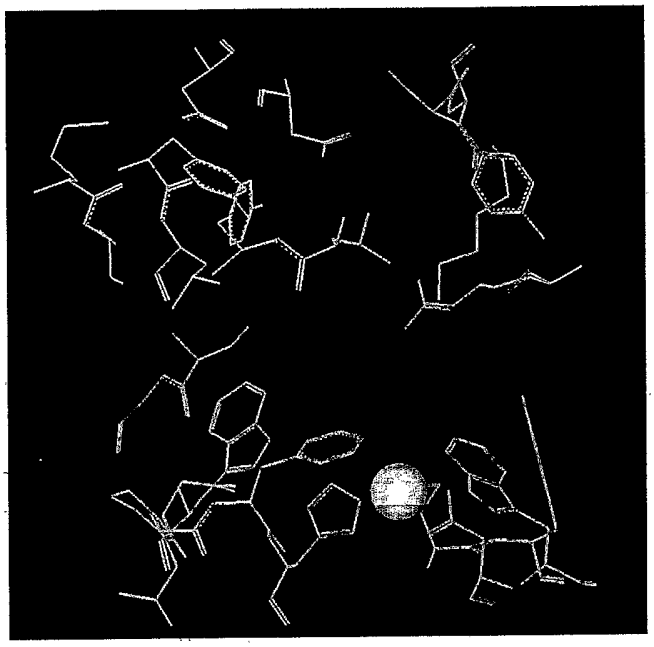


FIG. 14B

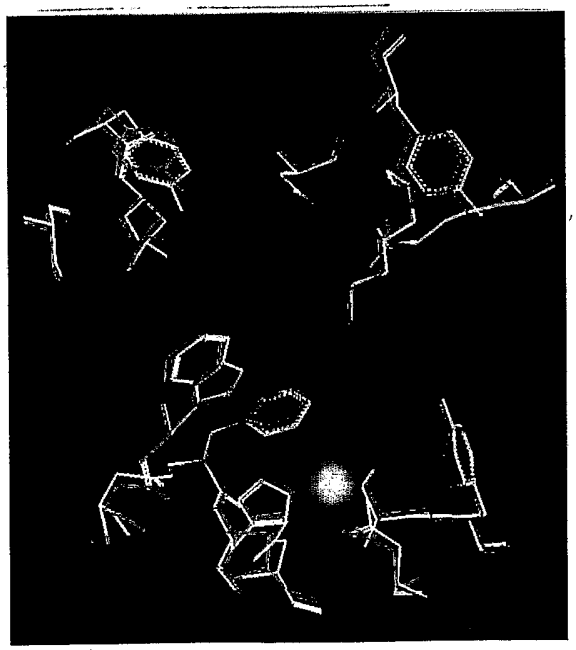


FIG. 14C

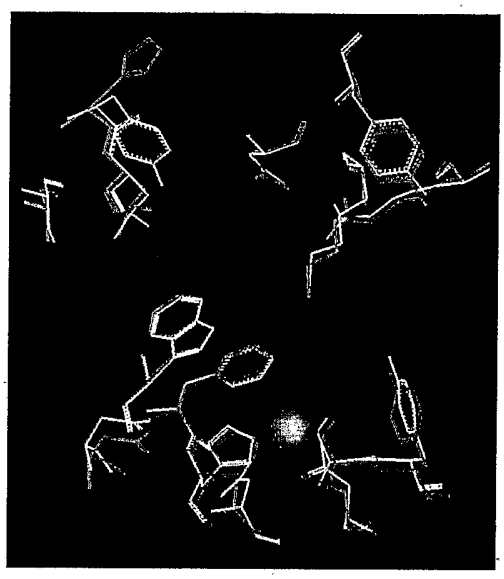
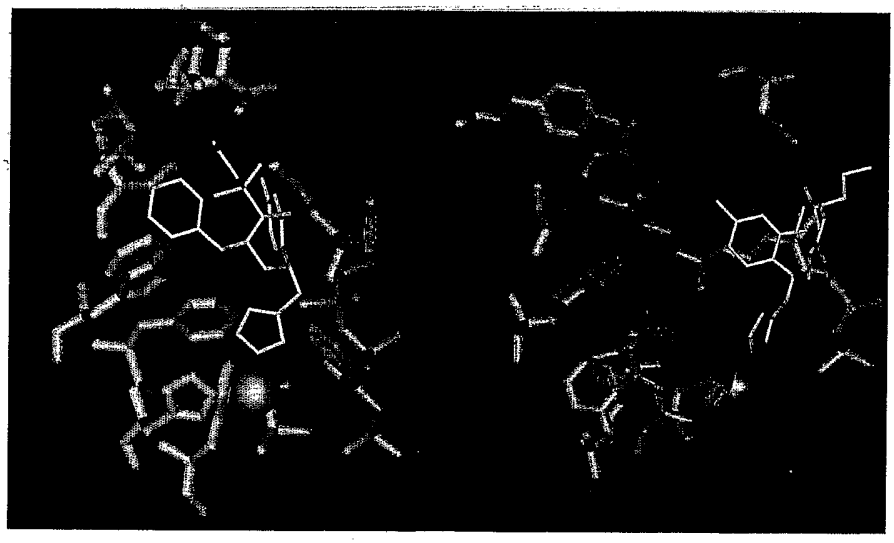


