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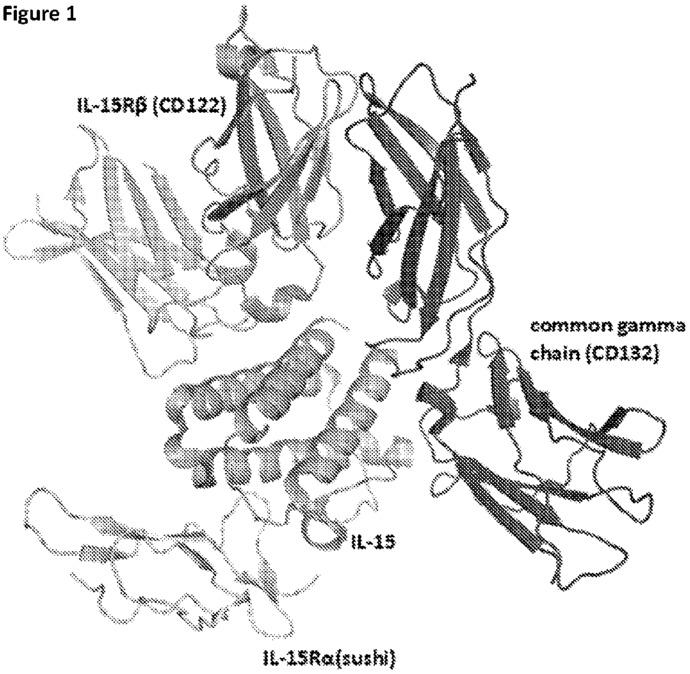
(54) Title: PD-1 TARGETED HETERODIMERIC FUSION PROTEINS CONTAINING IL-15/IL-15RA FC-FUSION PROTEINS AND PD-1 ANTIGEN BINDING DOMAINS AND USES THEREOF

Figure 1



(57) Abstract: The present invention is directed to novel PD-1-targeted IL-15/Ra-Fc fusion proteins comprising an IL-15/IL-15Ra Fc-fusion protein and a PD-1 antigen binding domain. The PD-1-targeted IL-15/Ra-Fc fusion proteins can be administered to a patient to treat cancer.

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WO 2019/204665 A1

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PD-1 TARGETED HETERODIMERIC FUSION PROTEINS CONTAINING IL-15/IL-15Ra Fc-FUSION PROTEINS AND PD-1 ANTIGEN BINDING DOMAINS AND USES THEREOF

CROSS-REFERENCING TO RELATED APPLICATIONS

[0001] This application claims priority to U.S. Provisional Application No. 62/659,571, filed April 18, 2018, the disclosure is herein incorporated by reference in its entirety.

BACKGROUND OF THE INVENTION

[0002] Cytokines such as IL-2 and IL-15 function in aiding the proliferation and differentiation of B cells, T cells, and NK cells. Both cytokines exert their cell signaling function through binding to a trimeric complex consisting of two shared receptors, the common gamma chain (γc; CD132) and IL-2 receptor beta-chain (IL-2Rß; CD122), as well as an alpha chain receptor unique to each cytokine: IL-2 receptor alpha (IL-2Rα; CD25) or IL-15 receptor alpha (IL-15Rα; CD215). Both cytokines are considered as potentially valuable therapeutics in oncology, and IL-2 has been approved for use in patients with metastatic renal-cell carcinoma and malignant melanoma. Currently, there are no approved uses of recombinant IL-15, although several clinical trials are ongoing. However, as potential drugs, both cytokines suffer from a very fast clearance, with half-lives measured in minutes. IL-2 immunotherapy has been associated with systemic toxicity when administered in high doses to overcome fast clearance. Such systemic toxicity has also been reported with IL-15 immunotherapy in recent clinical trials (Guo et al., *J Immunol*, 2015, 195(5):2353-64).

[0003] Immune checkpoint proteins such as PD-1 are up-regulated following T cell activation to preclude autoimmunity by exhausting activated T cells upon binding to immune checkpoint ligands such as PD-L1. However, immune checkpoint proteins are also up-regulated in tumor-infiltrating lymphocytes (TILs), and immune checkpoint ligands are overexpressed on tumor cells, contributing to immune escape by tumor cells.

[0004] There remains an unmet need in oncology treatment for therapeutic strategies with cytokines which do not require high doses and are targeted to tumors to avoid systemic toxicity. The present invention addresses this need by providing PD-1-targeted IL-15 fusion proteins (Figure 2) with enhanced half-life and more selective targeting of TILs to improve safety profile.

BRIEF SUMMARY OF THE INVENTION

[0005] The present invention is directed to novel PD-1 targeted IL-15/Rα heterodimeric Fc fusion proteins, their uses, and methods of making the heterodimeric Fc fusion proteins. comprising:

[0006] Accordingly in some aspects, the invention provides PD-1 targeted IL-15/Rα heterodimeric Fc fusion proteins. In this aspect, the PD-1 targeted IL-15/Rα heterodimeric Fc fusion protein comprises:

(a) a first monomer comprising, from N- to C-terminal:

(i) an IL-15 receptor alpha (IL-15Rα) sushi domain,

(ii) a first domain linker,

(iii) a variant IL-15 domain, and

(iv) a second domain linker, and

(v) a first variant Fc domain comprising CH2-CH3; and

(b) a second monomer comprising, from N- to C-terminal: a heavy chain comprising VH-CH1-hinge-CH2-CH3, wherein said CH2-CH3 is a second variant Fc domain; and

(c) a light chain comprising VL-CL;

wherein said VH and VL form an antigen binding domain that binds human PD-1 and have sequences selected from the pairs consisting of 1C11[PD-1]_H3L3 from XENP22553(SEQ ID NOS:186 and 187), 1C11[PD-1]_H3.234_L3.144 from XENP25806 (SEQ ID NOS:578-57), 1C11[PD-1]_H3.240_L3.148 from XENP25812 (SEQ ID NO:584), 1C11[PD-1]_H3.241_L3.148 from XENP25813 (SEQ ID NO:585), 1C11[PD-1]_H3.241_L3.92 from XENP25819 (SEQ ID NO:591), 1C11[PD-1]_H3.303_L3.152 from XENP26940 (SEQ ID NOS:642 and 1103), 1C11[PD-1]_H3.329_L3.220 from XENP28026 (SEQ ID NOS:708 and 1169), and 1C11[PD-1]_H3.328_L3.152 from XENP28652 (SEQ ID NOS:719 and 1180); and

wherein said first variant and said second variant Fc domains have a set of amino acid substitutions selected from the group consisting of S267K/L368D/K370S : S267K/LS364K/E357Q; S364K/E357Q : L368D/K370S; L368D/K370S : S364K;

L368E/K370S : S364K; T411E/K360E/Q362E : D401K; L368D/K370S : S364K/E357L; L368D/K370S : S364K/E357Q; and K370S : S364K/E357Q, respectively and according to EU numbering.

[0007] In some embodiments, the first variant Fc domain and/or the second variant Fc domain of the PD-1 targeted IL-15/Rα heterodimeric Fc fusion protein have amino acid substitutions comprising Q295E/N384D/Q418E/N421D, according to EU numbering.

[0008] In some embodiments, the first variant and the variant second Fc domains each have amino acid substitutions selected from the group consisting of G236R/L328R, E233P/L234V/L235A/G236del/S239K, E233P/L234V/L235A/G236del/S267K, E233P/L234V/L235A/G236del/S239K/A327G, E233P/L234V/L235A/G236del/S267K/A327G and E233P/L234V/L235A/G236del, according to EU numbering.

[0009] In some embodiments, the first variant and the second variant Fc domains each have amino acid substitution M428L/N434S, according to EU numbering.

[0010] In some embodiments, the variant IL-15 domain comprises the amino acid sequence of SEQ ID NO:2. In other embodiments, the variant IL-15 domain comprises the amino acid sequence of SEQ ID NO:2 and amino acid substitutions selected from the group consisting of N4D/N65D, D30N/N65D, and D30N/E64Q/N65D.

[0011] In some embodiments, the IL-15Rα sushi domain comprises the amino acid sequence of SEQ ID NO:4.

[0012] In some embodiments, the PD-1 targeted IL-15/Rα heterodimeric Fc fusion protein is selected from the group consisting of XENP29482 set forth in SEQ ID NOS:925,926, and 1216, XENP25937 set forth in SEQ ID NOS:370-372, and any one depicted in Figure 126A (SEQ ID NOS:925-929), Figure 126B (SEQ ID NOS:930-935), Figure 126C (SEQ ID NOS:936-941), Figure 126D (SEQ ID NOS:942-947), Figure 127A (SEQ ID NOS:948-953), Figure 127B (SEQ ID NOS:954-959), Figure 127C (SEQ ID NOS:960-965), Figure 127D (SEQ ID NOS:966-971), Figure 128A (SEQ ID NOS:972-977), Figure 128B (SEQ ID NOS:978-983), Figure 128C (SEQ ID NOS:984-989), Figure 128D (SEQ ID NOS:990-995), Figure 128E (SEQ ID NOS:996-1001), Figure 128F (SEQ ID NOS:1002-1007), Figure 128G (SEQ ID NOS:1008-1013), Figure 128H (SEQ ID NOS:1014-1019), Figure 128I (SEQ ID

NOS:1020-1025), Figure 128J (SEQ ID NOS:1026-1031), Figure 128K (SEQ ID NOS:1032-1035), Figure 128L (SEQ ID NOS:1036-1041).

[0013] In further aspects, provided herein is a PD-1 targeted IL-15/Rα heterodimeric Fc fusion protein comprising:

(a) a first monomer comprising, from N- to C-terminal:

(i) an IL-15 receptor alpha (IL-15Rα) sushi domain,

(ii) a first domain linker,

(iii) a variant IL-15 domain,

(iv) a second domain linker, and

(v) a first variant Fc domain comprising CH2-CH3; and

(b) a second monomer comprising, from N- to C-terminal: a

(i) a single chain Fv domain (scFv) that binds human PD-1, wherein said scFv comprises:

(1) a variable heavy domain (VH),

(2) a scFv linker, and

(3) a variable light domain (VL), and

(ii) a second variant Fc domain;

wherein the VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2, and VLCDR3 are selected from the group consisting of the CDRs from 1C11[PD-1]_H3L3 from XENP22538 (SEQ ID NO:417), 1C11[PD-1]_H3.234_L3.144 from XENP25806 (SEQ ID NOS:578-579), 1C11[PD-1]_H3.240_L3.148 from XENP25812 (SEQ ID NO:584), 1C11[PD-1]_H3.241_L3.148 from XENP25813 (SEQ ID NO:585), 1C11[PD-1]_H3.241_L3.92 from XENP25819 (SEQ ID NO:591), 1C11[PD-1]_H3.303_L3.152 from XENP26940 (SEQ ID NOS:642 and 1103), 1C11[PD-1]_H3.329_L3.220 from XENP28026 (SEQ ID NOS:708 and 1169), and 1C11[PD-1]_H3.328_L3.152 from XENP28652 (SEQ ID NOS:719 and 1180); and

wherein said first variant and said second variant Fc domains have a set of amino acid substitutions selected from the group consisting of S267K/L368D/K370S :

S267K/LS364K/E357Q; S364K/E357Q : L368D/K370S; L368D/K370S : S364K; L368E/K370S : S364K; T411E/K360E/Q362E : D401K; L368D/K370S : S364K/E357L; L368D/K370S : S364K/E357Q; and K370S : S364K/E357Q, respectively and according to EU numbering.

[0014] In some embodiments, the VH and VL of the second monomer are selected from the pairs consisting of 1C11[PD-1]_H3L3 from XENP22538 (SEQ ID NO:417), 1C11[PD-1]_H3.234_L3.144 from XENP25806 (SEQ ID NOS:578-579), 1C11[PD-1]_H3.240_L3.148 from XENP25812 (SEQ ID NO:584), 1C11[PD-1]_H3.241_L3.148 from XENP25813 (SEQ ID NO:585), 1C11[PD-1]_H3.241_L3.92 from XENP25819 (SEQ ID NO:591), 1C11[PD-1]_H3.303_L3.152 from XENP26940 (SEQ ID NOS:642 and 1103), 1C11[PD-1]_H3.329_L3.220 from XENP28026 (SEQ ID NOS:708 and 1169), and 1C11[PD-1]_H3.328_L3.152 from XENP28652 (SEQ ID NOS:719 and 1180).

[0015] In some embodiments, the first variant and the second variant Fc domains have an additional set of amino acid substitutions comprising Q295E/N384D/Q418E/N421D, according to EU numbering.

[0016] In some embodiments, the first variant and the variant second Fc domains each have an additional set of amino acid substitutions consisting of G236R/L328R, E233P/L234V/L235A/G236del/S239K, E233P/L234V/L235A/G236del/S267K, E233P/L234V/L235A/G236del/S239K/A327G, E233P/L234V/L235A/G236del/S267K/A327G and E233P/L234V/L235A/G236del, according to EU numbering.

[0017] In some embodiments, the first variant and the second variant Fc domains each have an additional amino acid substitution M428L/N434S, according to EU numbering.

[0018] In some embodiments, the variant IL-15 domain comprises the amino acid sequence of SEQ ID NO:2. In certain embodiments, the variant IL-15 domain comprises the amino acid sequence of SEQ ID NO:2 and amino acid substitutions selected from the group consisting of N4D/N65D, D30N/N65D, and D30N/E64Q/N65D.

[0019] In some embodiments, the IL-15Rα sushi domain has the amino acid sequence of SEQ ID NO:4.

In some embodiments, the first monomer comprises: the IL-15Rα sushi domain of SEQ ID NO:4 and the variant IL-15 domain of SEQ ID NO:2 having amino acid substitutions selected from the group consisting of N4D/N65D, D30N/N65D, and D30N/E64Q/N65D; and the scFv comprises: the VH and VL are selected from the pairs consisting of 1C11[PD-1]_H3.234_L3.144 from XENP25806 (SEQ ID NOS:578-579), 1C11[PD-1]_H3.240_L3.148 from XENP25812 (SEQ ID NO:584), 1C11[PD-1]_H3.241_L3.148 from XENP25813 (SEQ ID NO:585), 1C11[PD-1]_H3.241_L3.92 from XENP25819 (SEQ ID NO:591), 1C11[PD-1]_H3.303_L3.152 from XENP26940 (SEQ ID NOS:642 and 1103), 1C11[PD-1]_H3.329_L3.220 from XENP28026 (SEQ ID NOS:708 and 1169), and 1C11[PD-1]_H3.328_L3.152 from XENP28652 (SEQ ID NOS:719 and 1180).

[0020] In other aspects, provided herein is a nucleic acid composition encoding the first monomer of any heterodimeric Fc fusion protein outlined herein. Also, provided herein is a nucleic acid composition encoding the second monomer of any heterodimeric Fc fusion protein outlined herein. Also, provided is a nucleic acid composition encoding the light chain of any heterodimeric Fc fusion protein outlined herein.

[0021] In some aspects, provided herein is an expression vector comprising any of the nucleic acid composition encoding any one of the first monomers described herein. Also, provided herein is an expression vector comprising any of the nucleic acid composition encoding any one of the second monomers described herein. Also, provided herein is an expression vector comprising any of the nucleic acid composition encoding any one of the light chains described herein such that the VL and VH of the heterodimeric Fc fusion protein binds human PD-1.

[0022] Provided herein is an expression vector comprising one or more of the nucleic acid compositions described herein. Provided herein is a host cell comprising one or more expression vectors.

[0023] In some aspects, provided herein is a method of producing a PD-1 targeted IL-15/Rα heterodimeric Fc fusion protein comprising: culturing the host cell described herein under suitable conditions, wherein the heterodimeric Fc fusion protein is expressed; and recovering the protein.

[0024] In some aspects, the invention provides a PD-1 targeted IL-15/Rα heterodimeric Fc fusion protein selected from the group consisting of XENP29482 set forth in SEQ ID NOS:925, 926, and 1216, XENP25937 set forth in SEQ ID NOS: 370-372, and any one depicted in Figure 126A (SEQ ID NOS:925-929), Figure 126B (SEQ ID NOS: 930-935),

Figure 126C (SEQ ID NOS:936-941), Figure 126D (SEQ ID NOS:942-947), Figure 127A (SEQ ID NOS:948-953), Figure 127B (SEQ ID NOS:954-959), Figure 127C (SEQ ID NOS:960-965), Figure 127D (SEQ ID NOS:966-971), Figure 128A (SEQ ID NOS:972-977), Figure 128B (SEQ ID NOS:978-983), Figure 128C (SEQ ID NOS:984-989), Figure 128D (SEQ ID NOS:990-995), Figure 128E (SEQ ID NOS:996-1001), Figure 128F (SEQ ID NOS:1002-1007), Figure 128G (SEQ ID NOS:1008-1013), Figure 128H (SEQ ID NOS:1014-1019), Figure 128I (SEQ ID NOS:1020-1025), Figure 128J (SEQ ID NOS:1026-1031), Figure 128K (SEQ ID NOS:1032-1035), Figure 128L (SEQ ID NOS:1036-1041).

[0025] In other aspects, the invention provides a pharmaceutical composition comprising a PD-1 targeted IL-15/Rα heterodimeric Fc fusion protein selected from the group consisting of XENP29482 set forth in SEQ ID NOS:925, 926, and 1216, XENP25937 set forth in SEQ ID NOS: 370-372, and any one depicted in Figure 126A (SEQ ID NOS:925-929), Figure 126B (SEQ ID NOS: 930-935), Figure 126C (SEQ ID NOS:936-941), Figure 126D (SEQ ID NOS:942-947), Figure 127A (SEQ ID NOS:948-953), Figure 127B (SEQ ID NOS:954-959), Figure 127C (SEQ ID NOS:960-965), Figure 127D (SEQ ID NOS:966-971), Figure 128A (SEQ ID NOS:972-977), Figure 128B (SEQ ID NOS:978-983), Figure 128C (SEQ ID NOS:984-989), Figure 128D (SEQ ID NOS:990-995), Figure 128E (SEQ ID NOS:996-1001), Figure 128F (SEQ ID NOS:1002-1007), Figure 128G (SEQ ID NOS:1008-1013), Figure 128H (SEQ ID NOS:1014-1019), Figure 128I (SEQ ID NOS:1020-1025), Figure 128J (SEQ ID NOS:1026-1031), Figure 128K (SEQ ID NOS:1032-1035), Figure 128L (SEQ ID NOS:1036-1041), and a pharmaceutically acceptable carrier.

[0026] In certain aspects, the invention provides method of treating cancer in a patient in need thereof comprising administering a therapeutically effective amount of any one of the PD-1 targeted IL-15/Rα heterodimeric Fc fusion proteins described herein, or a pharmaceutical composition thereof.

[0027] In some embodiments, the method also comprises administering a therapeutically effective amount of a checkpoint blockade antibody.

[0028] In some embodiments, the checkpoint blockade antibody is selected from the group consisting of an anti-PD-1 antibody, an anti-PD-L1 antibody, an anti-TIM3 antibody, an anti-TIGIT antibody, an anti-LAG3 antibody, and an anti-CTLA-4 antibody.

[0029] In some embodiments, the said anti-PD-1 antibody is nivolumab, pembrolizumab, or pidilizumab. In some embodiments, the anti-PD-L1 antibody is atezolizumab, avelumab, or durbalumab.

BRIEF DESCRIPTION OF THE DRAWINGS

[0030] Figure 1 depicts the structure of IL-15 in complex with its receptors IL-15Rα (CD215), IL-15Rβ (CD122), and the common gamma chain (CD132).

[0031] Figure 2 depicts selectivity of PD-1-targeted IL-15/Rα-Fc fusion proteins for tumor-reactive tumor-infiltrating lymphocytes expressing PD-1.

[0032] Figure 3A-Figure 3B depict the sequences for IL-15 and its receptors.

[0033] Figure 4A-Figure 4E depict useful pairs of Fc heterodimerization variant sets (including skew and pI variants). There are variants for which there are no corresponding “monomer 2” variants; these are pI variants which can be used alone on either monomer.

[0034] Figure 5 depicts a list of isosteric variant antibody constant regions and their respective substitutions. pI_(-) indicates lower pI variants, while pI_(+) indicates higher pI variants. These can be optionally and independently combined with other heterodimerization variants of the inventions (and other variant types as well, as outlined herein).

[0035] Figure 6 depicts useful ablation variants that ablate FcγR binding (sometimes referred to as “knock outs” or “KO” variants). Generally, ablation variants are found on both monomers, although in some cases they may be on only one monomer.

[0036] Figure 7A-Figure 7E show a particularly useful embodiments of “non-cytokine” components of the IL-15/Rα-Fc fusion proteins of the invention.

[0037] Figure 8A-Figure 8F show particularly useful embodiments of “non-cytokine”/“non-Fv” components of the PD-1-targeted IL-15/Rα-Fc fusion proteins of the invention.

[0038] Figure 9 depicts a number of exemplary variable length linkers for use in IL-15/Rα-Fc fusion proteins. In some embodiments, these linkers find use linking the C-terminus of IL-15 and/or IL-15Rα(sushi) to the N-terminus of the Fc region. In some embodiments, these linkers find use fusing IL-15 to the IL-15Rα(sushi).

[0039] Figure 10 depicts a number of charged scFv linkers that find use in increasing or decreasing the pI of heterodimeric antibodies that utilize one or more scFv as a component.

The (+H) positive linker finds particular use herein. A single prior art scFv linker with single charge is referenced as "Whitlow", from Whitlow et al., Protein Engineering 6(8):989-995 (1993). It should be noted that this linker was used for reducing aggregation and enhancing proteolytic stability in scFvs.

[0040] Figure 11A-Figure 11D show the sequences of several useful IL-15/Rα-Fc format backbones based on human IgG1, without the cytokine sequences (e.g., the IL-15 and/or IL-15Rα(sushi)). It is important to note that these backbones can also find use in certain embodiments of PD-1 targeted IL-15/Rα-Fc proteins. Backbone 1 is based on human IgG1 (356E/358M allotype), and includes C220S on both chain, the S364K/E357Q : L368D/K370S skew variants, the Q295E/N384D/Q418E/N421D pI variants on the chain with L368D/K370S skew variants and the E233P/L234V/L235A/G236del/S267K ablation variants on both chains. Backbone 2 is based on human IgG1 (356E/358M allotype), and includes C220S on both chain, the S364K : L368D/K370S skew variants, the Q295E/N384D/Q418E/N421D pI variants on the chain with L368D/K370S skew variants and the E233P/L234V/L235A/G236del/S267K ablation variants on both chains. Backbone 3 is based on human IgG1 (356E/358M allotype), and includes C220S on both chain, the S364K : L368E/K370S skew variants, the Q295E/N384D/Q418E/N421D pI variants on the chain with L368E/K370S skew variants and the E233P/L234V/L235A/G236del/S267K ablation variants on both chains. Backbone 4 is based on human IgG1 (356E/358M allotype), and includes C220S on both chain, the D401K : K360E/Q362E/T411E skew variants, the Q295E/N384D/Q418E/N421D pI variants on the chain with K360E/Q362E/T411E skew variants and the E233P/L234V/L235A/G236del/S267K ablation variants on both chains. Backbone 5 is based on human IgG1 (356D/358L allotype), and includes C220S on both chain, the S364K/E357Q : L368D/K370S skew variants, the Q295E/N384D/Q418E/N421D pI variants on the chain with L368D/K370S skew variants and the E233P/L234V/L235A/G236del/S267K ablation variants on both chains. Backbone 6 is based on human IgG1 (356E/358M allotype), and includes C220S on both chain, the S364K/E357Q : L368D/K370S skew variants, Q295E/N384D/Q418E/N421D pI variants on the chain with L368D/K370S skew variants and the E233P/L234V/L235A/G236del/S267K ablation variants on both chains, as well as an N297A variant on both chains. Backbone 7 is identical to 6 except the mutation is N297S. Alternative formats for backbones 6 and 7 can exclude the ablation variants E233P/L234V/L235A/G236del/S267K in both chains.

Backbone 8 is based on human IgG4, and includes the S364K/E357Q : L368D/K370S skew variants, the Q295E/N384D/Q418E/N421D pI variants on the chain with L368D/K370S skew variants, as well as a S228P (EU numbering, this is S241P in Kabat) variant on both chains that ablates Fab arm exchange as is known in the art. Backbone 9 is based on human IgG2, and includes the S364K/E357Q : L368D/K370S skew variants, the Q295E/N384D/Q418E/N421D pI variants on the chain with L368D/K370S skew variants. Backbone 10 is based on human IgG2, and includes the S364K/E357Q : L368D/K370S skew variants, the Q295E/N384D/Q418E/N421D pI variants on the chain with L368D/K370S skew variants as well as a S267K variant on both chains. Backbone 11 is identical to backbone 1, except it includes M428L/N434S Xtend mutations. Backbone 12 is based on human IgG1 (356E/358M allotype), and includes C220S on both identical chain, the E233P/L234V/L235A/G236del/S267K ablation variants on both identical chains. Backbone 13 is based on human IgG1 (356E/358M allotype), and includes C220S on both chain, the S364K/E357Q : L368D/K370S skew variants, the P217R/P229R/N276K pI variants on the chain with S364K/E357Q skew variants and the E233P/L234V/L235A/G236del/S267K ablation variants on both chains.

[0041] As will be appreciated by those in the art and outlined below, these sequences can be used with any IL-15 and IL-15Rα(sushi) pairs outlined herein, including but not limited to IL-15/Rα-heteroFc, ncIL-15/Rα, and scIL-15/Rα, as schematically depicted in Figures 22 and 36. Additionally, any IL-15 and/or IL-15Rα(sushi) variants can be incorporated into these Figures 11A-11D backbones in any combination.

[0042] Included within each of these backbones are sequences that are 90%, 95%, 98%, and 99% identical (as defined herein) to the recited sequences, and/or contain from 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 additional amino acid substitutions (as compared to the “parent” of the Figure, which, as will be appreciated by those in the art, already contain a number of amino acid modifications as compared to the parental human IgG1 (or IgG2 or IgG4, depending on the backbone). That is, the recited backbones may contain additional amino acid modifications (generally amino acid substitutions) in addition to the skew, pI and ablation variants contained within the backbones of Figures 11A-11D.

[0043] Figure 12 shows the sequences of several useful PD-1-targeted IL-15/Rα-Fc fusion format backbones based on human IgG1, without the cytokine sequences (e.g., the Il-15 and/or IL-15Rα(sushi)) or VH, and further excluding light chain backbones which are depicted in Figure 13. Backbone 1 is based on human IgG1 (356E/358M allotype), and includes the S364K/E357Q : L368D/K370S skew variants, C220S and the Q295E/N384D/Q418E/N421D pI variants on the chain with L368D/K370S skew variants and the E233P/L234V/L235A/G236del/S267K ablation variants on both chains. Backbone 2 is based on human IgG1 (356E/358M allotype), and includes the S364K/E357Q : L368D/K370S skew variants, the N208D/Q295E/N384D/Q418E/N421D pI variants on the chain with L368D/K370S skew variants, C220S in the chain with S364K/E357Q variants, and the E233P/L234V/L235A/G236del/S267K ablation variants on both chains. Backbone 3 is based on human IgG1 (356E/358M allotype), and includes the S364K/E357Q : L368D/K370S skew variants, the N208D/Q295E/N384D/Q418E/N421D pI variants on the chains with L368D/K370S skew variants, the Q196K/I199T/P217R/P228R/N276K pI variants on the chains with S364K/E357Q variants, and the E233P/L234V/L235A/G236del/S267K ablation variants on both chains.

[0044] In certain embodiments, these sequences can be of the 356D/358L allotype. In other embodiments, these sequences can include either the N297A or N297S substitutions. In some other embodiments, these sequences can include the M428L/N434S Xtend mutations. In yet other embodiments, these sequences can instead be based on human IgG4, and include a S228P (EU numbering, this is S241P in Kabat) variant on both chains that ablates Fab arm exchange as is known in the art. In yet further embodiments, these sequences can instead be based on human IgG2. Further, these sequences may instead utilize the other skew variants, pI variants, and ablation variants depicted in Figures 4A-4E, 5 and 6.

[0045] As will be appreciated by those in the art and outlined below, these sequences can be used with any IL-15 and IL-15Rα(sushi) pairs outlined herein, including but not limited to scIL-15/Rα, ncIL-15/Rα, and dsIL-15Rα, as schematically depicted in Figures 65A-65K. Further as will be appreciated by those in the art and outlined below, any IL-15 and/or IL-15Rα(sushi) variants can be incorporated in these backbones. Furthermore as will be appreciated by those in the art and outlined below, these sequences can be used with any VH and VL pairs outlined herein, including either a scFv or a Fab.

[0046] Included within each of these backbones are sequences that are 90%, 95%, 98% and 99% identical (as defined herein) to the recited sequences, and/or contain from 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 additional amino acid substitutions (as compared to the “parent” of the Figure, which, as will be appreciated by those in the art, already contain a number of amino acid modifications as compared to the parental human IgG1 (or IgG2 or IgG4, depending on the backbone). That is, the recited backbones may contain additional amino acid modifications (generally amino acid substitutions) in addition to the skew, pI and ablation variants contained within the backbones of this figure.

[0047] Figure 13 depicts the "non-Fv" backbone of light chains (i.e., constant light chain) which find use in PD-1-targeted IL-15/Rα-Fc fusion proteins of the invention.

[0048] Figure 14 depicts the variable region sequences for an illustrative anti-PD-1 binding domain. The CDRs are underlined. As noted herein and is true for every sequence herein containing CDRs, the exact identification of the CDR locations may be slightly different depending on the numbering used as is shown in Table 1, and thus included herein are not only the CDRs that are underlined but also CDRs included within the V_H and V_L domains using other numbering systems. Furthermore, as for all the sequences in the figures, these V_H and V_L sequences can be used either in a scFv format or in a Fab format.

[0049] Figure 15A-Figure 15F depict the variable regions of additional PD-1-3 ABDs which may find use in the PD-1-targeted IL-15/Rα-Fc fusion proteins of the invention. The CDRs are underlined. As noted herein and is true for every sequence herein containing CDRs, the exact identification of the CDR locations may be slightly different depending on the numbering used as is shown in Table 1, and thus included herein are not only the CDRs that are underlined but also CDRs included within the V_H and V_L domains using other numbering systems. Furthermore, as for all the sequences in the Figures, these V_H and V_L sequences can be used either in a scFv format or in a Fab format.

[0050] Figure 16 depicts the sequences for XENP21575, a chimeric anti-PD-1 antibody based on the variable regions of hybridoma clone 1C11 and human IgG1 with E233P/L234V/L235A/G236del/S267K substitutions in the heavy chain. The CDRs are in bold, and the slashes indicate the borders of the variable domains. As note herein and is true for every sequence herein containing CDRs, the exact identification of the CDR locations may be slightly different depending on numbering used as is shown in Table 1, and thus included herein are not only the CDRs that are underlined but also CDRs included within the V_H and V_L domains using other numbering systems.

[0051] Figure 17 depicts blocking of PD-1/PD-L1 interaction on PD-1 transfected HEK293T cells by anti-PD-1 clone 1C11.

[0052] Figure 18 depicts the binding of anti-PD-1 clone 1C11 to SEB-stimulated T cells.

[0053] Figure 19A-Figure 19B depict cytokine release assays (Figure 19A: IL-2; Figure 19B: IFNγ) after SEB stimulation of human PBMCs and treatment with anti-PD-1 clone 1C11.

[0054] Figure 20A-Figure 20C depict the sequences for illustrative humanized variants of anti-PD-1 clone 1C11 as a bivalent antibodies in the human IgG1 format with E233P/L234V/L235A/G236del/S267K substitutions in the heavy chain. The CDRs are in bold, and the slashes indicate the borders of the variable domains. As note herein and is true for every sequence herein containing CDRs, the exact identification of the CDR locations may be slightly different depending on numbering used as is shown in Table 1, and thus included herein are not only the CDRs that are bolded but also CDRs included within the V_H and V_L domains using other numbering systems. As will be appreciated by those in the art, the V_H and V_L domains can be formatted as Fab or scFvs for use in the PD-1 targeted IL-15/Rα-Fc fusion proteins of the invention.

[0055] Figure 21 depicts the affinity of XENP22553 for PD-1 as determined by Octet (as well as the associated sensorgram).

[0056] Figure 22A- Figure 22G depict several formats for the IL-15/Rα-Fc fusion proteins of the present invention. IL-15Rα Heterodimeric Fc fusion or "IL-15/Rα-heteroFc" (Figure 22A) comprises IL-15 recombinantly fused to one side of a heterodimeric Fc and IL-15Rα(sushi) recombinantly fused to the other side of a heterodimeric Fc. The IL-15 and IL-15Rα(sushi) may have a variable length Gly-Ser linker between the C-terminus and the N-terminus of the Fc region. Single-chain IL-15/Rα-Fc fusion or "scIL-15/Rα-Fc" (Figure 22B) comprises IL-15Rα(sushi) fused to IL-15 by a variable length linker (termed a "single-chain" IL-15/IL-15Rα(sushi) complex or "scIL-15/Rα") which is then fused to the N-terminus of a heterodimeric Fc-region, with the other side of the molecule being "Fc-only" or "empty Fc". Non-covalent IL-15/Rα-Fc or "ncIL-15/Rα-Fc" (Figure 22C) comprises IL-15Rα(sushi) fused to a heterodimeric Fc region, while IL-15 is transfected separately so that a non-covalent IL-15/Rα complex is formed, with the other side of the molecule being "Fc-only" or "empty Fc". Bivalent non-covalent IL-15/Rα-Fc fusion or "bivalent ncIL-15/Rα-Fc" (Figure 22D) comprises IL-15Rα(sushi) fused to the N-terminus of a homodimeric Fc region, while IL-15 is transfected separately so that a non-covalent IL-15/Rα complex is formed. Bivalent single-chain IL-15/Rα-Fc fusion or "bivalent scIL-15/Rα-Fc" (Figure 22E) comprises IL-15 fused to IL-15Rα(sushi) by a variable length linker (termed a "single-chain" IL-15/IL-15Rα(sushi) complex or “scIL-15/Rα”) which is then fused to the N-terminus of a homodimeric Fc-region. Fc-non-covalent IL-15/Rα fusion or “Fc-ncIL-15/Rα” (Figure 22F) comprises IL-15Rα(sushi) fused to the C-terminus of a heterodimeric Fc region, while IL-15 is transfected separately so that a non-covalent IL-15/Rα complex is formed, with the other side of the molecule being “Fc-only” or “empty Fc”. Fc-single-chain IL-15/Rα fusion or “Fc-scIL-15/Rα” (Figure 22G) comprises IL-15 fused to IL-15Rα(sushi) by a variable length linker (termed a “single-chain” IL-15/IL-15Rα(sushi) complex or “scIL-15/Rα”) which is then fused to the C-terminus of a heterodimeric Fc region, with the other side of the molecule being “Fc-only” or “empty Fc”.

[0057] Figure 23 depicts sequences of XENP20818 and XENP21475, illustrative IL-15/Rα-Fc fusion proteins of the “IL-15/Rα-heteroFc” format. IL-15 and IL-15Rα(sushi) are underlined, linkers are double underlined (although as will be appreciated by those in the art, the linkers can be replaced by other linkers, some of which are depicted in Figures 9 and 10), and slashes (/) indicate the border(s) between IL-15, IL-15Rα, linkers, and Fc regions.

[0058] Figure 24 depicts sequences of XENP21478, an illustrative IL-15/Rα-Fc fusion protein of the “scIL-15/Rα-Fc” format. IL-15 and IL-15Rα(sushi) are underlined, linkers are double underlined (although as will be appreciated by those in the art, the linkers can be replaced by other linkers, some of which are depicted in Figures 9 and 10), and slashes (/) indicate the border(s) between IL-15, IL-15Rα, linkers, and Fc regions.

[0059] Figure 25A and Figure 25B depict sequences of XENP21479, XENP22366 and XENP24348, illustrative IL-15/Rα-Fc fusion proteins of the “ncIL-15/Rα-Fc” format. IL-15 and IL-15Rα(sushi) are underlined, linkers are double underlined (although as will be appreciated by those in the art, the linkers can be replaced by other linkers, some of which are depicted in Figures 9 and 10), and slashes (/) indicate the border(s) between IL-15, IL-15Rα, linkers, and Fc regions.

[0060] Figure 26 depicts sequences of XENP21978, an illustrative IL-15/Rα-Fc fusion protein of the “bivalent ncIL-15/Rα-Fc” format. IL-15 and IL-15Rα(sushi) are underlined, linkers are double underlined (although as will be appreciated by those in the art, the linkers can be replaced by other linkers, some of which are depicted in Figures 9 and 10), and slashes (/) indicate the border(s) between IL-15, IL-15Rα, linkers, and Fc regions.

[0061] Figure 27 depicts sequences of an illustrative IL-15/Rα-Fc fusion protein of the "bivalent scIL-15/Rα-Fc" format. IL-15 and IL-15Rα(sushi) are underlined, linkers are double underlined (although as will be appreciated by those in the art, the linkers can be replaced by other linkers, some of which are depicted in Figures 9 and 10), and slashes (/) indicate the border(s) between IL-15, IL-15Rα, linkers, and Fc regions.

[0062] Figure 28 depicts sequences of XENP22637, an illustrative IL-15/Rα-Fc fusion protein of the "Fc-ncIL-15/Rα" format. IL-15 and IL-15Rα(sushi) are underlined, linkers are double underlined (although as will be appreciated by those in the art, the linkers can be replaced by other linkers, some of which are depicted in Figures 9 and 10), and slashes (/) indicate the border(s) between IL-15, IL-15Rα, linkers, and Fc regions.

[0063] Figure 29 depicts sequences of an illustrative IL-15/Rα-Fc fusion protein of the "Fc-scIL-15/Rα" format. IL-15 and IL-15Rα(sushi) are underlined, linkers are double underlined (although as will be appreciated by those in the art, the linkers can be replaced by other linkers, some of which are depicted in Figures 9 and 10), and slashes (/) indicate the border(s) between IL-15, IL-15Rα, linkers, and Fc regions.

[0064] Figure 30A-Figure 30C depict the induction of (Figure 30A) NK ($CD56^+$/$CD16^+$) cells, (Figure 30B) $CD4^+$ T cells, and (Figure 30C) $CD8^+$ T cells proliferation by illustrative IL-15/Rα-Fc fusion proteins of Format A with different linker lengths based on Ki67 expression as measured by FACS.

[0065] Figure 31A-Figure 31C depict the induction of (Figure 31A) NK ($CD56^+$/$CD16^+$) cells, (Figure 31B) $CD4^+$ T cells, and (Figure 31C) $CD8^+$ T cells proliferation by illustrative IL-15/Rα-Fc fusion proteins of scIL-15/Rα-Fc format (XENP21478) and ncIL-15/Rα-Fc format (XENP21479) based on Ki67 expression as measured by FACS.

[0066] Figure 32 depicts a structural model of the IL-15/Rα heterodimer showing locations of engineered disulfide bond pairs.

[0067] Figure 33 depicts sequences for illustrative IL-15Rα(sushi) variants engineered with additional residues at the C-terminus to serve as a scaffold for engineering cysteine residues.

[0068] Figure 34 depicts sequences for illustrative IL-15 variants engineered with cysteines in order to form covalent disulfide bonds with IL-15Rα(sushi) variants engineered with cysteines.

[0069] Figure 35 depicts sequences for illustrative IL-15Rα(sushi) variants engineered with cysteines in order to form covalent disulfide bonds with IL-15 variants engineered with cysteines.

[0070] Figure 36A-Figure 36D depict additional formats for the IL-15/Rα-Fc fusion proteins of the present invention with engineered disulfide bonds. Disulfide-bonded IL-15/Rα heterodimeric Fc fusion or "dsIL-15/Rα-heteroFc" (Figure 36A) is the same as "IL-15/Rα-heteroFc", but wherein IL-15Rα(sushi) and IL-15 are further covalently linked as a result of engineered cysteines. Disulfide-bonded IL-15/Rα Fc fusion or "dsIL-15/Rα-Fc" (Figure 36B) is the same as "ncIL-15/Rα-Fc", but wherein IL-15Rα(sushi) and IL-15 are further covalently linked as a result of engineered cysteines. Bivalent disulfide-bonded IL-15/Rα-Fc or "bivalent dsIL-15/Rα-Fc" (Figure 36C) is the same as "bivalent ncIL-15/Rα-Fc", but wherein IL-15Rα(sushi) and IL-15 are further covalently linked as a result of engineered cysteines. Fc-disulfide-bonded IL-15/Rα fusion or "Fc-dsIL-15/Rα" (Figure 36D) is the same as "Fc-ncIL-15/Rα", but wherein IL-15Rα(sushi) and IL-15 are further covalently linked as a result of engineered cysteines.

[0071] Figure 37A-Figure 37B depict sequences of XENP22013, XENP22014, XENP22015, and XENP22017, illustrative IL-15/Rα-Fc fusion protein of the "dsIL-15/Rα-heteroFc" format. IL-15 and IL-15Rα(sushi) are underlined, linkers are double underlined (although as will be appreciated by those in the art, the linkers can be replaced by other linkers, some of which are depicted in Figure 9), and slashes (/) indicate the border(s) between IL-15, IL-15Rα, linkers, and Fc regions.

[0072] Figure 38A-Figure 38B depict sequences of XENP22357, XENP22358, XENP22359, XENP22684, and XENP22361, illustrative IL-15/Rα-Fc fusion proteins of the "dsIL-15/Rα-Fc" format. IL-15 and IL-15Rα(sushi) are underlined, linkers are double underlined (although as will be appreciated by those in the art, the linkers can be replaced by other linkers, some of which are depicted in Figures 9 and 10), and slashes (/) indicate the border(s) between IL-15, IL-15Rα, linkers, and Fc regions.

[0073] Figure 39 depicts sequences of XENP22634, XENP22635, and XENP22636, illustrative IL-15/Rα-Fc fusion proteins of the "bivalent dsIL-15/Rα-Fc" format. IL-15 and IL-15Rα(sushi) are underlined, linkers are double underlined (although as will be appreciated by those in the art, the linkers can be replaced by other linkers, some of which are depicted in

Figure 9 and Figure 10), and slashes (/) indicate the border(s) between IL-15, IL-15Rα, linkers, and Fc regions.

[0074] Figure 40 depicts sequences of XENP22639 and XENP22640, illustrative IL-15/Rα-Fc fusion proteins of the "Fc-dsIL-15/Rα" format. IL-15 and IL-15Rα(sushi) are underlined, linkers are double underlined (although as will be appreciated by those in the art, the linkers can be replaced by other linkers, some of which are depicted in Figures 9 and 10), and slashes (/) indicate the border(s) between IL-15, IL-15Rα, linkers, and Fc regions.

[0075] Figure 41 depicts the purity and homogeneity of illustrative IL-15/Rα-Fc fusion proteins with and without engineered disulfide bonds as determined by CEF.

[0076] Figure 42 depicts the induction of A) NK (CD56+/CD16+) cell, B) $CD8^+$ T cell, and C) $CD4^+$ T cell proliferation by illustrative IL-15/Rα-Fc fusion proteins with and without engineered disulfide bonds based on Ki67 expression as measured by FACS.

[0077] Figure 43 depicts the structure of IL-15 complexed with IL-15Rα, IL-2Rß, and common gamma chain. Locations of substitutions designed to reduce potency are shown.

[0078] Figure 44 depicts sequences for illustrative IL-15 variants engineered for reduced potency. Included within each of these variant IL-15 sequences are sequences that are 90, 95, 98 and 99% identical (as defined herein) to the recited sequences, and/or contain from 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 additional amino acid substitutions. In a non-limiting example, the recited sequences may contain additional amino acid modifications such as those contributing to formation of covalent disulfide bonds as described in Example 3B.

[0079] Figure 45A-Figure 45D depict sequences of XENP22821, XENP22822, XENP23554, XENP23557, XENP23561, XENP24018, XENP24019, XENP24045, XENP24051, and XENP24052, illustrative IL-15/Rα-Fc fusion proteins of the "IL-15/Rα-heteroFc" format engineered for reduced potency. IL-15 and IL-15Rα(sushi) are underlined, linkers are double underlined (although as will be appreciated by those in the art, the linkers can be replaced by other linkers, some of which are depicted in Figures 9 and 10), and slashes (/) indicate the border(s) between IL-15, IL-15Rα, linkers, and Fc regions.

[0080] Figure 46A-Figure 46C depict sequences of XENP24015, XENP24050, XENP24475, XENP24476, XENP24478, XENP24479, and XENP24481, illustrative IL-15/Rα-Fc fusion proteins of the "scIL-15/Rα-Fc" format engineered for reduced potency. IL-15 and IL-15Rα(sushi) are underlined, linkers are double underlined (although as will be appreciated by those in the art, the linkers can be replaced by other linkers, some of which are depicted in Figures 9 and 10), and slashes (/) indicate the border(s) between IL-15, IL-15Rα, linkers, and Fc regions.

[0081] Figure 47A-Figure 47B depict sequences of XENP24349, XENP24890, and XENP25138, illustrative IL-15/Rα-Fc fusion proteins of the "ncIL-15/Rα-Fc" format engineered for reduced potency. IL-15 and IL-15Rα(sushi) are underlined, linkers are double underlined (although as will be appreciated by those in the art, the linkers can be replaced by other linkers, some of which are depicted in Figure 9 and Figure 10), and slashes (/) indicate the border(s) between IL-15, IL-15Rα, linkers, and Fc regions.

[0082] Figure 48 depicts sequences of XENP22801 and XENP22802, illustrative ncIL-15/Rα heterodimers engineered for reduced potency. It is important to note that these sequences were generated using polyhistidine (Hisx6 or HHHHHH) C-terminal tags at the C-terminus of IL-15Rα(sushi).

[0083] Figure 49 depicts sequences of XENP24342, an illustrative IL-15/Rα-Fc fusion protein of the "bivalent ncIL-15/Rα-Fc" format engineered for reduced potency. IL-15 and IL-15Rα(sushi) are underlined, linkers are double underlined (although as will be appreciated by those in the art, the linkers can be replaced by other linkers, some of which are depicted in Figure 9 and Figure 10), and slashes (/) indicate the border(s) between IL-15, IL-15Rα, linkers, and Fc regions.

[0084] Figure 50 depicts sequences of XENP23472 and XENP23473, illustrative IL-15/Rα-Fc fusion proteins of the "dsIL-15/Rα-Fc" format engineered for reduced potency. IL-15 and IL-15Rα(sushi) are underlined, linkers are double underlined (although as will be appreciated by those in the art, the linkers can be replaced by other linkers, some of which are depicted in Figures 9 and 10), and slashes (/) indicate the border(s) between IL-15, IL-15Rα, linkers, and Fc regions.

[0085] Figure 51 depicts the induction of A) NK cell, B) $CD8^+$ (CD45RA-) T cell, and C) $CD4^+$ (CD45RA-) T cell proliferation by variant IL-15/Rα-Fc fusion proteins based on Ki67 expression as measured by FACS.

[0086] Figure 52 depicts EC50 for induction of NK and $CD8^+$ T cells proliferation by variant IL-15/Rα-Fc fusion proteins, and fold reduction in EC50 relative to XENP20818.

[0087] Figure 53A-Figure 53C depict the gating of lymphocytes and subpopulations for the experiments depicted in Figure 56. Figure 53A shows the gated lymphocyte population. Figure 53B shows the CD3-negative and CD3-positive subpopulations. Figure 53C shows the CD16=negative and CD16-positive subpopulations of the CD3-negative cells.

[0088] Figure 54A-Figure 54C depict the gating of $CD3^+$ lymphocyte subpopulations for the experiments depicted in Figure 56. Figure 54A shows the $CD4^+$, $CD8^+$ and γδ T cell subpopulations of the $CD3^+$ T cells. Figure 54B shows the CD45RA(-) and CD45RA(+) subpopulations of the $CD4^+$ T cells. Figure 54C shows the CD45RA(-) and CD45RA(+) subpopulation s of the $CD8^+$ T cells.

[0089] Figure 55A-Figure 55B depict CD69 and CD25 expression before (Figure 55A) and after (Figure 55B) incubation of human PBMCs with XENP22821.

[0090] Figure 56A-Figure 56D depict cell proliferation in human PBMCs incubated for four days with the indicated variant IL-15/Rα-Fc fusion proteins. Figures 56A-56C show the percentage of proliferating NK cells (CD3-CD16+) (Figure 56A), $CD8^+$ T cells (CD3+CD8+CD45RA-) (Figure 56B) and $CD4^+$ T cells (CD3+CD4+CD45RA-) (Figure 56C). Figure 56D shows the fold change in EC50 of various IL15/IL15Rα Fc heterodimers relative to control (XENP20818).

[0091] Figure 57A-Figure 57D depict cell proliferation in human PBMCs incubated for three days with the indicated variant IL-15/Rα-Fc fusion proteins. Figures 57A-C show the percentage of proliferating $CD8^+$ (CD45RA-) T cells (Figure 57A), $CD4^+$ (CD45RA-) T cells (Figure 57B), γδ T cells (Figure 57C), and NK cells (Figure 57D).

[0092] Figure 58A-Figure 58C depict the percentage of Ki67 expression on (Figure 58A) $CD8^+$ T cells, (Figure 58B) $CD4^+$ T cells, and (Figure 58C) NK cells following treatment with additional IL-15/Rα variants.

[0093] Figure 59A-Figure 59E depict the percentage of Ki67 expression on (Figure 59A) $CD8^+$ (CD45RA-) T cells, (Figure 59B) $CD4^+$ (CD45RA-) T cells, (Figure 59C) γδ T cells, (Figure 59D) NK (CD16+CD8α-) cells, and (Figure 59E) NK (CD56+CD8α-) cells following treatment with IL-15/Rα variants.

[0094] Figure 60A-Figure 60E depict the percentage of Ki67 expression on (Figure 60A) $CD8^+$ (CD45RA-) T cells, (Figure 60B) $CD4^+$ (CD45RA-) T cells, (Figure 60C) γδ T cells,

(Figure 60D) NK (CD16+CD8α-) cells, and (Figure 60E) NK (CD56+CD8α-) cells following treatment with IL-15/Rα variants.

[0095] Figure 61A-Figure 61D depict the percentage of Ki67 expression on (Figure 61A) $CD8^+$ T cells, (Figure 61B) $CD4^+$ T cells, (Figure 61C) γδ T cells and (Figure 61D) NK (CD16+) cells following treatment with additional IL-15/Rα variants.

[0096] Figure 62A-Figure 62D depict the percentage of Ki67 expression on (Figure 62A) $CD8^+$ T cells, (Figure 62B) $CD4^+$ T cells, (Figure 62C) γδ T cells and (Figure 62D) NK (CD16+) cells following treatment with additional IL-15/Rα variants.

[0097] Figure 63 depicts IV-TV Dose PK of various IL-15/Rα Fc fusion proteins or controls in C57BL/6 mice at 0.1 mg/kg single dose.

[0098] Figure 64 depicts the correlation of half-life vs NK cell potency following treatment with IL-15/Rα-Fc fusion proteins engineered for lower potency.

[0099] Figure 65A-Figure 65K depict several formats for the PD-1-targeted IL-15/Rα-Fc fusion proteins of the present invention. The “scIL-15/Rα x scFv” format (Figure 65A) comprises IL-15Rα(sushi) fused to IL-15 by a variable length linker (termed “scIL-15/Rα”) which is then fused to the N-terminus of a heterodimeric Fc-region, with an scFv fused to the other side of the heterodimeric Fc. The “scFv x ncIL-15/Rα” format (Figure 65B) comprises an scFv fused to the N-terminus of a heterodimeric Fc-region, with IL-15Rα(sushi) fused to the other side of the heterodimeric Fc, while IL-15 is transfected separately so that a non-covalent IL-15/Rα complex is formed. The “scFv x dsIL-15/Rα” format (Figure 65C) is the same as the “scFv x ncIL-15/Rα” format, but wherein IL-15Rα(sushi) and IL-15 are covalently linked as a result of engineered cysteines. The “scIL-15/Rα x Fab” format (Figure 65D) comprises IL-15Rα(sushi) fused to IL-15 by a variable length linker (termed “scIL-15/Rα”) which is then fused to the N-terminus of a heterodimeric Fc-region, with a variable heavy chain (VH) fused to the other side of the heterodimeric Fc, while a corresponding light chain is transfected separately so as to form a Fab with the VH. The “ncIL-15/Rα x Fab” format (Figure 65E) comprises a VH fused to the N-terminus of a heterodimeric Fc-region, with IL-15Rα(sushi) fused to the other side of the heterodimeric Fc, while a corresponding light chain is transfected separately so as to form a Fab with the VH, and while IL-15 is transfected separately so that a non-covalent IL-15/Rα complex is formed. The “dsIL-15/Rα x Fab” format (Figure 65F) is the same as the “ncIL-15/Rα x Fab” format, but wherein IL-

15Rα(sushi) and IL-15 are covalently linked as a result of engineered cysteines. The "mAb-scIL-15/Rα" format (Figure 65G) comprises VH fused to the N-terminus of a first and a second heterodimeric Fc, with IL-15 is fused to IL-15Rα(sushi) which is then further fused to the C-terminus of one of the heterodimeric Fc-region, while corresponding light chains are transfected separately so as to form Fabs with the VHs. The "mAb-ncIL-15/Rα" format (Figure 65H) comprises VH fused to the N-terminus of a first and a second heterodimeric Fc, with IL-15Rα(sushi) fused to the C-terminus of one of the heterodimeric Fc-region, while corresponding light chains are transfected separately so as to form a Fabs with the VHs, and while and while IL-15 is transfected separately so that a non-covalent IL-15/Rα complex is formed. The "mAb-dsIL-15/Rα" format (Figure 65I) is the same as the "mAb-ncIL-15/Rα" format, but wherein IL-15Rα(sushi) and IL-15 are covalently linked as a result of engineered cysteines. The "central-IL-15/Rα" format (Figure 65J) comprises a VH recombinantly fused to the N-terminus of IL-15 which is then further fused to one side of a heterodimeric Fc and a VH recombinantly fused to the N-terminus of IL-15Rα(sushi) which is then further fused to the other side of the heterodimeric Fc, while corresponding light chains are transfected separately so as to form a Fabs with the VHs. The "central-scIL-15/Rα" format (Figure 65K) comprises a VH fused to the N-terminus of IL-15Rα(sushi) which is fused to IL-15 which is then further fused to one side of a heterodimeric Fc and a VH fused to the other side of the heterodimeric Fc, while corresponding light chains are transfected separately so as to form a Fabs with the VHs.

[00100] Figure 66 depicts sequences of XENP21480, an illustrative PD-1-targeted IL-15/Rα-Fc fusion protein of the "scIL-15/Rα x scFv" format. The CDRs are in bold. As noted herein and is true for every sequence herein containing CDRs, the exact identification of the CDR locations may be slightly different depending on the numbering used as is shown in Table 1, and thus included herein are not only the CDRs that are in bold but also CDRs included within the V_H and V_L domains using other numbering systems. IL-15 and IL-15Rα(sushi) are underlined, linkers are double underlined (although as will be appreciated by those in the art, the linkers can be replaced by other linkers, some of which are depicted in Figure 9 and Figure 10), and slashes (/) indicate the border(s) between IL-15, IL-15Rα, linkers, variable regions, and constant/Fc regions.

[00101] Figure 67 depicts sequences of an illustrative PD-1-targeted IL-15/Rα-Fc fusion protein of the "scFv x ncIL-15/Rα" format. The CDRs are in bold. As noted herein and

is true for every sequence herein containing CDRs, the exact identification of the CDR locations may be slightly different depending on the numbering used as is shown in Table 1, and thus included herein are not only the CDRs that are in bold but also CDRs included within the V_H and V_L domains using other numbering systems. IL-15 and IL-15Rα(sushi) are underlined, linkers are double underlined (although as will be appreciated by those in the art, the linkers can be replaced by other linkers, some of which are depicted in Figure 9 and Figure 10), and slashes (/) indicate the border(s) between IL-15, IL-15Rα, linkers, variable regions, and constant/Fc regions.

[00102] Figure 68 depicts sequences of an illustrative PD-1-targeted IL-15/Rα-Fc fusion protein of the “scFv x dsIL-15/Rα” format. The CDRs are in bold. As noted herein and is true for every sequence herein containing CDRs, the exact identification of the CDR locations may be slightly different depending on the numbering used as is shown in Table 1, and thus included herein are not only the CDRs that are in bold but also CDRs included within the V_H and V_L domains using other numbering systems. IL-15 and IL-15Rα(sushi) are underlined, linkers are double underlined (although as will be appreciated by those in the art, the linkers can be replaced by other linkers, some of which are depicted in Figure 9 and Figure 10), and slashes (/) indicate the border(s) between IL-15, IL-15Rα, linkers, variable regions, and constant Fc regions.

[00103] Figure 69A-Figure 69C depict sequences of illustrative PD-1-targeted IL-15/Rα-Fc fusion proteins of the “scIL-15/Rα x Fab” format. The CDRs are in bold. As noted herein and is true for every sequence herein containing CDRs, the exact identification of the CDR locations may be slightly different depending on the numbering used as is shown in Table 1, and thus included herein are not only the CDRs that are in bold but also CDRs included within the V_H and V_L domains using other numbering systems. IL-15 and IL-15Rα(sushi) are underlined, linkers are double underlined (although as will be appreciated by those in the art, the linkers can be replaced by other linkers, some of which are depicted in Figure 9 and Figure 10), and slashes (/) indicate the border(s) between IL-15, IL-15Rα, linkers, variable regions, and constant Fc regions.

[00104] Figure 70 depicts sequences of XENP22112, an illustrative PD-1-targeted IL-15/Rα-Fc fusion protein of the “Fab x ncIL-15/Rα” format. The CDRs are in bold. As noted herein and is true for every sequence herein containing CDRs, the exact identification of the CDR locations may be slightly different depending on the numbering used as is shown in

Table 1, and thus included herein are not only the CDRs that are in bold but also CDRs included within the V_H and V_L domains using other numbering systems. IL-15 and IL-15Rα(sushi) are underlined, linkers are double underlined (although as will be appreciated by those in the art, the linkers can be replaced by other linkers, some of which are depicted in Figure 9 and Figure 10), and slashes (/) indicate the border(s) between IL-15, IL-15Rα, linkers, variable regions, and constant Fc regions.

[00105] Figure 71 depicts sequences of XENP22641, an illustrative PD-1-targeted IL-15/Rα-Fc fusion protein of the "Fab x dsIL-15/Rα" format. The CDRs are in bold. As noted herein and is true for every sequence herein containing CDRs, the exact identification of the CDR locations may be slightly different depending on the numbering used as is shown in Table 1, and thus included herein are not only the CDRs that are in bold but also CDRs included within the V_H and V_L domains using other numbering systems. IL-15 and IL-15Rα(sushi) are underlined, linkers are double underlined (although as will be appreciated by those in the art, the linkers can be replaced by other linkers, some of which are depicted in Figure 9 and Figure 10), and slashes (/) indicate the border(s) between IL-15, IL-15Rα, linkers, variable regions, and constant/Fc regions.

[00106] Figure 72A-Figure 72B depict sequences of an illustrative PD-1-targeted IL-15/Rα-Fc fusion protein of the "mAb x scIL-15/Rα" format. The CDRs are in bold. As noted herein and is true for every sequence herein containing CDRs, the exact identification of the CDR locations may be slightly different depending on the numbering used as is shown in Table 1, and thus included herein are not only the CDRs that are in bold but also CDRs included within the V_H and V_L domains using other numbering systems. IL-15 and IL-15Rα(sushi) are underlined, linkers are double underlined (although as will be appreciated by those in the art, the linkers can be replaced by other linkers, some of which are depicted in Figure 9 and Figure 10), and slashes (/) indicate the border(s) between IL-15, IL-15Rα, linkers, variable regions, and constant/Fc regions.

[00107] Figure 73A-Figure 73B depict sequences of XENP22642 and XENP22643, illustrative PD-1-targeted IL-15/Rα-Fc fusion proteins of the "mAb x ncIL-15/Rα" format. The CDRs are in bold. As noted herein and is true for every sequence herein containing CDRs, the exact identification of the CDR locations may be slightly different depending on the numbering used as is shown in Table 1, and thus included herein are not only the CDRs that are in bold but also CDRs included within the V_H and V_L domains using other numbering

systems. IL-15 and IL-15Rα(sushi) are underlined, linkers are double underlined (although as will be appreciated by those in the art, the linkers can be replaced by other linkers, some of which are depicted in Figure 9 and Figure 10), and slashes (/) indicate the border(s) between IL-15, IL-15Rα, linkers, variable regions, and constant/Fc regions.

[00108] Figure 74 depicts sequences of XENP22644 and XENP22645, illustrative PD-1-targeted IL-15/Rα-Fc fusion proteins of the "mAb x dsIL-15/Rα" format. The CDRs are in bold. As noted herein and is true for every sequence herein containing CDRs, the exact identification of the CDR locations may be slightly different depending on the numbering used as is shown in Table 1, and thus included herein are not only the CDRs that are in bold but also CDRs included within the V_H and V_L domains using other numbering systems. IL-15 and IL-15Rα(sushi) are underlined, linkers are double underlined (although as will be appreciated by those in the art, the linkers can be replaced by other linkers, some of which are depicted in Figure 9 and Figure 10), and slashes (/) indicate the border(s) between IL-15, IL-15Rα, linkers, variable regions, and constant/Fc regions.

[00109] Figure 75 depicts sequences of illustrative PD-1-targeted IL-15/Rα-Fc fusion proteins of the "central-IL-15/Rα" format. The CDRs are in bold. As noted herein and is true for every sequence herein containing CDRs, the exact identification of the CDR locations may be slightly different depending on the numbering used as is shown in Table 1, and thus included herein are not only the CDRs that are in bold but also CDRs included within the V_H and V_L domains using other numbering systems. IL-15 and IL-15Rα(sushi) are underlined, linkers are double underlined (although as will be appreciated by those in the art, the linkers can be replaced by other linkers, some of which are depicted in Figure 9 and Figure 10), and slashes (/) indicate the border(s) between IL-15, IL-15Rα, linkers, variable regions, and constant/Fc regions.

[00110] Figure 76 depicts sequences of illustrative PD-1-targeted IL-15/Rα-Fc fusion proteins of the "central-scIL-15/Rα" format. The CDRs are in bold. As noted herein and is true for every sequence herein containing CDRs, the exact identification of the CDR locations may be slightly different depending on the numbering used as is shown in Table 1, and thus included herein are not only the CDRs that are in bold but also CDRs included within the V_H and V_L domains using other numbering systems. IL-15 and IL-15Rα(sushi) are underlined, linkers are double underlined (although as will be appreciated by those in the art, the linkers can be replaced by other linkers, some of which are depicted in Figure 9 and

Figure 10), and slashes (/) indicate the border(s) between IL-15, IL-15Rα, linkers, variable regions, and constant/Fc regions.

[00111] Figure 77A-Figure 77F provide data for an illustrative PD-1-targeted IL-15/Rα-Fc fusion protein XENP21480. Figure 77A depicts the format for an illustrative PD-1 targeted IL-15/Rα-Fc fusion protein XENP21480. Figure 77B depicts the purity and homogeneity of XENP21480 as determined by SEC. Figure 77C depicts the purity and homogeneity of XENP21480 as determined by CEF. Figure 77D depicts the affinity of XENP21480 for IL-2Rβ as determined by Octet. Figure 77E depicts the affinity of XENP21480 for PD-1 as determined by Octet. Figure 77F depicts the stability of XENP21480 as determined by DSF.

[00112] Figure 78A-Figure 78B depict the sensorgrams from Octet experiment for confirming the binding of two batches of XENP25850 to IL-2Rß:common gamma chain complex (Figure 78A) and PD-1 (Figure 78B).

[00113] Figure 79A-Figure 79C depict the induction of NK ($CD56^+$/$CD16^+$) cells (Figure79A), $CD4^+$ T cells (Figure79B), and $CD8^+$ T cells (Figure79C) proliferation by illustrative PD-1 targeted IL-15/Rα-Fc fusion proteins and controls.

[00114] Figure 80 depicts enhancement of IL-2 secretion by an illustrative PD-1 targeted IL-15/Rα-Fc fusion protein and controls over PBS in an SEB-stimulated PBMC assay.

[00115] Figure 81 depicts IFNγ level on Days 4, 7, and 11 in serum of huPBMC engrafted mice following treatment with an illustrative PD-1 targeted IL-15/Rα-Fc fusion protein XENP25850 and controls.

[00116] Figure 82A-Figure 82C depict $CD8^+$ T cell count on Day 4 (Figure 82A), Day 7 (Figure 82B), and Day 11 (Figure 82C) in whole blood of huPBMC engrafted mice following treatment with an illustrative PD-1 targeted IL-15/Rα-Fc fusion protein XENP25850 and controls.

[00117] Figure 83A-Figure 83C depict $CD4^+$ T cell count on Day 4 (Figure 83A), Day 7 (Figure 83B), and Day 11 (Figure 83C) in whole blood of huPBMC engrafted mice following treatment with an illustrative PD-1 targeted IL-15/Rα-Fc fusion protein XENP25850 and controls.

[00118] Figure 84A-Figure 84C depict CD45+ cell count on Day 4 (Figure 84A), Day 7 (Figure 84A), and Day 11 (Figure 84A) in whole blood of huPBMC engrafted mice following treatment with an illustrative PD-1 targeted IL-15/Rα-Fc fusion protein XENP25850 and controls.

[00119] Figure 85A-Figure 85C depict the body weight as a percentage of initial body weight of huPBMC engrafted mice on Day 4 (Figure 85A), Day 7 (Figure 85B), and Day 11 (Figure 85C) following treatment with an illustrative PD-1 targeted IL-15/Rα-Fc fusion protein XENP25850 and controls. Each point represents a single NSG mouse. Mice whose body weights dropped below 70% initial body weight were euthanized. Dead mice are represented as 70%.

[00120] Figure 86 depicts the sequences for XENP16432, a bivalent anti-PD-1 mAb with an ablation variant (E233**P**/L234**V**/L235**A**/G236**del**/S267**K**, “IgG1_PVA_/S267k”). The CDRs are underlined. As noted herein and is true for every sequence herein containing CDRs, the exact identification of the CDR locations may be slightly different depending on the numbering used as is shown in Table 1, and thus included herein are not only the CDRs that are underlined but also CDRs included within the V_H and V_L domains using other numbering systems.

[00121] Figure 87 depicts the sequences for an illustrative humanized variant of anti-PD-1 clone 1C11 one-armed antibody (XENP25951) in the human IgG1 format with E233P/L234V/L235A/G236del/S267K substitutions in the heavy chain. The CDRs are in bold, and the slashes indicate the borders of the variable domains. As note herein and is true for every sequence herein containing CDRs, the exact identification of the CDR locations may be slightly different depending on numbering used as is shown in Table 1, and thus included herein are not only the CDRs that are underlined but also CDRs included within the V_H and V_L domains using other numbering systems. As will be appreciated by those in the art, the V_H and V_L domains can be formatted as Fab or scFvs for use in the IL-15/Rα x anti-PD-1 heterodimeric proteins of the invention.

[00122] Figure 88A-Figure 88C depict the $CD45^+$ cell count in NSG mice on Day 4 (Figure 88A), Day 7 (Figure 88B), and Day 11 (Figure 88C) following treatment with the indicated test articles.

[00123] Figure 89A-Figure 89C depict the $CD3^+$ cell count in NSG mice on Day 4 (Figure 89A), Day 7 (Figure 89B), and Day 11 (Figure 89C) following treatment with the indicated test articles.

[00124] Figure 90A-Figure 90C depict the $CD4^+$ cell count in NSG mice on Day 4 (Figure 90A), Day 7 (Figure 90B), and Day 11 (Figure 90C) following treatment with XENP24050 (0.61 mg/kg), XENP25951 (0.82 mg/kg), XENP25951 (0.82 mg/kg) + XENP24050 (0.61 mg/kg), or XENP25850 (1.0 mg/kg).

[00125] Figure 91A-Figure 91C depict the $CD8^+$ cell count in NSG mice on Day 4 (Figure 91A), Day 7 (Figure 91B), and Day 11 (Figure 91C) following treatment with the indicated test articles.

[00126] Figure 92A-Figure 92H depict induction of STAT5 phosphorylation on $CD4^+CD45RA^+CD25^-$ (Figure 92A), $CD4^+CD45RA^+CD25^+$ (Figure 92B), $CD4^+CD45RA^-CD25^+$ (Figure 92C), $CD4^+CD45RA^-CD25^-$ (Figure 92D), $CD8^+CD45RA^+CD25^-$ (Figure 92E), $CD8^+CD45RA^+CD25^+$ (Figure 92F), $CD8^+CD45RA^-CD25^+$ (Figure 92G), and $CD8^+CD45RA^-CD25^-$ (Figure 92H) by XENP20818 (WT IL-15/Rα-Fc), XENP24050 (an illustrative reduced potency IL-15/Rα-Fc), and XENP25850 (an illustrative PD-1-targeted IL-15/Rα-Fc fusion). Fresh cells are indicated in dotted lines, and activated cells are indicated in solid lines. Fresh cells are all $CD25^-$.

[00127] Figure 93A-Figure 93T depict sequences for illustrative scFv variants of anti-PD-1 clone 1C11. The scFv variant name is in bold and the CDRs are underlined, the scFv linker is double underlined (in the sequences, the scFv linker is a positively charged scFv $(GKPGS)_4$ linker, although as will be appreciated by those in the art, this linker can be replaced by other linkers, including uncharged or negatively charged linkers, such as but not limit to those in Figure 9 and Figure 10), and the slashes indicate the borders of the variable domains. As noted herein and is true for every sequence herein containing CDRs, the exact identification of the CDR locations may be slightly different depending on numbering used as is shown in Table 1, and thus included herein are not only the CDRs that are underlined but also CDRs included within the V_H and V_L domains using other numbering systems. Further, the naming convention illustrates the orientation of the scFv from N- to C-terminus; some of the sequences in this Figure are oriented as V_H-scFv linker-V_L (from N- to C-terminus), while some are oriented as V_L-scFv linker-V_H (from N- to C-terminus), although as will be appreciated by those in the art, these sequences may also be used in the opposition orientation

from their depiction herein. Furthermore, as will be appreciated by those in the art, the V_H and V_L domains can be formatted as Fabs or scFvs. Additionally, each CDR has its own SEQ ID NO: or sequence identifier in the sequence listing, and each VH and VL domain has its own SEQ ID NO: or sequence identifier in the sequence listing.

[00128] Figure 94A-Figure 94AP depict sequences for illustrative variant anti-PD-1 mAbs based on clone 1C11. The variant anti-PD-1 mAb name is in bold and the CDRs are underlined, and the slashes indicate the borders of the variable domains. As noted herein and is true for every sequence herein containing CDRs, the exact identification of the CDR locations may be slightly different depending on numbering used as is shown in Table 1, and thus included herein are not only the CDRs that are underlined but also CDRs included within the V_H and V_L domains using other numbering systems. As will be appreciated by those in the art, the V_H and V_L domains can be formatted as Fabs or scFvs. Additionally, each CDR has its own SEQ ID NO or sequence identifier in the sequence listing, and each VH and VL domain has its own SEQ ID NO or sequence identifier in the sequence listing.

[00129] Figure 95A-Figure 95J depict sequences for variant heavy chains based on the heavy chain of XENP22553. The variable heavy chain name is in bold and the CDRs are underlined. As noted herein and is true for every sequence herein containing CDRs, the exact identification of the CDR locations may be slightly different depending on numbering used as is shown in Table 1, and thus included herein are not only the CDRs that are underlined but also CDRs included within the V_H domain. As will be appreciated by those in the art, the V_H domains can be used in Fabs or scFvs. Additionally, each CDR has its own SEQ ID NO or sequence identifier in the sequence listing, and each VH domain has its own SEQ ID NO or sequence identifier in the sequence listing.

[00130] Figure 96A-Figure 96F depict sequences for variant light chains based on the light chain of XENP22553. The variable light chain name is in bold and the CDRs are underlined. As noted herein and is true for every sequence herein containing CDRs, the exact identification of the CDR locations may be slightly different depending on numbering used as is shown in Table 1, and thus included herein are not only the CDRs that are underlined but also CDRs included within the V_L domains using other numbering systems. As will be appreciated by those in the art, the V_L domains can be used in Fabs or scFvs. Additionally, each CDR has its own SEQ ID NO or sequence identifier in the sequence listing, and each VL domain has its own SEQ ID NO or sequence identifier in the sequence listing.

[00131] Figure 97A-Figure 97P depict the stability of variant anti-PD-1 scFvs as determined by DSF and equilibrium dissociation constants (K_D), association rates (k_a), and dissociation rates (k_d) of anti-PD-1 mAbs based on the VH/VL from the variant scFvs as determined by Octet. XENP for scFvs are in bold, and XENP for full-length mAb are in parentheses.

[00132] Figure 98 depicts the of equilibrium dissociation constants (K_D), association rates (k_a), and dissociation rates (k_d) of variant anti-PD-1 mAbs as determined by Octet.

[00133] Figure 99 depicts the of equilibrium dissociation constants (K_D), association rates (k_a), and dissociation rates (k_d) of variant anti-PD-1 mAbs as determined by Octet.

[00134] Figure 100 depicts the affinity/dissociation constants (K_D), association rates (k_a), and dissociation rates (k_d) of anti-PD-1 1C11 variants for human PD-1 as determined by Octet.

[00135] Figure 101 depicts the affinity/dissociation constants (K_D), association rates (k_a), and dissociation rates (k_d) of anti-PD-1 1C11 variants for human PD-1 as determined by Octet.

[00136] Figure 102 depicts the affinity/dissociation constants (K_D), association rates (k_a), and dissociation rates (k_d) of anti-PD-1 1C11 variants for human PD-1 as determined by Octet.

[00137] Figure 103 depicts the affinity/dissociation constants (K_D), association rates (k_a), and dissociation rates (k_d) of anti-PD-1 1C11 variants for human PD-1 as determined by Octet.

[00138] Figure 104 depicts the affinity/dissociation constants (K_D), association rates (k_a), and dissociation rates (k_d) of anti-PD-1 1C11 variants for human PD-1 and cynomolgus PD-1 as determined by Octet.

[00139] Figure 105A-Figure 105E depict the of equilibrium dissociation constants (K_D), association rates (k_a), and dissociation rates (k_d) of variant anti-PD-1 mAbs as determined by Octet. Variants are defined by heavy chain and light chain XenDs as depicted in Figure 95A-Figure 95J and Figure 96A-Figure 96F.

[00140] Figure 106 depicts the of equilibrium dissociation constants (K_D), association rates (k_a), and dissociation rates (k_d) of variant anti-PD-1 mAbs as determined by Octet.

Variants are defined by heavy chain and light chain XenDs as depicted in Figure 95A-Figure 95J and Figure 96A-Figure 96F.

[00141] Figure 107 depicts the affinity (K_D) of anti-PD-1 1C11 variants as determined by Biacore.

[00142] Figure 108 depicts the binding of affinity optimized anti-PD-1 1C11 variants to SEB-stimulated T cells.

[00143] Figure 109A-Figure 109D depict sequences of illustrative PD-1-targeted IL-15/Rα-Fc fusions comprising affinity-optimized PD-1-targeting arms. The CDRs are in bold. As noted herein and is true for every sequence herein containing CDRs, the exact identification of the CDR locations may be slightly different depending on the numbering used as is shown in Table 1 and thus included herein are not only the CDRs that are in bold but also CDRs included within the V_H and V_L domains using other numbering systems. IL-15 and IL-15Rα(sushi) are underlined, linkers are double underlined (although as will be appreciated by those in the art, the linkers can be replaced by other linkers, some of which are depicted in Figure 9 and Figure 10 and slashes (/) indicate the border(s) between IL-15, IL-15Rα, linkers, variable regions, and constant/Fc regions.

[00144] Figure 110A-Figure 110B depict induction of A) $CD8^+$ T cells and B) $CD4^+$ T cells proliferation by PD-1-targeted IL-15/Rα-Fc fusions (and controls) as indicated by percentage proliferating cells (determined based on CFSE dilution). The data show that PD-1-targeted IL-15/Rα-Fc fusions are more potent in inducing proliferation of $CD4^+$ T cells in comparison to untargeted IL-15(D30N/E64Q/N65D)/Rα-Fc fusion (as well as control RSV-targeted IL-15/Rα-Fc fusion). Notably, XENP29159 which has a higher-affinity PD-1 binding domain was more potent than XENP25850 (as well as XENP24306 and XENP26007) in proliferation of both $CD8^+$ and $CD4^+$ T cells.

[00145] Figure 111A-Figure 111B depict induction of A) CD8 memory T cell and B) CD8 naive T cell proliferation by PD-1-targeted IL-15/Rα-Fc fusions (and controls) as indicated by percentage proliferating cells (determined based on CFSE dilution). The data show that PD-1-targeted IL-15/Rα-Fc fusions are more potent in inducing proliferation of CD8 memory T cells in comparison to untargeted IL-15(D30N/E64Q/N65D)/Rα-Fc fusion (as well as control RSV-targeted IL-15/Rα-Fc fusion). Notably, XENP29159 which has a

higher-affinity PD-1 binding domain was more potent than XENP25850 in proliferation of CD8 memory T cells.

[00146] Figure 112A-Figure 112B depict induction of A) CD8 memory T cell and B) CD8 naive T cell proliferation by PD-1-targeted IL-15/Rα-Fc fusions (and controls) as indicated by cell counts.

[00147] Figure 113A-Figure 113B depict induction of A) CD4 memory T cell and B) CD4 naive T cell proliferation by PD-1-targeted IL-15/Rα-Fc fusions (and controls) as indicated by percentage proliferating cells (determined based on CFSE dilution). The data show that PD-1-targeted IL-15/Rα-Fc fusions are more potent in inducing proliferation of CD4 memory T cells in comparison to untargeted IL-15(D30N/E64Q/N65D)/Rα-Fc fusion (as well as control RSV-targeted IL-15/Rα-Fc fusion). Notably, XENP29159 which has a higher-affinity PD-1 binding domain was more potent than XENP25850 in proliferation of CD4 memory T cells.

[00148] Figure 114A-Figure 143B depict induction of A) CD4 memory T cell and B) CD4 naive T cell proliferation by PD-1-targeted IL-15/Rα-Fc fusions (and controls) as indicated by cell counts. The data show that PD-1-targeted IL-15/Rα-Fc fusions are more potent in expanding CD4 memory T cells in comparison to untargeted IL-15(D30N/E64Q/N65D)/Rα-Fc fusion (as well as control RSV-targeted IL-15/Rα-Fc fusion). Notably, XENP29159 which has a higher-affinity PD-1 binding domain was more potent than XENP25850 in proliferation of CD4 memory T cells.

[00149] Figure 115A-Figure 115B depict induction of NK cells proliferation by PD-1-targeted IL-15/Rα-Fc fusions (and controls) as indicated A) by percentage proliferating cells (determined based on CFSE dilution) and B) by cell counts.

[00150] Figure 116A-Figure 116D depict activation of T cells as indicated by A) percentage CD8 memory T cells expressing CD25, B) percentage CD8 naive T cells expressing CD25, C) percentage CD4 memory T cells expressing CD25, and D) percentage CD4 naive T cells expressing CD25 following incubation with PD-1-targeted IL-15/Rα-Fc fusions (and controls). The data show that PD-1-targeted IL-15/Rα-Fc fusions appear to upregulate CD25 on $CD8^+$ and $CD4^+$ T cells more potently in comparison to untargeted IL-15(D30N/E64Q/N65D)/Rα-Fc fusion (as well as control RSV-targeted IL-15/Rα-Fc fusion).

[00151] Figure 117A-Figure 117D depict activation of CD8$^+$ T cells as indicated by A) HLA-DR MFI on CD8 memory T cells, B) percentage CD8 memory T cells expressing HLA-DR, C) HLA-DR MFI on CD8 naive T cells, and D) percentage CD8 naive T cells expressing HLA-DR following incubation with PD-1-targeted IL-15/Rα-Fc fusions (and controls).

[00152] Figure 118A-Figure 118D depict activation of CD4$^+$ T cells as indicated by A) HLA-DR MFI on CD4 memory T cells, B) percentage CD4 memory T cells expressing HLA-DR, C) HLA-DR MFI on CD4 naive T cells, and D) percentage CD4 naive T cells expressing HLA-DR following incubation with PD-1-targeted IL-15/Rα-Fc fusions (and controls).

[00153] Figure 119 depicts the sequences of XENP22853, an IL-15/Rα-heteroFc fusion comprising a wild-type IL-15 and Xtend Fc (M428L/N434S) variant. IL-15 and IL-15Rα(sushi) are underlined, linkers are double underlined (although as will be appreciated by those in the art, the linkers can be replaced by other linkers, some of which are depicted in Figure 9 and Figure 10, and slashes (/) indicate the border(s) between IL-15, IL-15Rα, linkers, and constant/Fc regions.

[00154] Figure 120 depicts the sequences of XENP4113, an IL-15/Rα-heteroFc fusion comprising a IL-15(N4D/N65D) variant and Xtend Fc (M428L/N434S) variant. IL-15 and IL-15Rα(sushi) are underlined, linkers are double underlined (although as will be appreciated by those in the art, the linkers can be replaced by other linkers, some of which are depicted in Figure 9 and Figure 10, and slashes (/) indicate the border(s) between IL-15, IL-15Rα, linkers, and constant/Fc regions.

[00155] Figure 121 depicts the sequences of XENP24294, an scIL-15/Rα-Fc fusion comprising an IL-15(N4D/N65D) variant and Xtend Fc (M428L/N434S) substitution. IL-15 and IL-15Rα(sushi) are underlined, linkers are double underlined (although as will be appreciated by those in the art, the linkers can be replaced by other linkers, some of which are depicted in Figure 9 and Figure 10, and slashes (/) indicate the border(s) between IL-15, IL-15Rα, linkers, and constant/Fc regions.

[00156] Figure 122 depicts the sequences of XENP24306, an IL-15/Rα-heteroFc fusion comprising an IL-15(D30N/E64Q/N65D) variant and Xtend Fc (M428L/N434S) substitution. IL-15 and IL-15Rα(sushi) are underlined, linkers are double underlined

(although as will be appreciated by those in the art, the linkers can be replaced by other linkers, some of which are depicted in Figure 9 and Figure 10, and slashes (/) indicate the border(s) between IL-15, IL-15Rα, linkers, and constant/Fc regions.

[00157] Figure 123 depicts the serum concentration of the indicated test articles over time in cynomolgus monkeys following a first dose at the indicated relative concentrations.

[00158] Figure 124A-Figure 124C depict sequences of illustrative scIL-15/Rα-Fc fusions comprising additional IL-15 potency variants. IL-15 and IL-15Rα(sushi) are underlined, linkers are double underlined (although as will be appreciated by those in the art, the linkers can be replaced by other linkers, some of which are depicted in Figure 9 and Figure 10), and slashes (/) indicate the border(s) between IL-15, IL-15Rα, linkers, variable regions, and constant/Fc regions. Additionally, each component of the scIL-15/Rα-Fc fusion protein has its own SEQ ID NO: in the sequence listing.

[00159] Figure 125A-Figure 125G depict percentage of A) $CD4^+CD45RA^-$, B) $CD4^+CD45RA^+$, C) $CD8^+CD45RA^-$, D) $CD8^+CD45RA^+$, E) $CD16^+$ NK cells, F) $CD56^+$ NK cells, and G) γδ cells expression Ki67 following incubation of PBMCs with the indicated test articles for 3 days.

[00160] Figure 126A-Figure 126D depict sequences of illustrative PD-1-targeted IL-15/Rα-Fc fusions comprising IL-15(D30N/N65D) variant. The CDRs are in bold. As noted herein and is true for every sequence herein containing CDRs, the exact identification of the CDR locations may be slightly different depending on the numbering used as is shown in Table 1, and thus included herein are not only the CDRs that are in bold but also CDRs included within the V_H and V_L domains using other numbering systems. IL-15 and IL-15Rα(sushi) are underlined, linkers are double underlined (although as will be appreciated by those in the art, the linkers can be replaced by other linkers, some of which are depicted in Figure 9 and Figure 10), and slashes (/) indicate the border(s) between IL-15, IL-15Rα, linkers, variable regions, and constant/Fc regions. Additionally, each CDR has its own SEQ ID NO: in the sequence listing, and each VL domain has its own SEQ ID NO: in the sequence listing.

[00161] Figure 127A-Figure 127D depict sequences of illustrative PD-1-targeted IL-15/Rα-Fc fusions comprising IL-15(D30N/E64Q/N65D) variant. The CDRs are in bold. As noted herein and is true for every sequence herein containing CDRs, the exact identification

of the CDR locations may be slightly different depending on the numbering used as is shown in Table 1, and thus included herein are not only the CDRs that are in bold but also CDRs included within the V_H and V_L domains using other numbering systems. IL-15 and IL-15Rα(sushi) are underlined, linkers are double underlined (although as will be appreciated by those in the art, the linkers can be replaced by other linkers, some of which are depicted in Figure 9 and Figure 10), and slashes (/) indicate the border(s) between IL-15, IL-15Rα, linkers, variable regions, and constant/Fc regions. Additionally, each CDR has its own SEQ ID NO: in the sequence listing, and each VL domain has its own SEQ ID NO: in the sequence listing.