FIG. 15A



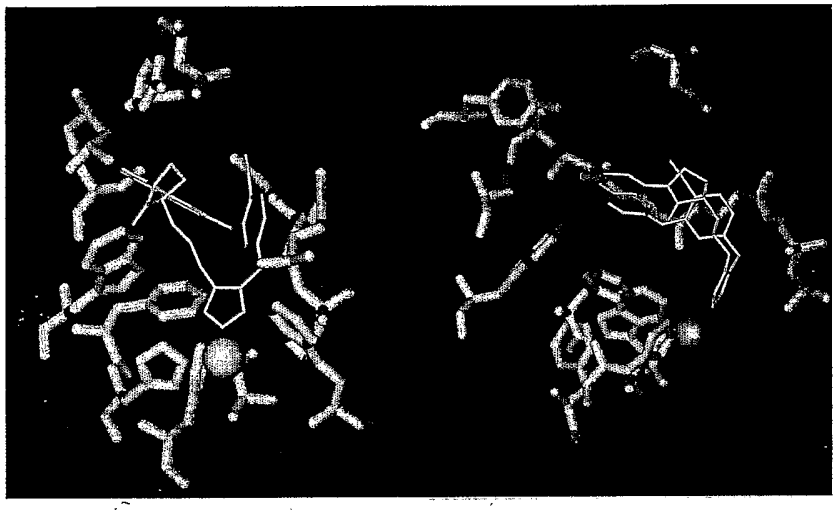


FIG. 15B

FIG. 16A

```
   1  gaattccctcgcgctctggnccgggcgaatcgggntataggaagggccacacggatggaa   60

  61  gtcctagtccgggtgctcacctcttgtggaacgtgcaaagcctgtcccaggacctctcta  120

 121  cactctgggggtctctgcccaggcacgcttgctgcttccggacacagctgtgggcggagc  180

 181  tagtaggggcgggctacgtgattgacacttctctcctcagacttcaagggctaccactgg  240

 241  acccttcccctgtcttgaaccctgagccggcaccatgcacggacgcctgaaggtgaagac  300
   1                                  M  H  G  R  L  K  V  K  T    9

 301  gtcagaagagcaggcggaggccaaaaggctagagcgagagcagaagctgaagctatacca  360
  10   S  E  E  Q  A  E  A  K  R  L  E  R  E  Q  K  L  K  L  Y  Q   29

 361  gtcagccacccaggccgtattccagaagcgccaggctggtgagctggatgagtccgtgct  420
  30   S  A  T  Q  A  V  F  Q  K  R  Q  A  G  E  L  D  E  S  V  L   49

 421  ggaactgacaagccagattctgggagccaaccctgattttgccaccctctggaactgccg  480
  50   E  L  T  S  Q  I  L  G  A  N  P  D  F  A  T  L  W  N  C  R   69

 481  acgagaggtgctccagcagctggagactcagaagtctcctgaagagttggctgctctggt  540
  70   R  E  V  L  Q  Q  L  E  T  Q  K  S  P  E  E  L  A  A  L  V   89

 541  gaaggcagaactgggcttcctggagagctgcctgcgggtgaaccccaagtcttatggtac  600
  90   K  A  E  L  G  F  L  E  S  C  L  R  V  N  P  K  S  Y  G  T  109

 601  ctggcaccaccgatgctggctgctaggccgcctgcctgagcccaactggacccgagagct  660
 110   W  H  H  R  C  W  L  L  G  R  L  P  E  P  N  W  T  R  E  L  129

 661  ggagctctgtgcccgtttcctggaggtggatgagcggaactttcactgctgggactatcg  720
 130   E  L  C  A  R  F  L  E  V  D  E  R  N  F  H  C  W  D  Y  R  149

 721  gcggtttgtggccacacaggcagccgtgccccctgcagaagagctagccttcactgacag  780
 150   R  F  V  A  T  Q  A  A  V  P  P  A  E  E  L  A  F  T  D  S  169

 781  cctcatcacccgaaacttctccaactactcttcctggcattaccgctcctgtctcttgcc  840
 170   L  I  T  R  N  F  S  N  Y  S  S  W  H  Y  R  S  C  L  L  P  189

 841  ccagttgcacccccagccggattctggaccacaggggcgcctccctgaggatgtgctgct  900
 190   Q  L  H  P  Q  P  D  S  G  P  Q  G  R  L  P  E  D  V  L  L  209

 901  caaagagctggagctggtgcagaatgccttcttcactgaccccaatgaccagagtgcctg  960
 210   K  E  L  E  L  V  Q  N  A  F  F  T  D  P  N  D  Q  S  A  W  229

 961  gttttatcaccggtggctcctaggtcgagctgacccccaggatgcactgcgctgtctgca 1020
 230   F  Y  H  R  W  L  L  G  R  A  D  P  Q  D  A  L  R  C  L  H  249

1021  tgtgagccgggacgaggcctgtctgactgtctccttctctcggcccctcttagtgggctc 1080
 250   V  S  R  D  E  A  C  L  T  V  S  F  S  R  P  L  L  V  G  S  269

1081  caggatggagatcttgctgctcatggttgatgattctcccctgattgtggagtggaggac 1140
 270   R  M  E  I  L  L  L  M  V  D  D  S  P  L  I  V  E  W  R  T  289
```