[00162] Figure 128A-Figure 128L depict sequences of illustrative PD-1-targeted IL-15/Rα-Fc fusions comprising Xtend (M428L/N434S) substitutions for enhancing serum half-life. The CDRs are in bold. As noted herein and is true for every sequence herein containing CDRs, the exact identification of the CDR locations may be slightly different depending on the numbering used as is shown in Table 1, and thus included herein are not only the CDRs that are in bold but also CDRs included within the V_H and V_L domains using other numbering systems. IL-15 and IL-15Rα(sushi) are underlined, linkers are double underlined (although as will be appreciated by those in the art, the linkers can be replaced by other linkers, some of which are depicted in Figure 9 and Figure 10), and slashes (/) indicate the border(s) between IL-15, IL-15Rα, linkers, variable regions, and constant/Fc regions. It should be noted that any of the sequences depicted herein may include or exclude the M428L/N434S substitutions. Additionally, each CDR has its own SEQ ID NO: in the sequence listing, and each VL domain has its own SEQ ID NO: in the sequence listing.

[00163] Figure 129A-Figure 129B depict the sequences of XENP26007, XENP29481, and XENP30432, control RSV-targeted IL-15/Rα-Fc fusions. The CDRs are underlined. As noted herein and is true for every sequence herein containing CDRs, the exact identification of the CDR locations may be slightly different depending on the numbering used as is shown in Table 1, and thus included herein are not only the CDRs that are in bold but also CDRs included within the V_H and V_L domains using other numbering systems. IL-15 and IL-15Rα(sushi) are italicized, linkers are double underlined (although as will be appreciated by those in the art, the linkers can be replaced by other linkers, some of which are depicted in Figure 9 and Figure 10), and slashes (/) indicate the border(s) between IL-15, IL-15Rα, linkers, variable regions, and constant/Fc regions. Additionally, each CDR has its own SEQ

ID NO: in the sequence listing, and each VL domain has its own SEQ ID NO: in the sequence listing.

DETAILED DESCRIPTION OF THE INVENTION

I. Incorporation of Materials

A. Figures and Legends

[00164] All the figures, accompanying legends and sequences (with their identifiers and/or descriptions) of U.S. Provisional Application No. 62/659,571 filed April 18, 2018, and International Application No. WO2018/071918 filed October 16, 2017, and U.S. Patent Application No. 2018/0118828 filed October 16, 2017, all which are expressly and independently incorporated by reference herein in their entirety, particularly the amino acid sequences depicted therein.

[00165] Additional IL-15/IL-15Rα heterodimeric Fc fusion proteins are described in detail, for example, in U.S. Provisional Application titled "IL-15/IL-Ra Heterodimeric Fc Fusion Proteins and Uses Thereof" and filed concurrently, U.S. Provisional Application No. 62/408,655, filed Oct. 14, 2016, U.S. Provisional Application No. 62/416,087, filed Nov. 1, 2016, U.S. Provisional Application No. 62/443,465, filed Jan. 6, 2017, U.S. Provisional Application No. 62/477,926, filed Mar. 28, 2017, U.S. Patent Application No. 15/785,401, filed on October 16, 2017, and PCT International Application No. PCT/US2017/056829, filed on October 16, 2017, which are expressly incorporated herein by reference in their entirety, with particular reference to the figures, legends and claims therein.

[00166] Additional PD-1-targeted IL-15/IL-15Rα-Fc fusion proteins are described in detail, for example, in U.S. Provisional Application No. 62/408,655, filed on October 14, 2016, U.S. Provisional Application No. 62/416,087, filed on November 1, 2016, U.S. Provisional Application No. 62/443,465, filed on January 6, 2017, U.S. Provisional Application No. 62/477,926, filed on March 28, 2017, U.S. Patent Application No. 15/785,393, filed on October 16, 2017, and PCT International Application No. PCT/US2017/056826, filed on October 16, 2017, which are expressly incorporated herein by reference in their entirety, with particular reference to the figures, legends and claims therein.

B. Sequences

[00167] Reference is made to the accompanying sequence listing as following: anti-PD-1 sequences suitable for use as ABDs include SEQ ID NOS of the PD-1 scFv sequences of Figures 93A-93S, although the Fv sequences therein can be formatted as scFvs) and SEQ ID NOS of the PD-1 Fab sequences of Figures 94A-94AP, although the Fab sequences therein can be formatted as scFvs). As will be understood from those in the art, these sequence identifiers come in "pairs" for the variable heavy and light chains, as will be apparent from the sequence identifiers.

[00168] IL-15 sequences suitable for use in the PD-1-targeted IL-15/IL-15Rα-Fc fusion proteins include the SEQ ID NO of human mature IL-15 of Figure 3A, the SEQ ID NO of human mature IL-15 of Figure 3A having amino acid substitutions N4D/N65D, the SEQ ID NO: of human mature IL-15 of Figure 3A having amino acid substitutions D30N/N65D, and the SEQ ID NO: of human mature IL-15 of Figure 3A having amino acid substitutions D30N/E64Q/N65D. In some embodiments, the IL-15 of the PD-1-targeted IL-15/IL-15Rα-Fc fusion protein of the invention includes the SEQ ID NO of human mature IL-15 of Figure 3A having one or more amino acid substitutions selected from the group consisting of N1D, N4D, D8N, D30N, D61N, E64Q, N65D, Q108E, and those depicted in Figures 44A-44C and the corresponding sequence identifiers. IL-15 Rα sequences suitable for use in the PD-1-targeted IL-15/IL-15Rα-Fc fusion proteins include the SEQ ID NO of human IL-15Rα(sushi) domain of Figure 3A.

C. Nomenclature

[00169] The PD-1-targeted IL-15/IL-15Rα-Fc fusion proteins of the invention are listed in several formats. In some cases, a polypeptide is given a unique "XENP" number (or in some cases, a "XENCS" number), although as will be appreciated in the art, a longer sequence might contain a shorter one. These XENP numbers are in the sequence listing as well as identifiers, and used in the Figures. In addition, one molecule, comprising the three components, gives rise to multiple sequence identifiers. For example, the listing of the Fab monomer has the full length sequence, the variable heavy sequence and the three CDRs of the variable heavy sequence; the light chain has a full length sequence, a variable light sequence and the three CDRs of the variable light sequence; and the scFv-Fc domain has a full length sequence, an scFv sequence, a variable light sequence, 3 light CDRs, a scFv linker, a variable heavy sequence and 3 heavy CDRs. In some cases, molecules herein with a scFv domain use a single charged scFv linker (+H), although others can be used. In addition, the naming

nomenclature of particular variable domains uses a "Hx.xx_Ly.yy" type of format, with the numbers being unique identifiers to particular variable chain sequences. Thus, the variable domain of the Fab side of XENP25937 is "1C11 [PD-1]_H3L3", which indicates that the variable heavy domain H3 was combined with the light domain L3. In the case of scFv sequences such as XENP25812, the designation "1C11_H3.240_L3.148", indicates that the variable heavy domain H3.240 was combined with the light domain L3.148 and is in vh-linker-vl orientation, from N- to C-terminus. This molecule with the identical sequences of the heavy and light variable domains but in the reverse order would be named "1C11_L3.148_ H3.240". Similarly, different constructs may "mix and match" the heavy and light chains as will be evident from the sequence listing and the Figures.

II. **Definitions**

[00170] In order that the application may be more completely understood, several definitions are set forth below. Such definitions are meant to encompass grammatical equivalents.

[00171] By "ablation" herein is meant a decrease or removal of activity. Thus for example, "ablating FcγR binding" means the Fc region amino acid variant has less than 50% starting binding as compared to an Fc region not containing the specific variant, with less than 70-80-90-95-98% loss of activity being preferred, and in general, with the activity being below the level of detectable binding in a Biacore assay. Of particular use in the ablation of FcγR binding are those shown in Figure 6. However, unless otherwise noted, the Fc monomers of the invention retain binding to the FcRn receptor.

[00172] By "ADCC" or "antibody dependent cell-mediated cytotoxicity" as used herein is meant the cell-mediated reaction wherein nonspecific cytotoxic cells that express FcγRs recognize bound antibody on a target cell and subsequently cause lysis of the target cell. ADCC is correlated with binding to FcγRIIIa; increased binding to FcγRIIIa leads to an increase in ADCC activity. As is discussed herein, many embodiments of the invention ablate ADCC activity entirely.

[00173] By "ADCP" or antibody dependent cell-mediated phagocytosis as used herein is meant the cell-mediated reaction wherein nonspecific cytotoxic cells that express FcγRs recognize bound antibody on a target cell and subsequently cause phagocytosis of the target cell.

[00174] By "antigen binding domain" or "ABD" herein is meant a set of six **C**omplementary **D**etermining **R**egions (CDRs) that, when present as part of a polypeptide sequence, specifically binds a target antigen as discussed herein. Thus, a "checkpoint antigen binding domain" binds a target checkpoint antigen as outlined herein. As is known in the art, these CDRs are generally present as a first set of variable heavy CDRs (vhCDRs or V_HCDRs) and a second set of variable light CDRs (vlCDRs or V_LCDRs), each comprising three CDRs: vhCDR1, vhCDR2, vhCDR3 for the heavy chain and vlCDR1, vlCDR2 and vlCDR3 for the light. The CDRs are present in the variable heavy and variable light domains, respectively, and together form an Fv region. Thus, in some cases, the six CDRs of the antigen binding domain are contributed by a variable heavy and variable light chain. In a "Fab" format, the set of 6 CDRs are contributed by two different polypeptide sequences, the variable heavy domain (vh or V_H; containing the vhCDR1, vhCDR2 and vhCDR3) and the variable light domain (vl or V_L; containing the vlCDR1, vlCDR2 and vlCDR3), with the C-terminus of the vh domain being attached to the N-terminus of the CH1 domain of the heavy chain and the C-terminus of the vl domain being attached to the N-terminus of the constant light domain (and thus forming the light chain). In a scFv format, the vh and vl domains are covalently attached, generally through the use of a linker as outlined herein, into a single polypeptide sequence, which can be either (starting from the N-terminus) vh-linker-vl or vl-linker-vh, with the former being generally preferred (including optional domain linkers on each side, depending on the format used (e.g., from Figure 1 of US 62/353,511).

[00175] By "modification" herein is meant an amino acid substitution, insertion, and/or deletion in a polypeptide sequence or an alteration to a moiety chemically linked to a protein. For example, a modification may be an altered carbohydrate or PEG structure attached to a protein. By "amino acid modification" herein is meant an amino acid substitution, insertion, and/or deletion in a polypeptide sequence. For clarity, unless otherwise noted, the amino acid modification is always to an amino acid coded for by DNA, e.g., the 20 amino acids that have codons in DNA and RNA.

[00176] By "amino acid substitution" or "substitution" herein is meant the replacement of an amino acid at a particular position in a parent polypeptide sequence with a different amino acid. In particular, in some embodiments, the substitution is to an amino acid that is not naturally occurring at the particular position, either not naturally occurring within the organism or in any organism. For example, the substitution E272Y refers to a variant

polypeptide, in this case an Fc variant, in which the glutamic acid at position 272 is replaced with tyrosine. For clarity, a protein which has been engineered to change the nucleic acid coding sequence but not change the starting amino acid (for example exchanging CGG (encoding arginine) to CGA (still encoding arginine) to increase host organism expression levels) is not an "amino acid substitution"; that is, despite the creation of a new gene encoding the same protein, if the protein has the same amino acid at the particular position that it started with, it is not an amino acid substitution.

[00177] By "amino acid insertion" or "insertion" as used herein is meant the addition of an amino acid sequence at a particular position in a parent polypeptide sequence. For example, -233E or 233E designates an insertion of glutamic acid after position 233 and before position 234. Additionally, -233ADE or A233ADE designates an insertion of AlaAspGlu after position 233 and before position 234.

[00178] By "amino acid deletion" or "deletion" as used herein is meant the removal of an amino acid sequence at a particular position in a parent polypeptide sequence. For example, E233- or E233#, E233() or E233del designates a deletion of glutamic acid at position 233. Additionally, EDA233- or EDA233# designates a deletion of the sequence GluAspAla that begins at position 233.

[00179] By "variant protein" or "protein variant", or "variant" as used herein is meant a protein that differs from that of a parent protein by virtue of at least one amino acid modification. Protein variant may refer to the protein itself, a composition comprising the protein, or the amino sequence that encodes it. Preferably, the protein variant has at least one amino acid modification compared to the parent protein, e.g. from about one to about seventy amino acid modifications, and preferably from about one to about five amino acid modifications compared to the parent. As described below, in some embodiments the parent polypeptide, for example an Fc parent polypeptide, is a human wild type sequence, such as the Fc region from IgG1, IgG2, IgG3 or IgG4, although human sequences with variants can also serve as “parent polypeptides”, for example the IgG1/2 hybrid can be included. The protein variant sequence herein will preferably possess at least about 80% identity with a parent protein sequence, and most preferably at least about 90% identity, more preferably at least about 95-98-99% identity . Variant protein can refer to the variant protein itself, compositions comprising the protein variant, or the DNA sequence that encodes it.

[00180] Accordingly, by "antibody variant" or "variant antibody" as used herein is meant an antibody that differs from a parent antibody by virtue of at least one amino acid modification, "IgG variant" or "variant IgG" as used herein is meant an antibody that differs from a parent IgG (again, in many cases, from a human IgG sequence) by virtue of at least one amino acid modification, and "immunoglobulin variant" or "variant immunoglobulin" as used herein is meant an immunoglobulin sequence that differs from that of a parent immunoglobulin sequence by virtue of at least one amino acid modification. "Fc variant" or "variant Fc" as used herein is meant a protein comprising an amino acid modification in an Fc domain as compared to an Fc domain of human IgG1, IgG2, IgG3 or IgG4. The Fc variants of the present invention are defined according to the amino acid modifications that compose them. Thus, for example, N434S or 434S is an Fc variant with the substitution serine at position 434 relative to the parent Fc polypeptide, wherein the numbering is according to the EU index. Likewise, M428L/N434S defines an Fc variant with the substitutions M428L and N434S relative to the parent Fc polypeptide. The identity of the WT amino acid may be unspecified, in which case the aforementioned variant is referred to as 428L/434S. It is noted that the order in which substitutions are provided is arbitrary, that is to say that, for example, 428L/434S is the same Fc variant as M428L/N434S, and so on. For all positions discussed in the present invention that relate to antibodies, unless otherwise noted, amino acid position numbering is according to the EU index. The EU index or EU index as in Kabat or EU numbering scheme refers to the numbering of the EU antibody (Edelman et al., 1969, Proc Natl Acad Sci USA 63:78-85, hereby entirely incorporated by reference.) The modification can be an addition, deletion, or substitution. Substitutions can include naturally occurring amino acids and, in some cases, synthetic amino acids. Examples include US 6,586,207; WO 98/48032; WO 03/073238; US2004/0214988A1; WO 05/35727A2; WO 05/74524A2; J. W. Chin et al., (2002), Journal of the American Chemical Society 124:9026-9027; J. W. Chin, & P. G. Schultz, (2002), ChemBioChem 11:1135-1137; J. W. Chin, et al., (2002), PICAS United States of America 99:11020-11024; and, L. Wang, & P. G. Schultz, (2002), Chem. 1-10, all entirely incorporated by reference.

[00181] As used herein, "protein" herein is meant at least two covalently attached amino acids, which includes proteins, polypeptides, oligopeptides and peptides. In addition, polypeptides may include synthetic derivatization of one or more side chains or termini,

glycosylation, PEGylation, circular permutation, cyclization, linkers to other molecules, fusion to proteins or protein domains, and addition of peptide tags or labels.

[00182] By "residue" as used herein is meant a position in a protein and its associated amino acid identity. For example, Asparagine 297 (also referred to as Asn297 or N297) is a residue at position 297 in the human antibody IgG1.

[00183] By "Fab" or "Fab region" as used herein is meant the polypeptide that comprises the VH, CH1, VL, and CL immunoglobulin domains. Fab may refer to this region in isolation, or this region in the context of a full length antibody, antibody fragment or Fab fusion protein. In the context of a Fab, the Fab comprises an Fv region in addition to the CH1 and CL domains.

[00184] By "Fv" or "Fv fragment" or "Fv region" as used herein is meant a polypeptide that comprises the VL and VH domains of a single antibody. As will be appreciated by those in the art, these generally are made up of two chains, or can be combined (generally with a linker as discussed herein) to form an scFv.

[00185] By “single chain Fv” or “scFv” herein is meant a variable heavy domain covalently attached to a variable light domain, generally using a scFv linker as discussed herein, to form a scFv or scFv domain. A scFv domain can be in either orientation from N- to C-terminus (vh-linker-vl or vl-linker-vh). In the sequences depicted in the sequence listing and in the figures, the order of the vh and vl domain is indicated in the name, e.g. H.X_L.Y means N- to C-terminal is vh-linker-vl, and L.Y_H.X is vl-linker-vh.

[00186] By "IgG subclass modification" or “isotype modification” as used herein is meant an amino acid modification that converts one amino acid of one IgG isotype to the corresponding amino acid in a different, aligned IgG isotype. For example, because IgG1 comprises a tyrosine and IgG2 a phenylalanine at EU position 296, a F296Y substitution in IgG2 is considered an IgG subclass modification.

[00187] By "non-naturally occurring modification" as used herein is meant an amino acid modification that is not isotypic. For example, because none of the IgGs comprise a serine at position 434, the substitution 434S in IgG1, IgG2, IgG3, or IgG4 (or hybrids thereof) is considered a non-naturally occurring modification.

[00188] By "amino acid" and "amino acid identity" as used herein is meant one of the 20 naturally occurring amino acids that are coded for by DNA and RNA.

[00189] By "effector function" as used herein is meant a biochemical event that results from the interaction of an antibody Fc region with an Fc receptor or ligand. Effector functions include but are not limited to ADCC, ADCP, and CDC.

[00190] By "IgG Fc ligand" as used herein is meant a molecule, preferably a polypeptide, from any organism that binds to the Fc region of an IgG antibody to form an Fc/Fc ligand complex. Fc ligands include but are not limited to FcγRIs, FcγRIIs, FcγRIIIs, FcRn, C1q, C3, mannan binding lectin, mannose receptor, staphylococcal protein A, streptococcal protein G, and viral FcγR. Fc ligands also include Fc receptor homologs (FcRH), which are a family of Fc receptors that are homologous to the FcγRs (Davis et al., 2002, Immunological Reviews 190:123-136, entirely incorporated by reference). Fc ligands may include undiscovered molecules that bind Fc. Particular IgG Fc ligands are FcRn and Fc gamma receptors. By "Fc ligand" as used herein is meant a molecule, preferably a polypeptide, from any organism that binds to the Fc region of an antibody to form an Fc/Fc ligand complex.

[00191] By "Fc gamma receptor", "FcγR" or "FcgammaR" as used herein is meant any member of the family of proteins that bind the IgG antibody Fc region and is encoded by an FcγR gene. In humans this family includes but is not limited to FcγRI (CD64), including isoforms FcγRIa, FcγRIb, and FcγRIc; FcγRII (CD32), including isoforms FcγRIIa (including allotypes H131 and R131), FcγRIIb (including FcγRIIb-1 and FcγRIIb-2), and FcγRIIc; and FcγRIII (CD16), including isoforms FcγRIIIa (including allotypes V158 and F158) and FcγRIIIb (including allotypes FcγRIIb-NA1 and FcγRIIb-NA2) (Jefferis et al., 2002, Immunol Lett 82:57-65, entirely incorporated by reference), as well as any undiscovered human FcγRs or FcγR isoforms or allotypes. An FcγR may be from any organism, including but not limited to humans, mice, rats, rabbits, and monkeys. Mouse FcγRs include but are not limited to FcγRI (CD64), FcγRII (CD32), FcγRIII (CD16), and FcγRIII-2 (CD16-2), as well as any undiscovered mouse FcγRs or FcγR isoforms or allotypes.

[00192] By "FcRn" or "neonatal Fc Receptor" as used herein is meant a protein that binds the IgG antibody Fc region and is encoded at least in part by an FcRn gene. The FcRn may be from any organism, including but not limited to humans, mice, rats, rabbits, and monkeys. As is known in the art, the functional FcRn protein comprises two polypeptides, often referred to as the heavy chain and light chain. The light chain is beta-2-microglobulin

and the heavy chain is encoded by the FcRn gene. Unless otherwise noted herein, FcRn or an FcRn protein refers to the complex of FcRn heavy chain with beta-2-microglobulin. A variety of FcRn variants can be used to increase binding to the FcRn receptor, and in some cases, to increase serum half-life. In general, unless otherwise noted, the Fc monomers of the invention retain binding to the FcRn receptor (and, as noted below, can include amino acid variants to increase binding to the FcRn receptor).

[00193] By "parent polypeptide" as used herein is meant a starting polypeptide that is subsequently modified to generate a variant. The parent polypeptide may be a naturally occurring polypeptide, or a variant or engineered version of a naturally occurring polypeptide. Parent polypeptide may refer to the polypeptide itself, compositions that comprise the parent polypeptide, or the amino acid sequence that encodes it. Accordingly, by "parent immunoglobulin" as used herein is meant an unmodified immunoglobulin polypeptide that is modified to generate a variant, and by "parent antibody" as used herein is meant an unmodified antibody that is modified to generate a variant antibody. It should be noted that "parent antibody" includes known commercial, recombinantly produced antibodies as outlined below.

[00194] By "Fc" or "Fc region" or "Fc domain" as used herein is meant the polypeptide comprising the constant region of an antibody excluding the first constant region immunoglobulin domain (e.g., CH1) and in some cases, part of the hinge. Thus Fc refers to the last two constant region immunoglobulin domains (e.g., CH2 and CH3) of IgA, IgD, and IgG, the last three constant region immunoglobulin domains of IgE and IgM, and the flexible hinge N-terminal to these domains. For IgA and IgM, Fc may include the J chain. For IgG, the Fc domain comprises immunoglobulin domains Cγ2 and Cγ3 (Cγ2 and Cγ3) and the lower hinge region between Cγ1 (Cγ1) and Cγ2 (Cγ2). Although the boundaries of the Fc region may vary, the human IgG heavy chain Fc region is usually defined to include residues C226 or P230 to its carboxyl-terminus, wherein the numbering is according to the EU index as in Kabat. In some embodiments, as is more fully described below, amino acid modifications are made to the Fc region, for example to alter binding to one or more FcγR receptors or to the FcRn receptor.

[00195] By “heavy constant region” herein is meant the CH1-hinge-CH2-CH3 portion of an antibody.

[00196] By "Fc fusion protein" or "immunoadhesin" herein is meant a protein comprising an Fc region, generally linked (optionally through a linker moiety, as described herein) to a different protein, such as to IL-15 and/or IL-15R, as described herein. In some instances, two Fc fusion proteins can form a homodimeric Fc fusion protein or a heterodimeric Fc fusion protein with the latter being preferred. In some cases, one monomer of the heterodimeric Fc fusion protein comprises an Fc domain alone (e.g., an empty Fc domain) and the other monomer is a Fc fusion, comprising a variant Fc domain and a protein domain, such as a receptor, ligand or other binding partner.

[00197] By "position" as used herein is meant a location in the sequence of a protein. Positions may be numbered sequentially, or according to an established format, for example the EU index for antibody numbering.

[00198] By "strandedness" in the context of the monomers of the heterodimeric antibodies of the invention herein is meant that, similar to the two strands of DNA that "match", heterodimerization variants are incorporated into each monomer so as to preserve the ability to "match" to form heterodimers. For example, if some pI variants are engineered into monomer A (e.g., making the pI higher) then steric variants that are "charge pairs" that can be utilized as well do not interfere with the pI variants, e.g., the charge variants that make a pI higher are put on the same "strand" or "monomer" to preserve both functionalities. Similarly, for "skew" variants that come in pairs of a set as more fully outlined below, the skilled artisan will consider pI in deciding into which strand or monomer that incorporates one set of the pair will go, such that pI separation is maximized using the pI of the skews as well.

[00199] By "target antigen" as used herein is meant the molecule that is bound specifically by the variable region of a given antibody. A target antigen may be a protein, carbohydrate, lipid, or other chemical compound. A wide number of suitable target antigens are described below.

[00200] By "target cell" as used herein is meant a cell that expresses a target antigen.

[00201] By "variable region" as used herein is meant the region of an immunoglobulin that comprises one or more Ig domains substantially encoded by any of the Vκ, Vλ, and/or VH genes that make up the kappa, lambda, and heavy chain immunoglobulin genetic loci respectively.

[00202] By "wild type or WT" herein is meant an amino acid sequence or a nucleotide sequence that is found in nature, including allelic variations. A WT protein has an amino acid sequence or a nucleotide sequence that has not been intentionally modified.

[00203] The biospecific heterodimeric proteins of the present invention are generally isolated or recombinant. "Isolated," when used to describe the various polypeptides disclosed herein, means a polypeptide that has been identified and separated and/or recovered from a cell or cell culture from which it was expressed. Ordinarily, an isolated polypeptide will be prepared by at least one purification step. An "isolated protein," refers to a protein which is substantially free of other proteins having different binding specificities. "Recombinant" means the proteins are generated using recombinant nucleic acid techniques in exogeneous host cells.

[00204] "Percent (%) amino acid sequence identity" with respect to a protein sequence is defined as the percentage of amino acid residues in a candidate sequence that are identical with the amino acid residues in the specific (parental) sequence, after aligning the sequences and introducing gaps, if necessary, to achieve the maximum percent sequence identity, and not considering any conservative substitutions as part of the sequence identity. Alignment for purposes of determining percent amino acid sequence identity can be achieved in various ways that are within the skill in the art, for instance, using publicly available computer software such as BLAST, BLAST-2, ALIGN or Megalign (DNASTAR) software. Those skilled in the art can determine appropriate parameters for measuring alignment, including any algorithms needed to achieve maximal alignment over the full length of the sequences being compared. One particular program is the ALIGN-2 program outlined at paragraphs [0279] to [0280] of US Pub. No. 20160244525, hereby incorporated by reference.

[00205] The degree of identity between an amino acid sequence of the present invention ("invention sequence") and the parental amino acid sequence is calculated as the number of exact matches in an alignment of the two sequences, divided by the length of the "invention sequence," or the length of the parental sequence, whichever is the shortest. The result is expressed in percent identity.

[00206] In some embodiments, two or more amino acid sequences are at least 50%, 60%, 70%, 80%, or 90% identical. In some embodiments, two or more amino acid sequences are at least 95%, 97%, 98%, 99%, or even 100% identical.

[00207] "Specific binding" or "specifically binds to" or is "specific for" a particular antigen or an epitope means binding that is measurably different from a non-specific interaction. Specific binding can be measured, for example, by determining binding of a molecule compared to binding of a control molecule, which generally is a molecule of similar structure that does not have binding activity. For example, specific binding can be determined by competition with a control molecule that is similar to the target.

[00208] Specific binding for a particular antigen or an epitope can be exhibited, for example, by an antibody having a KD for an antigen or epitope of at least about 10^{-4} M, at least about 10^{-5} M, at least about 10^{-6} M, at least about 10^{-7} M, at least about 10^{-8} M, at least about 10^{-9} M, alternatively at least about 10^{-10} M, at least about 10^{-11} M, at least about 10^{-12} M, or greater, where KD refers to a dissociation rate of a particular antibody-antigen interaction. Typically, an antibody that specifically binds an antigen will have a KD that is 20-, 50-, 100-, 500-, 1000-, 5,000-, 10,000- or more times greater for a control molecule relative to the antigen or epitope.

[00209] Also, specific binding for a particular antigen or an epitope can be exhibited, for example, by an antibody having a KA or Ka for an antigen or epitope of at least 20-, 50-, 100-, 500-, 1000-, 5,000-, 10,000- or more times greater for the epitope relative to a control, where KA or Ka refers to an association rate of a particular antibody-antigen interaction. Binding affinity is generally measured using a Biacore assay.

III. **Introduction**

[00210] The invention provides targeted heterodimeric fusion proteins that can bind to the checkpoint inhibitor PD-1 antigen and can complex with the common gamma chain (γc; CD132) and/or the Il-2 receptor β-chain (IL-2Rβ; CD122). In general, the heterodimeric fusion proteins of the invention have three functional components: an IL-15/IL-15Rα(sushi) component, generally referred to herein as an "IL-15 complex", an anti-PD-1 component, and an Fc component, each of which can take different forms and each of which can be combined with the other components in any configuration. The IL-15/IL-15Rα-Fc fusion protein can include as IL-15 protein covalently attached to an IL-15Rα, and an Fc domain. In some embodiments, the IL-15 protein and IL-15Rα protein are noncovalently attached.

[00211] As shown in the figures, the IL-15 complex can take several forms. As stated above, the IL-15 protein on its own is less stable than when complexed with the IL-15Rα protein. As is known in the art, the IL-15Rα protein contains a "sushi domain", which is the shortest region of the receptor that retains IL-15 binding activity. Thus, while heterodimeric fusion proteins comprising the entire IL-15Rα protein can be made, preferred embodiments herein include complexes that just use the sushi domain, the sequence of which is shown in the figures.

[00212] Accordingly, the IL-15 complex of the PD-1-targeted IL-15/Rα heterodimeric Fc fusion proteins of the invention generally comprises the human mature IL-15 protein (including human mature IL-15 protein variants) and the sushi domain of IL-15Rα (unless otherwise noted that the full length sequence is used, "IL-15Rα", "IL-15Rα(sushi)" and "sushi" are used interchangeably throughout). This complex can be used in multiple different formats. As shown in Figures 22A, 22C, 22D, and 22F, the IL-15 protein and the IL-15Rα(sushi) are not covalently attached, but rather are self-assembled through regular ligand-ligand interactions. As is more fully described herein, it can be either the IL-15 variant or the IL-15Rα sushi domain that is covalently linked to the Fc domain (generally using an optional domain linker). Amino acid sequences of the formats are provided in Figure 23 ("IL-15/Rα-heteroFc" format), Figure 24 ("scIL-15/Rα-Fc" format), Figures 25A-25B ("ncIL-15/Rα-Fc" format), Figure 26 ("bivalent ncIL-15/Rα-Fc" format), Figure 27 ("bivalent scIL-15/Rα-Fc" format), Figure 28 ("Fc-ncIL-15/Rα" format), and Figure 29 ("Fc-scIL-15/Rα" format). Alternatively, they can be covalently attached using a domain linker as generally shown in Figures 22B, 22E, and 22G. Figure 22E depicts the sushi domain as the N-terminal domain, although this can be reversed. Finally, each of the IL-15 and IL-15Rα sushi domains can be engineered to contain a cysteine amino acid, that forms a disulfide bond to form the complex as is generally shown in Figures 36A, 36B, 36C, and 36D, again, with either the IL-15 domain or the IL-15Rα sushi domain being covalently attached (using an optional domain linker) to the Fc domain. Amino acid sequences of the formats are provided in Figures 37A-37B ("dsIL-15/Rα-heteroFc" format), Figure 38A-38B ("dsIL-15/Rα-Fc" format), Figure 39 ("bivalent dsIL-15/Rα-Fc" format), and Figure 40 ("Fc-dsIL-15/Rα" format).

[00213] In some embodiments, the PD-1-targeted IL-15/Rα Fc fusion proteins have been engineered to exhibit reduced potency compared to their parental construct. For instance, one or more amino acid substitutions can be introduced into the amino acid

sequence of the human mature IL-15 protein of the IL-15/Rα complex. In some embodiments, the PD-1-targeted IL-15/Rα Fc fusion protein of the invention comprises human mature IL-15 protein variant having amino acid substitutions N4D/N65D. In certain embodiments, the PD-1-targeted IL-15/Rα Fc fusion protein of the invention comprises human mature IL-15 protein variant having amino acid substitutions D30N/N65D. In particular embodiments, the PD-1-targeted IL-15/Rα Fc fusion protein of the invention comprises human mature IL-15 protein variant having amino acid substitutions D30N/E64Q/N65D. Exemplary embodiments of PD-1-targeted IL-15/Rα Fc fusion proteins with reduced potency and amino acid sequences thereof are provided in Figures 45A-45D, 46A-46C, 47A-47B, 48, 49, 50, 126, and 127.

A. PD-1 Antigen Binding Domains

[00214] The PD-1 antigen binding domain (ABD) (e.g., the anti-PD-1 component) of the invention is generally a set of 6 CDRs and/or a variable heavy domain and a variable light domain that form an Fv domain that can bind human PD-1. As shown herein, the anti-PD-1 ABD can be in the form of a scFv, wherein the vh and vl domains are joined using an scFv linker, which can be optionally a charged scFv linker. As will be appreciated by those in the art, the scFv can be assembled from N- to C-terminus as N-vh-scFv linker-vl-C or as N-vl-scFv linker-vh-C, with the C terminus of the scFv domain generally being linked to the hinge-CH2-CH3 Fc domain. Suitable Fvs (including CDR sets and variable heavy/variable light domains) can be used in scFv formats or Fab formats are shown in the Figures as well as disclosed in WO2017/218707 and PCT/US2018/059887 filed November 8, 2018, hereby expressly incorporated in their entirety, and specifically for Figures, Legends, and SEQ identifiers that depict anti-PD-1 sequences. In some embodiments, PD-1 ABDs of the present invention are based on the 1C11 clone, shown in the Figures, specifically Figures 93A-93S and 94A-94AP. In some embodiments, PD-1 ABDs of the present invention are based on a variant heavy chain based on the heavy chain of 1C11 clone (XENP22553) shown in Figures 96A-96F. In some embodiments, PD-1 ABDs of the present invention are based on a variant light chain based on the light chain of 1C11 clone (XENP22553) shown in Figures 97A-97Q.

[00215] In useful embodiments, the PD-1-targeted IL-15/Rα Fc fusion proteins of the invention include an ABD to human PD-1. In some embodiments, the six CDRs that confer binding to PD-1 are selected from those depicted in any of Figures 93A-93S and 94A-94AP.

[00216] In some embodiments, the PD-1-targeted IL-15/Rα Fc fusion proteins of the invention include an ABD to human PD-1 in a scFv format. In some embodiments, ABD to human PD-1 contains the six CDRs that confer binding to PD-1 are selected from those depicted in any of Figures 93A-93S, or the VH and VL domain of any ABD of Figures 93A-93S.

[00217] In particular embodiments, the PD-1-targeted IL-15/Rα Fc fusion proteins of the invention include an ABD to human PD-1 in a Fab format. In some embodiments, ABD to human PD-1 contains the six CDRs that confer binding to PD-1 are selected from those depicted in any of Figures 94A-94AP, or the VH and VL domain of any ABD of Figures 94A-94AP. As will be understood from those in the art, these sequence identifiers come in "pairs" for the variable heavy and light chains, as will be apparent from the sequence identifiers.

[00218] In certain embodiments, the PD-1-targeted IL-15/Rα Fc fusion proteins of the invention include an ABD to human PD-1. In some instances, the CDRs of the variable heavy domain of the ABD are selected from those depicted in any of Figures 95A-95J and the CDRs of the variable light domain of the ABD are selected from those depicted in any of Figures 96A-96F.

[00219] Of particular use in many embodiments that have a scFv ABD to human PD-1 is the ABD of XENP25806 1C11[PD-1]_H3.234_L3.144 as depicted in Figure 93R, including SEQ ID NOS: 578-579. Thus, the six CDRs and/or the VH and VL domains from XENP25806 (SEQ ID NOS: 578-579) can be used in the constructs of the invention.

[00220] Of particular use in many embodiments that have a scFv ABD to human PD-1 is the ABD of XENP25812 1C11[PD-1]_H3.240_L3.148 as depicted in Figure 93R, including SEQ ID NO:584. Thus, the six CDRs and/or the VH and VL domains from XENP25812 (SEQ ID NO:584) can be used in the constructs of the invention.

[00221] Of particular use in many embodiments that have a scFv ABD to human PD-1 is the ABD of XENP25813 1C11[PD-1]_H3.241_L3.148 as depicted in Figure 93R, including SEQ ID NO:585. Thus, the six CDRs and/or the VH and VL domains from XENP25813 (SEQ ID NO:585) can be used in the constructs of the invention.

[00222] Of particular use in many embodiments that have a scFv ABD to human PD-1 is the ABD of XENP25819 1C11[PD-1]_H3.241_L3.92 as depicted in Figure 93S, including

SEQ ID NO:591. Thus, the six CDRs and/or the VH and VL domains from XENP25819 (SEQ ID NO:591) can be used in the constructs of the invention.

[00223] Of particular use in many embodiments that have a Fab ABD to human PD-1 is the ABD of XENP26940 1C11[PD-1]_H3.303_L3.152 as depicted in Figure 94N, including SEQ ID NOS:642 and 1103. Thus, the six CDRs and/or the VH and VL domains from XENP26940 (SEQ ID NOS:642 and 1103) can be used in the constructs of the invention.

[00224] Of particular use in many embodiments that have a Fab ABD to human PD-1 is the ABD of XENP28026 1C11[PD-1]_H3.329_L3.220 as depicted in Figure 94AE, including SEQ ID NOS:708 and 1169. Thus, the six CDRs and/or the VH and VL domains from XENP28026 (SEQ ID NOS:708 and 1169) can be used in the constructs of the invention.

[00225] Of particular use in many embodiments that have a Fab ABD to human PD-1 is the ABD of XENP28652 1C11[PD-1]_H3.328_L3.152 as depicted in Figure 94AG, including SEQ ID NOS:719 and 1180. Thus, the six CDRs and/or the VH and VL domains from XENP28652 (SEQ ID NOS:719 and 1180) can be used in the constructs of the invention.

B. Fc domains

[00226] The Fc domain component of the invention is as described herein, which generally contains skew variants and/or optional pI variants and/or ablation variants are outlined herein.

[00227] The Fc domains can be derived from IgG Fc domains, e.g., IgG1, IgG2, IgG3 or IgG4 Fc domains, with IgG1 Fc domains finding particular use in the invention. The following describes Fc domains that are useful for IL-15/IL-15Rα Fc fusion monomers and checkpoint antibody fragments of the bispecific heterodimer proteins of the present invention.

[00228] The carboxy-terminal portion of each chain defines a constant region primarily responsible for effector function Kabat et al. collected numerous primary sequences of the variable regions of heavy chains and light chains. Based on the degree of conservation of the sequences, they classified individual primary sequences into the CDR and the framework and made a list thereof (see SEQUENCES OF IMMUNOLOGICAL INTEREST, 5th edition, NIH publication, No. 91-3242, E.A. Kabat et al., entirely incorporated by reference).

Throughout the present specification, the Kabat numbering system is generally used when referring to a residue in the variable domain (approximately, residues 1-107 of the light chain variable region and residues 1-113 of the heavy chain variable region) and the EU numbering system for Fc regions (e.g., Kabat et al., supra (1991)).

[00229] In the IgG subclass of immunoglobulins, there are several immunoglobulin domains in the heavy chain. By "immunoglobulin (Ig) domain" herein is meant a region of an immunoglobulin having a distinct tertiary structure. Of interest in the present invention are the heavy chain domains, including, the constant heavy (CH) domains and the hinge domains. In the context of IgG antibodies, the IgG isotypes each have three CH regions. Accordingly, "CH" domains in the context of IgG are as follows: "CH1" refers to positions 118-220 according to the EU index as in Kabat. "CH2" refers to positions 237-340 according to the EU index as in Kabat, and "CH3" refers to positions 341-447 according to the EU index as in Kabat. As shown herein and described below, the pI variants can be in one or more of the CH regions, as well as the hinge region, discussed below.

[00230] Another type of Ig domain of the heavy chain is the hinge region. By "hinge" or "hinge region" or "antibody hinge region" or "immunoglobulin hinge region" herein is meant the flexible polypeptide comprising the amino acids between the first and second constant domains of an antibody. Structurally, the IgG CH1 domain ends at EU position 220, and the IgG CH2 domain begins at residue EU position 237. Thus for IgG the antibody hinge is herein defined to include positions 221 (D221 in IgG1) to 236 (G236 in IgG1), wherein the numbering is according to the EU index as in Kabat. In some embodiments, for example in the context of an Fc region, the lower hinge is included, with the "lower hinge" generally referring to positions 226 or 230. As noted herein, pI variants can be made in the hinge region as well.

[00231] Thus, the present invention provides different antibody domains, e.g., different Fc domains. As described herein and known in the art, the heterodimeric proteins of the invention comprise different domains, which can be overlapping as well. These domains include, but are not limited to, the Fc domain, the CH1 domain, the CH2 domain, the CH3 domain, the hinge domain, and the heavy constant domain (CH1-hinge-Fc domain or CH1-hinge-CH2-CH3).

[00232] Thus, the "Fc domain" includes the -CH2-CH3 domain, and optionally a hinge domain, and can be from human IgG1, IgG2, IgG3 or IgG4. When from IgG1, the Fc domain

can be a variant human IgG1 domain, for example including amino acid substitutions 427L/434S. Additionally, the variant IgG1 Fc domain can comprises ablation variants such as E233P/L234V/L235A/G236del/S267K substitutions.

[00233] In some of the embodiments herein, when a protein fragment, e.g., IL-15 or IL-15Rα is attached to an Fc domain, it is the C-terminus of the IL-15 or IL-15Rα construct that is attached to all or part of the hinge of the Fc domain; for example, it is generally attached to the sequence EPKS which is the beginning of the hinge. In other embodiments, when a protein fragment, e.g., IL-15 or IL-15Rα, is attached to an Fc domain, it is the C-terminus of the IL-15 or IL-15Rα construct that is attached to the CH1 domain of the Fc domain.

[00234] In some of the constructs and sequences outlined herein of an Fc domain protein, the C-terminus of the IL-15 or IL-15Rα protein fragment is attached to the N-terminus of a domain linker, the C-terminus of which is attached to the N-terminus of a constant Fc domain (N-IL-15 or IL-15Rα protein fragment-linker-Fc domain-C) although that can be switched (N- Fc domain-linker- IL-15 or IL-15Rα protein fragment -C). In other constructs and sequence outlined herein, C-terminus of a first protein fragment is attached to the N-terminus of a second protein fragment, optionally via a domain linker, the C-terminus of the second protein fragment is attached to the N-terminus of a constant Fc domain, optionally via a domain linker. In yet other constructs and sequences outlined herein, a constant Fc domain that is not attached to a first protein fragment or a second protein fragment is provided. A heterodimer Fc fusion protein can contain two or more of the exemplary monomeric Fc domain proteins described herein.

[00235] In some embodiments, the linker is a "domain linker", used to link any two domains as outlined herein together, some of which are depicted in Figure 9. While any suitable linker can be used, many embodiments utilize a glycine-serine polymer, including for example (GS)n, (GSGGS)n (SEQ ID NO:1217), (GGGGS)n (SEQ ID NO:1218), and (GGGS)n (SEQ ID NO:1219), where n is an integer of at least one (and generally from 1 to 2 to 3 to 4 to 5) as well as any peptide sequence that allows for recombinant attachment of the two domains with sufficient length and flexibility to allow each domain to retain its biological function. In some cases, and with attention being paid to "strandedness", as outlined below, charged domain linkers.

[00236] In one embodiment, heterodimeric Fc fusion proteins contain at least two constant domains which can be engineered to produce heterodimers, such as pI engineering. Other Fc domains that can be used include fragments that contain one or more of the CH1, CH2, CH3 ,and hinge domains of the invention that have been pI engineered. In particular, the formats depicted in Figure 21 and Figure 64 are heterodimeric Fc fusion proteins, meaning that the protein has two associated Fc sequences self-assembled into a heterodimeric Fc domain and at least one protein fragment (e.g., 1, 2 or more protein fragments) as more fully described below. In some cases, a first protein fragment is linked to a first Fc sequence and a second protein fragment is linked to a second Fc sequence. In other cases, a first protein fragment is linked to a first Fc sequence, and the first protein fragment is non-covalently attached to a second protein fragment that is not linked to an Fc sequence. In some cases, the heterodimeric Fc fusion protein contains a first protein fragment linked to a second protein fragment which is linked a first Fc sequence, and a second Fc sequence that is not linked to either the first or second protein fragments.

[00237] Accordingly, in some embodiments the present invention provides heterodimeric Fc fusion proteins that rely on the use of two different heavy chain variant Fc sequences, that will self-assemble to form a heterodimeric Fc domain fusion polypeptide.

[00238] The present invention is directed to novel constructs to provide heterodimeric Fc fusion proteins that allow binding to one or more binding partners, ligands or receptors. The heterodimeric Fc fusion constructs are based on the self-assembling nature of the two Fc domains of the heavy chains of antibodies, e.g., two “monomers” that assemble into a “dimer”. Heterodimeric Fc fusions are made by altering the amino acid sequence of each monomer as more fully discussed below. Thus, the present invention is generally directed to the creation of heterodimeric Fc fusion proteins which can co-engage binding partner(s) or ligand(s) or receptor(s) in several ways, relying on amino acid variants in the constant regions that are different on each chain to promote heterodimeric formation and/or allow for ease of purification of heterodimers over the homodimers.

[00239] There are a number of mechanisms that can be used to generate the heterodimers of the present invention. In addition, as will be appreciated by those in the art, these mechanisms can be combined to ensure high heterodimerization. Thus, amino acid variants that lead to the production of heterodimers are referred to as “heterodimerization variants”. As discussed below, heterodimerization variants can include steric variants (e.g.

the "knobs and holes" or "skew" variants described below and the "charge pairs" variants described below) as well as "pI variants", which allows purification of homodimers away from heterodimers. As is generally described in WO2014/145806, hereby incorporated by reference in its entirety and specifically as below for the discussion of "heterodimerization variants", useful mechanisms for heterodimerization include "knobs and holes" ("KIH"; sometimes herein as "skew" variants (see discussion in WO2014/145806), "electrostatic steering" or "charge pairs" as described in WO2014/145806, pI variants as described in WO2014/145806, and general additional Fc variants as outlined in WO2014/145806 and below.

[00240] In the present invention, there are several basic mechanisms that can lead to ease of purifying heterodimeric antibodies; one relies on the use of pI variants, such that each monomer has a different pI, thus allowing the isoelectric purification of A-A, A-B and B-B dimeric proteins. Alternatively, some formats also allow separation on the basis of size. As is further outlined below, it is also possible to "skew" the formation of heterodimers over homodimers. Thus, a combination of steric heterodimerization variants and pI or charge pair variants find particular use in the invention.

[00241] In general, embodiments of particular use in the present invention rely on sets of variants that include skew variants, that encourage heterodimerization formation over homodimerization formation, coupled with pI variants, which increase the pI difference between the two monomers.

[00242] Additionally, as more fully outlined below, depending on the format of the heterodimer Fc fusion protein, pI variants can be either contained within the constant and/or Fc domains of a monomer, or domain linkers can be used. That is, the invention provides pI variants that are on one or both of the monomers, and/or charged domain linkers as well. In addition, additional amino acid engineering for alternative functionalities may also confer pI changes, such as Fc, FcRn and KO variants.

[00243] In the present invention that utilizes pI as a separation mechanism to allow the purification of heterodimeric proteins, amino acid variants can be introduced into one or both of the monomer polypeptides; that is, the pI of one of the monomers (referred to herein for simplicity as "monomer A") can be engineered away from monomer B, or both monomer A and B change be changed, with the pI of monomer A increasing and the pI of monomer B decreasing. As discussed, the pI changes of either or both monomers can be done by

removing or adding a charged residue (e.g., a neutral amino acid is replaced by a positively or negatively charged amino acid residue, e.g., glycine to glutamic acid), changing a charged residue from positive or negative to the opposite charge (e.g. aspartic acid to lysine) or changing a charged residue to a neutral residue (e.g., loss of a charge; lysine to serine.). A number of these variants are shown in the Figures.

[00244] Accordingly, this embodiment of the present invention provides for creating a sufficient change in pI in at least one of the monomers such that heterodimers can be separated from homodimers. As will be appreciated by those in the art, and as discussed further below, this can be done by using a “wild type” heavy chain constant region and a variant region that has been engineered to either increase or decrease its pI (wt A-+B or wt A - -B), or by increasing one region and decreasing the other region (A+ -B- or A- B+).

[00245] Thus, in general, a component of some embodiments of the present invention are amino acid variants in the constant regions that are directed to altering the isoelectric point (pI) of at least one, if not both, of the monomers of a dimeric protein by incorporating amino acid substitutions (“pI variants” or “pI substitutions”) into one or both of the monomers. As shown herein, the separation of the heterodimers from the two homodimers can be accomplished if the pIs of the two monomers differ by as little as 0.1 pH unit, with 0.2, 0.3, 0.4 and 0.5 or greater all finding use in the present invention.

[00246] As will be appreciated by those in the art, the number of pI variants to be included on each or both monomer(s) to get good separation will depend in part on the starting pI of the components. As is known in the art, different Fcs will have different starting pIs which are exploited in the present invention. In general, as outlined herein, the pIs are engineered to result in a total pI difference of each monomer of at least about 0.1 logs, with 0.2 to 0.5 being preferred as outlined herein.

[00247] As will be appreciated by those in the art, the number of pI variants to be included on each or both monomer(s) to get good separation will depend in part on the starting pI of the components. That is, to determine which monomer to engineer or in which “direction” (e.g., more positive or more negative), the sequences of the Fc domains, and in some cases, the protein domain(s) linked to the Fc domain are calculated and a decision is made from there. As is known in the art, different Fc domains and/or protein domains will have different starting pIs which are exploited in the present invention. In general, as

outlined herein, the pIs are engineered to result in a total pI difference of each monomer of at least about 0.1 logs, with 0.2 to 0.5 being preferred as outlined herein.

[00248] Furthermore, as will be appreciated by those in the art and outlined herein, in some embodiments, heterodimers can be separated from homodimers on the basis of size. As shown in the Figures, for example, several of the formats allow separation of heterodimers and homodimers on the basis of size.

[00249] In the case where pI variants are used to achieve heterodimerization, by using the constant region(s) of Fc domains(s), a more modular approach to designing and purifying heterodimeric Fc fusion proteins is provided. Thus, in some embodiments, heterodimerization variants (including skew and purification heterodimerization variants) must be engineered. In addition, in some embodiments, the possibility of immunogenicity resulting from the pI variants is significantly reduced by importing pI variants from different IgG isotypes such that pI is changed without introducing significant immunogenicity. Thus, an additional problem to be solved is the elucidation of low pI constant domains with high human sequence content, e.g. the minimization or avoidance of non-human residues at any particular position.

[00250] A side benefit that can occur with this pI engineering is also the extension of serum half-life and increased FcRn binding. That is, as described in US8,637,641 (incorporated by reference in its entirety), lowering the pI of antibody constant domains (including those found in antibodies and Fc fusions) can lead to longer serum retention in vivo. These pI variants for increased serum half-life also facilitate pI changes for purification.

[00251] In addition, it should be noted that the pI variants of the heterodimerization variants give an additional benefit for the analytics and quality control process of Fc fusion proteins, as the ability to either eliminate, minimize and distinguish when homodimers are present is significant. Similarly, the ability to reliably test the reproducibility of the heterodimeric Fc fusion protein production is important.

C. Heterodimerization Variants

[00252] The present invention provides heterodimeric proteins, including heterodimeric Fc fusion proteins in a variety of formats, which utilize heterodimeric variants to allow for heterodimeric formation and/or purification away from homodimers. The heterodimeric fusion constructs are based on the self-assembling nature of the two Fc domains, e.g., two “monomers” that assemble into a “dimer”.

[00253] There are a number of suitable pairs of sets of heterodimerization skew variants. These variants come in "pairs" of "sets". That is, one set of the pair is incorporated into the first monomer and the other set of the pair is incorporated into the second monomer. It should be noted that these sets do not necessarily behave as "knobs in holes" variants, with a one-to-one correspondence between a residue on one monomer and a residue on the other; that is, these pairs of sets form an interface between the two monomers that encourages heterodimer formation and discourages homodimer formation, allowing the percentage of heterodimers that spontaneously form under biological conditions to be over 90%, rather than the expected 50% (25 % homodimer A/A:50% heterodimer A/B:25% homodimer B/B).

D. Steric Variants

[00254] In some embodiments, the formation of heterodimers can be facilitated by the addition of steric variants. That is, by changing amino acids in each heavy chain, different heavy chains are more likely to associate to form the heterodimeric structure than to form homodimers with the same Fc amino acid sequences. Suitable steric variants are included in in the Figure 29 of US2016/0355608, all of which is hereby incorporated by reference in its entirety, as well as in Figures 1A-1E.

[00255] One mechanism is generally referred to in the art as "knobs and holes", referring to amino acid engineering that creates steric influences to favor heterodimeric formation and disfavor homodimeric formation can also optionally be used; this is sometimes referred to as "knobs and holes", as described in Ridgway et al., Protein Engineering 9(7):617 (1996); Atwell et al., J. Mol. Biol. 1997 270:26; US Patent No. 8,216,805, all of which are hereby incorporated by reference in their entirety. The Figures identify a number of "monomer A – monomer B" pairs that rely on "knobs and holes". In addition, as described in Merchant et al., Nature Biotech. 16:677 (1998), these "knobs and hole" mutations can be combined with disulfide bonds to skew formation to heterodimerization.

[00256] An additional mechanism that finds use in the generation of heterodimers is sometimes referred to as "electrostatic steering" as described in Gunasekaran et al., J. Biol. Chem. 285(25):19637 (2010), hereby incorporated by reference in its entirety. This is sometimes referred to herein as "charge pairs". In this embodiment, electrostatics are used to skew the formation towards heterodimerization. As those in the art will appreciate, these may also have an effect on pI, and thus on purification, and thus could in some cases also be

considered pI variants. However, as these were generated to force heterodimerization and were not used as purification tools, they are classified as "steric variants". These include, but are not limited to, D221E/P228E/L368E paired with D221R/P228R/K409R (e.g., these are "monomer corresponding sets) and C220E/P228E/368E paired with C220R/E224R/P228R/K409R.

[00257] Additional monomer A and monomer B variants that can be combined with other variants, optionally and independently in any amount, such as pI variants outlined herein or other steric variants that are shown in Figure 37 of US 2012/0149876, all of which are incorporated expressly by reference herein.

[00258] In some embodiments, the steric variants outlined herein can be optionally and independently incorporated with any pI variant (or other variants such as Fc variants, FcRn variants, etc.) into one or both monomers, and can be independently and optionally included or excluded from the proteins of the invention.

[00259] A list of suitable skew variants is found in Figures 4A-4C. Of particular use in many embodiments are the pairs of sets including, but not limited to, S364K/E357Q : L368D/K370S; L368D/K370S : S364K; L368E/K370S : S364K; T411E/K360E/Q362E : D401K; L368D/K370S : S364K/E357L, K370S : S364K/E357Q and T366S/L368A/Y407V : T366W (optionally including a bridging disulfide, T366S/L368A/Y407V/Y349C : T366W/S354C). In terms of nomenclature, the pair "S364K/E357Q : L368D/K370S" means that one of the monomers has the double variant set S364K/E357Q and the other has the double variant set L368D/K370S; as above, the "strandedness" of these pairs depends on the starting pI.

E. pI (Isoelectric point) Variants for Heterodimers

[00260] In general, as will be appreciated by those in the art, there are two general categories of pI variants: those that increase the pI of the protein (basic changes) and those that decrease the pI of the protein (acidic changes). As described herein, all combinations of these variants can be done: one monomer may be wild type, or a variant that does not display a significantly different pI from wild-type, and the other can be either more basic or more acidic. Alternatively, each monomer is changed, one to more basic and one to more acidic.

[00261] Preferred combinations of pI variants are shown in Figure 30 of US2016/0355608, all of which are herein incorporated by reference in its entirety. As

outlined herein and shown in the figures, these changes are shown relative to IgG1, but all isotypes can be altered this way, as well as isotype hybrids. In the case where the heavy chain constant domain is from IgG2-4, R133E and R133Q can also be used.

[00262] In one embodiment, a preferred combination of pI variants has one monomer comprising 208D/295E/384D/418E/421D variants (N208D/Q295E/N384D/Q418E/N421D when relative to human IgG1) if one of the Fc monomers includes a CH1 domain. In some instances, the second monomer comprising a positively charged domain linker, including $(GKPGS)_4$. In some cases, the first monomer includes a CH1 domain, including position 208. Accordingly, in constructs that do not include a CH1 domain (for example for heterodimeric Fc fusion proteins that do not utilize a CH1 domain on one of the domains), a preferred negative pI variant Fc set includes 295E/384D/418E/421D variants (Q295E/N384D/Q418E/N421D when relative to human IgG1).

[00263] In some embodiments, mutations are made in the hinge domain of the Fc domain, including positions 221, 222, 223, 224, 225, 233, 234, 235 and 236. It should be noted that changes in 233-236 can be made to increase effector function (along with 327A) in the IgG2 backbone. Thus, pI mutations and particularly substitutions can be made in one or more of positions 221-225, with 1, 2, 3, 4 or 5 mutations finding use in the present invention. Again, all possible combinations are contemplated, alone or with other pI variants in other domains.

[00264] Specific substitutions that find use in lowering the pI of hinge domains include, but are not limited to, a deletion at position 221, a non-native valine or threonine at position 222, a deletion at position 223, a non-native glutamic acid at position 224, a deletion at position 225, a deletion at position 235 and a deletion or a non-native alanine at position 236. In some cases, only pI substitutions are done in the hinge domain, and in others, these substitution(s) are added to other pI variants in other domains in any combination.

[00265] In some embodiments, mutations can be made in the CH2 region, including positions 274, 296, 300, 309, 320, 322, 326, 327, 334 and 339. Again, all possible combinations of these 10 positions can be made; e.g., a pI antibody may have 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 CH2 pI substitutions.

[00266] Specific substitutions that find use in lowering the pI of CH2 domains include, but are not limited to, a non-native glutamine or glutamic acid at position 274, a non-native

phenylalanine at position 296, a non-native phenylalanine at position 300, a non-native valine at position 309, a non-native glutamic acid at position 320, a non-native glutamic acid at position 322, a non-native glutamic acid at position 326, a non-native glycine at position 327, a non-native glutamic acid at position 334, a non-native threonine at position 339, and all possible combinations within CH2 and with other domains.

[00267] In this embodiment, the mutations can be independently and optionally selected from position 355, 359, 362, 384, 389,392, 397, 418, 419, 444 and 447. Specific substitutions that find use in lowering the pI of CH3 domains include, but are not limited to, a non-native glutamine or glutamic acid at position 355, a non-native serine at position 384, a non-native asparagine or glutamic acid at position 392, a non-native methionine at position 397, a non-native glutamic acid at position 419, a non-native glutamic acid at position 359, a non-native glutamic acid at position 362, a non-native glutamic acid at position 389, a non-native glutamic acid at position 418, a non-native glutamic acid at position 444, and a deletion or non-native aspartic acid at position 447. Exemplary embodiments of pI variants are provided in the Figures including Figure 5.

F. Isotypic Variants

[00268] In addition, many embodiments of the invention rely on the “importation” of pI amino acids at particular positions from one IgG isotype into another, thus reducing or eliminating the possibility of unwanted immunogenicity being introduced into the variants. A number of these are shown in Figure 21 of US2014/0370013, hereby incorporated by reference. That is, IgG1 is a common isotype for therapeutic antibodies for a variety of reasons, including high effector function. However, the heavy constant region of IgG1 has a higher pI than that of IgG2 (8.10 versus 7.31). By introducing IgG2 residues at particular positions into the IgG1 backbone, the pI of the resulting monomer is lowered (or increased) and additionally exhibits longer serum half-life. For example, IgG1 has a glycine (pI 5.97) at position 137, and IgG2 has a glutamic acid (pI 3.22); importing the glutamic acid will affect the pI of the resulting protein. As is described below, a number of amino acid substitutions are generally required to significant affect the pI of the variant Fc fusion protein. However, it should be noted as discussed below that even changes in IgG2 molecules allow for increased serum half-life.

[00269] In other embodiments, non-isotypic amino acid changes are made, either to reduce the overall charge state of the resulting protein (e.g., by changing a higher pI amino acid to a lower pI amino acid), or to allow accommodations in structure for stability, etc. as is more further described below.

[00270] In addition, by pI engineering both the heavy and light constant domains, significant changes in each monomer of the heterodimer can be seen. As discussed herein, having the pIs of the two monomers differ by at least 0.5 can allow separation by ion exchange chromatography or isoelectric focusing, or other methods sensitive to isoelectric point.

G. Calculating pI

[00271] The pI of each monomer can depend on the pI of the variant heavy chain constant domain and the pI of the total monomer, including the variant heavy chain constant domain and the fusion partner. Thus, in some embodiments, the change in pI is calculated on the basis of the variant heavy chain constant domain, using the chart in the Figure 19 of US2014/0370013. As discussed herein, which monomer to engineer is generally decided by the inherent pI of each monomer.

H. pI Variants that also confer better FcRn in vivo binding

[00272] In the case where the pI variant decreases the pI of the monomer, they can have the added benefit of improving serum retention in vivo.

[00273] Although still under examination, Fc regions are believed to have longer half-lives in vivo, because binding to FcRn at pH 6 in an endosome sequesters the Fc (Ghetie and Ward, 1997 Immunol Today. 18(12): 592-598, entirely incorporated by reference). The endosomal compartment then recycles the Fc to the cell surface. Once the compartment opens to the extracellular space, the higher pH, ~7.4, induces the release of Fc back into the blood. In mice, Dall' Acqua et al. showed that Fc mutants with increased FcRn binding at pH 6 and pH 7.4 actually had reduced serum concentrations and the same half-life as wild-type Fc (Dall' Acqua et al. 2002, J. Immunol. 169:5171-5180, entirely incorporated by reference). The increased affinity of Fc for FcRn at pH 7.4 is thought to forbid the release of the Fc back into the blood. Therefore, the Fc mutations that will increase Fc's half-life in vivo will ideally increase FcRn binding at the lower pH while still allowing release of Fc at higher pH. The

amino acid histidine changes its charge state in the pH range of 6.0 to 7.4. Therefore, it is not surprising to find His residues at important positions in the Fc/FcRn complex.

[00274] Exemplary embodiments of pI variants are provided in the Figures including Figure 5.

I. Additional Fc Variants for Additional Functionality

[00275] In addition to pI amino acid variants, there are a number of useful Fc amino acid modification that can be made for a variety of reasons, including, but not limited to, altering binding to one or more FcγR receptors, altered binding to FcRn receptors, etc.

[00276] Accordingly, the proteins of the invention can include amino acid modifications, including the heterodimerization variants outlined herein, which includes the pI variants and steric variants. Each set of variants can be independently and optionally included or excluded from any particular heterodimeric protein.

J. FcγR Variants

[00277] Accordingly, there are a number of useful Fc substitutions that can be made to alter binding to one or more of the FcγR receptors. Substitutions that result in increased binding as well as decreased binding can be useful. For example, it is known that increased binding to FcγRIIIa results in increased ADCC (antibody dependent cell-mediated cytotoxicity; the cell-mediated reaction wherein nonspecific cytotoxic cells that express FcγRs recognize bound antibody on a target cell and subsequently cause lysis of the target cell). Similarly, decreased binding to FcγRIIb (an inhibitory receptor) can be beneficial as well in some circumstances. Amino acid substitutions that find use in the present invention include those listed in USSNs 11/124,620 (particularly Figure 41), 11/174,287, 11/396,495, 11/538,406, all of which are expressly incorporated herein by reference in their entirety and specifically for the variants disclosed therein. Particular variants that find use include, but are not limited to, 236A, 239D, 239E, 332E, 332D, 239D/332E, 267D, 267E, 328F, 267E/328F, 236A/332E, 239D/332E/330Y, 239D, 332E/330L, 243A, 243L, 264A, 264V and 299T.

[00278] In addition, amino acid substitutions that increase affinity for FcγRIIc can also be included in the Fc domain variants outlined herein. The substitutions described in, for example, USSNs 11/124,620 and 14/578,305 are useful.

[00279] In addition, there are additional Fc substitutions that find use in increased binding to the FcRn receptor and increased serum half-life, as specifically disclosed in USSN 12/341,769, hereby incorporated by reference in its entirety, including, but not limited to, 434S, 434A, 428L, 308F, 259I, 428L/434S, 259I/308F, 436I/428L, 436I or V/434S, 436V/428L and 259I/308F/428L.

K. Ablation Variants

[00280] Similarly, another category of functional variants are "FcγR ablation variants" or "Fc knock out (FcKO or KO)" variants. In these embodiments, for some therapeutic applications, it is desirable to reduce or remove the normal binding of the Fc domain to one or more or all of the Fcγ receptors (e.g., FcγR1, FcγRIIa, FcγRIIb, FcγRIIIa, etc.) to avoid additional mechanisms of action. That is, for example, in many embodiments, particularly in the use of bispecific immunomodulatory antibodies desirable to ablate FcγRIIIa binding to eliminate or significantly reduce ADCC activity such that one of the Fc domains comprises one or more Fcγ receptor ablation variants. These ablation variants are depicted in Figure 31 of USSN 15/141,350, all of which are herein incorporated by reference in its entirety, and each can be independently and optionally included or excluded, with preferred aspects utilizing ablation variants selected from the group consisting of G236R/L328R, E233P/L234V/L235A/G236del/S239K, E233P/L234V/L235A/G236del/S267K, E233P/L234V/L235A/G236del/S239K/A327G, E233P/L234V/L235A/G236del/S267K/A327G and E233P/L234V/L235A/G236del, according to the EU index. It should be noted that the ablation variants referenced herein ablate FcγR binding but generally not FcRn binding.

L. Combination of Heterodimeric and Fc Variants

[00281] As will be appreciated by those in the art, all of the recited heterodimerization variants (including skew and/or pI variants) can be optionally and independently combined in any way, as long as they retain their "strandedness" or "monomer partition". In addition, all of these variants can be combined into any of the heterodimerization formats.

[00282] In the case of pI variants, while embodiments finding particular use are shown in the Figures, other combinations can be generated, following the basic rule of altering the pI difference between two monomers to facilitate purification.

[00283] In addition, any of the heterodimerization variants, skew and pI, are also independently and optionally combined with Fc ablation variants, Fc variants, FcRn variants, as generally outlined herein.

[00284] In addition, a monomeric Fc domain can comprise a set of amino acid substitutions that includes C220S/S267K/L368D/K370S or C220S/S267K/S364K/E357Q.

[00285] In addition, the heterodimeric Fc fusion proteins can comprise skew variants (e.g., a set of amino acid substitutions as shown in Figures 1A-1C of USSN 15/141,350, all of which are herein incorporated by reference in its entirety), with particularly useful skew variants being selected from the group consisting of S364K/E357Q : L368D/K370S; L368D/K370S : S364K; L368E/K370S : S364K; T411E/K360E/Q362E : D401K; L368D/K370S : S364K/E357L, K370S : S364K/E357Q, T366S/L368A/Y407V : T366W and T366S/L368A/Y407V/Y349C : T366W/S354C, optionally ablation variants, optionally charged domain linkers and the heavy chain comprises pI variants.

[00286] In some embodiments, the Fc domain comprising an amino acid substitution selected from the group consisting of: 236R, 239D, 239E, 243L, M252Y, V259I, 267D, 267E, 298A, V308F, 328F, 328R, 330L, 332D, 332E, M428L, N434A, N434S, 236R/328R, 239D/332E, M428L, 236R/328F, V259I/V308F, 267E/328F, M428L/N434S, Y436I/M428L, Y436V/M428L, Y436I/N434S, Y436V/N434S, 239D/332E/330L, M252Y/S254T/T256E, V259I/V308F/M428L, E233P/L234V/L235A/G236del/S267K, G236R/L328R and PVA/S267K. In some cases, the Fc domain comprises the amino acid substitution 239D/332E. In other cases, the Fc domain comprises the amino acid substitution G236R/L328R or PVA/S267K.

[00287] In one embodiment, a particular combination of skew and pI variants that finds use in the present invention is T366S/L368A/Y407V : T366W (optionally including a bridging disulfide, T366S/L368A/Y407V/Y349C : T366W/S354C) with one monomer comprises Q295E/N384D/Q418E/N481D and the other a positively charged domain linker. As will be appreciated in the art, the "knobs in holes" variants do not change pI, and thus can be used on either monomer.

[00288] Useful pairs of Fc dimermization variant sets (including skew and pI variants) are provided in Figures 4A-4E. Additional pI variants are provided in Figure 5. Useful ablation variants are provided in Figure 6. Useful embodiments of the non-cytokine

components of the PD-1-targeted IL-15/IL-15Rα-Fc fusion proteins of the present invention are provided in Figures 7A-7E and 8A-8F. In addition, useful IL-15/Rα-Fc format backbones based on human IgG1, without the IL-15 and IL-15Rα (sushi) domain sequences.

IV. **Useful Formats of the Invention**

[00289] As shown in Figures 65A-65K, there are a number of useful formats of the PD-1-targeted IL-15/IL-15Rα-Fc fusion proteins (also referred to as PD-1-targeted IL-15/IL-15Rα heterodimeric proteins or heterodimeric fusion proteins) of the invention. In general, the heterodimeric fusion proteins of the invention have three functional components: an IL-15/IL-15Rα(sushi) component, an anti-PD-1 component, and an Fc component, each of which can take different forms as outlined herein and each of which can be combined with the other components in any configuration.

[00290] The first and the second Fc domains of the Fc component can have a set of amino acid substitutions selected from the group consisting of a) S267K/L368D/K370S : S267K/LS364K/E357Q; b) S364K/E357Q : L368D/K370S; c) L368D/K370S : S364K; d) L368E/K370S : S364K; e) T411E/K360E/Q362E : D401K; f) L368D/K370S : S364K/E357L; and g) K370S : S364K/E357Q, according to EU numbering.

[00291] In some instances, the first and second Fc domains have the substitutions L368D/K370S : S364K/E357Q, respectively. In certain instances, the first and second Fc domains have the substitutions S364K/E357Q : L368D/K370S, respectively.

[00292] In some embodiments, the first and/or the second Fc domains have an additional set of amino acid substitutions comprising Q295E/N384D/Q418E/N421D, according to EU numbering.

[00293] Optionally, the first and/or the second Fc domains have an additional set of amino acid substitutions consisting of G236R/L328R, E233P/L234V/L235A/G236del/S239K, E233P/L234V/L235A/G236del/S267K, E233P/L234V/L235A/G236del/S239K/A327G, E233P/L234V/L235A/G236del/S267K/A327G and E233P/L234V/L235A/G236del, according to EU numbering.

Optionally, the first and/or second Fc domains have M428L/N434S variants for half-life extension. In some embodiments, the first and/or second Fc domains have 428L/434S variants for half-life extension. In some embodiments, the first and the second Fc domains each have M428L/N434S variants.

A. scIL-15/Rα X scFv

[00294] One embodiment is shown in Figure 65A, and comprises two monomers. This is generally referred to as "scIL-15/Rα X scFv", with the "sc" standing for "single chain" referring to the attachment of the IL-15 and IL-15Rα sushi domain using a covalent linker. The "scIL-15/Rα x scFv" format (see Figure 65A) comprises a human IL-15Rα(sushi) domain fused to a human mature IL-15 by a variable length linker (termed "scIL-15/Rα") which is then fused to the N-terminus of a first Fc monomer, with an scFv fused to the N-terminus of a second Fc monomer. In some embodiments, the second Fc monomer comprises all or part of the hinge-CH2-CH3.

[00295] In some embodiments, the first monomer comprises, from N- to C-terminus, the human IL-15Rα sushi domain-domain linker-human IL-15-optional domain linker-CH2-CH3, and the second monomer comprises vh-scFv linker-vl-hinge-CH2-CH3 or vl-scFv linker-vh-hinge-CH2-CH3, although in either orientation a domain linker can be substituted for the hinge. Such combinations of Fc variants for this embodiment are found in Figures 8A and 8B.

[00296] As noted in Figures 93A-93S, Figures 94A-94AP, Figures 95A-95J, and Figures 96A-96F and is true for every sequence herein containing CDRs, the exact identification of the CDR locations may be slightly different depending on numbering used as is shown in Table 1, and thus included herein are not only the CDRs that are underlined but also CDRs included wherein the VH and VL domain using other numbering systems. Additionally, each CDR has its own SEQ ID NO: or sequence identifier, and each VH and VL domain has its own SEQ ID NO: or sequence identifier in the sequence listing.

[00297] In the scIL-15/Rα X scFv format, one embodiment utilizes the anti-PD-1 ABD having the sequence 1G6_L1.194_H1.279 as shown in Figure 66 including the sequence identifiers. Amino acid sequences of an illustrative PD-1-targeted IL-15/IL-15Rα-Fc fusion protein of the scIL-15/Rα x scFv format such as XENP21480 is provided in Figure 66. In the scIL-15/Rα X scFv format, one embodiment utilizes the skew variant pair S364K/E357Q : L368D/K370S. In the scIL-15/Rα X scFv format, one embodiment utilizes the anti-PD-1 ABD having the sequence 1G6_L1.194_H1.279 as shown in Figure 66 and the skew variant pair S364K/E357Q : L368D/K370S. In the scIL-15/Rα X scFv format, one embodiment

utilizes the anti-PD-1 ABD having the sequence 1G6_L1.194_H1.279 as shown in Figure 66, in the Figure 8A format: e.g., the skew variants S364K/E357Q (on the scFv-Fc monomer) and L368D/K370S (on the IL-15 complex monomer), the pI variants Q295E/N384D/Q418E/N421D (on the IL-15 complex side), the ablation variants E233P/L234V/L235A/G236del/S267K on both monomers, and optionally the 428L/434S variants on both sides.

[00298] In the scIL-15/Rα X scFv format, one embodiment utilizes the anti-PD-1 ABD having the variable heavy and variable light sequences from 1C11[PD-1]_H3L3 of XENP22538 as shown in Figure 93A. In the scIL-15/Rα X scFv format, one embodiment utilizes an anti-PD-1 ABD having the sequence 1C11[PD-1]_H3L3 of XENP22538 as shown in Figure 93A in the Figure 8A format. One embodiment utilizes an anti-PD-1 ABD having the sequence of a scFv variant of 1C11[PD-1]_H3L3 as depicted in Figure 93A-Figure 93S, including the sequence identifiers. One embodiment utilizes an anti-PD-1 ABD having a variable heavy chain sequence of a variant of 1C11[PD-1]_H3L3 as depicted in Figure 95A–Figure 95J including the sequence identifiers and a variable light chain sequence of a variant of 1C11[PD-1]_H3L3 as depicted in Figure 96A–Figure 96F including the sequence identifiers. In some embodiments, an anti-PD-1 ABD of an scIL-15/Rα X scFv fusion protein comprises CDRs of the variable heavy chain sequence of a variant of 1C11[PD-1]_H3L3 depicted in Figure 95A–Figure 95J including the sequence identifiers and CDRs of the variable light chain sequence of a variant of 1C11[PD-1]_H3L3 depicted in Figure 96A–Figure 96F including the sequence identifiers.

[00299] In some embodiments of an scIL-15/Rα X scFv fusion protein, the anti-PD-1 scFv utilizes the sequences of the ABD of any one of the XENP or corresponding SEQ ID NOS as depicted in Figures 93A-93S. In some instances, the anti-PD-1 scFv has a sequence of the ABD selected from the group consisting of XENP22538, XENP23577, XENP23579, XENP23589, XENP23601, XENP23605, XENP23609, XENP23615, XENP23616, XENP23624, XENP23626, XENP23628, XENP23629, XENP23633, XENP23636, XENP23640, XENP23755, XENP23758, XENP23760, XENP23765, XENP23770, XENP23776, XENP23779, XENP23780, XENP23781, XENP23789, XENP23793, XENP23796, XENP23811, XENP24201, XENP24207, XENP24208, XENP24209, XENP24210, XENP24211, XENP24212, XENP24213, XENP24214, XENP24215, XENP24216, XENP24217, XENP24218, XENP24221, XENP24222, XENP24226,

XENP24227, XENP24228, XENP24247, XENP42450, XENP24254, XENP24256, XENP24263, XENP24266, XENP24267, XENP24268, XENP24270, XENP24274, XENP24278, XENP24279, XENP24287, XENP24291, XENP24372, XENP24373, XENP24374, XENP24375, XENP24376, XENP24377, XENP24378, XENP24379, XENP24380, XENP24381, XENP24382, XENP24414, XENP24415, XENP24416, XENP24417, XENP24418, XENP24419, XENP24420, XENP24421, XENP24422, XENP24423, XENP24424, XENP24425, XENP24426, XENP24427, XENP24428, XENP24429, XENP24430, XENP24431, XENP24432, XENP24433, XENP24434, XENP24435, XENP24436, XENP24437, XENP24438, XENP24439, XENP24440, XENP24441, XENP24442, XENP24443, XENP24827, XENP24828, XENP24829, XENP24830, XENP24831, XENP24832, XENP24833, XENP24834, XENP24835, XENP24836, XENP24837, XENP24838, XENP24839, XENP24840, XENP24841, XENP24842, XENP24843, XENP24844, XENP24845, XENP24846, XENP24847, XENP24848, XENP24849, XENP24850, XENP24851, XENP24852, XENP24853, XENP24854, XENP24855, XENP24856, XENP24857, XENP24858, XENP25295, XENP25296, XENP25301, XENP23502, XENP25303, XENP25304, XENP25305, XENP25306, XENP25307, XENP25308, XENP25309, XENP25310, XENP25311, XENP25312, XENP25313, XENP25314, XENP25315, XENP25316, XENP25317, XENP25318, XENP25319, XENP25320, XENP25321, XENP25802, XENP25803, XENP25804, XENP25805, XENP25806, XENP25807, XENP25808, XENP25809, XENP25810, XENP25811, XENP25812, XENP25813, XENP25814, XENP25815, XENP25816, XENP25817, XENP25818, and XENP25819, including the corresponding SEQ ID NOS.

[00300] In some embodiments, the scIL-15/Rα X scFv format utilizes a scFv ABD to human PD-1 having the sequence of the ABD of XENP25806 or 1C11[PD-1]_H3.234_L3.144, as depicted in Figure 93R including the SEQ ID NOS. In other words, the six CDRs and/or the VH and VL domains from XENP25806 can be used in an exemplary scIL-15/Rα X anti-PD-1 scFv format.

[00301] In certain embodiments, the scIL-15/Rα X scFv format utilizes a scFv ABD to human PD-1 having the sequence of the ABD of XENP25812 or 1C11[PD-1]_H3.240_L3.148, as depicted in Figure 93R including the SEQ ID NOS. In other words,

the six CDRs and/or the VH and VL domains from XENP25812 can be used in an exemplary scIL-15/Rα X anti-PD-1 scFv format.

[00302] In particular embodiments, the scIL-15/Rα X scFv format utilizes a scFv ABD to human PD-1 having the sequence of the ABD of XENP25813 or 1C11[PD-1]_H3.241_L3.148, as depicted in Figure 93R including the SEQ ID NOS. In other words, the six CDRs and/or the VH and VL domains from XENP25813 can be used in an exemplary scIL-15/Rα X anti-PD-1 scFv format.

[00303] In other embodiments, the scIL-15/Rα X scFv format utilizes a scFv ABD to human PD-1 having the sequence of the ABD of XENP25819 or 1C11[PD-1]_H3.241_L3.92, as depicted in Figure 93S including the SEQ ID NOS. In other words, the six CDRs and/or the VH and VL domains from XENP25819 can be used in an exemplary scIL-15/Rα X anti-PD-1 scFv format.

[00304] In the scIL-15/Rα X scFv format, a preferred embodiment utilizes the IL-15 complex (sushi domain-linker-IL-15) of chain 1 of XENP22022 as depicted in Figure 69A including the SEQ ID NOS. In the scIL-15/Rα X scFv format, one preferred embodiment utilizes the IL-15 complex (sushi domain-linker-IL-15 variant N4D/N65D) of chain 2 of XENP25850 as depicted in Figure 69C. In the scIL-15/Rα X scFv format, another preferred embodiment utilizes the IL-15 complex (sushi domain-linker-IL-15 variant D30N/N65D) of chain 1 of XENP29482 as depicted in Figure 126A. In the scIL-15/Rα X scFv format, another preferred embodiment utilizes the IL-15 complex (sushi domain-linker-IL-15 variant D30N/E64Q/N65D) of chain 1 of XENP29286 as depicted in Figure 124C.

[00305] In the scIL-15/Rα X anti-PD-1 scFv format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence 1G6_L1.194_H1.279 as shown in Figure 66 and the IL-15 complex (sushi domain-linker-IL-15) of chain 1 of XENP22022 as depicted in Figure 69A. In some instances, the scIL-15/Rα X anti-PD-1 scFv Fc fusion protein contains an anti-PD-1 ABD having the sequence 1G6_L1.194_H1.279 as shown in Figure 66 and an IL-15 complex (sushi domain-linker-IL-15 variant N4D/N65D) of chain 2 of XENP25850 as depicted in Figure 69C. In other instances, the Fc fusion protein contains an anti-PD-1 ABD having the sequence 1G6_L1.194_H1.279 as shown in Figure 66 and an IL-15 complex (sushi domain-linker-IL-15 variant D30N/N65D) of chain 1 of XENP29482 as depicted in Figure 126A. In certain instances, the Fc fusion protein contains an anti-PD-1 ABD having

the sequence 1G6_L1.194_H1.279 as shown in Figure 66 and an IL-15 complex (sushi domain-linker-IL-15 variant D30N/E64Q/N65D) of XENP29286 as depicted in Figure 124C.

[00306] In the scIL-15/Rα X anti-PD-1 scFv format, some embodiments include an anti-PD-1 ABD having the sequence 1C11[PD-1]_H3L3 of XENP22538 as shown in Figure 93A and an IL-15 complex (sushi domain-linker-IL-15) of chain 1 of XENP22022 as depicted in Figure 69A. In some embodiments, the scIL-15/Rα X anti-PD-1 scFv Fc fusion protein contains an anti-PD-1 ABD having the sequence 1C11[PD-1]_H3L3 of XENP22538 as shown in Figure 93A and an IL-15 complex (sushi domain-linker-IL-15 variant N4D/N65D) of chain 2 of XENP25850 as depicted in Figure 69C. In other embodiments, such Fc fusion proteins contain an anti-PD-1 ABD having the sequence 1C11[PD-1]_H3L3 of XENP22538 as shown in Figure 93A and an IL-15 complex (sushi domain-linker-IL-15 variant D30N/N65D) of chain 1 of XENP29482 as depicted in Figure 126A. In certain embodiments, such Fc fusion proteins contain an anti-PD-1 ABD having the sequence 1C11[PD-1]_H3L3 of XENP22538 as shown in Figure 93A and an IL-15 complex (sushi domain-linker-IL-15 variant D30N/E64Q/N65D) of chain 1 of XENP29286 as depicted in Figure 124C.

[00307] In the scIL-15/Rα X anti-PD-1 scFv format, some embodiments include an anti-PD-1 ABD having a variable heavy chain sequence of a variant of 1C11[PD-1]_H3L3 as depicted in Figure 95A –Figure 95J and a variable light chain sequence of a variant of 1C11[PD-1]_H3L3 as depicted in Figure 96A–Figure 96F and the IL-15 complex (sushi domain-linker-IL-15) of chain 1 of XENP22022 as depicted in Figure 69A. In some embodiments, the scIL-15/Rα X anti-PD-1 scFv Fc fusion protein contains an anti-PD-1 ABD having a variable heavy chain sequence of a variant of 1C11[PD-1]_H3L3 as depicted in Figure 95A–Figure 95J and a variable light chain sequence of a variant of 1C11[PD-1]_H3L3 as depicted in Figure 96A–Figure 96F and the IL-15 complex (sushi domain-linker-IL-15 variant N4D/N65D) of chain 2 of XENP25850 as depicted in Figure 69C. In other embodiments, such Fc fusion proteins contain an anti-PD-1 ABD having a variable heavy chain sequence of a variant of 1C11[PD-1]_H3L3 as depicted in Figure 95A–Figure 95J and a variable light chain sequence of a variant of 1C11[PD-1]_H3L3 as depicted in Figure 96A–Figure 96F and the IL-15 complex (sushi domain-linker-IL-15 variant D30N/N65D) of chain 1 of XENP29482 as depicted in Figure 126A. In some embodiments, such Fc fusion proteins contain an anti-PD-1 ABD having a variable heavy chain sequence of a variant of 1C11[PD-

1]_H3L3 as depicted in Figure 95A–Figure 95J and a variable light chain sequence of a variant of 1C11[PD-1]_H3L3 as depicted in Figure 96A–Figure 96F and the IL-15 complex (sushi domain-linker-IL-15 variant D30N/E64Q/N65D) of chain 1 of XENP29286 as depicted in Figure 124C.

[00308] In the scIL-15/Rα X anti-PD-1 scFv format, some embodiments include an anti-PD-1 ABD having the sequence of XENP25806 or 1C11[PD-1]_H3.234_L3.144 as depicted in Figure 93R and the IL-15 complex (sushi domain-linker-IL-15) of chain 1 of XENP22022 as depicted in Figure 69A. In some embodiments, the scIL-15/Rα X anti-PD-1 scFv Fc fusion protein contains an anti-PD-1 ABD having the sequence of XENP25806 or 1C11[PD-1]_H3.234_L3.144 as depicted in Figure 93R and an IL-15 complex (sushi domain-linker-IL-15 variant N4D/N65D) of chain 2 of XENP25850 as depicted in Figure 69C. In some embodiments, such Fc fusion proteins contain an anti-PD-1 ABD having the sequence of XENP25806 or 1C11[PD-1]_H3.234_L3.144 as depicted in Figure 93R and an IL-15 complex (sushi domain-linker-IL-15 variant D30N/N65D) of chain 1 of XENP29482 as depicted in Figure 126A. In some embodiments, such Fc fusion proteins contain an anti-PD-1 ABD having the sequence of XENP25806 or 1C11[PD-1]_H3.234_L3.144 as depicted in Figure 93R and the IL-15 complex (sushi domain-linker-IL-15 variant D30N/E64Q/N65D) of chain 1 of XENP29286 as depicted in Figure 124C.