FIG. 16B

```
1141  cccagatggcaggaaccggcccagccatgtctggctctgtgacctgcctgctgcctccct  1200
 290   P  D  G  R  N  R  P  S  H  V  W  L  C  D  L  P  A  A  S  L   309

1201  caacgaccagttgccccaacatacatttcgcgtcatttggacagcaggcgatgtccagaa  1260
 310   N  D  Q  L  P  Q  H  T  F  R  V  I  W  T  A  G  D  V  Q  K   329

1261  agaatgcgtgcttttaaaaggccgccaggagggctggtgccgggactccacgacagacga  1320
 330   E  C  V  L  L  K  G  R  Q  E  G  W  C  R  D  S  T  T  D  E   349

1321  gcagctattcaggtgtgagctgtcagtggagaagtccacagtgctgcagtctgagctgga  1380
 350   Q  L  F  R  C  E  L  S  V  E  K  S  T  V  L  Q  S  E  L  E   369

1381  atcctgtaaggagctgcaggagctggagcctgagaataaatggtgcctgcttaccatcat  1440
 370   S  C  K  E  L  Q  E  L  E  P  E  N  K  W  C  L  L  T  I  I   389

1441  cctgctgatgcgggcactggacccccctgctgtatgagaaggagaccctgcagtacttcca  1500
 390   L  L  M  R  A  L  D  P  L  L  Y  E  K  E  T  L  Q  Y  F  Q   409

1501  gaccctcaaggccgtggaccccatgcgggcaacgtatctggatgacctgcgcagcaagtt  1560
 410   T  L  K  A  V  D  P  M  R  A  T  Y  L  D  D  L  R  S  K  F   429

1561  cttgctggagaatagcgtgctcaagatggagtatgccgaggtgcgtgtgctgcacctggc  1620
 430   L  L  E  N  S  V  L  K  M  E  Y  A  E  V  R  V  L  H  L  A   449

1621  tcacaaggatctgacagtgctctgccatctggaacagctgctcttggtcacccatcttga  1680
 450   H  K  D  L  T  V  L  C  H  L  E  Q  L  L  L  V  T  H  L  D   469

1681  cttgtcacacaatcgcctccgaaccctgccacctgcactggctgccctgcgctgccttga  1740
 470   L  S  H  N  R  L  R  T  L  P  P  A  L  A  A  L  R  C  L  E   489

1741  ggtgctgcaggccagtgataatgcaatagagtccctggacggcgtcaccaacctaccccg  1800
 490   V  L  Q  A  S  D  N  A  I  E  S  L  D  G  V  T  N  L  P  R   509

1801  gctgcaggagctgctactgtgcaacaaccgcctccagcagcctgcagtgctccagcctct  1860
 510   L  Q  E  L  L  L  C  N  N  R  L  Q  Q  P  A  V  L  Q  P  L   529

1861  tgcctcctgccccaggctggtcctcctcaacctgcagggtaacccgctgtgccaagcggt  1920
 530   A  S  C  P  R  L  V  L  L  N  L  Q  G  N  P  L  C  Q  A  V   549

1921  gggcatcttggagcaactggctgaactgctgccttcagttagcagcgtcctcacctaaga  1980
 550   G  I  L  E  Q  L  A  E  L  L  P  S  V  S  S  V  L  T  *      568

1981  ggccctgccccctaccttgccctttaacttattgggactgaataaagaatggagaggcc  2040

2041  cctctcaggctaccaaaaaaaaaaaaa  2067
```