[00309] In the scIL-15/Rα X anti-PD-1 scFv format, some embodiments include an anti-PD-1 ABD having the sequence of XENP25812 or 1C11[PD-1]_H3.240_L3.148, as depicted in Figure 93R and the IL-15 complex (sushi domain-linker-IL-15) of chain 1 of XENP22022 as depicted in Figure 69A. In some embodiments, the scIL-15/Rα X anti-PD-1 scFv Fc fusion protein contains an anti-PD-1 ABD having the sequence of XENP25812 or 1C11[PD-1]_H3.240_L3.148, as depicted in Figure 93R and an IL-15 complex (sushi domain-linker-IL-15 variant N4D/N65D) of chain 2 of XENP25850 as depicted in Figure 69C. In some embodiments, such Fc fusion proteins contain an anti-PD-1 ABD having the sequence of XENP25812 or 1C11[PD-1]_H3.240_L3.148, as depicted in Figure 93R and an IL-15 complex (sushi domain-linker-IL-15 variant D30N/N65D) of chain 1 of XENP29482 as depicted in Figure 126A. In some embodiments, such Fc fusion proteins contain an anti-PD-1 ABD having the sequence of XENP25812 or 1C11[PD-1]_H3.240_L3.148, as depicted in Figure 93R and an IL-15 complex (sushi domain-linker-IL-15 variant D30N/E64Q/N65D) of chain 1 of XENP29286 as depicted in Figure 124C.

[00310] In the scIL-15/Rα X anti-PD-1 scFv format, some embodiments include an anti-PD-1 ABD having the sequence of XENP25813 or 1C11[PD-1]_H3.241_L3.148 as depicted in Figure 93R and the IL-15 complex (sushi domain-linker-IL-15) of chain 1 of XENP22022 as depicted in Figure 69A. In some embodiments, the scIL-15/Rα X anti-PD-1 scFv Fc fusion protein contains an anti-PD-1 ABD having the sequence of XENP25813 or 1C11[PD-1]_H3.241_L3.148 as depicted in Figure 93R and an IL-15 complex (sushi domain-linker-IL-15 variant N4D/N65D) of chain 2 of XENP25850 as depicted in Figure 69C. In some embodiments, such Fc fusion proteins contain an anti-PD-1 ABD having the sequence of XENP25813 or 1C11[PD-1]_H3.241_L3.148 as depicted in Figure 93R and an IL-15 complex (sushi domain-linker-IL-15 variant D30N/N65D) of chain 1 of XENP29482 as depicted in Figure 126A. In some embodiments, such Fc fusion proteins contain an anti-PD-1 ABD having the sequence of XENP25813 or 1C11[PD-1]_H3.241_L3.148 as depicted in Figure 93R and an IL-15 complex (sushi domain-linker-IL-15 variant D30N/E64Q/N65D) of chain 1 of XENP29286 as depicted in Figure 124C.

[00311] In the scIL-15/Rα X anti-PD-1 scFv format, some embodiments include an anti-PD-1 ABD having the sequence of XENP25819 or 1C11[PD-1]_H3.241_L3.92 as depicted in Figure 93S and the IL-15 complex (sushi domain-linker-IL-15) of chain 1 of XENP22022 as depicted in Figure 69A. In some embodiments, the scIL-15/Rα X anti-PD-1 scFv Fc fusion protein contains an anti-PD-1 ABD having the sequence XENP25819 or 1C11[PD-1]_H3.241_L3.92 as depicted in Figure 93S and the IL-15 complex (sushi domain-linker-IL-15 variant N4D/N65D) of chain 2 of XENP25850 as depicted in Figure 69C. In some embodiments, such Fc fusion proteins contain an anti-PD-1 ABD having the sequence XENP25819 or 1C11[PD-1]_H3.241_L3.92 as depicted in Figure 93S and the IL-15 complex (sushi domain-linker-IL-15 variant D30N/N65D) of chain 1 of XENP29482 as depicted in Figure 126A. In some embodiments, such Fc fusion proteins contain an anti-PD-1 ABD having the sequence XENP25819 or 1C11[PD-1]_H3.241_L3.92 as depicted in Figure 93S and the IL-15 complex (sushi domain-linker-IL-15 variant D30N/E64Q/N65D) of chain 1 of XENP29286 as depicted in Figure 124C.

[00312] In the scIL-15/Rα X anti-PD-1 scFv format, one preferred embodiment utilizes the anti-PD-1 ABD having the VH and VL sequences of XENP26940 or 1C11_H3.303_L3.152 as depicted in Figure 94N and the IL-15 complex (sushi domain-linker-IL-15) of chain 1 of XENP22022 as depicted in Figure 69A. In some embodiments,

the scIL-15/Rα X scFv comprises anti-PD-1 ABD having the VH and VL sequences of XENP26940 or 1C11_H3.303_L3.152 as depicted in Figure 94N and the IL-15 complex (sushi domain-linker-IL-15 variant N4D/N65D) of chain 2 of XENP25850 as depicted in Figure 69C. In some embodiments, the scIL-15/Rα X scFv comprises anti-PD-1 ABD having the VH and VL sequences of XENP26940 or 1C11_H3.303_L3.152 as depicted in Figure 94N and the IL-15 complex (sushi domain-linker-IL-15 variant D30N/N65D) of chain 1 of XENP29482 as depicted in Figure 126A. In some embodiments, the scIL-15/Rα X scFv comprises anti-PD-1 ABD having the VH and VL sequences of XENP26940 or 1C11_H3.303_L3.152 as depicted in Figure 94N and the IL-15 complex (sushi domain-linker-IL-15 variant D30N/E64Q/N65D) of chain 1 of XENP29286 as depicted in Figure 124C.

[00313] In the scIL-15/Rα X anti-PD-1 scFv format, one preferred embodiment utilizes the anti-PD-1 ABD having the VH and VL sequences of XENP28026 or 1C11_H3.329_L3.220 as shown in Figure 94AE and the IL-15 complex (sushi domain-linker-IL-15) of chain 1 of XENP22022 as depicted in Figure 69A. In some embodiments, the scIL-15/Rα X scFv comprises anti-PD-1 ABD having the VH and VL sequences of XENP28026 or 1C11_H3.329_L3.220 as shown in Figure 94AE and the IL-15 complex (sushi domain-linker-IL-15 variant N4D/N65D) of chain 2 of XENP25850 as depicted in Figure 69C. In some embodiments, the scIL-15/Rα X scFv comprises anti-PD-1 ABD having the VH and VL sequences of XENP28026 or 1C11_H3.329_L3.220 as shown in Figure 94AE and the IL-15 complex (sushi domain-linker-IL-15 variant D30N/N65D) of chain 1 of XENP29482 as depicted in Figure 126A. In some embodiments, the scIL-15/Rα X scFv comprises anti-PD-1 ABD having the VH and VL sequences of XENP28026 or 1C11_H3.329_L3.220 as shown in Figure 94AE and the IL-15 complex (sushi domain-linker-IL-15 variant D30N/E64Q/N65D) of chain 1 of XENP29286 as depicted in Figure 124C.

[00314] In the scIL-15/Rα X scFv format, one preferred embodiment utilizes the anti-PD-1 ABD having the VH and VL sequences of XENP28652 or 1C11_H3.328_L3.152 as depicted in Figure 94AG and the IL-15 complex (sushi domain-linker-IL-15) of chain 1 of XENP22022 as depicted in Figure 69A. In some embodiments, the scIL-15/Rα X scFv comprises anti-PD-1 ABD having the VH and VL sequences of XENP28652 or 1C11_H3.328_L3.152 as depicted in Figure 94AG and the IL-15 complex (sushi domain-

linker-IL-15 variant N4D/N65D) of chain 2 of XENP25850 as depicted in Figure 69C. In some embodiments, the scIL-15/Rα X scFv comprises anti-PD-1 ABD having the VH and VL sequences of XENP28652 or 1C11_H3.328_L3.152 as depicted in Figure 94AG and the IL-15 complex (sushi domain-linker-IL-15 variant D30N/N65D) of chain 1 of XENP29482 as depicted in Figure 126A. In some embodiments, the scIL-15/Rα X scFv comprises anti-PD-1 ABD having the VH and VL sequences of XENP28652 or 1C11_H3.328_L3.152 as depicted in Figure 94AG and the IL-15 complex (sushi domain-linker-IL-15 variant D30N/E64Q/N65D) of chain 1 of XENP29286 as depicted in Figure 124C.

B. scFv X ncIL-15/Rα

[00315] This embodiment is shown in Figure 65B, and comprises three monomers. This is generally referred to as “ncIL-15/Rα X scFv” or “scFv X ncIL-15/Rα” with the “nc” standing for “non-covalent” referring to the self-assembling non-covalent attachment of the IL-15 and IL-15Rα sushi domain. The “scFv x ncIL-15/Rα” format (see Figure 65B) comprises an scFv fused to the N-terminus of a first Fc monomer, with human IL-15Rα(sushi) fused to a second Fc monomer, while human mature IL-15 (such as a human mature IL-15 variant) is transfected separately so that a non-covalent IL-15/Rα complex is formed.

[00316] In some embodiments, the first monomer comprises, from N- to C-terminus, the sushi domain-domain linker-CH2-CH3, and the second monomer comprises vh-scFv linker-vl-hinge-CH2-CH3 or vl-scFv linker-vh-hinge-CH2-CH3, although in either orientation a domain linker can be substituted for the hinge. The third monomer is the mature IL-15 domain. Preferred combinations of variants for this embodiment are found in Figures 8A and 8B.

[00317] In the ncIL-15/Rα X scFv format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence 1G6_L1.194_H1.279 as shown in Figure 66. Amino acid sequences of an illustrative IL-15/Rα x anti-PD-1 heterodimeric protein of the scFv x ncIL-15/Rα format is provided in Figure 67. In some embodiments, the anti-PD-1 ABD has the sequence 1G6_L1.194_H1.279_scFv as shown in chain 1 of Figure 67.

[00318] In the ncIL-15/Rα X scFv format, one preferred embodiment utilizes the skew variant pair S364K/E357Q : L368D/K370S. In the ncIL-15/Rα X scFv format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence 1G6_L1.194_H1.279 as shown in Figure 66 and the skew variant pair S364K/E357Q : L368D/K370S. In the ncIL-15/Rα X

scFv format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence 1G6_L1.194_H1.279 as shown in Figure 66, in the Figure 8B format: e.g., the skew variants S364K/E357Q (on the IL-15Rα(sushi)-Fc monomer) and L368D/K370S (on the scFv-Fc monomer), the pI variants Q295E/N384D/Q418E/N421D (on the scFv-Fc monomer), the ablation variants E233P/L234V/L235A/G236del/S267K on both monomers, and optionally the 428L/434S variants on both sides. In the ncIL-15/Rα X scFv format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence 1G6_L1.194_H1.279 as shown in Figure 66, in the Figure 8B format.

[00319] In the ncIL-15/Rα X scFv format, one preferred embodiment utilizes the anti-PD-1 ABD having the variable heavy and variable light sequences from 1C11[PD-1]_H3L3 of XENP22538 as shown in Figure 93A. In the ncIL-15/Rα X scFv format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence 1C11[PD-1]_H3L3 of XENP22538 as shown in Figure 93A, in the Figure 8B format: e.g., the skew variants S364K/E357Q (on the IL-15Rα(sushi)-Fc monomer) and L368D/K370S (on the scFv-Fc monomer), the pI variants Q295E/N384D/Q418E/N421D (on the scFv-Fc monomer), the ablation variants E233P/L234V/L235A/G236del/S267K on both monomers, and optionally the 428L/434S variants on both sides. In the ncIL-15/Rα X scFv format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence 1C11[PD-1]_H3L3 of XENP22538 as shown in Figure 93A in the Figure 8B format. In the ncIL-15/Rα X scFv format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence of a scFv variant of 1C11[PD-1]_H3L3 as depicted in Figure 93A-Figure 93S. In the ncIL-15/Rα X scFv format, one preferred embodiment utilizes the anti-PD-1 ABD having a variable heavy chain sequence of a variant of 1C11[PD-1]_H3L3 as depicted in Figure 95A–Figure 95J and a variable light chain sequence of a variant of 1C11[PD-1]_H3L3 as depicted in Figure 96A–Figure 96F.

[00320] In some embodiments, the ncIL-15/Rα X scFv format utilizes a scFv ABD to human PD-1 having the sequence of the ABD of XENP25806 or 1C11[PD-1]_H3.234_L3.144, as depicted in Figure 93R. In other words, the six CDRs and/or the VH and VL domains from XENP25806 can be used in an exemplary ncIL-15/Rα X anti-PD-1 scFv format. In some embodiments, the ncIL-15/Rα X scFv format utilizes a scFv ABD to human PD-1 having the sequence of the ABD of XENP25806 or 1C11[PD-1]_H3.234_L3.144, as depicted in Figure 93R in the Figure 8B format: e.g., the skew variants

S364K/E357Q (on the IL-15Rα(sushi)-Fc monomer) and L368D/K370S (on the scFv-Fc monomer), the pI variants Q295E/N384D/Q418E/N421D (on the scFv-Fc monomer), the ablation variants E233P/L234V/L235A/G236del/S267K on both monomers, and optionally the 428L/434S variants on both sides.

[00321] In certain embodiments, the ncIL-15/Rα X scFv format utilizes a scFv ABD to human PD-1 having the sequence of the ABD of XENP25812 or 1C11[PD-1]_H3.240_L3.148, as depicted in Figure 93R. In other words, the six CDRs and/or the VH and VL domains from XENP25812 can be used in an exemplary ncIL-15/Rα X anti-PD-1 scFv format. In some embodiments, the ncIL-15/Rα X scFv format utilizes a scFv ABD to human PD-1 having the sequence of the ABD of XENP25812 or 1C11[PD-1]_H3.240_L3.148, as depicted in Figure 93R in the Figure 8B format: e.g., the skew variants S364K/E357Q (on the IL-15Rα(sushi)-Fc monomer) and L368D/K370S (on the scFv-Fc monomer), the pI variants Q295E/N384D/Q418E/N421D (on the scFv-Fc monomer), the ablation variants E233P/L234V/L235A/G236del/S267K on both monomers, and optionally the 428L/434S variants on both sides.

[00322] In particular embodiments, the ncIL-15/Rα X scFv format utilizes a scFv ABD to human PD-1 having the sequence of the ABD of XENP25813 or 1C11[PD-1]_H3.241_L3.148, as depicted in Figure 93R. In other words, the six CDRs and/or the VH and VL domains from XENP25813 can be used in an exemplary ncIL-15/Rα X anti-PD-1 scFv format. In some embodiments, the ncIL-15/Rα X scFv format utilizes a scFv ABD to human PD-1 having the sequence of the ABD of XENP25813 or 1C11[PD-1]_H3.241_L3.148, as depicted in Figure 93R in the Figure 8B format: e.g., the skew variants S364K/E357Q (on the IL-15Rα(sushi)-Fc monomer) and L368D/K370S (on the scFv-Fc monomer), the pI variants Q295E/N384D/Q418E/N421D (on the scFv-Fc monomer), the ablation variants E233P/L234V/L235A/G236del/S267K on both monomers, and optionally the 428L/434S variants on both sides.

[00323] In other embodiments, the ncIL-15/Rα X scFv format utilizes a scFv ABD to human PD-1 having the sequence of the ABD of XENP25819 or 1C11[PD-1]_H3.241_L3.92, as depicted in Figure 93S. In other words, the six CDRs and/or the VH and VL domains from XENP25819 can be used in an exemplary ncIL-15/Rα X anti-PD-1 scFv format. In some embodiments, the ncIL-15/Rα X scFv format utilizes a scFv ABD to human PD-1 having the sequence of the ABD of XENP25819 or 1C11[PD-

1]_H3.241_L3.92, as depicted in Figure 93S in the Figure 8B format: e.g., the skew variants S364K/E357Q (on the IL-15Rα(sushi)-Fc monomer) and L368D/K370S (on the scFv-Fc monomer), the pI variants Q295E/N384D/Q418E/N421D (on the scFv-Fc monomer), the ablation variants E233P/L234V/L235A/G236del/S267K on both monomers, and optionally the 428L/434S variants on both sides.

[00324] In some embodiments, the anti-PD-1 scFv of any of the ncIL-15/Rα X scFv fusion protein outlined herein comprises the VH and VL sequences of XENP26940 or 1C11_H3.303_L3.152 as depicted in Figure 94N, the VH and VL sequences of XENP28026 or 1C11_H3.329_L3.220 as shown in Figure 94AE, or the VH and VL sequences of XENP28652 or 1C11_H3.328_L3.152 as depicted in Figure 94AG.

[00325] In some embodiments, the ncIL-15/Rα X scFv comprises a human IL-15Rα(sushi) domain and a human mature IL-15. In certain embodiments, the ncIL-15/Rα X scFv comprises a human IL-15Rα(sushi) domain and a human mature IL-15 variant having amino acid substitutions N4D/N65D. In particular embodiments, the ncIL-15/Rα X scFv comprises a human IL-15Rα(sushi) domain and a human mature IL-15 variant having amino acid substitutions D30N/N65D. In certain embodiments, the ncIL-15/Rα X scFv comprises a human IL-15Rα(sushi) domain and a human mature IL-15 variant having amino acid substitutions D30N/E64Q/N65D.

[00326] In the ncIL-15/Rα X scFv format, one preferred embodiment utilizes the anti-PD-1 ABD having the variable heavy and variable light sequences from 1C11[PD-1]_H3L3 of XENP22538 as shown in Figure 93A. In the ncIL-15/Rα X scFv format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence 1C11[PD-1]_H3L3 of XENP22538 as shown in Figure 93A in the Figure 8B format: e.g., the skew variants S364K/E357Q (on the IL-15Rα(sushi)-Fc monomer) and L368D/K370S (on the scFv-Fc monomer), the pI variants Q295E/N384D/Q418E/N421D (on the scFv-Fc monomer), the ablation variants E233P/L234V/L235A/G236del/S267K on both monomers, and optionally the 428L/434S variants on both sides. In the ncIL-15/Rα X scFv format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence 1C11[PD-1]_H3L3 of XENP22538 as shown in Figure 93A in the Figure 8B format. In the ncIL-15/Rα X scFv format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence of a scFv variant of 1C11[PD-1]_H3L3 as depicted in Figure 93A-Figure 93S. In the ncIL-15/Rα X scFv format, one preferred embodiment utilizes the anti-PD-1 ABD having a variable heavy

chain sequence of a variant of 1C11[PD-1]_H3L3 as depicted in Figure 95A –Figure 95J and a variable light chain sequence of a variant of 1C11[PD-1]_H3L3 as depicted in Figure 96A–Figure 96F. In some embodiments, the ncIL-15/Rα X scFv comprises a human IL-15Rα(sushi) domain and a human mature IL-15. In certain embodiments, the ncIL-15/Rα X scFv comprises a human IL-15Rα(sushi) domain and a human mature IL-15 variant having amino acid substitutions N4D/N65D. In particular embodiments, the ncIL-15/Rα X scFv comprises a human IL-15Rα(sushi) domain and a human mature IL-15 variant having amino acid substitutions D30N/N65D. In certain embodiments, the ncIL-15/Rα X scFv comprises a human IL-15Rα(sushi) domain and a human mature IL-15 variant having amino acid substitutions D30N/E64Q/N65D.

[00327] In the ncIL-15/Rα X scFv format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence of a scFv variant of 1C11[PD-1]_H3L3 as depicted in Figure 93A-Figure 93S, a human IL-15Rα(sushi) domain and a human mature IL-15 (such as a human mature IL-15 variant). In certain embodiments, the ncIL-15/Rα X scFv comprises of a scFv variant of 1C11[PD-1]_H3L3 as depicted in Figure 93A-Figure 93S, a human IL-15Rα(sushi) domain and a human mature IL-15 variant having amino acid substitutions N4D/N65D. In particular embodiments, the ncIL-15/Rα X scFv comprises of a scFv variant of 1C11[PD-1]_H3L3 as depicted in Figure 93A-Figure 93S, a human IL-15Rα(sushi) domain and a human mature IL-15 variant having amino acid substitutions D30N/N65D. In certain embodiments, the ncIL-15/Rα X scFv comprises of a scFv variant of 1C11[PD-1]_H3L3 as depicted in Figure 93A-Figure 93S, a human IL-15Rα(sushi) domain and a human mature IL-15 variant having amino acid substitutions D30N/E64Q/N65D.

[00328] In some embodiments, the ncIL-15/Rα X scFv format utilizes a scFv ABD to human PD-1 having the sequence of the ABD of XENP25806 or 1C11[PD-1]_H3.234_L3.144 as depicted in Figure 93R, a human IL-15Rα(sushi) domain and a human mature IL-15 (such as a human mature IL-15 variant). In certain embodiments, the ncIL-15/Rα X scFv comprises a scFv ABD to human PD-1 having the sequence of the ABD of XENP25806 or 1C11[PD-1]_H3.234_L3.144 as depicted in Figure 93R, a human IL-15Rα(sushi) domain and a human mature IL-15 variant having amino acid substitutions N4D/N65D. In particular embodiments, the ncIL-15/Rα X scFv comprises a scFv ABD to human PD-1 having the sequence of the ABD of XENP25806 or 1C11[PD-1]_H3.234_L3.144 as depicted in Figure 93R, a human IL-15Rα(sushi) domain and a human

mature IL-15 variant having amino acid substitutions D30N/N65D. In certain embodiments, the ncIL-15/Rα X scFv comprises a scFv ABD to human PD-1 having the sequence of the ABD of XENP25806 or 1C11[PD-1]_H3.234_L3.144 as depicted in Figure 93R, a human IL-15Rα(sushi) domain and a human mature IL-15 variant having amino acid substitutions D30N/E64Q/N65D.

[00329] In certain embodiments, the ncIL-15/Rα X scFv format utilizes a scFv ABD to human PD-1 having the sequence of the ABD of XENP25812 or 1C11[PD-1]_H3.240_L3.148 as depicted in Figure 93R, a human IL-15Rα(sushi) domain and a human mature IL-15 (such as a human mature IL-15 variant). In certain embodiments, the ncIL-15/Rα X scFv comprises a scFv ABD to human PD-1 having the sequence of the ABD of XENP25812 or 1C11[PD-1]_H3.240_L3.148 as depicted in Figure 93R, a human IL-15Rα(sushi) domain and a human mature IL-15 variant having amino acid substitutions N4D/N65D. In particular embodiments, the ncIL-15/Rα X scFv comprises a scFv ABD to human PD-1 having the sequence of the ABD of XENP25812 or 1C11[PD-1]_H3.240_L3.148 as depicted in Figure 93R, a human IL-15Rα(sushi) domain and a human mature IL-15 variant having amino acid substitutions D30N/N65D. In certain embodiments, the ncIL-15/Rα X scFv comprises a scFv ABD to human PD-1 having the sequence of the ABD of XENP25812 or 1C11[PD-1]_H3.240_L3.148 as depicted in Figure 93R, a human IL-15Rα(sushi) domain and a human mature IL-15 variant having amino acid substitutions D30N/E64Q/N65D.

[00330] In particular embodiments, the ncIL-15/Rα X scFv format utilizes a scFv ABD to human PD-1 having the sequence of the ABD of XENP25813 or 1C11[PD-1]_H3.241_L3.148 as depicted in Figure 93R, a human IL-15Rα(sushi) domain and a human mature IL-15 (such as a human mature IL-15 variant). In certain embodiments, the ncIL-15/Rα X scFv comprises a scFv ABD to human PD-1 having the sequence of the ABD of XENP25813 or 1C11[PD-1]_H3.241_L3.148 as depicted in Figure 93R, a human IL-15Rα(sushi) domain and a human mature IL-15 variant having amino acid substitutions N4D/N65D. In particular embodiments, the ncIL-15/Rα X scFv comprises a scFv ABD to human PD-1 having the sequence of the ABD of XENP25813 or 1C11[PD-1]_H3.241_L3.148 as depicted in Figure 93R, a human IL-15Rα(sushi) domain and a human mature IL-15 variant having amino acid substitutions D30N/N65D. In certain embodiments, the ncIL-15/Rα X scFv comprises a scFv ABD to human PD-1 having the sequence of the

ABD of XENP25813 or 1C11[PD-1]_H3.241_L3.148 as depicted in Figure 93R, a human IL-15Rα(sushi) domain and a human mature IL-15 variant having amino acid substitutions D30N/E64Q/N65D.

[00331] In other embodiments, the ncIL-15/Rα X scFv format utilizes a scFv ABD to human PD-1 having the sequence of the ABD of XENP25819 or 1C11[PD-1]_H3.241_L3.92, as depicted in Figure 93S, a human IL-15Rα(sushi) domain and a human mature IL-15 (such as a human mature IL-15 variant). In certain embodiments, the ncIL-15/Rα X scFv comprises a scFv ABD to human PD-1 having the sequence of the ABD of XENP25819 or 1C11[PD-1]_H3.241_L3.92, as depicted in Figure 93S, a human IL-15Rα(sushi) domain and a human mature IL-15 variant having amino acid substitutions N4D/N65D. In particular embodiments, the ncIL-15/Rα X scFv comprises a scFv ABD to human PD-1 having the sequence of the ABD of XENP25819 or 1C11[PD-1]_H3.241_L3.92, as depicted in Figure 93S, a human IL-15Rα(sushi) domain and a human mature IL-15 variant having amino acid substitutions D30N/N65D. In certain embodiments, the ncIL-15/Rα X scFv comprises a scFv ABD to human PD-1 having the sequence of the ABD of XENP25819 or 1C11[PD-1]_H3.241_L3.92, as depicted in Figure 93S, a human IL-15Rα(sushi) domain and a human mature IL-15 variant having amino acid substitutions D30N/E64Q/N65D.

C. scFv X dsIL-15/Rα

[00332] This embodiment is shown in Figure 65C, and comprises three monomers. This is generally referred to as "scFv X dsIL-15/Rα" or dsIL-15/Rα X scFv, with the "ds" standing for "disulfide". The "scFv x dsIL-15/Rα" format (Figure 65C) is the same as the "scFv x ncIL-15/Rα" format, but wherein IL-15Rα(sushi) and IL-15 are covalently linked as a result of engineered cysteines. The "scFv x dsIL-15/Rα" format comprises an scFv fused to the N-terminus of a first Fc monomer, with human IL-15Rα(sushi) fused to a second Fc monomer, while human mature IL-15 (such as a human mature IL-15 variant) is transfected separately so that a covalently linked IL-15/Rα complex is formed.

[00333] In some embodiments, the first monomer comprises, from N- to C-terminus, the sushi domain-domain linker-CH2-CH3, wherein the sushi domain has an engineered cysteine residue and the second monomer comprises vh-scFv linker-vl-hinge-CH2-CH3 or vl-scFv linker-vh-hinge-CH2-CH3, although in either orientation a domain linker can be substituted for the hinge. The third monomer is the IL-15 domain, also engineered to have a

cysteine variant amino acid, thus allowing a disulfide bridge to form between the sushi domain and the IL-15 domain. Preferred combinations of variants for this embodiment are found in Figures 8A and 8B.

[00334] In the dsIL-15/Rα X scFv format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence 1G6_L1.194_H1.279 as shown in Figure 66. Amino acid sequences of an illustrative IL-15/Rα x anti-PD-1 heterodimeric protein of the "scFv x dsIL-15/Rα" format is provided in Figure 68. In some embodiments, the anti-PD-1 ABD includes the sequence 1G6_L1.194_H1.279_scFv as shown in chain 1 of Figure 66.

[00335] In the dsIL-15/Rα X scFv format, one preferred embodiment utilizes the skew variant pair S364K/E357Q : L368D/K370S. In the dsIL-15/Rα X scFv format, one preferred embodiment utilizes the skew variant pair S364K/E357Q : L368D/K370S and the anti-PD-1 ABD having the sequence 1G6_L1.194_H1.279 as shown in Figure 66. In the dsIL-15/Rα X scFv format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence 1G6_L1.194_H1.279 as shown in Figure 66, in the Figure 8B format: e.g., the skew variants S364K/E357Q (on the IL-15Rα(sushi)-Fc monomer) and L368D/K370S (on the scFv-Fc monomer), the pI variants Q295E/N384D/Q418E/N421D (on the scFv-Fc monomer), the ablation variants E233P/L234V/L235A/G236del/S267K on both monomers, and optionally the 428L/434S variants on both sides. In the dsIL-15/Rα X scFv format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence 1G6_L1.194_H1.279 as shown in Figure 66, in the Figure 8B format.

[00336] In the dsIL-15/Rα X scFv format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence 1C11[PD-1]_H3L3 as shown in Figure 93A. In the dsIL-15/Rα X scFv format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence 1C11[PD-1]_H3L3 as shown in Figure 93A in the Figure 8B format: e.g., the skew variants S364K/E357Q (on the IL-15Rα(sushi)-Fc monomer) and L368D/K370S (on the scFv-Fc monomer), the pI variants Q295E/N384D/Q418E/N421D (on the scFv-Fc monomer), the ablation variants E233P/L234V/L235A/G236del/S267K on both monomers, and optionally the 428L/434S variants on both sides. In the dsIL-15/Rα X scFv format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence 1C11[PD-1]_H3L3 as shown in Figure 93A in the Figure 8B format.

[00337] In the dsIL-15/Rα X scFv format, one preferred embodiment utilizes the anti-PD-1 ABD having the variable heavy and variable light sequences from 1C11[PD-1]_H3L3

of XENP22538 as shown in Figure 93A. In the dsIL-15/Rα X scFv format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence 1C11[PD-1]_H3L3 of XENP22538 as shown in Figure 93A in the Figure 8B format: e.g., the skew variants S364K/E357Q (on the IL-15Rα(sushi)-Fc monomer) and L368D/K370S (on the scFv-Fc monomer), the pI variants Q295E/N384D/Q418E/N421D (on the scFv-Fc monomer), the ablation variants E233P/L234V/L235A/G236del/S267K on both monomers, and optionally the 428L/434S variants on both sides. In the dsIL-15/Rα X scFv format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence 1C11[PD-1]_H3L3 of XENP22538 as shown in Figure 93A in the Figure 8B format. In the dsIL-15/Rα X scFv format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence of a scFv variant of 1C11[PD-1]_H3L3 as depicted in Figure 93A-Figure 93S. In the dsIL-15/Rα X scFv format, one preferred embodiment utilizes the anti-PD-1 ABD having a variable heavy chain sequence of a variant of 1C11[PD-1]_H3L3 as depicted in Figure 95A–Figure 95J and a variable light chain sequence of a variant of 1C11[PD-1]_H3L3 as depicted in Figure 96A–Figure 96F.

[00338] In some embodiments, the dsIL-15/Rα X scFv format utilizes a scFv ABD to human PD-1 having the sequence of the ABD of XENP25806 or 1C11[PD-1]_H3.234_L3.144, as depicted in Figure 93R in the Figure 8B format: e.g., the skew variants S364K/E357Q (on the IL-15Rα(sushi)-Fc monomer) and L368D/K370S (on the scFv-Fc monomer), the pI variants Q295E/N384D/Q418E/N421D (on the scFv-Fc monomer), the ablation variants E233P/L234V/L235A/G236del/S267K on both monomers, and optionally the 428L/434S variants on both sides. In other words, the six CDRs and/or the VH and VL domains from XENP25806 can be used in an exemplary dsIL-15/Rα X anti-PD-1 scFv format.

[00339] In certain embodiments, the dsIL-15/Rα X scFv format utilizes a scFv ABD to human PD-1 having the sequence of the ABD of XENP25812 or 1C11[PD-1]_H3.240_L3.148, as depicted in Figure 93R. In other words, the six CDRs and/or the VH and VL domains from XENP25812 can be used in an exemplary dsIL-15/Rα X anti-PD-1 scFv format.

[00340] In particular embodiments, the dsIL-15/Rα X scFv format utilizes a scFv ABD to human PD-1 having the sequence of the ABD of XENP25813 or 1C11[PD-1]_H3.241_L3.148, as depicted in Figure 93R in the Figure 8B format: e.g., the skew variants

S364K/E357Q (on the IL-15Rα(sushi)-Fc monomer) and L368D/K370S (on the scFv-Fc monomer), the pI variants Q295E/N384D/Q418E/N421D (on the scFv-Fc monomer), the ablation variants E233P/L234V/L235A/G236del/S267K on both monomers, and optionally the 428L/434S variants on both sides. In other words, the six CDRs and/or the VH and VL domains from XENP25813 can be used in an exemplary dsIL-15/Rα X anti-PD-1 scFv format.

[00341] In other embodiments, the dsIL-15/Rα X scFv format utilizes a scFv ABD to human PD-1 having the sequence of the ABD of XENP25819 or 1C11[PD-1]_H3.241_L3.92, as depicted in Figure 93S in the Figure 8B format: e.g., the skew variants S364K/E357Q (on the IL-15Rα(sushi)-Fc monomer) and L368D/K370S (on the scFv-Fc monomer), the pI variants Q295E/N384D/Q418E/N421D (on the scFv-Fc monomer), the ablation variants E233P/L234V/L235A/G236del/S267K on both monomers, and optionally the 428L/434S variants on both sides. In other words, the six CDRs and/or the VH and VL domains from XENP25819 can be used in an exemplary dsIL-15/Rα X anti-PD-1 scFv format.

[00342] In the dsIL-15/Rα X scFv format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence of a scFv variant of 1C11[PD-1]_H3L3 as depicted in Figure 93A-Figure 93S, a human IL-15Rα(sushi) domain and a human mature IL-15 (such as a human mature IL-15 variant). In certain embodiments, the dsIL-15/Rα X scFv comprises a scFv variant of 1C11[PD-1]_H3L3 as depicted in Figure 93A-Figure 93S, a human IL-15Rα(sushi) domain and a human mature IL-15 variant having amino acid substitutions N4D/N65D. In particular embodiments, the dsIL-15/Rα X scFv comprises a scFv variant of 1C11[PD-1]_H3L3 as depicted in Figure 93A-Figure 93S, a human IL-15Rα(sushi) domain and a human mature IL-15 variant having amino acid substitutions D30N/N65D. In certain embodiments, the dsIL-15/Rα X scFv comprises a scFv variant of 1C11[PD-1]_H3L3 as depicted in Figure 93A-Figure 93S, a human IL-15Rα(sushi) domain and a human mature IL-15 variant having amino acid substitutions D30N/E64Q/N65D.

[00343] In the dsIL-15/Rα X scFv format, one preferred embodiment utilizes the anti-PD-1 ABD having a variable heavy chain sequence of a variant of 1C11[PD-1]_H3L3 as depicted in Figure 95A–Figure 95J and a variable light chain sequence of a variant of 1C11[PD-1]_H3L3 as depicted in Figure 96A–Figure 96F, a human IL-15Rα(sushi) domain and a human mature IL-15 (such as a human mature IL-15 variant). In some embodiments,

the dsIL-15/Rα X scFv comprises an anti-PD-1 ABD having a variable heavy chain sequence of a variant of 1C11[PD-1]_H3L3 as depicted in Figure 95A–Figure 95J and a variable light chain sequence of a variant of 1C11[PD-1]_H3L3 as depicted in Figure 96A–Figure 96F, a human IL-15Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions N4D/N65D. In particular embodiments, the dsIL-15/Rα X scFv comprises an anti-PD-1 ABD having a variable heavy chain sequence of a variant of 1C11[PD-1]_H3L3 as depicted in Figure 95A–Figure 95J and a variable light chain sequence of a variant of 1C11[PD-1]_H3L3 as depicted in Figure 96A–Figure 96F, a human IL-15Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions D30N/N65D. In certain embodiments, the dsIL-15/Rα X scFv comprises an anti-PD-1 ABD having a variable heavy chain sequence of a variant of 1C11[PD-1]_H3L3 as depicted in Figure 95A–Figure 95J and a variable light chain sequence of a variant of 1C11[PD-1]_H3L3 as depicted in Figure 96A–Figure 96F, a human IL-15Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions D30N/E64Q/N65D.

[00344] In some embodiments, the dsIL-15/Rα X scFv format utilizes a scFv ABD to human PD-1 having the sequence of the ABD of XENP25806 or 1C11[PD-1]_H3.234_L3.144 as depicted in Figure 93R, a human IL-15Rα(sushi) domain and a human mature IL-15 variant. In certain embodiments, the dsIL-15/Rα X scFv comprises a scFv ABD to human PD-1 having the sequence of the ABD of XENP25806 or 1C11[PD-1]_H3.234_L3.144 as depicted in Figure 93R, a human IL-15Rα(sushi) domain and a human mature IL-15 variant having amino acid substitutions N4D/N65D. In particular embodiments, the dsIL-15/Rα X scFv comprises a scFv ABD to human PD-1 having the sequence of the ABD of XENP25806 or 1C11[PD-1]_H3.234_L3.144 as depicted in Figure 93R, a human IL-15Rα(sushi) domain and a human mature IL-15 variant having amino acid substitutions D30N/N65D. In certain embodiments, the dsIL-15/Rα X scFv comprises a scFv ABD to human PD-1 having the sequence of the ABD of XENP25806 or 1C11[PD-1]_H3.234_L3.144 as depicted in Figure 93R, a human IL-15Rα(sushi) domain and a human mature IL-15 variant having amino acid substitutions D30N/E64Q/N65D.

[00345] In certain embodiments, the dsIL-15/Rα X scFv format utilizes a scFv ABD to human PD-1 having the sequence of the ABD of XENP25812 or 1C11[PD-1]_H3.240_L3.148 as depicted in Figure 93R, a human IL-15Rα(sushi) domain and a human mature IL-15 variant. In certain embodiments, the dsIL-15/Rα X scFv comprises a scFv

ABD to human PD-1 having the sequence of the ABD of XENP25812 or 1C11[PD-1]_H3.240_L3.148 as depicted in Figure 93R, a human IL-15Rα(sushi) domain and a human mature IL-15 variant having amino acid substitutions N4D/N65D. In particular embodiments, the dsIL-15/Rα X scFv comprises a scFv ABD to human PD-1 having the sequence of the ABD of XENP25812 or 1C11[PD-1]_H3.240_L3.148 as depicted in Figure 93R, a human IL-15Rα(sushi) domain and a human mature IL-15 variant having amino acid substitutions D30N/N65D. In certain embodiments, the dsIL-15/Rα X scFv comprises a scFv ABD to human PD-1 having the sequence of the ABD of XENP25812 or 1C11[PD-1]_H3.240_L3.148 as depicted in Figure 93R, a human IL-15Rα(sushi) domain and a human mature IL-15 variant having amino acid substitutions D30N/E64Q/N65D.

[00346] In particular embodiments, the dsIL-15/Rα X scFv format utilizes a scFv ABD to human PD-1 having the sequence of the ABD of XENP25813 or 1C11[PD-1]_H3.241_L3.148 as depicted in Figure 93R, a human IL-15Rα(sushi) domain and a human mature IL-15 variant. In certain embodiments, the dsIL-15/Rα X scFv comprises a scFv ABD to human PD-1 having the sequence of the ABD of XENP25813 or 1C11[PD-1]_H3.241_L3.148 as depicted in Figure 93R, a human IL-15Rα(sushi) domain and a human mature IL-15 variant having amino acid substitutions N4D/N65D. In particular embodiments, the dsIL-15/Rα X scFv comprises a scFv ABD to human PD-1 having the sequence of the ABD of XENP25813 or 1C11[PD-1]_H3.241_L3.148 as depicted in Figure 93R, a human IL-15Rα(sushi) domain and a human mature IL-15 variant having amino acid substitutions D30N/N65D. In certain embodiments, the dsIL-15/Rα X scFv comprises a scFv ABD to human PD-1 having the sequence of the ABD of XENP25813 or 1C11[PD-1]_H3.241_L3.148 as depicted in Figure 93R, a human IL-15Rα(sushi) domain and a human mature IL-15 variant having amino acid substitutions D30N/E64Q/N65D.

[00347] In other embodiments, the dsIL-15/Rα X scFv format utilizes a scFv ABD to human PD-1 having the sequence of the ABD of XENP25819 or 1C11[PD-1]_H3.241_L3.92 as depicted in Figure 93S, a human IL-15Rα(sushi) domain and a human mature IL-15 variant. In certain embodiments, the dsIL-15/Rα X scFv comprises a scFv ABD to human PD-1 having the sequence of the ABD of XENP25819 or 1C11[PD-1]_H3.241_L3.92 as depicted in Figure 93S, a human IL-15Rα(sushi) domain and a human mature IL-15 variant having amino acid substitutions N4D/N65D. In particular embodiments, the dsIL-15/Rα X scFv comprises a scFv ABD to human PD-1 having the sequence of the ABD of XENP25819

or 1C11[PD-1]_H3.241_L3.92 as depicted in Figure 93S, a human IL-15Rα(sushi) domain and a human mature IL-15 variant having amino acid substitutions D30N/N65D. In certain embodiments, the dsIL-15/Rα X scFv comprises a scFv ABD to human PD-1 having the sequence of the ABD of XENP25819 or 1C11[PD-1]_H3.241_L3.92 as depicted in Figure 93S, a human IL-15Rα(sushi) domain and a human mature IL-15 variant having amino acid substitutions D30N/E64Q/N65D.

[00348] In some embodiments, the anti-PD-1 scFv of any of the dsIL-15/Rα X scFv fusion protein outlined herein comprises the VH and VL sequences of XENP26940 or 1C11_H3.303_L3.152 as depicted in Figure 94N, the VH and VL sequences of XENP28026 or 1C11_H3.329_L3.220 as shown in Figure 94AE, or the VH and VL sequences of XENP28652 or 1C11_H3.328_L3.152 as depicted in Figure 94AG.

D. scIL-15/Rα X Fab

[00349] This embodiment is shown in Figure 65D, and comprises three monomers. This is generally referred to as "scIL-15/Rα X Fab" or "Fab X scIL-15/Rα," as used interchangeably, with the "sc" standing for "single chain". The "scIL-15/Rα x Fab" format (Figure 65D) comprises IL-15Rα(sushi) fused to IL-15 by a variable length linker (termed "scIL-15/Rα") which is then fused to the N-terminus of a first Fc monomer, with a variable heavy chain (VH) fused to the other side of a second Fc monomer, while a corresponding light chain is transfected separately so as to form a Fab with the VH.

[00350] As noted in Figures 94A-94AP, Figures 95A-95J, Figures 96A-96F, Figures 126A-126D, Figures 127A-127D, and Figures 128A-128L and is true for every sequence herein containing CDRs, the exact identification of the CDR locations may be slightly different depending on numbering used as is shown in Table 1, and thus included herein are not only the CDRs that are bolded but also CDRs included wherein the VH and VL domain using other numbering systems. Additionally, each CDR has its own SEQ ID NO: or sequence identifier, and each VH and VL domain has its own SEQ ID NO: or sequence identifier in the sequence listing.

[00351] In some embodiments, the first monomer comprises, from N- to C-terminus, the human IL-15Rα sushi domain-domain linker-human mature IL-15-optional domain linker-CH2-CH3 and the second monomer comprises a heavy chain, VH-CH1-hinge-CH2-CH3. The third monomer is a light chain, VL-CL. Preferred combinations of Fc variants for this embodiment are found in Figure 8C.