FIG. 17

```
   1  atgggcactccacagaaggatgttattatcaagtcagatgcaccggacactttgttattg   60
   1  M  G  T  P  Q  K  D  V  I  I  K  S  D  A  P  D  T  L  L  L    20

  61  gagaaacatgcagattatatcgcatcctatggctcaaagaaagatgattatgaatactgt   120
  21  E  K  H  A  D  Y  I  A  S  Y  G  S  K  K  D  D  Y  E  Y  C    40

 121  atgtctgagtatttgagaatgagtggcatctattggggtctgacagtaatggatctcatg   180
  41  M  S  E  Y  L  R  M  S  G  I  Y  W  G  L  T  V  M  D  L  M    60

 181  ggacaacttcatcgcatgaatagagaagagattctggcatttattaagtcttgccaacat   240
  61  G  Q  L  H  R  M  N  R  E  E  I  L  A  F  I  K  S  C  Q  H    80

 241  gaatgtggtggaataagtgctagtatcggacatgatcctcatcttttatacactcttagt   300
  81  E  C  G  G  I  S  A  S  I  G  H  D  P  H  L  L  Y  T  L  S   100

 301  gctgtccagattcttacgctgtatgacagtattaatgttattgacgtaaataaagttgtg   360
 101  A  V  Q  I  L  T  L  Y  D  S  I  N  V  I  D  V  N  K  V  V   120

 361  gaatatgttaaaggtctacagaaagaagatggttcttttgctggagatatttggggagaa   420
 121  E  Y  V  K  G  L  Q  K  E  D  G  S  F  A  G  D  I  W  G  E   140

 421  attgacacaagattctctttttgtgcggtggcaactttcgctttgttggggaagcttgat   480
 141  I  D  T  R  F  S  F  C  A  V  A  T  F  A  L  L  G  K  L  D   160

 481  gctattaatgtggaaaaggcaatcgaatttgttttatcctgtatgaactttgacggtgga   540
 161  A  I  N  V  E  K  A  I  E  F  V  L  S  C  M  N  F  D  G  G   180

 541  tttggttgcagaccaggttctgaatcccatgctgggcagatctattgttgcacaggattt   600
 181  F  G  C  R  P  G  S  E  S  H  A  G  Q  I  Y  C  C  T  G  F   200

 601  ctggctattacaagtcagttgcatcaagtaaattctgatttacttggctggtggctttgt   660
 201  L  A  I  T  S  Q  L  H  Q  V  N  S  D  L  L  G  W  W  L  C   220

 661  gaacgacaattaccctcaggcgggctcaatggaaggccggagaagttaccagatgtatgc   720
 221  E  R  Q  L  P  S  G  G  L  N  G  R  P  E  K  L  P  D  V  C   240

 721  tactcatggtgggtcctggcttccctaaagataattggaagacttcattggattgataga   780
 241  Y  S  W  W  V  L  A  S  L  K  I  I  G  R  L  H  W  I  D  R   260

 781  gagaaactgcgtaatttcattttagcatgtcaagatgaagaaacgggggatttgcagac   840
 261  E  K  L  R  N  F  I  L  A  C  Q  D  E  E  T  G  G  F  A  D   280

 841  aggccaggagatatggtggatccttttcataccttatttggaattgctggattgtcactt   900
 281  R  P  G  D  M  V  D  P  F  H  T  L  F  G  I  A  G  L  S  L   300

 901  ttgggagaagaacagattaaacctgttaatcctgtcttttgcatgcctgaagaagtgctt   960
 301  L  G  E  E  Q  I  K  P  V  N  P  V  F  C  M  P  E  E  V  L   320

 961  cagagagtgaatgttcagcctgagctagtgagctagattcattgaattgaaagttgcata  1020
 321  Q  R  V  N  V  Q  P  E  L  V  S  *                          332

1021  gtatagttttgccattttaacatttctgtatttgaagtgcttatcgaatctaaaagtgac  1080

1081  tactgttaatattttgtatattgtgttaaattaattttaataaattatataattatat    1138
```