[00352] In some embodiments, the illustrative PD-1-targeted X IL-15/Rα-Fc fusion proteins of the scIL-15/Rα x Fab format comprises amino acid sequences of XENP22022, XENP25849, XENP24535, XENP24536, XENP25850, and XENP25937 are provided in Figures 69A-69C.

[00353] In some embodiments, the scIL-15/Rα X Fab comprises the skew variants S364K/E357Q (on the second monomer or heavy chain-Fc monomer) and L368D/K370S (on the first monomer or IL-15 complex-Fc monomer), the pI variants Q295E/N384D/Q418E/N421D (on the IL-15 complex side), the ablation variants E233P/L234V/L235A/G236del/S267K on both monomers, and optionally the 428L/434S variants on both sides. In the scIL-15/Rα X Fab format, one preferred embodiment utilizes the skew variant pair S364K/E357Q : L368D/K370S.

[00354] In the scIL-15/Rα X Fab format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence 1G6_H1.279_L1.194 as shown in Figure 14. In some embodiments, the anti-PD-1 ABD has CDRs and/or the VH and VL domains of 1G6_H1.279_L1.194. In the scIL-15/Rα X Fab format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence 1G6_H1.279_L1.194 as shown in Figure 14, in the Figure 8C format: e.g., the skew variants L368D/K370S (on the IL-15 complex Fc-monomer) and S364K/E357Q (on the heavy chain-Fc monomer), the pI variants Q295E/N384D/Q418E/N421D (on the IL-15 complex side), the ablation variants E233P/L234V/L235A/G236del/S267K on both monomers, and optionally the 428L/434S variants on both sides. In the scIL-15/Rα X Fab format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence 1G6_H1.279_L1.194 as shown in Figure 14 in the Figure 8C format. In the scIL-15/Rα X Fab format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence 1G6_H1.279_L1.194 as shown in Figure 14 and the skew variant pair S364K/E357Q : L368D/K370S.

[00355] In some embodiments, the anti-PD-1 Fab utilizes the sequences 1G6_H1.278 [PD-1] as shown in chain 2 of XENP22022 and 1G6_L1.188[PD-1] as shown in chain 3 of XENP22022 of Figure 69A. In certain embodiments, the anti-PD-1 Fab utilizes the sequences 1C11[PD-1]_H3 as shown in chain 1 of XENP25849 and 1C11[PD-1]_L3 as shown in chain 3 of XENP25849 of Figure 69A. In other embodiments, the anti-PD-1 Fab utilizes the sequences 1C11[PD-1]_H3 as shown in chain 1 of XENP24535 and 1C11[PD-1]_L3 as shown in chain 3 of XENP24535 of Figure 69B. In some embodiments,

the anti-PD-1 Fab utilizes the sequences 1C11[PD-1]_H3 as shown in chain 1 of XENP24536 and 1C11[PD-1]_L3 as shown in chain 3 of XENP24536 of Figure 69B. In some embodiments, the anti-PD-1 Fab utilizes the sequences 1C11[PD-1]_H3L3 as shown in chain 1 of XENP25850 and 1C11[PD-1]_L3 as shown in chain 3 of XENP25850 of Figure 69C. In certain embodiments, the anti-PD-1 Fab utilizes the sequences 1C11[PD-1]_H3 as shown in chain 1 of XENP259357 and 1C11[PD-1]_L3 as shown in chain 3 of XENP25937 of Figure 69C. In some embodiments, the anti-PD-1 Fab utilizes the sequences of XENP22553 or 1C11_H3L3 as depicted in Figure 94A. In some instances, the anti-PD-1 Fab utilizes the CDRs and/or the VH and VL domains from XENP22553 or 1C11_H3L3. In the scIL-15/Rα X Fab format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence 1C11[PD-1]_H3L3 as shown in Figure 94. In the scIL-15/Rα X Fab format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence 1C11[PD-1]_H3L3 as shown in Figure 94 in the Figure 8C format: e.g., the skew variants L368D/K370S (on the IL-15 complex Fc-monomer) and S364K/E357Q (on the heavy chain-Fc monomer), the pI variants Q295E/N384D/Q418E/N421D (on the IL-15 complex side), the ablation variants E233P/L234V/L235A/G236del/S267K on both monomers, and optionally the 428L/434S variants on both sides.

[00356] In some embodiments, the anti-PD-1 Fab utilizes the sequences of XENP26940 or 1C11_H3.303_L3.152 as depicted in Figure 94N. In some instances, the anti-PD-1 Fab utilizes the CDRs and/or the VH and VL domains from XENP26940 or 1C11_H3.303_L3.152. In the scIL-15/Rα X Fab format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence of XENP26940 or 1C11_H3.303_L3.152. In the scIL-15/Rα X Fab format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence of XENP26940 or 1C11_H3.303_L3.152 as shown in Figure 94N, in the Figure 8C format: e.g., the skew variants L368D/K370S (on the IL-15 complex Fc-monomer) and S364K/E357Q (on the heavy chain-Fc monomer), the pI variants Q295E/N384D/Q418E/N421D (on the IL-15 complex side), the ablation variants E233P/L234V/L235A/G236del/S267K on both monomers, and optionally the 428L/434S variants on both sides. In the scIL-15/Rα X Fab format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence of XENP26940 or 1C11_H3.303_L3.152 as shown in Figure 94N in the Figure 8C format. In the scIL-15/Rα X Fab format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence of XENP26940 or

1C11_H3.303_L3.152 as shown in Figure 94N and the skew variant pair S364K/E357Q : L368D/K370S.

[00357] In some embodiments, the anti-PD-1 Fab utilizes the sequences of XENP28026 or 1C11_H3.329_L3.220 as depicted in Figure 94AE. In some instances, the anti-PD-1 Fab utilizes the CDRs and/or the VH and VL domains from XENP28026 or 1C11_H3.329_L3.220. In the scIL-15/Rα X Fab format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence of 1C11_H3.329_L3.220. In the scIL-15/Rα X Fab format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence of XENP28026 or 1C11_H3.329_L3.220 as shown in Figure 94AE, in the Figure 8C format: e.g., the skew variants L368D/K370S (on the IL-15 complex Fc-monomer) and S364K/E357Q (on the heavy chain-Fc monomer), the pI variants Q295E/N384D/Q418E/N421D (on the IL-15 complex side), the ablation variants E233P/L234V/L235A/G236del/S267K on both monomers, and optionally the 428L/434S variants on both sides. In the scIL-15/Rα X Fab format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence of XENP28026 or 1C11_H3.329_L3.220 as shown in Figure 94AE in the Figure 8C format. In the scIL-15/Rα X Fab format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence of XENP28026 or 1C11_H3.329_L3.220 as shown in Figure 94AE and the skew variant pair S364K/E357Q : L368D/K370S.

[00358] In some embodiments, the anti-PD-1 Fab utilizes the sequences of XENP28652 or 1C11_H3.328_L3.152 as depicted in Figure 94AG. In some instances, the anti-PD-1 Fab utilizes the CDRs and/or the VH and VL domains from XENP28652 or 1C11_H3.328_L3.152. In the scIL-15/Rα X Fab format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence of XENP28652 or 1C11_H3.328_L3.152. In the scIL-15/Rα X Fab format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence of XENP28652 or 1C11_H3.328_L3.152 as shown in Figure 94AG, in the Figure 8C format: e.g., the skew variants L368D/K370S (on the IL-15 complex Fc-monomer) and S364K/E357Q (on the heavy chain-Fc monomer), the pI variants Q295E/N384D/Q418E/N421D (on the IL-15 complex side), the ablation variants E233P/L234V/L235A/G236del/S267K on both monomers, and optionally the 428L/434S variants on both sides. In the scIL-15/Rα X Fab format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence of XENP28652 or 1C11_H3.328_L3.152 as shown

in Figure 94AG in the Figure 8C format. In the scIL-15/Rα X Fab format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence of XENP28652 or 1C11_H3.328_L3.152 as shown in Figure 94AG and the skew variant pair S364K/E357Q : L368D/K370S.

[00359] In one embodiment, the anti-PD-1 Fab utilizes the sequences of any one of the XENP or corresponding SEQ ID NO identifiers as depicted in Figures 94A-94AP. In some instances, the anti-PD-1 Fab has a sequence selected from the group consisting of XENP22553, XENP25338, XENP25339, XENP26321, XENP26322, XENP26323, XENP26324, XENP26325, XENP26326, XENP26327, XENP26328, XENP26329, XENP26330, XENP26331, XENP26332, XENP26333, XENP26334, XENP26335, XENP26336, XENP26337, XENP26338, XENP26339, XENP26340, XENP26341, XENP26342, XENP26343, XENP26344, XENP26917, XENP26918, XENP26919, XENP26920, XENP26921, XENP26922, XENP26923, XENP26924, XENP26925, XENP26926, XENP26927, XENP26928, XENP26929, XENP26930, XENP26931, XENP26932, XENP26933, XENP26934, XENP26935, XENP26936, XENP26937, XENP26938, XENP26939, XENP26940, XENP26941, XENP26942, XENP26943, XENP26944, XENP26945, XENP26946, XENP26947, XENP26949, XENP26950, XENP26951, XENP26952, XENP26953, XENP26954, XENP26955, XENP27643, XENP27644, XENP27645, XENP27646, XENP27647, XENP47648, XENP27649, XENP27650, XENP27651, XENP27652, XENP27839, XENP27840, XENP27841, XENP27842, XENP27843, XENP27844, XENP27845, XENP27846, XENP27847, XENP27848, XENP27849, XENP27850, XENP27851, XENP27852, XENP27853, XENP27854, XENP27855, XENP27856, XENP27857, XENP27858, XENP27859, XENP27860, XENP27861, XENP27862, XENP27863, XENP27864, XENP27865, XENP27866, XENP27867, XENP27868, XENP27869, XENP27870, XENP27871, XENP27872, XENP27959, XENP27960, XENP27961, XENP27962, XENP27963, XENP28024, XENP28025, XENP28026, XENP28027, XENP28028, XENP28029, XENP28030, XENP28031, XENP28032, XENP28033, XENP28034, XENP28035, XENP28651, XENP28652, XENP28653, XENP28654, XENP28655, XENP28656, XENP28657, XENP28658, XENP28659, XENP29029, XENP29030, XENP29031, XENP29032, XENP29033, XENP29034, XENP29035, XENP29036, XENP29037, XENP29038, XENP29039, XENP29040, XENP29041, XENP29042, XENP29043,

XENP29044, XENP29045, XENP29046, XENP29047, XENP29048, XENP29049, XENP29050, XENP29051, XENP29052, XENP29053, XENP29054, XENP29055, and XENP29056, including the corresponding SEQ ID NO identifiers.

[00360] In another embodiment, the anti-PD-1 Fab utilizes the variable heavy chain sequence of any one of the XenD or corresponding SEQ ID NO identifier as depicted in Figures 95A-95J and the variable light chain sequence of any one of the XenD or corresponding SEQ ID NO identifier as depicted in Figures 96A-96F. In some cases, the sequence of the variable heavy chain is selected from the group consisting of XenD17478, XenD18576, XenD22097, XenD22098, XenD22099, XenD22100, XenD22101, XenD22102, XenD22103, XenD22104, XenD22105, XenD22106, XenD22107, XenD22108, XenD22109, XenD22110, XenD22111, XenD22112, XenD22113, XenD22114, XenD22115, XenD22116, XenD22117, XenD22118, XenD22119, XenD22120, XenD22121, XenD22122, XenD22123, XenD22124, XenD22125, XenD22126, XenD22127, XenD22128, XenD22129, XenD22130, XenD22131, XenD22132, XenD22133, XenD22134, XenD22135, XenD22136, XenD22137, XenD22138, XenD22139, XenD22140, XenD22141, XenD22142, XenD22143, XenD22144, XenD22145, XenD22146, XenD22147, XenD22148, XenD22149, XenD22150, XenD22150, XenD22152, XenD22153, XenD22154, XenD22155, XenD22156, XenD22157, XenD22158, XenD22159, XenD22160, XenD22161, and XenD22162, including the corresponding SEQ ID NO identifiers. In some cases, the sequence of the variable light chain is selected from the group consisting of XenD17482, XenD18472, XenD22163, XenD22164, XenD22165, XenD22166, XenD22167, XenD22168, XenD22169, XenD22170, XenD22157, XenD22158, XenD22159, XenD22161, XenD22162, XenD22171, XenD22172, XenD22173, XenD22174, XenD22175, XenD22176, XenD22177, XenD22178, XenD22179, XenD22180, XenD22181, XenD22182, XenD22183, XenD22184, XenD22185, XenD22186, XenD22184, XenD22185, XenD22186, XenD22187, XenD22188, XenD22189, XenD22190, XenD22191, XenD22192, XenD22193, XenD22194, XenD22195, XenD22196, XenD22197, XenD22198, XenD22199, XenD22200, XenD22201, XenD22202, XenD22203, XenD22204, XenD22205, XenD22206, XenD22207, XenD22208, XenD22209, XenD22210, XenD22211, XenD22212, XenD22213, XenD22214, XenD22215, XenD22216, XenD22217, XenD22218, XenD22219, XenD22220, XenD22221, XenD22222, and XenD22223 of Figure 96, including the corresponding SEQ ID NO identifiers.

[00361] In the scIL-15/Rα X Fab format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence of 1G6_H1.279_L1.194 (1G6_L1.194_H1.279) as shown in Figure 14 and the IL-15 complex (sushi domain-linker-IL-15) of chain 1 of XENP22022 as depicted in Figure 69A. In some embodiments, the scIL-15/Rα X Fab comprises anti-PD-1 ABD having the sequence of 1G6_H1.279_L1.194 (1G6_L1.194_H1.279) as shown in Figure 14 and the IL-15 complex (sushi domain-linker-IL-15 variant N4D/N65D) of chain 2 of XENP25850 as depicted in Figure 69C. In some embodiments, the scIL-15/Rα X Fab comprises anti-PD-1 ABD having the sequence of 1G6_H1.279_L1.194 (1G6_L1.194_H1.279) as shown in Figure 14 and the IL-15 complex (sushi domain-linker-IL-15 variant D30N/N65D) of chain 1 of XENP29482 as depicted in Figure 126A. In some embodiments, the scIL-15/Rα X Fab comprises anti-PD-1 ABD having the sequence of 1G6_H1.279_L1.194 (1G6_L1.194_H1.279) as shown in Figure 14 and the IL-15 complex (sushi domain-linker-IL-15 variant D30N/E64Q/N65D) of chain 1 of the constructs as depicted in Figure 124C.

[00362] In the scIL-15/Rα X Fab format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence of 1C11_H3L3 as shown in Figure 94A and the IL-15 complex (sushi domain-linker-IL-15) of chain 1 of XENP22022 as depicted in Figure 69A. In some embodiments, the scIL-15/Rα X Fab comprises anti-PD-1 ABD having the sequence of 1C11_H3L3 as shown in Figure 94A and the IL-15 complex (sushi domain-linker-IL-15 variant N4D/N65D) of chain 2 of XENP25850 as depicted in Figure 69C. In some embodiments, the scIL-15/Rα X Fab comprises anti-PD-1 ABD having the sequence of 1C11_H3L3 as shown in Figure 94A and the IL-15 complex (sushi domain-linker-IL-15 variant D30N/N65D) of chain 1 of XENP29482 as depicted in Figure 126A. In some embodiments, the scIL-15/Rα X Fab comprises anti-PD-1 ABD having the sequence of 1C11_H3L3 as shown in Figure 94A and the IL-15 complex (sushi domain-linker-IL-15 variant D30N/E64Q/N65D) of chain 1 of XENP29286 as depicted in Figure 124C.

[00363] In the scIL-15/Rα X Fab format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence of XENP26940 or 1C11_H3.303_L3.152 as depicted in Figure 94N and the IL-15 complex (sushi domain-linker-IL-15) of chain 1 of XENP22022 as depicted in Figure 69A. In some embodiments, the scIL-15/Rα X Fab comprises anti-PD-1 ABD having the sequence of XENP26940 or 1C11_H3.303_L3.152 as depicted in Figure 94N and the IL-15 complex (sushi domain-linker-IL-15 variant N4D/N65D) of chain 2 of

XENP25850 as depicted in Figure 69C. In some embodiments, the scIL-15/Rα X Fab comprises anti-PD-1 ABD having the sequence of XENP26940 or 1C11_H3.303_L3.152 as depicted in Figure 94N and the IL-15 complex (sushi domain-linker-IL-15 variant D30N/N65D) of chain 1 of XENP29482 as depicted in Figure 126A. In some embodiments, the scIL-15/Rα X Fab comprises anti-PD-1 ABD having the sequence of XENP26940 or 1C11_H3.303_L3.152 as depicted in Figure 94N and the IL-15 complex (sushi domain-linker-IL-15 variant D30N/E64Q/N65D) of chain 1 of XENP29286 as depicted in Figure 124C.

[00364] In the scIL-15/Rα X Fab format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence of XENP28026 or 1C11_H3.329_L3.220 as shown in Figure 94AE and the IL-15 complex (sushi domain-linker-IL-15) of chain 1 of XENP22022 as depicted in Figure 69A. In some embodiments, the scIL-15/Rα X Fab comprises anti-PD-1 ABD having the sequence of XENP28026 or 1C11_H3.329_L3.220 as shown in Figure 94AE and the IL-15 complex (sushi domain-linker-IL-15 variant N4D/N65D) of chain 2 of XENP25850 as depicted in Figure 69C. In some embodiments, the scIL-15/Rα X Fab comprises anti-PD-1 ABD having the sequence of XENP28026 or 1C11_H3.329_L3.220 as shown in Figure 94AE and the IL-15 complex (sushi domain-linker-IL-15 variant D30N/N65D) of chain 1 of XENP29482 as depicted in Figure 126A. In some embodiments, the scIL-15/Rα X Fab comprises anti-PD-1 ABD having the sequence of XENP28026 or 1C11_H3.329_L3.220 as shown in Figure 94AE and the IL-15 complex (sushi domain-linker-IL-15 variant D30N/E64Q/N65D) of chain 1 of XENP29286 as depicted in Figure 124C.

[00365] In the scIL-15/Rα X Fab format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence of XENP28652 or 1C11_H3.328_L3.152 as depicted in Figure 94AG and the IL-15 complex (sushi domain-linker-IL-15) of chain 1 of XENP22022 as depicted in Figure 69A. In some embodiments, the scIL-15/Rα X Fab comprises anti-PD-1 ABD having the sequence of XENP28652 or 1C11_H3.328_L3.152 as depicted in Figure 94AG and the IL-15 complex (sushi domain-linker-IL-15 variant N4D/N65D) of chain 2 of XENP25850 as depicted in Figure 69C. In some embodiments, the scIL-15/Rα X Fab comprises anti-PD-1 ABD having the sequence of XENP28652 or 1C11_H3.328_L3.152 as depicted in Figure 94AG and the IL-15 complex (sushi domain-linker-IL-15 variant D30N/N65D) of chain 1 of XENP29482 as depicted in Figure 126A. In some embodiments,

the scIL-15/Rα X Fab comprises anti-PD-1 ABD having the sequence of XENP28652 or 1C11_H3.328_L3.152 as depicted in Figure 94AG and the IL-15 complex (sushi domain-linker-IL-15 variant D30N/E64Q/N65D) of chain 1 of XENP29286 as depicted in Figure 124C.

[00366] In some embodiments, the anti-PD-1 Fab of the scIL-15/Rα X Fab format has the heavy chain and light chain sequences of XENP25806 or 1C11[PD-1]_H3.234_L3.144, as depicted in Figure 93R, the heavy chain and light chain sequences of the ABD of XENP25812 or 1C11[PD-1]_H3.240_L3.148, as depicted in Figure 93R, the heavy chain and light chain sequences of XENP25813 or 1C11[PD-1]_H3.241_L3.148, as depicted in Figure 93R, or the heavy chain and light chain sequences of XENP25819 or 1C11[PD-1]_H3.241_L3.92, as depicted in Figure 93S.

E. **ncIL-15/Rα X Fab**

[00367] This embodiment is shown in Figure 65E, and comprises three monomers. This is generally referred to as "ncIL-15/Rα X Fab" or "Fab X ncIL-15/Rα," as used interchangeably, with the "nc" standing for "non-covalent" referring to the self-assembing non-covalent attachment of the IL-15 and IL-15Rα sushi domain. The ncIL-15/Rα x Fab format (see Figure 65E) comprises a VH fused to the N-terminus of a heterodimeric Fc-region, with IL-15Rα(sushi) fused to the other side of the heterodimeric Fc, while a corresponding light chain is transfected separately so as to form a Fab with the VH, and while IL-15 is transfected separately so that a non-covalent IL-15/Rα complex is formed. Amino acid sequences of an illustrative PD-1-targeted x IL-15/Rα-Fc fusion proteins of the Fab x ncIL-15/Rα format such as XENP22112 is provided in Figure 70.

[00368] In some embodiments, the first monomer comprises, from N- to C-terminus, the IL-15Rα sushi domain-optional domain linker-CH2-CH3, and the second monomer comprises a heavy chain, VH-CH1-hinge-CH2-CH3. The third monomer is the IL-15 domain. Preferred combinations of Fc variants for this embodiment are found in Figure 8D.

[00369] In the ncIL-15/Rα X Fab format, one preferred embodiment utilizes the skew variant pair S364K/E357Q : L368D/K370S. In the ncIL-15/Rα X Fab format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence 1G6_L1.194_H1.279 as shown in Figure 14. In the ncIL-15/Rα X Fab format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence 1G6_L1.194_H1.279 (1G6_H1.279_L1.194) as shown in Figure 14, in the Figure 8D format: e.g., the skew variants L368D/K370S (on the heavy

chain-Fc monomer) and S364K/E357Q (on the sushi domain-Fc-monomer), the pI variants Q295E/N384D/Q418E/N421D (on the heavy chain-Fc monomer), the ablation variants E233P/L234V/L235A/G236del/S267K on both monomers, and optionally the 428L/434S variants on both sides.

[00370] In the ncIL-15/Rα X Fab format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence 1C11[PD-1]_H3L3 as shown in Figure 20C and the skew variant pair S364K/E357Q : L368D/K370S. In the ncIL-15/Rα X Fab format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence 1C11[PD-1]_H3L3 as shown in Figure 20C in the Figure 8D format: e.g., the skew variants L368D/K370S (on the heavy chain-Fc monomer) and S364K/E357Q (on the sushi domain-Fc-monomer), the pI variants Q295E/N384D/Q418E/N421D (on the heavy chain-Fc monomer), the ablation variants E233P/L234V/L235A/G236del/S267K on both monomers, and optionally the 428L/434S variants on both sides.

[00371] In some embodiments, ncIL-15/Rα X Fab of the invention comprises an anti-PD-1 ABD having the sequence of XENP26940 or 1C11_H3.303_L3.152 as shown in Figure 94N, a human IL-15 Rα(sushi) domain, and a human mature IL-15 (including a human mature IL-15 variant). In some embodiments, ncIL-15/Rα X Fab of the invention comprises an anti-PD-1 ABD having the sequence of XENP26940 or 1C11_H3.303_L3.152 as shown in Figure 94N, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions N4D/N65D. In some embodiments, ncIL-15/Rα X Fab comprises an anti-PD-1 ABD having the sequence of XENP26940 or 1C11_H3.303_L3.152 as shown in Figure 94N, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions D30N/N65D. In some embodiments, ncIL-15/Rα X Fab comprises an anti-PD-1 ABD having the sequence of XENP26940 or 1C11_H3.303_L3.152 as shown in Figure 94N, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions D30N/E64Q/N65D.

[00372] In some embodiments, ncIL-15/Rα X Fab of the invention comprises an anti-PD-1 ABD having the sequence of XENP28026 or 1C11_H3.329_L3.220 as shown in Figure 94AE, a human IL-15 Rα(sushi) domain, and a human mature IL-15 (including a human mature IL-15 variant). In some embodiments, ncIL-15/Rα X Fab of the invention comprises an anti-PD-1 ABD having the sequence of XENP28026 or 1C11_H3.329_L3.220 as shown in Figure 94AE, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having

amino acid substitutions N4D/N65D. In some embodiments, ncIL-15/Rα X Fab comprises an anti-PD-1 ABD having the sequence of XENP28026 or 1C11_H3.329_L3.220 as shown in Figure 94AE, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions D30N/N65D. In some embodiments, ncIL-15/Rα X Fab comprises an anti-PD-1 ABD having the sequence of XENP28026 or 1C11_H3.329_L3.220 as shown in Figure 94AE, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions D30N/E64Q/N65D.

[00373] In some embodiments, ncIL-15/Rα X Fab of the invention comprises an anti-PD-1 ABD having the sequence of XENP28652 or 1C11_H3.328_L3.152 as shown in Figure 94AG, a human IL-15 Rα(sushi) domain, and a human mature IL-15 (including a human mature IL-15 variant). In some embodiments, ncIL-15/Rα X Fab of the invention comprises an anti-PD-1 ABD having the sequence of XENP28652 or 1C11_H3.328_L3.152 as shown in Figure 94AG, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions N4D/N65D. In some embodiments, ncIL-15/Rα X Fab comprises an anti-PD-1 ABD having the sequence of XENP28652 or 1C11_H3.328_L3.152 as shown in Figure 94AG, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions D30N/N65D. In some embodiments, ncIL-15/Rα X Fab comprises an anti-PD-1 ABD having the sequence of XENP28652 or 1C11_H3.328_L3.152 as shown in Figure 94AG, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions D30N/E64Q/N65D.

[00374] In some embodiments, the anti-PD-1 Fab of the ncIL-15/Rα X Fab format has the heavy chain and light chain sequences of XENP25806 or 1C11[PD-1]_H3.234_L3.144, as depicted in Figure 93R, the heavy chain and light chain sequences of the ABD of XENP25812 or 1C11[PD-1]_H3.240_L3.148, as depicted in Figure 93R, the heavy chain and light chain sequences of XENP25813 or 1C11[PD-1]_H3.241_L3.148, as depicted in Figure 93R, or the heavy chain and light chain sequences of XENP25819 or 1C11[PD-1]_H3.241_L3.92, as depicted in Figure 93S.

F. **dsIL-15/Rα X Fab**

[00375] This embodiment is shown in Figure 65F, and comprises three monomers. This is generally referred to as "dsIL-15/Rα X Fab" or "Fab X dsIL-15/Rα," as used interchangeably, with the "ds" standing for "disulfide" referring to the self-assembing non-covalent attachment of the IL-15 and sushi domain. The dsIL-15/Rα x Fab format (see Figure

65F) is the same as the "ncIL-15/Rα x Fab" format, but wherein IL-15Rα(sushi) and IL-15 are covalently linked as a result of engineered cysteines. Amino acid sequences of an illustrative PD-1-targeted x IL-15/Rα-Fc fusion protein of the Fab x dsIL-15/Rα format such as XENP22641 is provided in Figure 71.

[00376] In some embodiments, the first monomer comprises, from N- to C-terminus, the sushi domain-domain linker-CH2-CH3, wherein the sushi domain has been engineered to contain a cysteine residue, and the second monomer comprises a heavy chain, VH-CH1-hinge-CH2-CH3. The third monomer is the IL-15 domain, also engineered to have a cysteine residue, such that a disulfide bridge is formed under native cellular conditions. Preferred combinations of variants for this embodiment are found in Figure 7 of WO2018/071918.

[00377] In the dsIL-15/Rα X Fab format, one preferred embodiment utilizes the skew variant pair S364K/E357Q : L368D/K370S. In the dsIL-15/Rα X Fab format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence 1G6_L1.194_H1.279 as shown in Figure 14. In the dsIL-15/Rα X Fab format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence 1G6_L1.194_H1.279 (1G6_H1.279_L1.194) as shown in Figure 14, in the Figure 8D format: e.g., the skew variants L368D/K370S (on the heavy chain-Fc monomer) and S364K/E357Q (on the IL-15 complex Fc-monomer), the pI variants Q295E/N384D/Q418E/N421D (on the heavy chain-Fc monomer), the ablation variants E233P/L234V/L235A/G236del/S267K on both monomers, and optionally the 428L/434S variants on both sides.

[00378] In the dsIL-15/Rα X Fab format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence 1C11[PD-1]_H3L3 as shown in Figure 20C and the skew variant pair S364K/E357Q : L368D/K370S. In the dsIL-15/Rα X Fab format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence 1C11[PD-1]_H3L3 as shown in Figure 20C in the Figure 8D format.

[00379] In some embodiments, dsIL-15/Rα X Fab of the invention comprises an anti-PD-1 ABD having the sequence of XENP26940 or 1C11_H3.303_L3.152 as shown in Figure 94N. In some embodiments, dsIL-15/Rα X Fab of the invention comprises an anti-PD-1 ABD having the sequence of XENP28026 or 1C11_H3.329_L3.220 as shown in Figure 94AE. In some embodiments, dsIL-15/Rα X Fab of the invention comprises an anti-PD-1 ABD having the sequence of XENP28652 or 1C11_H3.328_L3.152 as shown in Figure 94AG.

[00380] In some embodiments, dsIL-15/Rα X Fab of the invention comprises an anti-PD-1 ABD having the sequence of XENP26940 or 1C11_H3.303_L3.152 as shown in Figure 94N, a human IL-15 Rα(sushi) domain, and a human mature IL-15 (including a human mature IL-15 variant). In some embodiments, dsIL-15/Rα X Fab of the invention comprises an anti-PD-1 ABD having the sequence o of XENP26940 or f 1C11_H3.303_L3.152 as shown in Figure 94N, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions N4D/N65D. In some embodiments, dsIL-15/Rα X Fab comprises an anti-PD-1 ABD having the sequence of XENP26940 or 1C11_H3.303_L3.152 as shown in Figure 94N, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions D30N/N65D. In some embodiments, dsIL-15/Rα X Fab comprises an anti-PD-1 ABD having the sequence of XENP26940 or 1C11_H3.303_L3.152 as shown in Figure 94N, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions D30N/E64Q/N65D.

[00381] In some embodiments, dsIL-15/Rα X Fab of the invention comprises an anti-PD-1 ABD having the sequence of XENP28026 or 1C11_H3.329_L3.220 as shown in Figure 94AE, a human IL-15 Rα(sushi) domain, and a human mature IL-15 (including a human mature IL-15 variant). In some embodiments, dsIL-15/Rα X Fab of the invention comprises an anti-PD-1 ABD having the sequence of XENP28026 or 1C11_H3.329_L3.220 as shown in Figure 94AE, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions N4D/N65D. In some embodiments, dsIL-15/Rα X Fab comprises an anti-PD-1 ABD having the sequence of XENP28026 or 1C11_H3.329_L3.220 as shown in Figure 94AE, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions D30N/N65D. In some embodiments, dsIL-15/Rα X Fab comprises an anti-PD-1 ABD having the sequence of XENP28026 or 1C11_H3.329_L3.220 as shown in Figure 94AE, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions D30N/E64Q/N65D.

[00382] In some embodiments, dsIL-15/Rα X Fab of the invention comprises an anti-PD-1 ABD having the sequence of XENP28652 or 1C11_H3.328_L3.152 as shown in Figure 94AG, a human IL-15 Rα(sushi) domain, and a human mature IL-15 (including a human mature IL-15 variant). In some embodiments, dsIL-15/Rα X Fab of the invention comprises an anti-PD-1 ABD having the sequence of XENP28652 or 1C11_H3.328_L3.152 as shown in Figure 94AG, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having

amino acid substitutions N4D/N65D. In some embodiments, dsIL-15/Rα X Fab comprises an anti-PD-1 ABD having the sequence of XENP28652 or 1C11_H3.328_L3.152 as shown in Figure 94AG, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions D30N/N65D. In some embodiments, dsIL-15/Rα X Fab comprises an anti-PD-1 ABD having the sequence of XENP28652 or 1C11_H3.328_L3.152 as shown in Figure 94AG, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions D30N/E64Q/N65D.

[00383] In some embodiments, the anti-PD-1 Fab of the dsIL-15/Rα X Fab format has the heavy chain and light chain sequences of XENP25806 or 1C11[PD-1]_H3.234_L3.144, as depicted in Figure 93R, the heavy chain and light chain sequences of the ABD of XENP25812 or 1C11[PD-1]_H3.240_L3.148, as depicted in Figure 93R, the heavy chain and light chain sequences of XENP25813 or 1C11[PD-1]_H3.241_L3.148, as depicted in Figure 93R, or the heavy chain and light chain sequences of XENP25819 or 1C11[PD-1]_H3.241_L3.92, as depicted in Figure 93S.

G. **mAb-scIL-15/Rα**

[00384] This embodiment is shown in Figure 65G, and comprises three monomers (although the fusion protein is a tetramer). This is generally referred to as “mAb-scIL-15/Rα”, with the “sc” standing for “single chain”. The mAb-scIL-15/Rα format (see Figure 65G) comprises VH fused to the N-terminus of a first and a second heterodimeric Fc, with IL-15 is fused to IL-15Rα(sushi) which is then further fused to the C-terminus of one of the heterodimeric Fc-region, while corresponding light chains are transfected separately so as to form Fabs with the VHs. Amino acid sequences of illustrative PD-1-targeted x IL-15/Rα-Fc fusion protein of the mAb x scIL-15/Rα format are provided in Figures 72A-72B.

[00385] In some embodiments, the first monomer comprises a heavy chain, VH-CH1-hinge-CH2-CH3. The second monomer comprises a heavy chain with a scIL-15 complex, VH-CH1-hinge-CH2-CH3-domain linker- IL-15Rα sushi domain-domain linker-IL-15. The third (and fourth) monomer are light chains, VL-CL. This is generally referred to as “mAb-scIL-15/Rα”, with the “sc” standing for “single chain”.

[00386] In the mAb-scIL-15/Rα format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence 1G6_L1.194_H1.279 as shown in Figure 14. In the mAb-scIL-15/Rα format, one preferred embodiment utilizes the skew variant pair S364K/E357Q : L368D/K370S. In the mAb-scIL-15/Rα format, one preferred embodiment utilizes the anti-

PD-1 ABD having the sequence 1G6_L1.194_H1.279 as shown in Figure 14, in a useful format of Figures 8A-8F.

[00387] In the mAb-scIL-15/Rα format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence 1C11[PD-1]_H3L3 as shown in Figure 20C.

[00388] In the mAb-scIL-15/Rα format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence 1C11[PD-1]_H3L3 as shown in Figure 20C and the skew variant pair S364K/E357Q : L368D/K370S. In the mAb-scIL-15/Rα format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence 1C11[PD-1]_H3L3 as shown in Figure 20C in a useful format of Figures 8A-8F.

[00389] In some embodiments, the mAb-scIL-15/Rα comprises any of the anti-PD-1 ABDs described herein. In some embodiments, the mAb-scIL-15/Rα comprises an anti-PD-1 ABD comprising: heavy chain and light chain sequences of XENP25806 or 1C11[PD-1]_H3.234_L3.144, as depicted in Figure 93R, heavy chain and light chain sequences of the ABD of XENP25812 or 1C11[PD-1]_H3.240_L3.148, as depicted in Figure 93R, heavy chain and light chain sequences of XENP25813 or 1C11[PD-1]_H3.241_L3.148, as depicted in Figure 93R, or heavy chain and light chain sequences of XENP25819 or 1C11[PD-1]_H3.241_L3.92, as depicted in Figure 93S. In some embodiments, the mAb-scIL-15/Rα of the invention comprises an anti-PD-1 ABD having the sequence of XENP26940 or 1C11_H3.303_L3.152 as shown in Figure 94N. In some embodiments, the mAb-scIL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP28026 or 1C11_H3.329_L3.220 as shown in Figure 94AE. In some embodiments, the mAb-scIL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP28652 or 1C11_H3.328_L3.152 as shown in Figure 94AG.

[00390] In the mAb-scIL-15/Rα format, one preferred embodiment utilizes any of the IL-15 complex sequences described herein. In some embodiments, the IL-15 complex comprises from N- to C-terminus: a human IL-15 Rα sushi domain, a domain linker, and a human mature IL-15 domain (such as a human mature IL-15 variant). In some embodiments, the IL-15 complex comprises from N- to C-terminus: a human IL-15 Rα sushi domain, a domain linker, and a human mature IL-15 variant having amino acid substitutions N4D/N65D. In some embodiments, the IL-15 complex comprises from N- to C-terminus: a human IL-15 Rα sushi domain, a domain linker, and a human mature IL-15 variant having amino acid substitutions D30N/N65D. In some embodiments, the IL-15 complex comprises

from N- to C-terminus: a human IL-15 Rα sushi domain, a domain linker, and a human mature IL-15 variant having amino acid substitutions D30N/E64Q/N65D.

[00391] In the mAb-scIL-15/Rα format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence of 1C11_H3L3 as shown in Figure 94A and the IL-15 complex (sushi domain-linker-IL-15) such as in chain 1 of XENP22022 as depicted in Figure 69A. In some embodiments, the mAb-scIL-15/Rα comprises anti-PD-1 ABD having the sequence of 1C11_H3L3 as shown in Figure 94A and the IL-15 complex (sushi domain-linker-IL-15 variant N4D/N65D) such as in chain 2 of XENP25850 as depicted in Figure 69C. In some embodiments, the mAb-scIL-15/Rα comprises anti-PD-1 ABD having the sequence of 1C11_H3L3 as shown in Figure 94A and the IL-15 complex (sushi domain-linker-IL-15 variant D30N/N65D) such as in chain 1 of XENP29482 as depicted in Figure 126A. In some embodiments, the mAb-scIL-15/Rα comprises anti-PD-1 ABD having the sequence of 1C11_H3L3 as shown in Figure 94A and the IL-15 complex (sushi domain-linker-IL-15 variant D30N/E64Q/N65D) such as in chain 1 of XENP29286 as depicted in Figure 124C.

[00392] In some embodiments, the mAb-scIL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP26940 or 1C11_H3.303_L3.152 as shown in Figure 94N, a human IL-15 Rα(sushi) domain, and a human mature IL-15 (including a human mature IL-15 variant). In some embodiments, the mAb-scIL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP26940 or 1C11_H3.303_L3.152 as shown in Figure 94N, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions N4D/N65D. In some embodiments, the mAb-scIL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP26940 or 1C11_H3.303_L3.152 as shown in Figure 94N, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions D30N/N65D. In some embodiments, the mAb-scIL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP26940 or 1C11_H3.303_L3.152 as shown in Figure 94N, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions D30N/E64Q/N65D.

[00393] In some embodiments, the mAb-scIL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP28026 or 1C11_H3.329_L3.220 as shown in Figure 94AE, a human IL-15 Rα(sushi) domain, and a human mature IL-15 (including a human mature IL-15 variant). In some embodiments, the mAb-scIL-15/Rα comprises an anti-PD-1 ABD having

the sequence of XENP28026 or 1C11_H3.329_L3.220 as shown in Figure 94AE, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions N4D/N65D. In some embodiments, the mAb-scIL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP28026 or 1C11_H3.329_L3.220 as shown in Figure 94AE, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions D30N/N65D. In some embodiments, the mAb-scIL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP28026 or 1C11_H3.329_L3.220 as shown in Figure 94AE, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions D30N/E64Q/N65D.

[00394] In some embodiments, the mAb-scIL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP28652 or 1C11_H3.328_L3.152 as shown in Figure 94AG, a human IL-15 Rα(sushi) domain, and a human mature IL-15 (including a human mature IL-15 variant). In some embodiments, the mAb-scIL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP28652 or 1C11_H3.328_L3.152 as shown in Figure 94AG, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions N4D/N65D. In some embodiments, the mAb-scIL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP28652 or 1C11_H3.328_L3.152 as shown in Figure 94AG, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions D30N/N65D. In some embodiments, the mAb-scIL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP28652 or 1C11_H3.328_L3.152 as shown in Figure 94AG, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions D30N/E64Q/N65D.

H. mAb-ncIL-15/Rα

[00395] This embodiment is shown in Figure 65H, and comprises four monomers (although the heterodimeric fusion protein is a pentamer). This is generally referred to as "mAb-ncIL-15/Rα", with the "nc" standing for "non-covalent". The mAb-ncIL-15/Rα format (Figure 65H) comprises VH fused to the N-terminus of a first and a second heterodimeric Fc, with IL-15Rα(sushi) fused to the C-terminus of one of the heterodimeric Fc-region, while corresponding light chains are transfected separately so as to form Fabs with the VHs, and while IL-15 is transfected separately so that a non-covalent IL-15/Rα complex is formed. Amino acid sequences of illustrative IL-15/Rα x anti-PD-1 heterodimeric proteins

of the mAb x ncIL-15/Rα format such as XENP22642 and XENP22643 are provided in Figures 73A-73B.

[00396] In some embodiments, the first monomer comprises a heavy chain, VH-CH1-hinge-CH2-CH3. The second monomer comprises a heavy chain with an IL-15Rα(sushi) domain, VH-CH1-hinge-CH2-CH3-domain linker-sushi domain. The third monomer is an IL-15 domain. The fourth (and fifth) monomer are light chains, VL-CL. Preferred combinations of Fc variants for this embodiment are found in Figures 8A-8F.

[00397] In the mAb-ncIL-15/Rα format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence 1G6_L1.194_H1.279 as shown in Figure 14. In the mAb-ncIL-15/Rα format, one preferred embodiment utilizes the skew variant pair S364K/E357Q : L368D/K370S. In the mAb-ncIL-15/Rα format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence 1G6_L1.194_H1.279 as shown in Figure 14, in a useful format of Figures 8A-8F.

[00398] In the mAb-ncIL-15/Rα format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence 1C11[PD-1]_H3L3 as shown in Figure 20C.

[00399] In the mAb-ncIL-15/Rα format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence 1C11[PD-1]_H3L3 as shown in Figure 20C and the skew variant pair S364K/E357Q : L368D/K370S. In the mAb-ncIL-15/Rα format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence 1C11[PD-1]_H3L3 as shown in Figure 20C in a useful format of Figures 8A-8F.

[00400] In some embodiments, the mAb-ncIL-15/Rα comprises any of the anti-PD-1 ABDs described herein. In some embodiments, the mAb-ncIL-15/Rα comprises an anti-PD-1 ABD comprising: heavy chain and light chain sequences of XENP25806 or 1C11[PD-1]_H3.234_L3.144, as depicted in Figure 93R, heavy chain and light chain sequences of the ABD of XENP25812 or 1C11[PD-1]_H3.240_L3.148, as depicted in Figure 93R, heavy chain and light chain sequences of XENP25813 or 1C11[PD-1]_H3.241_L3.148, as depicted in Figure 93R, or heavy chain and light chain sequences of XENP25819 or 1C11[PD-1]_H3.241_L3.92, as depicted in Figure 93S. In some embodiments, mAb-ncIL-15/Rα of the invention comprises an anti-PD-1 ABD having the sequence of XENP26940 or 1C11_H3.303_L3.152 as shown in Figure 94N. In some embodiments, the mAb-ncIL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP28026 or 1C11_H3.329_L3.220

as shown in Figure 94AE. In some embodiments, the mAb-ncIL-15/Rα comprises an anti-PD-1 ABD having the sequence XENP28652 or 1C11_H3.328_L3.152 as shown in Figure 94AG.

[00401] In the mAb-ncIL-15/Rα format, one preferred embodiment utilizes any of the IL-15 complex sequences described herein.

[00402] In the mAb-ncIL-15/Rα format, one preferred embodiment utilizes any of the IL-15 complex sequences described herein. In some embodiments, the IL-15 complex comprises a human IL-15 Rα sushi domain and a human mature IL-15 domain (such as a human mature IL-15 variant). In some embodiments, the IL-15 complex comprises a human IL-15 Rα sushi domain and a human mature IL-15 variant having amino acid substitutions N4D/N65D. In some embodiments, the IL-15 complex comprises a human IL-15 Rα sushi domain and a human mature IL-15 variant having amino acid substitutions D30N/N65D. In some embodiments, the IL-15 complex comprises a human IL-15 Rα sushi domain and a human mature IL-15 variant having amino acid substitutions D30N/E64Q/N65D.

[00403] In some embodiments, the mAb-ncIL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP26940 or 1C11_H3.303_L3.152 as shown in Figure 94N, a human IL-15 Rα(sushi) domain, and a human mature IL-15 (including a human mature IL-15 variant). In some embodiments, the mAb-ncIL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP26940 or 1C11_H3.303_L3.152 as shown in Figure 94N, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions N4D/N65D. In some embodiments, the mAb-ncIL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP26940 or 1C11_H3.303_L3.152 as shown in Figure 94N, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions D30N/N65D. In some embodiments, the mAb-ncIL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP26940 or 1C11_H3.303_L3.152 as shown in Figure 94N, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions D30N/E64Q/N65D.

[00404] In some embodiments, the mAb-ncIL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP28026 or 1C11_H3.329_L3.220 as shown in Figure 94AE, a human IL-15 Rα(sushi) domain, and a human mature IL-15 (including a human mature IL-15 variant). In some embodiments, the mAb-ncIL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP28026 or 1C11_H3.329_L3.220 as shown in Figure 94AE, a human

IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions N4D/N65D. In some embodiments, the mAb-ncIL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP28026 or 1C11_H3.329_L3.220 as shown in Figure 94AE, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions D30N/N65D. In some embodiments, the mAb-ncIL-15/Rα comprises an anti-PD-1 ABD having the sequence o of XENP28026 or f 1C11_H3.329_L3.220 as shown in Figure 94AE, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions D30N/E64Q/N65D.

[00405] In some embodiments, the mAb-ncIL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP28652 or 1C11_H3.328_L3.152 as shown in Figure 94AG, a human IL-15 Rα(sushi) domain, and a human mature IL-15 (including a human mature IL-15 variant). In some embodiments, the mAb-ncIL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP28652 or 1C11_H3.328_L3.152 as shown in Figure 94AG, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions N4D/N65D. In some embodiments, the mAb-ncIL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP28652 or 1C11_H3.328_L3.152 as shown in Figure 94AG, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions D30N/N65D. In some embodiments, the mAb-ncIL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP28652 or 1C11_H3.328_L3.152 as shown in Figure 94AG, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions D30N/E64Q/N65D.

I. **mAb-dsIL-15/Rα**

[00406] This embodiment is shown in Figure 65I, and comprises four monomers (although the heterodimeric fusion protein is a pentamer). This is generally referred to as "mAb-ncIL-15/Rα", with the "nc" standing for "non-covalent". The mAb-ncIL-15/Rα format (see Figure 65H) comprises VH fused to the N-terminus of a first and a second heterodimeric Fc, with IL-15Rα(sushi) fused to the C-terminus of one of the heterodimeric Fc-region, while corresponding light chains are transfected separately so as to form a Fabs with the VHs, and while and while IL-15 is transfected separately so that a non-covalent IL-15/Rα complex is formed. Amino acid sequences of illustrative IL-15/Rα x anti-PD-1 heterodimeric proteins of the mAb x dsIL-15/Rα format such as XENP22644 and XENP22645 are provided in Figures 74A-74B.

[00407] In some embodiments, the anti-PD-1 ABD includes the sequence Nivolumab_H0 as shown in chain 2 and chain 3 of Figures 74A and 74B. In some embodiments, the anti-PD-1 ABD includes the sequence Nivolumab_L0 as shown in chain 4 of Figures 74A and 74B.

[00408] The first monomer comprises a heavy chain, VH-CH1-hinge-CH2-CH3. The second monomer comprises a heavy chain with an IL-15Rα(sushi) domain: VH-CH1-hinge-CH2-CH3-domain linker-sushi domain, where the sushi domain has been engineered to contain a cysteine residue. The third monomer is an IL-15 domain, which has been engineered to contain a cysteine residue, such that the IL-15 complex is formed under physiological conditions. The fourth (and fifth) monomer are light chains, VL-CL. Useful combinations of Fc variants for this embodiment are found in Figures 8A-8F.

[00409] In the mAb-dsIL-15/Rα format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence 1G6_L1.194_H1.279 as shown in Figure 14.

[00410] In the mAb-dsIL-15/Rα format, one preferred embodiment utilizes the skew variant pair S364K/E357Q : L368D/K370S. In some embodiments, the mAb-dsIL-15/Rα comprises an anti-PD-1 ABD having the sequence 1G6_L1.194_H1.279 as shown in Figure 14 and the skew variant pair S364K/E357Q : L368D/K370S. In some embodiments, the mAb-dsIL-15/Rα comprises an anti-PD-1 ABD having the sequence 1G6_L1.194_H1.279 as shown in Figure 14, in a useful format of Figures 8A-8F.

[00411] In the mAb-dsIL-15/Rα format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence 1C11[PD-1]_H3L3 as shown in Figure 20C.

[00412] In some embodiments, the mAb-dsIL-15/Rα comprises the skew variant pair S364K/E357Q : L368D/K370S. In some embodiments, the mAb-dsIL-15/Rα comprises the anti-PD-1 ABD having the sequence 1C11[PD-1]_H3L3 as shown in Figure 20C and the skew variant pair S364K/E357Q : L368D/K370S. In the mAb-dsIL-15/Rα format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence 1C11[PD-1]_H3L3 as shown in Figure 20C, in a useful format of Figures 8A-8F.

[00413] In some embodiments, the mAb-dsIL-15/Rα comprises any of the anti-PD-1 ABDs described herein. In some embodiments, the mAb-dsIL-15/Rα comprises an anti-PD-1 ABD comprising: heavy chain and light chain sequences of XENP25806 or 1C11[PD-1]_H3.234_L3.144, as depicted in Figure 93R, heavy chain and light chain sequences of the

ABD of XENP25812 or 1C11[PD-1]_H3.240_L3.148, as depicted in Figure 93R, heavy chain and light chain sequences of XENP25813 or 1C11[PD-1]_H3.241_L3.148, as depicted in Figure 93R, or heavy chain and light chain sequences of XENP25819 or 1C11[PD-1]_H3.241_L3.92, as depicted in Figure 93S. In some embodiments, mAb-dsIL-15/Rα of the invention comprises an anti-PD-1 ABD having the sequence of XENP26940 or 1C11_H3.303_L3.152 as shown in Figure 94N. In some embodiments, the mAb-dsIL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP28026 or 1C11_H3.329_L3.220 as shown in Figure 94AE. In some embodiments, the mAb-dsIL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP28652 or 1C11_H3.328_L3.152 as shown in Figure 94AG.

[00414] In the mAb-dsIL-15/Rα format, one preferred embodiment utilizes any of the IL-15 complex sequences described herein. In the mAb-dsIL-15/Rα format, one preferred embodiment utilizes any of the IL-15 complex sequences described herein. In some embodiments, the IL-15 complex comprises a human IL-15 Rα sushi domain and a human mature IL-15 domain (such as a human mature IL-15 variant). In some embodiments, the IL-15 complex comprises a human IL-15 Rα sushi domain and a human mature IL-15 variant having amino acid substitutions N4D/N65D. In some embodiments, the IL-15 complex comprises a human IL-15 Rα sushi domain and a human mature IL-15 variant having amino acid substitutions D30N/N65D. In some embodiments, the IL-15 complex comprises a human IL-15 Rα sushi domain and a human mature IL-15 variant having amino acid substitutions D30N/E64Q/N65D.

[00415] In some embodiments, the mAb-dsIL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP26940 or 1C11_H3.303_L3.152 as shown in Figure 94N, a human IL-15 Rα(sushi) domain, and a human mature IL-15 (including a human mature IL-15 variant). In some embodiments, the mAb-dsIL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP26940 or 1C11_H3.303_L3.152 as shown in Figure 94N, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions N4D/N65D. In some embodiments, the mAb-dsIL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP26940 or 1C11_H3.303_L3.152 as shown in Figure 94N, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions D30N/N65D. In some embodiments, the mAb-dsIL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP26940 or 1C11_H3.303_L3.152 as shown in Figure

94N, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions D30N/E64Q/N65D.

[00416] In some embodiments, the mAb-dsIL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP28026 or 1C11_H3.329_L3.220 as shown in Figure 94AE, a human IL-15 Rα(sushi) domain, and a human mature IL-15 (including a human mature IL-15 variant). In some embodiments, the mAb-dsIL-15/Rα comprises an anti-PD-1 ABD having the sequence XENP28026 or 1C11_H3.329_L3.220 as shown in Figure 94AE, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions N4D/N65D. In some embodiments, the mAb-dsIL-15/Rα comprises an anti-PD-1 ABD having the sequence XENP28026 or 1C11_H3.329_L3.220 as shown in Figure 94AE, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions D30N/N65D. In some embodiments, the mAb-dsIL-15/Rα comprises an anti-PD-1 ABD having the sequence XENP28026 or 1C11_H3.329_L3.220 as shown in Figure 94AE, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions D30N/E64Q/N65D.

[00417] In some embodiments, the mAb-dsIL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP28652 or 1C11_H3.328_L3.152 as shown in Figure 94AG, a human IL-15 Rα(sushi) domain, and a human mature IL-15 (including a human mature IL-15 variant). In some embodiments, the mAb-dsIL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP28652 or 1C11_H3.328_L3.152 as shown in Figure 94AG, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions N4D/N65D. In some embodiments, the mAb-dsIL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP28652 or 1C11_H3.328_L3.152 as shown in Figure 94AG, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions D30N/N65D. In some embodiments, the mAb-dsIL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP28652 or 1C11_H3.328_L3.152 as shown in Figure 94AG, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions D30N/E64Q/N65D.

J. Central-IL-15/Rα

[00418] This embodiment is shown in Figure 65J, and comprises four monomers forming a tetramer. This is generally referred to as "Central-IL-15/Rα". The central-IL-15/Rα format (see Figure 65J) comprises a VH recombinantly fused to the N-terminus of IL-

15 which is then further fused to one side of a heterodimeric Fc and a VH recombinantly fused to the N-terminus of IL-15Rα(sushi) which is then further fused to the other side of the heterodimeric Fc, while corresponding light chains are transfected separately so as to form a Fabs with the VHs. Amino acid sequences of illustrative IL-15/Rα x anti-PD-1 heterodimeric proteins of the central-IL-15/Rα format are provided in Figure 75.

[00419] In some embodiments, the anti-PD-1 ABD includes the sequence 1C11[PD-1]_H3 as shown in chain 1 and chain 2 of Figure 75. In some embodiments, the anti-PD-1 ABD includes the sequence 1C11[PD-1]_L3 as shown in chain 3 of Figure 75.

[00420] In the central-IL-15/Rα format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence 1G6_L1.194_H1.279 as shown in Figure 14.

[00421] In the central-IL-15/Rα format, one preferred embodiment utilizes the skew variant pair S364K/E357Q : L368D/K370S. In some embodiments, the central-IL-15/Rα comprises an anti-PD-1 ABD having the sequence 1G6_L1.194_H1.279 as shown in Figure 14 and the skew variant pair S364K/E357Q : L368D/K370S. In some embodiments, the mAb-dsIL-15/Rα comprises an anti-PD-1 ABD having the sequence 1G6_L1.194_H1.279 as shown in Figure 14, in a useful format of Figures 8A-8F.

[00422] In the central-IL-15/Rα format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence 1C11[PD-1]_H3L3 as shown in Figure 20C.

[00423] In some embodiments, the central-IL-15/Rα comprises the skew variant pair S364K/E357Q : L368D/K370S. In some embodiments, the central-IL-15/Rα comprises the anti-PD-1 ABD having the sequence 1C11[PD-1]_H3L3 as shown in Figure 20C and the skew variant pair S364K/E357Q : L368D/K370S. In the central-IL-15/Rα format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence 1C11[PD-1]_H3L3 as shown in Figure 20C, in a useful format of Figures 8A-8F.

[00424] In some embodiments, the central-IL-15/Rα comprises any of the anti-PD-1 ABDs described herein. In some embodiments, the central-IL-15/Rα comprises an anti-PD-1 ABD comprising: heavy chain and light chain sequences of XENP25806 or 1C11[PD-1]_H3.234_L3.144, as depicted in Figure 93R, heavy chain and light chain sequences of the ABD of XENP25812 or 1C11[PD-1]_H3.240_L3.148, as depicted in Figure 93R, heavy chain and light chain sequences of XENP25813 or 1C11[PD-1]_H3.241_L3.148, as depicted in Figure 93R, or heavy chain and light chain sequences of XENP25819 or 1C11[PD-

1]_H3.241_L3.92, as depicted in Figure 93S. In some embodiments, central-IL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP26940 or 1C11_H3.303_L3.152 as shown in Figure 94N. In some embodiments, the central-IL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP28026 or 1C11_H3.329_L3.220 as shown in Figure 94AE. In some embodiments, the central-IL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP28652 or 1C11_H3.328_L3.152 as shown in Figure 94AG.

[00425] In the central-IL-15/Rα format, one preferred embodiment utilizes any of the IL-15 complex sequences described herein. In the central-IL-15/Rα format, one preferred embodiment utilizes any of the IL-15 complex sequences described herein. In some embodiments, the IL-15 complex comprises a human IL-15 Rα sushi domain and a human mature IL-15 domain (such as a human mature IL-15 variant). In some embodiments, the IL-15 complex comprises a human IL-15 Rα sushi domain and a human mature IL-15 variant having amino acid substitutions N4D/N65D. In some embodiments, the IL-15 complex comprises a human IL-15 Rα sushi domain and a human mature IL-15 variant having amino acid substitutions D30N/N65D. In some embodiments, the IL-15 complex comprises a human IL-15 Rα sushi domain and a human mature IL-15 variant having amino acid substitutions D30N/E64Q/N65D.

[00426] In some embodiments, the central-IL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP26940 or 1C11_H3.303_L3.152 as shown in Figure 94N, a human IL-15 Rα(sushi) domain, and a human mature IL-15 (including a human mature IL-15 variant). In some embodiments, the central-IL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP26940 or 1C11_H3.303_L3.152 as shown in Figure 94N, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions N4D/N65D. In some embodiments, the central-IL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP26940 or 1C11_H3.303_L3.152 as shown in Figure 94N, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions D30N/N65D. In some embodiments, the central-IL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP26940 or 1C11_H3.303_L3.152 as shown in Figure 94N, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions D30N/E64Q/N65D.

[00427] In some embodiments, the central-IL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP28026 or 1C11_H3.329_L3.220 as shown in Figure 94AE, a

human IL-15 Rα(sushi) domain, and a human mature IL-15 (including a human mature IL-15 variant). In some embodiments, the central-IL-15/Rα comprises an anti-PD-1 ABD having the sequence XENP28026 or 1C11_H3.329_L3.220 as shown in Figure 94AE, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions N4D/N65D. In some embodiments, the central-IL-15/Rα comprises an anti-PD-1 ABD having the sequence XENP28026 or 1C11_H3.329_L3.220 as shown in Figure 94AE, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions D30N/N65D. In some embodiments, the central-IL-15/Rα comprises an anti-PD-1 ABD having the sequence XENP28026 or 1C11_H3.329_L3.220 as shown in Figure 94AE, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions D30N/E64Q/N65D.

[00428] In some embodiments, the central-IL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP28652 or 1C11_H3.328_L3.152 as shown in Figure 94AG, a human IL-15 Rα(sushi) domain, and a human mature IL-15 (including a human mature IL-15 variant). In some embodiments, the central-IL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP28652 or 1C11_H3.328_L3.152 as shown in Figure 94AG, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions N4D/N65D. In some embodiments, the central-IL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP28652 or 1C11_H3.328_L3.152 as shown in Figure 94AG, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions D30N/N65D. In some embodiments, the central-IL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP28652 or 1C11_H3.328_L3.152 as shown in Figure 94AG, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions D30N/E64Q/N65D.

K. Central scIL-15/Rα

[00429] This embodiment is shown in Figure 64K, and comprises four monomers forming a tetramer. This is generally referred to as “central-scIL-15/Rα”, with the “sc” standing for “single chain”. The central-scIL-15/Rα format (see Figure 65K) comprises a VH fused to the N-terminus of IL-15Rα(sushi) which is fused to IL-15 which is then further fused to one side of a heterodimeric Fc and a VH fused to the other side of the heterodimeric Fc, while corresponding light chains are transfected separately so as to form a Fabs with the VHs.

Amino acid sequences of illustrative IL-15/Rα x anti-PD-1 heterodimeric proteins of the central-scIL-15/Rα format are provided in Figure 76.

[00430] In some embodiments, the anti-PD-1 ABD includes the sequence 1C11[PD-1]_H3 as shown in chain 1 and chain 2 of Figure 76. In some embodiments, the anti-PD-1 ABD includes the sequence 1C11[PD-1]_L3 as shown in chain 3 of Figure 76.

[00431] The first monomer comprises a VH-CH1-[optional domain linker]-sushi domain-domain linker-IL-15-[optional domain linker]-CH2-CH3, with the second optional domain linker sometimes being the hinge domain. The second monomer comprises a VH-CH1-hinge-CH2-CH3. The third (and fourth) monomers are light chains, VL-CL. Preferred combinations of variants for this embodiment are found in Figures 8A-8F.

[00432] In the central-scIL-15/Rα format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence 1G6_L1.194_H1.279 as shown in Figure 14.

[00433] In the central-scIL-15/Rα format, one preferred embodiment utilizes the skew variant pair S364K/E357Q : L368D/K370S. In some embodiments, the central-scIL-15/Rα comprises an anti-PD-1 ABD having the sequence 1G6_L1.194_H1.279 as shown in Figure 14 and the skew variant pair S364K/E357Q : L368D/K370S. In some embodiments, the central-scIL-15/Rα comprises an anti-PD-1 ABD having the sequence 1G6_L1.194_H1.279 as shown in Figure 14, in a useful format of Figures 8A-8F.

[00434] In the central-scIL-15/Rα format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence 1C11[PD-1]_H3L3 as shown in Figure 20C.

[00435] In some embodiments, the central-scIL-15/Rα comprises the skew variant pair S364K/E357Q : L368D/K370S. In some embodiments, the central-scIL-15/Rα comprises the anti-PD-1 ABD having the sequence 1C11[PD-1]_H3L3 as shown in Figure 20C and the skew variant pair S364K/E357Q : L368D/K370S. In the central-scIL-15/Rα format, one preferred embodiment utilizes the anti-PD-1 ABD having the sequence 1C11[PD-1]_H3L3 as shown in Figure 20C, in a useful format of Figures 8A-8F.

[00436] In some embodiments, the central-scIL-15/Rα comprises any of the anti-PD-1 ABDs described herein. I In some embodiments, the central-scIL-15/Rα comprises an anti-PD-1 ABD comprising: heavy chain and light chain sequences of XENP25806 or 1C11[PD-1]_H3.234_L3.144, as depicted in Figure 93R, heavy chain and light chain sequences of the ABD of XENP25812 or 1C11[PD-1]_H3.240_L3.148, as depicted in Figure 93R, heavy

chain and light chain sequences of XENP25813 or 1C11[PD-1]_H3.241_L3.148, as depicted in Figure 93R, or heavy chain and light chain sequences of XENP25819 or 1C11[PD-1]_H3.241_L3.92, as depicted in Figure 93S. n some embodiments, central-scIL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP26940 or 1C11_H3.303_L3.152 as shown in Figure 94N. In some embodiments, the central-scIL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP28026 or 1C11_H3.329_L3.220 as shown in Figure 94AE. In some embodiments, the central-scIL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP28652 or 1C11_H3.328_L3.152 as shown in Figure 94AG.

[00437] In the central-scIL-15/Rα format, one preferred embodiment utilizes any of the IL-15 complex sequences described herein. In some embodiments, the IL-15 complex comprises from N- to C-terminus: a human IL-15Rα sushi domain, a domain linker, and a human mature IL-15 domain (such as a human mature IL-15 variant). In some embodiments, the IL-15 complex comprises from N- to C-terminus: a human IL-15 Rα sushi domain, a domain linker, and a human mature IL-15 variant having amino acid substitutions N4D/N65D. In some embodiments, the IL-15 complex comprises from N- to C-terminus: a human IL-15 Rα sushi domain, a domain linker, and a human mature IL-15 variant having amino acid substitutions D30N/N65D. In some embodiments, the IL-15 complex comprises from N- to C-terminus: a human IL-15 Rα sushi domain, a domain linker, and a human mature IL-15 variant having amino acid substitutions D30N/E64Q/N65D.

[00438] In some embodiments, the central-scIL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP26940 or 1C11_H3.303_L3.152 as shown in Figure 94N, a human IL-15 Rα(sushi) domain, and a human mature IL-15 (including a human mature IL-15 variant). In some embodiments, the central-scIL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP26940 or 1C11_H3.303_L3.152 as shown in Figure 94N, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions N4D/N65D. In some embodiments, the central-scIL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP26940 or 1C11_H3.303_L3.152 as shown in Figure 94N, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions D30N/N65D. In some embodiments, the central-scIL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP26940 or 1C11_H3.303_L3.152 as shown in Figure 94N, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions D30N/E64Q/N65D.

[00439] In some embodiments, the central-scIL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP28026 or 1C11_H3.329_L3.220 as shown in Figure 94AE, a human IL-15 Rα(sushi) domain, and a human mature IL-15 (including a human mature IL-15 variant). In some embodiments, the central-scIL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP28026 or 1C11_H3.329_L3.220 as shown in Figure 94AE, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions N4D/N65D. In some embodiments, the central-scIL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP28026 or 1C11_H3.329_L3.220 as shown in Figure 94AE, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions D30N/N65D. In some embodiments, the central-scIL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP28026 or 1C11_H3.329_L3.220 as shown in Figure 94AE, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions D30N/E64Q/N65D.

[00440] In some embodiments, the central-scIL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP28652 or 1C11_H3.328_L3.152 as shown in Figure 94AG, a human IL-15 Rα(sushi) domain, and a human mature IL-15 (including a human mature IL-15 variant). In some embodiments, the central-scIL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP28652 or 1C11_H3.328_L3.152 as shown in Figure 94AG, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions N4D/N65D. In some embodiments, the central-scIL-15/Rα comprises an anti-PD-1 ABD having the sequence o of XENP28652 or f 1C11_H3.328_L3.152 as shown in Figure 94AG, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions D30N/N65D. In some embodiments, the central-scIL-15/Rα comprises an anti-PD-1 ABD having the sequence of XENP28652 or 1C11_H3.328_L3.152 as shown in Figure 94AG, a human IL-15 Rα(sushi) domain, and a human mature IL-15 variant having amino acid substitutions D30N/E64Q/N65D.

V. **IL-15/IL-15Rα –Fc Fusion Monomers**

[00441] The Fc fusion proteins of the present invention include an IL-15/IL-15 receptor alpha (IL-15Rα)-Fc fusion monomer; reference is made to WO2018/171918, WO2018/071919, US2018/0118805, US2018/0118828, USSN62/408,655, filed on October 14, 2016, USSN62/443,465, filed on January 6, 2017, and USSN62/477,926, filed on March

28, 2017, hereby incorporated by reference in their entirety and in particular for the figures, figure legends, and sequences outlined therein.

[00442] In some embodiments, the human IL-15 protein has the amino acid sequence set forth in NCBI Ref. Seq. No. NP_000576.1 or SEQ ID NO:1. In some cases, the coding sequence of human IL-15 is set forth in NCBI Ref. Seq. No. NM_000585. An exemplary IL-15 protein of the Fc fusion heterodimeric protein outlined herein can have the amino acid sequence of SEQ ID NO:2 or amino acids 49-162 of SEQ ID NO:1.

[00443] SEQ ID NO:1 is
MRISKPHLRSISIQCYLCLLLNSHFLTEAGIHVFILGCFSAGLPKTEANWVNVISDLKKI
EDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVENLIILAN
NSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS.

[00444] SEQ ID NO:2 is
NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDAS
IHDTVENLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS.

[00445] In some embodiments, the IL-15 protein has at least 90%, e.g., 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more sequence identity to SEQ ID NO:2. In some embodiments, the IL-15 protein has the amino acid sequence of SEQ ID NO:2 and one or more amino acid substitutions selected from the group consisting of C42S, L45C, Q48C, V49C, L52C, E53C, E87C, and E89C. In some embodiments, the IL-15 protein has one or more amino acid substitutions selected from the group consisting of N1D, N4D, D8N, D30N, D61N, E64Q, N65D, and Q108E. The IL-15 protein of the Fc fusion protein can have 1, 2, 3, 4, 5, 6, 7, 8, 9 or more amino acid substitutions. In some embodiments, the IL-15 protein has the amino acid sequence of SEQ ID NO:2 and one or more amino acid substitutions selected from the group consisting of N1D, N4D, D8N, D30N, D61N, E64Q, N65D, and Q108E. In other embodiments, the amino acid substitutions are N4D/N65D. In other embodiments, the amino acid substitutions are D30N/E64Q/N65D. In some instances, the amino acid substitutions are D30N/N65D. In some embodiments, the IL-15 protein has at least 97% or 98% sequence identity to SEQ ID NO:2 and N4D/N65D substitutions. In some embodiments, the IL-15 protein has at least 97% or 98% sequence identity to SEQ ID NO:2 and D30N/N65D substitutions. In some embodiments, the IL-15 protein has at least 96% or 97% sequence identity to SEQ ID NO:2 and D30N/N65D substitutions.

[00446] In some embodiments, the human IL-15 receptor alpha (IL-15Rα) protein has the amino acid sequence set forth in NCBI Ref. Seq. No. NP_002180.1 or SEQ ID NO:3. In some cases, the coding sequence of human IL-15Rα is set forth in NCBI Ref. Seq. No. NM_002189.3. An exemplary the IL-15Rα protein of the Fc fusion heterodimeric protein outlined herein can comprise or consist of the sushi domain of SEQ ID NO:3 (e.g., amino acids 31-95 of SEQ ID NO:3), or in other words, the amino acid sequence of SEQ ID NO:4.

[00447] SEQ ID NO:3 is MAPRRARGCRTLGLPALLLLLLLRPPATRGITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIRDPALVHQRPAPPSTVTTAGVTPQPESLSPSGKEPAASSPSSNNTAATTAAIVPGSQLMPSKSPSTGTTEISSHESSHGTPSQTTAKNWELTASASHQPPGVYPQGHSDTTVAISTSTVLLCGLSAVSLLACYLKSRQTPPLASVEMEAMEALPVTWGTSSRDEDLENCSHHL.

[00448] SEQ ID NO:4 is ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR.

[00449] In some embodiments, the IL-15Rα protein has the amino acid sequence of SEQ ID NO:4 and an amino acid insertion selected from the group consisting of D96, P97, A98, D96/P97, D96/C97, D96/P97/A98, D96/P97/C98, and D96/C97/A98, wherein the amino acid position is relative to full-length human IL-15Rα protein or SEQ ID NO:3. For instance, amino acid(s) such as D (e.g., Asp), P (e.g., Pro), A (e.g., Ala), DP (e.g., Asp-Pro), DC (e.g., Asp-Cys), DPA (e.g., Asp-Pro-Ala), DPC (e.g., Asp-Pro-Cys), or DCA (e.g., Asp-Cys-Ala) can be added to the C-terminus of the IL-15Rα protein of SEQ ID NO:4. In some embodiments, the IL-15Rα protein has the amino acid sequence of SEQ ID NO:4 and one or more amino acid substitutions selected from the group consisting of K34C, A37C, G38C, S40C, and L42C, wherein the amino acid position is relative to SEQ ID NO:4. The IL-15Rα protein can have 1, 2, 3, 4, 5, 6, 7, 8 or more amino acid mutations (e.g., substitutions, insertions and/or deletions).

VI. **Domain Linkers**

[00450] In some embodiments, an IL-15 protein is attached to the N-terminus of an Fc domain, and an IL-15Rα protein is attached to the N-terminus of the IL-15 protein. In other embodiments, an IL-15Rα protein is attached to the N-terminus of an Fc domain and the IL-

15Rα protein is non-covalently attached to an IL-15 protein. In yet other embodiments, an IL-15Rα protein is attached to the C-terminus of an Fc domain and the IL-15Rα protein is non-covalently attached to an IL-15 protein.

[00451] In some embodiments, the IL-15 protein and IL-15Rα protein are attached together via a linker (e.g., a "scIL-15/Rα" format). Optionally, the proteins are not attached via a linker, and utilize either native self-assembly or disulfide bonds as outlined herein. In other embodiments, the IL-15 protein and IL-15Rα protein are noncovalently attached. In some embodiments, the IL-15 protein is attached to an Fc domain via a linker. In certain embodiments, the IL-15 protein is attached to an Fc domain directly, such as without a linker. In particular embodiments, the IL-15 protein is attached to an Fc domain via a hinge region or a fragment thereof. In other embodiments, the IL-15Rα protein is attached to an Fc domain via a linker. In other embodiments, the IL-15Rα protein is attached to an Fc domain directly, such as without a linker. In particular embodiments, the IL-15Rα protein is attached to an Fc domain via a hinge region or a fragment thereof. Optionally, a linker is not used to attach the IL-15 protein or IL-15Rα protein to the Fc domain.

[00452] In some instances, the PD-1 ABD is covalently attached to the N-terminus of an Fc domain via a linker, such as a domain linker. In some embodiments, the PD-1 ABD is attached to an Fc domain directly, such as without a linker. In particular embodiments, the PD-1 ABD is attached to an Fc domain via a hinge region or a fragment thereof.

[00453] In some embodiments, the linker is a "domain linker", used to link any two domains as outlined herein together. While any suitable linker can be used, many embodiments utilize a glycine-serine polymer, including for example (GS)n, (GSGGS)n, (GGGGS)n, and (GGGS)n, where n is an integer of at least 1 (and generally from 1 to 2 to 3 to 4 to 5) as well as any peptide sequence that allows for recombinant attachment of the two domains with sufficient length and flexibility to allow each domain to retain its biological function. In some cases, and with attention being paid to "strandedness", as outlined below, charged domain linkers can be used as discussed herein and shown in Figures 9 and 10.

VII. **PD-1 Antibody Monomers**

[00454] The present invention relates to the generation of bispecific heterodimeric proteins that bind to a PD-1 and cells expressing IL-2Rβ and the common gamma chain (γc; CD132). The bispecific heterodimeric protein can include an antibody monomer of any

useful antibody format that can bind to an immune checkpoint antigen. In some embodiments, the antibody monomer includes a Fab or a scFv linked to an Fc domain. In some cases, the PD-1 antibody monomer contains an anti-PD1(VH)-CH1-Fc and an anti-PD-1 VL-Ckappa. In some cases, the PD-1 antibody monomer contains an anti-PD-1 scFv-Fc.

[00455] In some embodiments, the PD-1 targeting arm of the heterodimeric Fc fusion proteins of the invention comprises sequences for VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2, and VLCDR3 selected from the CDRs of the group consisting of 1C11[PD-1]_H3L3 from XENP22553, 1C11[PD-1]_H3.234_L3.144 from XENP25806, 1C11[PD-1]_H3.240_L3.148 from XENP25812, 1C11[PD-1]_H3.241_L3.148 from XENP25813, 1C11[PD-1]_H3.241_L3.92 from XENP25819, 1C11[PD-1]_H3.303_L3.152 from XENP26940, 1C11[PD-1]_H3.329_L3.220 from XENP28026, and 1C11[PD-1]_H3.328_L3.152 from XENP28652. In some embodiments, the sequences for VHCDR1, VHCD2, and VHCDR3 are selected from the sequences depicted in Figures 95A-95J, and the corresponding sequence identifiers. In some embodiments, the sequences for VHCDR1, VHCD2, and VHCDR3 are selected from the sequences depicted in Figures 96A-96F, and the corresponding sequence identifiers.

[00456] In some embodiments, the PD-1 targeting arm of the heterodimeric Fc fusion proteins of the invention comprises a variable heavy domain and a variable light domain from the pair selected from the group consisting of 1C11[PD-1]_H3L3 from XENP22553, 1C11[PD-1]_H3.234_L3.144 from XENP25806, 1C11[PD-1]_H3.240_L3.148 from XENP25812, 1C11[PD-1]_H3.241_L3.148 from XENP25813, 1C11[PD-1]_H3.241_L3.92 from XENP25819, 1C11[PD-1]_H3.303_L3.152 from XENP26940, 1C11[PD-1]_H3.329_L3.220 from XENP28026, and 1C11[PD-1]_H3.328_L3.152 from XENP28652. In some embodiments, the variable heavy domain of the PD-1 targeting arm has at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or more sequence identity to the sequence of the variable heavy domain and the variable light domain of the PD-1 targeting arm has at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or more sequence identity to the sequence of the variable light domain selected from the group consisting of the pair from 1C11[PD-1]_H3L3 from XENP22553, 1C11[PD-1]_H3.234_L3.144 from XENP25806, 1C11[PD-1]_H3.240_L3.148 from XENP25812, 1C11[PD-1]_H3.241_L3.148 from XENP25813, 1C11[PD-

1]_H3.241_L3.92 from XENP25819, 1C11[PD-1]_H3.303_L3.152 from XENP26940, 1C11[PD-1]_H3.329_L3.220 from XENP28026, 1C11[PD-1]_H3.328_L3.152 from XENP28652, and the corresponding sequence identifiers.

[00457] Additional exemplary embodiments of such antibody fragments are provided in XENP21480 (chain 2; Figure 65A), XENP22022 (chains 2 and 3; Figure 65D), XENP22112 (chains 1 and 4; Figure 65E), XENP22641 (chains 1 and 3; Figure 65F), XENP22642 (chains 1-3; Figure 65H), and XENP22644 (chains 1-3; Figure 65I).

[00458] The ABD can be in a variety of formats, such as in a Fab format or in an scFv format. Exemplary ABDs for use in the present invention are disclosed in WO2017/218707 and PCT/US2018/059887, the contents including the figures, figure legends, and sequence listings are hereby incorporated in its entirety for all purposes.

[00459] For instance, suitable ABDs that bind PD-1 are shown in Figures 11 and 12 of US2018/0118836, as well as those outlined in Figure 13 and Figure 14 and the SEQ ID NOS: herein. As will be appreciated by those in the art, suitable ABDs can comprise a set of 6 CDRs as depicted in the Figures herein, either as they are underlined or, in the case where a different numbering scheme is used as described above, as the CDRs that are identified using other alignments within the vh and vl sequences of Figures 11 and 12 of US2018/0118836. Suitable ABDs can also include the entire vh and vl sequences as depicted in these Figures, used as scFvs or as Fabs. Specific scFv sequences are shown in Figure 11 of US2018/0118836, with a particular charged linker, although other linkers, such as those depicted in Figure 7, can also be used. In many of the embodiments herein that contain an Fv to PD-1, it is the scFv monomer that binds PD-1. In US2018/0118836, Figure 11 shows preferred scFv sequences, and Figure 12 depicts suitable Fab sequences, although as discussed herein, vh and vl of can be used in either configuration.

B. Antibodies

[00460] As is discussed below, the term “antibody” is used generally. Antibodies that find use in the present invention can take on a number of formats as described herein, including traditional antibodies as well as antibody derivatives, fragments and mimetics, described herein and depicted in the figures. The present invention provides antibody fusion proteins containing a checkpoint antigen binding domain and an Fc domain. In some embodiments, the antibody fusion protein forms a bispecific heterodimeric protein with an IL-15/IL-15Rα-Fc protein described herein. In other embodiments, the antibody fusion

protein forms a bispecific heterodimeric protein with another antibody fusion protein comprising a checkpoint antigen binding domain and an Fc domain. Embodiments of such PD-1-targeted heterodimeric proteins include, but are not limited to, XENP21480, XENP22022, XENP22112, XENP22641, XENP22642, XENP22644, XENP25850, and XENP25937.

[00461] Traditional antibody structural units typically comprise a tetramer. Each tetramer is typically composed of two identical pairs of polypeptide chains, each pair having one “light” (typically having a molecular weight of about 25 kDa) and one “heavy” chain (typically having a molecular weight of about 50-70 kDa). Human light chains are classified as kappa and lambda light chains. The present invention is directed to antibodies or antibody fragments (antibody monomers) that generally are based on the IgG class, which has several subclasses, including, but not limited to IgG1, IgG2, IgG3, and IgG4. In general, IgG1, IgG2 and IgG4 are used more frequently than IgG3. It should be noted that IgG1 has different allotypes with polymorphisms at 356 (D or E) and 358 (L or M). The sequences depicted herein use the 356D/358M allotype, however the other allotype is included herein. That is, any sequence inclusive of an IgG1 Fc domain included herein can have 356E/358L replacing the 356D/358M allotype.

[00462] In addition, many of the sequences herein have at least one the cysteines at position 220 replaced by a serine; generally this is the on the “scFv monomer” side for most of the sequences depicted herein, although it can also be on the “Fab monomer” side, or both, to reduce disulfide formation. Specifically included within the sequences herein are one or both of these cysteines replaced (C220S).

[00463] Thus, “isotype” as used herein is meant any of the subclasses of immunoglobulins defined by the chemical and antigenic characteristics of their constant regions. It should be understood that therapeutic antibodies can also comprise hybrids of isotypes and/or subclasses. For example, as shown in US2009/0163699, incorporated by reference, the present invention covers pI engineering of IgG1/G2 hybrids.

[00464] The amino-terminal portion of each chain includes a variable region of about 100 to 110 or more amino acids primarily responsible for antigen recognition, generally referred to in the art and herein as the “Fv domain” or “Fv region”. In the variable region, three loops are gathered for each of the V domains of the heavy chain and light chain to form an antigen-binding site. Each of the loops is referred to as a complementarity-determining

region (hereinafter referred to as a "CDR"), in which the variation in the amino acid sequence is most significant. "Variable" refers to the fact that certain segments of the variable region differ extensively in sequence among antibodies. Variability within the variable region is not evenly distributed. Instead, the V regions consist of relatively invariant stretches called framework regions (FRs) of 15-30 amino acids separated by shorter regions of extreme variability called "hypervariable regions" that are each 9-15 amino acids long or longer.

[00465] Each VH and VL is composed of three hypervariable regions ("complementary determining regions," "CDRs") and four FRs, arranged from amino-terminus to carboxy-terminus in the following order: FR1-CDR1-FR2-CDR2-FR3-CDR3-FR4.

[00466] The hypervariable region generally encompasses amino acid residues from about amino acid residues 24-34 (LCDR1; "L" denotes light chain), 50-56 (LCDR2) and 89-97 (LCDR3) in the light chain variable region and around about 31-35B (HCDR1; "H" denotes heavy chain), 50-65 (HCDR2), and 95-102 (HCDR3) in the heavy chain variable region; Kabat et al., SEQUENCES OF PROTEINS OF IMMUNOLOGICAL INTEREST, 5th Ed. Public Health Service, National Institutes of Health, Bethesda, Md. (1991) and/or those residues forming a hypervariable loop (e.g. residues 26-32 (LCDR1), 50-52 (LCDR2) and 91-96 (LCDR3) in the light chain variable region and 26-32 (HCDR1), 53-55 (HCDR2) and 96-101 (HCDR3) in the heavy chain variable region; Chothia and Lesk (1987) J. Mol. Biol. 196:901-917. Specific CDRs of the invention are described below.

[00467] As will be appreciated by those in the art, the exact numbering and placement of the CDRs can be different among different numbering systems. However, it should be understood that the disclosure of a variable heavy and/or variable light sequence includes the disclosure of the associated (inherent) CDRs. Accordingly, the disclosure of each variable heavy region is a disclosure of the vhCDRs (e.g. vhCDR1, vhCDR2 and vhCDR3) and the disclosure of each variable light region is a disclosure of the vlCDRs (e.g., vlCDR1, vlCDR2 and vlCDR3).

[00468] A useful comparison of CDR numbering is as below, see Lafranc et al., Dev. Comp. Immunol. 27(1):55-77 (2003):

Table 1

	Kabat+ Chothia	IMGT	Kabat	AbM	Chothia	Contact	Xencor
vhCDR1	26-35	27-38	31-35	26-35	26-32	30-35	27-35
vhCDR2	50-65	56-65	50-65	50-58	52-56	47-58	54-61
vhCDR3	95-102	105-117	95-102	95-102	95-102	93-101	103-116
vlCDR1	24-34	27-38	24-34	24-34	24-34	30-36	27-38
vlCDR2	50-56	56-65	50-56	50-56	50-56	46-55	56-62
vlCDR3	89-97	105-117	89-97	89-97	89-97	89-96	97-105

[00469] Throughout the present specification, the Kabat numbering system is generally used when referring to a residue in the variable domain (approximately, residues 1-107 of the light chain variable region and residues 1-113 of the heavy chain variable region) and the EU numbering system for Fc regions (e.g, Kabat et al., supra (1991)).

[00470] The present invention provides a large number of different CDR sets. In this case, a "full CDR set" comprises the three variable light and three variable heavy CDRs, e.g. a vlCDR1, vlCDR2, vlCDR3, vhCDR1, vhCDR2 and vhCDR3. These can be part of a larger variable light or variable heavy domain, respectfully. In addition, as more fully outlined herein, the variable heavy and variable light domains can be on separate polypeptide chains, when a heavy and light chain is used (for example when Fabs are used), or on a single polypeptide chain in the case of scFv sequences.

[00471] The CDRs contribute to the formation of the antigen-binding, or more specifically, epitope binding site of antibodies. "Epitope" refers to a determinant that interacts with a specific antigen binding site in the variable region of an antibody molecule known as a paratope. Epitopes are groupings of molecules such as amino acids or sugar side chains and usually have specific structural characteristics, as well as specific charge characteristics. A single antigen may have more than one epitope.

[00472] The epitope may comprise amino acid residues directly involved in the binding (also called immunodominant component of the epitope) and other amino acid

residues, which are not directly involved in the binding, such as amino acid residues which are effectively blocked by the specifically antigen binding peptide; in other words, the amino acid residue is within the footprint of the specifically antigen binding peptide.

[00473] Epitopes may be either conformational or linear. A conformational epitope is produced by spatially juxtaposed amino acids from different segments of the linear polypeptide chain. A linear epitope is one produced by adjacent amino acid residues in a polypeptide chain. Conformational and nonconformational epitopes may be distinguished in that the binding to the former but not the latter is lost in the presence of denaturing solvents.

[00474] An epitope typically includes at least 3, and more usually, at least 5 or 8-10 amino acids in a unique spatial conformation. Antibodies that recognize the same epitope can be verified in a simple immunoassay showing the ability of one antibody to block the binding of another antibody to a target antigen, for example “binning.” As outlined below, the invention not only includes the enumerated antigen binding domains and antibodies herein, but those that compete for binding with the epitopes bound by the enumerated antigen binding domains.

[00475] The carboxy-terminal portion of each chain defines a constant region primarily responsible for effector function. Kabat et al. collected numerous primary sequences of the variable regions of heavy chains and light chains. Based on the degree of conservation of the sequences, they classified individual primary sequences into the CDR and the framework and made a list thereof (see SEQUENCES OF IMMUNOLOGICAL INTEREST, 5th edition, NIH publication, No. 91-3242, E.A. Kabat et al., entirely incorporated by reference).

[00476] In the IgG subclass of immunoglobulins, there are several immunoglobulin domains in the heavy chain. By “immunoglobulin (Ig) domain” herein is meant a region of an immunoglobulin having a distinct tertiary structure. Of interest in the present invention are the heavy chain domains, including, the constant heavy (CH) domains and the hinge domains. In the context of IgG antibodies, the IgG isotypes each have three CH regions. Accordingly, “CH” domains in the context of IgG are as follows: “CH1” refers to positions 118-220 according to the EU index as in Kabat. “CH2” refers to positions 237-340 according to the EU index as in Kabat, and “CH3” refers to positions 341-447 according to the EU index as in Kabat. As shown herein and described below, the pI variants can be in one or more of the CH regions, as well as the hinge region, discussed below.

[00477] Another type of Ig domain of the heavy chain is the hinge region. By "hinge" or "hinge region" or "antibody hinge region" or "immunoglobulin hinge region" herein is meant the flexible polypeptide comprising the amino acids between the first and second constant domains of an antibody. Structurally, the IgG CH1 domain ends at EU position 220, and the IgG CH2 domain begins at residue EU position 237. Thus for IgG the antibody hinge is herein defined to include positions 221 (D221 in IgG1) to 236 (G236 in IgG1), wherein the numbering is according to the EU index as in Kabat. In some embodiments, for example in the context of an Fc region, the lower hinge is included, with the "lower hinge" generally referring to positions 226 or 230. As noted herein, pI variants can be made in the hinge region as well.

[00478] The light chain generally comprises two domains, the variable light domain (containing the light chain CDRs and together with the variable heavy domains forming the Fv region), and a constant light chain region (often referred to as CL or Cκ).

[00479] Another region of interest for additional substitutions, outlined above, is the Fc region.

[00480] As described herein and known in the art, the ABDs of the invention comprise different domains within the heavy and light chains, which can be overlapping as well. These domains include, but are not limited to, the Fc domain, the CH1 domain, the CH2 domain, the CH3 domain, the hinge domain, the heavy constant domain (CH1-hinge-Fc domain or CH1-hinge-CH2-CH3), the variable heavy domain, the variable light domain, the light constant domain, Fab domains and scFv domains.

[00481] Thus, the "Fc domain" includes the -CH2-CH3 domain, and optionally a hinge domain. In the embodiments herein, when a scFv is attached to an Fc domain, it is the C-terminus of the scFv construct that is attached to all or part of the hinge of the Fc domain; for example, it is generally attached to the sequence EPKS (SEQ ID NO:1220) which is the beginning of the hinge. The heavy chain comprises a variable heavy domain and a constant domain, which includes a CH1-optional hinge-Fc domain comprising a CH2-CH3. The light chain comprises a variable light chain and the light constant domain. A scFv comprises a variable heavy chain, an scFv linker, and a variable light domain. In most of the constructs and sequences outlined herein, C-terminus of the variable light chain is attached to the N-terminus of the scFv linker, the C-terminus of which is attached to the N-terminus of a variable heavy chain (N-vh-linker-vl-C) although that can be switched (N-vl-linker-vh-C).

[00482] Some embodiments of the invention comprise at least one scFv domain, which, while not naturally occurring, generally includes a variable heavy domain and a variable light domain, linked together by a scFv linker. As outlined herein, while the scFv domain is generally from N- to C-terminus oriented as vh-scFv linker-vl, this can be reversed for any of the scFv domains (or those constructed using vh and vl sequences from Fabs), to vl-scFv linker-vh, with optional linkers at one or both ends depending on the format (see generally Figures 4A-4B of US 62/353,511).

[00483] As shown herein, there are a number of suitable scFv linkers that can be used, including traditional peptide bonds, generated by recombinant techniques. The linker peptide may predominantly include the following amino acid residues: Gly, Ser, Ala, or Thr. The linker peptide should have a length that is adequate to link two molecules in such a way that they assume the correct conformation relative to one another so that they retain the desired activity. In one embodiment, the linker is from about 1 to 50 amino acids in length, preferably about 1 to 30 amino acids in length. In one embodiment, linkers of 1 to 20 amino acids in length may be used, with from about 5 to about 10 amino acids finding use in some embodiments. Useful linkers include glycine-serine polymers, including for example (GS)n, (GSGGS)n, (GGGGS)n, and (GGGS)n, where n is an integer of at least one (and generally from 3 to 4), glycine-alanine polymers, alanine-serine polymers, and other flexible linkers. Alternatively, a variety of nonproteinaceous polymers, including but not limited to polyethylene glycol (PEG), polypropylene glycol, polyoxyalkylenes, or copolymers of polyethylene glycol and polypropylene glycol, may find use as linkers, that is may find use as linkers.

[00484] Other linker sequences may include any sequence of any length of CL/CH1 domain but not all residues of CL/CH1 domain; for example the first 5-12 amino acid residues of the CL/CH1 domains. Linkers can be derived from immunoglobulin light chain, for example Cκ or Cλ. Linkers can be derived from immunoglobulin heavy chains of any isotype, including for example Cγ1, Cγ2, Cγ3, Cγ4, Cα1, Cα2, Cδ, Cε, and Cμ. Linker sequences may also be derived from other proteins such as Ig-like proteins (e.g. TCR, FcR, KIR), hinge region-derived sequences, and other natural sequences from other proteins.

[00485] In some embodiments, the linker is a “domain linker”, used to link any two domains as outlined herein together. While any suitable linker can be used, many embodiments utilize a glycine-serine polymer, including for example (GS)n, (GSGGS)n,

(GGGGS)n, and (GGGS)n , where n is an integer of at least one (and generally from 3 to 4 to 5) as well as any peptide sequence that allows for recombinant attachment of the two domains with sufficient length and flexibility to allow each domain to retain its biological function. . In some cases, and with attention being paid to "strandedness", as outlined below, charged domain linkers, as used in some embodiments of scFv linkers can be used.

[00486] In some embodiments, the scFv linker is a charged scFv linker, a number of which are shown in Figure 10. Accordingly, the present invention further provides charged scFv linkers, to facilitate the separation in pI between a first and a second monomer (e.g., an IL-15/IL-15Rα monomer and PD-1 ABD monomer). That is, by incorporating a charged scFv linker, either positive or negative (or both, in the case of scaffolds that use scFvs on different monomers), this allows the monomer comprising the charged linker to alter the pI without making further changes in the Fc domains. These charged linkers can be substituted into any scFv containing standard linkers. Again, as will be appreciated by those in the art, charged scFv linkers are used on the correct "strand" or monomer, according to the desired changes in pI. For example, as discussed herein, to make triple F format heterodimeric antibody, the original pI of the Fv region for each of the desired antigen binding domains are calculated, and one is chosen to make an scFv, and depending on the pI, either positive or negative linkers are chosen.

[00487] Charged domain linkers can also be used to increase the pI separation of the monomers of the invention as well, and thus those included in Figure 10 can be used in any embodiment herein where a linker is utilized.

[00488] In one embodiment, the antibody is an antibody fragment, as long as it contains at least one constant domain which can be engineered to produce heterodimers, such as pI engineering. Other antibody fragments that can be used include fragments that contain one or more of the CH1, CH2, CH3, hinge and CL domains of the invention that have been pI engineered. In particular, the formats depicted in Figures 65A-65K are PD-1 targeted heterodimeric Fc fusion proteins, referred to as "bispecific heterodimeric fusion proteins", meaning that the protein has at least two associated Fc sequences self-assembled into a heterodimeric Fc domain and at least one Fv regions, whether as Fabs or as scFvs.

C. Chimeric and Humanized Antibodies

[00489] In some embodiments, the antibodies herein can be derived from a mixture from different species, e.g., a chimeric antibody and/or a humanized antibody. In general, both “chimeric antibodies” and “humanized antibodies” refer to antibodies that combine regions from more than one species. For example, “chimeric antibodies” traditionally comprise variable region(s) from a mouse (or rat, in some cases) and the constant region(s) from a human. “Humanized antibodies” generally refer to non-human antibodies that have had the variable-domain framework regions swapped for sequences found in human antibodies. Generally, in a humanized antibody, the entire antibody, except the CDRs, is encoded by a polynucleotide of human origin or is identical to such an antibody except within its CDRs. The CDRs, some or all of which are encoded by nucleic acids originating in a non-human organism, are grafted into the beta-sheet framework of a human antibody variable region to create an antibody, the specificity of which is determined by the engrafted CDRs. The creation of such antibodies is described in, e.g., WO 92/11018, Jones, 1986, Nature 321:522-525, Verhoeyen et al., 1988, Science 239:1534-1536, all entirely incorporated by reference. “Backmutation” of selected acceptor framework residues to the corresponding donor residues is often required to regain affinity that is lost in the initial grafted construct (US 5530101; US 5585089; US 5693761; US 5693762; US 6180370; US 5859205; US 5821337; US 6054297; US 6407213, all entirely incorporated by reference). The humanized antibody optimally also will comprise at least a portion of an immunoglobulin constant region, typically that of a human immunoglobulin, and thus will typically comprise a human Fc region Humanized antibodies can also be generated using mice with a genetically engineered immune system. Roque et al., 2004, Biotechnol. Prog. 20:639-654, entirely incorporated by reference. A variety of techniques and methods for humanizing and reshaping non-human antibodies are well known in the art (See Tsurushita & Vasquez, 2004, Humanization of Monoclonal Antibodies, Molecular Biology of B Cells, 533-545, Elsevier Science (USA), and references cited therein, all entirely incorporated by reference). Humanization methods include but are not limited to methods described in Jones et al., 1986, Nature 321:522-525; Riechmann et al., 1988; Nature 332:323-329; Verhoeyen et al., 1988, Science, 239:1534-1536; Queen et al., 1989, Proc Natl Acad Sci, USA 86:10029-33; He et al., 1998, J. Immunol. 160: 1029-1035; Carter et al., 1992, Proc Natl Acad Sci USA 89:4285-9, Presta et al., 1997, Cancer Res. 57(20):4593-9; Gorman et al., 1991, Proc. Natl. Acad. Sci. USA 88:4181-4185; O’Connor et al., 1998, Protein Eng 11:321-8, all entirely incorporated by reference. Humanization or other methods of reducing the immunogenicity of nonhuman

antibody variable regions may include resurfacing methods, as described for example in Roguska et al., 1994, Proc. Natl. Acad. Sci. USA 91:969-973, entirely incorporated by reference. In certain embodiments, the antibodies of the invention comprise a heavy chain variable region from a particular germline heavy chain immunoglobulin gene and/or a light chain variable region from a particular germline light chain immunoglobulin gene. For example, such antibodies may comprise or consist of a human antibody comprising heavy or light chain variable regions that are "the product of" or "derived from" a particular germline sequence. A human antibody that is "the product of" or "derived from" a human germline immunoglobulin sequence can be identified as such by comparing the amino acid sequence of the human antibody to the amino acid sequences of human germline immunoglobulins and selecting the human germline immunoglobulin sequence that is closest in sequence (i.e., greatest % identity) to the sequence of the human antibody. A human antibody that is "the product of" or "derived from" a particular human germline immunoglobulin sequence may contain amino acid differences as compared to the germline sequence, due to, for example, naturally-occurring somatic mutations or intentional introduction of site-directed mutation. However, a humanized antibody typically is at least 90% identical in amino acids sequence to an amino acid sequence encoded by a human germline immunoglobulin gene and contains amino acid residues that identify the antibody as being derived from human sequences when compared to the germline immunoglobulin amino acid sequences of other species (e.g., murine germline sequences). In certain cases, a humanized antibody may be at least 95, 96, 97, 98 or 99%, or even at least 96%, 97%, 98%, or 99% identical in amino acid sequence to the amino acid sequence encoded by the germline immunoglobulin gene. Typically, a humanized antibody derived from a particular human germline sequence will display no more than 10-20 amino acid differences from the amino acid sequence encoded by the human germline immunoglobulin gene (prior to the introduction of any skew, pI and ablation variants herein; that is, the number of variants is generally low, prior to the introduction of the variants of the invention). In certain cases, the humanized antibody may display no more than 5, or even no more than 4, 3, 2, or 1 amino acid difference from the amino acid sequence encoded by the germline immunoglobulin gene (again, prior to the introduction of any skew, pI and ablation variants herein; that is, the number of variants is generally low, prior to the introduction of the variants of the invention). In one embodiment, the parent antibody has been affinity matured, as is known in the art. Structure-based methods may be employed for humanization and affinity maturation, for example as described in US7,657,380. Selection based methods may be employed to humanize and/or affinity mature antibody variable regions, including but not limited to methods described in Wu et al., 1999, J. Mol. Biol. 294:151-162; Baca et al., 1997, J. Biol. Chem. 272(16):10678-10684; Rosok et al., 1996, J. Biol. Chem. 271(37): 22611-22618; Rader et al., 1998, Proc. Natl. Acad. Sci. USA 95: 8910-8915; Krauss et al., 2003, Protein Engineering 16(10):753-759, all entirely incorporated by reference. Other humanization methods may involve the grafting of only parts of the CDRs, including but not limited to methods described in USSN 09/810,510; Tan et al., 2002, J. Immunol. 169:1119-1125; De Pascalis et al., 2002, J. Immunol. 169:3076-3084, all entirely incorporated by reference.

VIII. **Useful Embodiments of the Invention**

[00490] As will be appreciated by those in the art and discussed more fully below, the PD-1-targeted IL-15/Rα-Fc heterodimeric fusion proteins of the present invention can take on a wide variety of configurations, as are generally depicted in Figures 65A-65K. The amino acid sequences of exemplary PD-1-targeted IL-15/Rα-Fc fusion proteins are provided in Figures 66, 67, 68, 69A, 69B, 69C, 70, 71, 72A, 72B, 73A, 73B, 74A, 74B, 75, 76, 126A-126D, 127A-127D, and 128A-128L.

[00491] Provided herein are PD-1-targeted IL-15/Rα-Fc fusion proteins of the scIL-15/Rα X Fab format. In some embodiments, the PD-1-targeted IL-15/Rα-Fc fusion protein comprises: (a) a first monomer comprising from N- to C-terminal: a human IL-15Rα(sushi) domain, a domain linker, a human mature IL-15 variant, a domain linker, and a first Fc variant domain comprising CH2-CH3; (b) a second monomer comprising from N- to C-terminal: a heavy chain comprising VH-CH1-hinge-CH2-CH3 such that CH2-CH3 of the second monomer is a second Fc variant domain; (c) a light chain comprising VL-CL such that the VH and VL form an antigen binding domain that binds human PD-1. In some embodiments, the VH and VL are selected from the group of pair consisting of 1C11[PD-1]_H3L3 from XENP22553, 1C11[PD-1]_H3.234_L3.144 from XENP25806, 1C11[PD-1]_H3.240_L3.148 from XENP25812, 1C11[PD-1]_H3.241_L3.148 from XENP25813, 1C11[PD-1]_H3.241_L3.92 from XENP25819, 1C11[PD-1]_H3.303_L3.152 from XENP26940, 1C11[PD-1]_H3.329_L3.220 from XENP28026, and 1C11[PD-1]_H3.328_L3.152 from XENP28652. In some embodiments, the sequences of the VH and VL of the antigen binding domain are depicted in Figures 93A-93S and Figures 94A-94AP and the corresponding sequence identifiers.

[00492] In some embodiments, the human IL-15Rα(sushi) domain is SEQ ID NO:4. In some embodiments, the human mature IL-15 variant is SEQ ID NO:2. In some embodiments, the human mature IL-15 variant is SEQ ID NO:2 with amino acid substitutions N4D/N65D. In certain embodiments, the human mature IL-15 variant is SEQ ID NO:2 with amino acid substitutions D30N/N65D. In some embodiments, the human mature IL-15 variant is SEQ ID NO:2 with amino acid substitutions D30N/E64Q/N65D.

[00493] In some embodiments, the first Fc variant domain of the scIL-15/Rα X Fab format comprises amino acid substitutions C220S, L368D/K370S, Q295E/N384D/Q418E/N421D, and E233P/L234V/L235A/G236del/S267K, and optionally, M248L/N434S; and the second Fc variant domain comprises amino acid substitutions S364K/E357Q and E233P/L234V/L235A/G236del/S267K, and optionally, M248L/N434S.

[00494] In some embodiments, the PD-1-targeted IL-15/Rα-Fc fusion protein comprises: a first monomer comprising from N- to C-terminal: a human IL-15Rα(sushi) domain of SEQ ID NO:4, a domain linker, a human mature IL-15 variant of SEQ ID NO:2 with N4D/N65D substitutions, and a first Fc variant domain comprising amino acid substitutions C220S, L368D/K370S, Q295E/N384D/Q418E/N421D, E233P/L234V/L235A/G236del/S267K, and optionally, M248L/N434S; a second monomer comprising a heavy chain comprising VH-CH1-hinge-CH2-CH3 wherein the CH2-CH3 is a second Fc variant domain comprising amino acid substitutions S364K/E357Q, E233P/L234V/L235A/G236del/S267K, and optionally, M248L/N434S; and a light chain comprising VL-CL, wherein the VH and VL are from 1C11[PD-1]_H3L3 from XENP22553. In some embodiments, the VH and VL of the PD-1-targeted IL-15/Rα-Fc fusion protein are from 1C11[PD-1]_H3.234_L3.144 from XENP25806. In some embodiments, the VH and VL of the PD-1-targeted IL-15/Rα-Fc fusion protein are from 1C11[PD-1]_H3.240_L3.148 from XENP25812. In some embodiments, the VH and of the PD-1-targeted IL-15/Rα-Fc fusion protein are from 1C11[PD-1]_H3.241_L3.148 from XENP25813. In some embodiments, the VH and VL of the PD-1-targeted IL-15/Rα-Fc fusion protein are from 1C11[PD-1]_H3.241_L3.92 from XENP25819. In some embodiments, the VH and VL of the PD-1-targeted IL-15/Rα-Fc fusion protein are from 1C11[PD-1]_H3.303_L3.152 from XENP26940. In some embodiments, the VH and VL are from 1C11[PD-1]_H3.329_L3.220 from XENP28026. In some embodiments, the VH and VL of the PD-1-targeted IL-15/Rα-Fc fusion protein are from 1C11[PD-1]_H3.328_L3.152 from XENP28652. As will be

understood from those in the art, the variable heavy and light domains of the scFv come in "pairs" as will be apparent from the sequence identifiers and corresponding Figures 93A-93S and Figures 94A-94AP. In some instances, the first Fc variant domain comprises CH2-CH3. In other instances, the first Fc variant domain comprises hinge-CH2-CH3. In some embodiments, the Fc variant domain (e.g., the first and/or second Fc variant domain) is selected from the group consisting of the Fc domain of human IgG1, IgG2, IgG3, and IgG4. In some embodiments, the Fc variant domains is selected from the group consisting of the Fc domain of human IgG1, IgG2, and IgG4. In some embodiments, the Fc variant domains is selected from the group consisting of the Fc domain of human IgG1.

[00495] In other embodiments, the PD-1-targeted IL-15/Rα-Fc fusion protein comprises: a first monomer comprising from N- to C-terminal: a human IL-15Rα(sushi) domain of SEQ ID NO:4, a domain linker, a human mature IL-15 variant of SEQ ID NO:2 with D30N/N65D substitutions, and a first Fc variant domain comprising amino acid substitutions C220S, L368D/K370S, Q295E/N384D/Q418E/N421D, E233P/L234V/L235A/G236del/S267K, and optionally, M248L/N434S; a second monomer comprising a heavy chain comprising VH-CH1-hinge-CH2-CH3 wherein the CH2-CH3 is a second Fc variant domain comprising amino acid substitutions S364K/E357Q, E233P/L234V/L235A/G236del/S267K, and optionally, M248L/N434S; and a light chain comprising VL-CL, wherein the VH and VL of the PD-1-targeted IL-15/Rα-Fc fusion protein are from 1C11[PD-1]_H3L3 from XENP22553. In some embodiments, the VH and VL of the PD-1-targeted IL-15/Rα-Fc fusion protein are from 1C11[PD-1]_H3.234_L3.144 from XENP25806. In some embodiments, the VH and VL of the PD-1-targeted IL-15/Rα-Fc fusion protein are from 1C11[PD-1]_H3.240_L3.148 from XENP25812. In some embodiments, the VH and VL of the PD-1-targeted IL-15/Rα-Fc fusion protein are from 1C11[PD-1]_H3.241_L3.148 from XENP25813. In some embodiments, the VH and VL of the PD-1-targeted IL-15/Rα-Fc fusion protein are from 1C11[PD-1]_H3.241_L3.92 from XENP25819. In some embodiments, the VH and VL of the PD-1-targeted IL-15/Rα-Fc fusion protein are from 1C11[PD-1]_H3.303_L3.152 from XENP26940. In some embodiments, the VH and VL of the PD-1-targeted IL-15/Rα-Fc fusion protein are from 1C11[PD-1]_H3.329_L3.220 from XENP28026. In some embodiments, the VH and VL of the PD-1-targeted IL-15/Rα-Fc fusion protein are from and 1C11[PD-1]_H3.328_L3.152 from XENP28652. As will be understood from those in the art, the variable heavy and light

domains of the scFv come in "pairs" as will be apparent from the sequence identifiers and corresponding Figures 93A-93S and Figures 94A-94AP. In some instances, the first Fc variant domain comprises CH2-CH3. In other instances, the first Fc variant domain comprises hinge-CH2-CH3. In some embodiments, the Fc variant domain (e.g., the first and/or second Fc variant domain) is selected from the group consisting of the Fc domain of human IgG1, IgG2, IgG3, and IgG4. In some embodiments, the Fc variant domains is selected from the group consisting of the Fc domain of human IgG1, IgG2, and IgG4. In some embodiments, the Fc variant domains is selected from the group consisting of the Fc domain of human IgG1.

[00496] In some embodiments, the PD-1-targeted IL-15/Rα-Fc fusion protein comprises: a first monomer comprising from N- to C-terminal: a human IL-15Rα(sushi) domain of SEQ ID NO:4, a domain linker, a human mature IL-15 variant of SEQ ID NO:2 with D30N/E64Q/N65D substitutions, and a first Fc variant domain comprising amino acid substitutions C220S, L368D/K370S, Q295E/N384D/Q418E/N421D, E233P/L234V/L235A/G236del/S267K, and optionally, M248L/N434S; a second monomer comprising a heavy chain comprising VH-CH1-hinge-CH2-CH3 wherein the CH2-CH3 is a second Fc variant domain comprising amino acid substitutions S364K/E357Q, E233P/L234V/L235A/G236del/S267K, and optionally, M248L/N434S; and a light chain comprising VL-CL, wherein the VH and VL of the PD-1-targeted IL-15/Rα-Fc fusion protein are from 1C11[PD-1]_H3L3 from XENP22553. In some embodiments, the VH and VL of the PD-1-targeted IL-15/Rα-Fc fusion protein are from 1C11[PD-1]_H3.234_L3.144 from XENP25806. In some embodiments, the VH and VL of the PD-1-targeted IL-15/Rα-Fc fusion protein are from 1C11[PD-1]_H3.240_L3.148 from XENP25812. In some embodiments, the VH and VL of the PD-1-targeted IL-15/Rα-Fc fusion protein are from 1C11[PD-1]_H3.241_L3.148 from XENP25813. In some embodiments, the VH and VL of the PD-1-targeted IL-15/Rα-Fc fusion protein are from 1C11[PD-1]_H3.241_L3.92 from XENP25819. In some embodiments, the VH and VL of the PD-1-targeted IL-15/Rα-Fc fusion protein are from 1C11[PD-1]_H3.303_L3.152 from XENP26940. In some embodiments, the VH and VL of the PD-1-targeted IL-15/Rα-Fc fusion protein are from 1C11[PD-1]_H3.329_L3.220 from XENP28026. In some embodiments, the VH and VL of the PD-1-targeted IL-15/Rα-Fc fusion protein are from and 1C11[PD-1]_H3.328_L3.152 from XENP28652. As will be understood from those in the art, the variable heavy and light

domains of the scFv come in "pairs" as will be apparent from the sequence identifiers and corresponding Figures 93A-93S and Figures 94A-94AP. In some instances, the first Fc variant domain comprises CH2-CH3. In other instances, the first Fc variant domain comprises hinge-CH2-CH3. In some embodiments, the Fc variant domain (e.g., the first and/or second Fc variant domain) is selected from the group consisting of the Fc domain of human IgG1, IgG2, IgG3, and IgG4. In some embodiments, the Fc variant domains is selected from the group consisting of the Fc domain of human IgG1, IgG2, and IgG4. In some embodiments, the Fc variant domains is selected from the group consisting of the Fc domain of human IgG1.

[00497] In some embodiments, the scIL-15/Rα X anti-PD-1 Fab is depicted in Figures 126A-126D, Figures 127A-127K, Figures 128A-128L, and the corresponding sequence identifiers and SEQ ID NOS of the sequence listing.

[00498] Provided herein are PD-1-targeted IL-15/Rα-Fc fusion proteins of the scIL-15/Rα X scFv format. In some embodiments, the PD-1-targeted IL-15/Rα-Fc fusion protein comprises: (a) a first monomer comprising from N- to C-terminal: a human IL-15Rα(sushi) domain, a domain linker, a human mature IL-15 variant, an optional domain linker, and a first Fc variant domain comprising CH2-CH3; and (b) a second monomer comprising from N- to C-terminal: a scFv domain that binds human PD-1 such that the scFv comprises a variable heavy domain (VH), an scFv linker, and a variable light domain (VL) (e.g., in some cases, the scFv comprises from N- to C-terminus: a VH-scFv linker-VL or in other cases, the scFv comprises from N- to C-terminus: a VL-scFv linker-VH); and a second Fc variant domain. In some embodiments, the VH and VL are selected from the group of pair consisting of 1C11[PD-1]_H3L3 from XENP22553, 1C11[PD-1]_H3.234_L3.144 from XENP25806, 1C11[PD-1]_H3.240_L3.148 from XENP25812, 1C11[PD-1]_H3.241_L3.148 from XENP25813, 1C11[PD-1]_H3.241_L3.92 from XENP25819, 1C11[PD-1]_H3.303_L3.152 from XENP26940, 1C11[PD-1]_H3.329_L3.220 from XENP28026, and 1C11[PD-1]_H3.328_L3.152 from XENP28652. In some embodiments, the sequences of the VH and VL of the antigen binding domain are depicted in Figures 93A-93S and Figures 94A-94AP and the corresponding sequence identifiers.

[00499] In some embodiments, the human IL-15Rα(sushi) domain is SEQ ID NO:4. In some embodiments, the human mature IL-15 variant is SEQ ID NO:2. In some embodiments, the human mature IL-15 variant is SEQ ID NO:2 with amino acid substitutions

N4D/N65D. In certain embodiments, the human mature IL-15 variant is SEQ ID NO:2 with amino acid substitutions D30N/N65D. In some embodiments, the human mature IL-15 variant is SEQ ID NO:2 with amino acid substitutions D30N/E64Q/N65D.

[00500] In some embodiments, the first Fc variant domain of the scIL-15/Rα X scFv format comprises amino acid substitutions C220S, L368D/K370S, Q295E/N384D/Q418E/N421D, and E233P/L234V/L235A/G236del/S267K, and optionally, M248L/N434S; and the second Fc variant domain comprises amino acid substitutions C220S, S364K/E357Q and E233P/L234V/L235A/G236del/S267K, and optionally, M248L/N434S.

[00501] In particular embodiments, the PD-1-targeted IL-15/Rα-Fc fusion protein comprises: a first monomer comprising from N- to C-terminal: a human IL-15Rα(sushi) domain of SEQ ID NO:4, a domain linker, a human mature IL-15 variant of SEQ ID NO:2, an optional domain linker, and a first Fc variant domain comprising amino acid substitutions C220S, L368D/K370S, Q295E/N384D/Q418E/N421D, E233P/L234V/L235A/G236del/S267K, and optionally, M248L/N434S; and a second monomer comprising an anti-PD-1 scFv and a second Fc variant domain comprising amino acid substitutions C220S, S364K/E357Q, E233P/L234V/L235A/G236del/S267K, and optionally, M248L/N434S. In some embodiments, the anti-PD-1 scFv comprises sequences for VHCDR1, VHCD2, VHCDR3, VLCDR1, VLCDR2, and VLCDR3 from 1C11[PD-1]_H3L3 from XENP22553. In some embodiments, the CDRs are from 1C11[PD-1]_H3.234_L3.144 from XENP25806. In some embodiments, the CDRs are from 1C11[PD-1]_H3.240_L3.148 from XENP25812. In some embodiments, the CDRs are from 1C11[PD-1]_H3.241_L3.148 from XENP25813. In some embodiments, the CDRs are from 1C11[PD-1]_H3.241_L3.92 from XENP25819. In some embodiments, the CDRs are from 1C11[PD-1]_H3.303_L3.152 from XENP26940. In some embodiments, the CDRs are from 1C11[PD-1]_H3.329_L3.220 from XENP28026. In some embodiments, the CDRs are from and 1C11[PD-1]_H3.328_L3.152 from XENP28652. As will be understood from those in the art, the CDRs for the variable heavy and light domains of the scFv come in “pairs” as will be apparent from the sequence identifiers. In some instances, the first Fc variant domain comprises CH2-CH3. In other instances, the first Fc variant domain comprises hinge-CH2-CH3. In some embodiments, the Fc variant domain (e.g., the first and/or second Fc variant domain) is selected from the group consisting of the Fc domain of human IgG1, IgG2, IgG3, and IgG4. In some embodiments, the Fc variant domains is selected from the group

consisting of the Fc domain of human IgG1, IgG2, and IgG4. In some embodiments, the Fc variant domains is selected from the group consisting of the Fc domain of human IgG1.

[00502] In some embodiments, the PD-1-targeted IL-15/Rα-Fc fusion protein comprises: a first monomer comprising from N- to C-terminal: a human IL-15Rα(sushi) domain of SEQ ID NO:4, a domain linker, a human mature IL-15 variant of SEQ ID NO:2 with N4D/N65D substitutions, an optional domain linker, and a first Fc variant domain comprising amino acid substitutions C220S, L368D/K370S, Q295E/N384D/Q418E/N421D, E233P/L234V/L235A/G236del/S267K, and optionally, M248L/N434S; and a second monomer comprising an anti-PD-1 scFv and a second Fc variant domain comprising amino acid substitutions C220S, S364K/E357Q, E233P/L234V/L235A/G236del/S267K, and optionally, M248L/N434S. In some embodiments, the anti-PD-1 scFv comprises sequences for VHCDR1, VHCD2, VHCDR3, VLCDR1, VLCDR2, and VLCDR3 from 1C11[PD-1]_H3L3 from XENP22553. In some embodiments, the CDRs are from 1C11[PD-1]_H3.234_L3.144 from XENP25806. In some embodiments, the CDRs are from 1C11[PD-1]_H3.240_L3.148 from XENP25812. In some embodiments, the CDRs are from 1C11[PD-1]_H3.241_L3.148 from XENP25813. In some embodiments, the CDRs are from 1C11[PD-1]_H3.241_L3.92 from XENP25819. In some embodiments, the CDRs are from 1C11[PD-1]_H3.303_L3.152 from XENP26940. In some embodiments, the CDRs are from 1C11[PD-1]_H3.329_L3.220 from XENP28026. In some embodiments, the CDRs are from and 1C11[PD-1]_H3.328_L3.152 from XENP28652. As will be understood from those in the art, the CDRs for the variable heavy and light domains of the scFv come in "pairs" as will be apparent from the sequence identifiers. In some instances, the first Fc variant domain comprises CH2-CH3. In other instances, the first Fc variant domain comprises hinge-CH2-CH3. In some embodiments, the Fc variant domain (e.g., the first and/or second Fc variant domain) is selected from the group consisting of the Fc domain of human IgG1, IgG2, IgG3, and IgG4. In some embodiments, the Fc variant domains is selected from the group consisting of the Fc domain of human IgG1, IgG2, and IgG4. In some embodiments, the Fc variant domains is selected from the group consisting of the Fc domain of human IgG1.

[00503] In some embodiments, the PD-1-targeted IL-15/Rα-Fc fusion protein comprises: a first monomer comprising from N- to C-terminal: a human IL-15Rα(sushi) domain of SEQ ID NO:4, a domain linker, a human mature IL-15 variant of SEQ ID NO:2 with D30N/N65D substitutions, an optional domain linker, and a first Fc variant domain

comprising amino acid substitutions C220S, L368D/K370S, Q295E/N384D/Q418E/N421D, E233P/L234V/L235A/G236del/S267K, and optionally, M248L/N434S; and a second monomer comprising an anti-PD-1 scFv and a second Fc variant domain comprising amino acid substitutions C220S, S364K/E357Q, E233P/L234V/L235A/G236del/S267K, and optionally, M248L/N434S. In some embodiments, the anti-PD-1 scFv comprises sequences for VHCDR1, VHCD2, VHCDR3, VLCDR1, VLCDR2, and VLCDR3 from 1C11[PD-1]_H3L3 from XENP22553. In some embodiments, the CDRs are from 1C11[PD-1]_H3.234_L3.144 from XENP25806. In some embodiments, the CDRs are from 1C11[PD-1]_H3.240_L3.148 from XENP25812. In some embodiments, the CDRs are from 1C11[PD-1]_H3.241_L3.148 from XENP25813. In some embodiments, the CDRs are from 1C11[PD-1]_H3.241_L3.92 from XENP25819. In some embodiments, the CDRs are from 1C11[PD-1]_H3.303_L3.152 from XENP26940. In some embodiments, the CDRs are from 1C11[PD-1]_H3.329_L3.220 from XENP28026. In some embodiments, the CDRs are from and 1C11[PD-1]_H3.328_L3.152 from XENP28652. As will be understood from those in the art, the CDRs for the variable heavy and light domains of the scFv come in “pairs” as will be apparent from the sequence identifiers. In some instances, the first Fc variant domain comprises CH2-CH3. In other instances, the first Fc variant domain comprises hinge-CH2-CH3. In some embodiments, the Fc variant domain (e.g., the first and/or second Fc variant domain) is selected from the group consisting of the Fc domain of human IgG1, IgG2, IgG3, and IgG4. In some embodiments, the Fc variant domains is selected from the group consisting of the Fc domain of human IgG1, IgG2, and IgG4. In some embodiments, the Fc variant domains is selected from the group consisting of the Fc domain of human IgG1.

[00504] In particular embodiments, the PD-1-targeted IL-15/Rα-Fc fusion protein comprises: a first monomer comprising from N- to C-terminal: a human IL-15Rα(sushi) domain of SEQ ID NO:4, a domain linker, a human mature IL-15 variant of SEQ ID NO:2 with D30N/E64Q/N65D substitutions, an optional domain linker, and a first Fc variant domain comprising amino acid substitutions C220S, L368D/K370S, Q295E/N384D/Q418E/N421D, E233P/L234V/L235A/G236del/S267K, and optionally, M248L/N434S; and a second monomer comprising an anti-PD-1 scFv and a second Fc variant domain comprising amino acid substitutions C220S, S364K/E357Q, E233P/L234V/L235A/G236del/S267K, and optionally, M248L/N434S. In some embodiments, the anti-PD-1 scFv comprises sequences for VHCDR1, VHCD2, VHCDR3,

VLCDR1, VLCDR2, and VLCDR3 from 1C11[PD-1]_H3L3 from XENP22553. In some embodiments, the CDRs are from 1C11[PD-1]_H3.234_L3.144 from XENP25806. In some embodiments, the CDRs are from 1C11[PD-1]_H3.240_L3.148 from XENP25812. In some embodiments, the CDRs are from 1C11[PD-1]_H3.241_L3.148 from XENP25813. In some embodiments, the CDRs are from 1C11[PD-1]_H3.241_L3.92 from XENP25819. In some embodiments, the CDRs are from 1C11[PD-1]_H3.303_L3.152 from XENP26940. In some embodiments, the CDRs are from 1C11[PD-1]_H3.329_L3.220 from XENP28026. In some embodiments, the CDRs are from and 1C11[PD-1]_H3.328_L3.152 from XENP28652. As will be understood from those in the art, the CDRs for the variable heavy and light domains of the scFv come in "pairs" as will be apparent from the sequence identifiers. In some instances, the first Fc variant domain comprises CH2-CH3. In other instances, the first Fc variant domain comprises hinge-CH2-CH3. In some embodiments, the Fc variant domain (e.g., the first and/or second Fc variant domain) is selected from the group consisting of the Fc domain of human IgG1, IgG2, IgG3, and IgG4. In some embodiments, the Fc variant domains is selected from the group consisting of the Fc domain of human IgG1, IgG2, and IgG4. In some embodiments, the Fc variant domains is selected from the group consisting of the Fc domain of human IgG1.

[00505] In some embodiments, the PD-1-targeted IL-15/Rα-Fc fusion proteins of the invention are administered to a patient, e.g., a human patient with cancer.

[00506] In some embodiments, provided herein is a nucleic acid composition comprising a nucleic acid encoding a first monomer of the present invention and a nucleic acid encoding a second monomer of the present invention.

[00507] In some embodiments, provided herein is an expression vector comprising a nucleic acid encoding a first monomer of the present invention. In some embodiments, provided herein is an expression vector comprising a nucleic acid encoding a second monomer of the present invention. In some embodiments, provided herein is an expression vector comprising a nucleic acid encoding the first monomer and a nucleic acid encoding the second monomer. In some embodiments, a host cell comprising one or more of the expression vectors described herein.

[00508] In some embodiments, provided herein is a nucleic acid composition comprising a nucleic acid encoding a first monomer of the present invention, a nucleic acid

encoding second monomer of the present invention, and a nucleic acid encoding a light chain, such that the VH and VL of the PD-1-targeted IL-15/Rα-Fc fusion protein can bind PD-1.

[00509] In some embodiments, provided herein is an expression vector comprising a nucleic acid encoding a first monomer. In some embodiments, provided herein is an expression vector comprising a nucleic acid encoding second monomer. In some embodiments, provided herein is an expression vector comprising a nucleic acid encoding a first monomer and a nucleic acid encoding second monomer. In some embodiments, provided herein is an expression vector comprising a nucleic acid encoding a light chain, such that the VH and VL of the PD-1-targeted IL-15/Rα-Fc fusion protein can bind PD-1. In some embodiments, provided herein is an expression vector comprising a nucleic acid encoding a first monomer and a nucleic acid encoding a light chain. In some embodiments, provided herein is an expression vector comprising a nucleic acid encoding a second monomer and a nucleic acid encoding a light chain. In some embodiments, provided herein is an expression vector comprising a nucleic acid encoding a first monomer, a nucleic acid encoding second monomer, and a nucleic acid encoding a light chain. In some embodiments, provided herein is a host cell comprising one or more of the expression vectors described herein.

[00510] Provided herein is a method of making any one of the PD-1-targeted IL-15/Rα-Fc fusion proteins outlined herein comprising: culturing the host cell under conditions, such as cell culture conditions such that the PD-1-targeted IL-15/Rα-Fc fusion protein is expressed by the cell, and recovering the fusion protein.

[00511] Provided herein is a method of treating cancer in a patient comprising administering the PD-1-targeted IL-15/Rα-Fc fusion protein to the patient.

IX. **Other Embodiments of the Invention**

[00512] As will be appreciated by those in the art and discussed more fully below, the PD-1-targeted IL-15/Rα-Fc heterodimeric fusion proteins of the present invention can take on a wide variety of configurations, as are generally depicted in Figures 65A-65K. The amino acid sequences of exemplary PD-1-targeted IL-15/Rα-Fc fusion proteins are provided in Figures 66, 67, 68, 69A, 69B, 69C, 70, 71, 72A, 72B, 73A, 73B, 74A, 74B, 75, 76, 126A-126D, 127A-127D, and 128A-128L.

[00513] The present invention provides a PD-1-targeted IL-15/Rα-Fc fusion protein comprising a fusion protein and an antibody fusion protein. The fusion protein comprises a first protein domain, a second protein domain, and a first Fc domain. In some cases, the first protein domain is covalently attached to the N-terminus of the second protein domain using a first domain linker, the second protein domain is covalently attached to the N-terminus of the first Fc domain using a second domain linker, and the first protein domain comprises an IL-15Rα protein and the second protein domain comprises an IL-15 protein. The antibody fusion protein comprises a PD-1 antigen binding domain and a second Fc domain such that the PD-1 antigen binding domain is covalently attached to the N-terminus of the second Fc domain, and the PD-1 antigen binding domain is a single chain variable fragment (scFv) or a Fab fragment. In some embodiments, the first and the second Fc domains have a set of amino acid substitutions selected from the group consisting of S267K/L368D/K370S : S267K/LS364K/E357Q; S364K/E357Q : L368D/K370S; L368D/K370S : S364K; L368E/K370S : S364K; T411E/K360E/Q362E : D401K; L368D/K370S : S364K/E357L, L368D/K370S : S364K/E357Q, and K370S : S364K/E357Q, according to EU numbering. In some instances, the first and/or the second Fc domains have an additional set of amino acid substitutions comprising Q295E/N384D/Q418E/N421D, according to EU numbering. In some cases, the first and/or the second Fc domains have an additional set of amino acid substitutions consisting of G236R/L328R, E233P/L234V/L235A/G236del/S239K, E233P/L234V/L235A/G236del/S267K, E233P/L234V/L235A/G236del/S239K/A327G, E233P/L234V/L235A/G236del/S267K/A327G and E233P/L234V/L235A/G236del, according to EU numbering.

[00514] In some embodiments, the IL-15 protein has a polypeptide sequence selected from the group consisting of full-length human IL-15 and mature human IL-15, and the IL-15Rα protein has a polypeptide sequence selected from the group consisting of full-length human IL-15Rα and the sushi domain of human IL-15Rα. The IL-15 protein of the Fc fusion protein can have 1, 2, 3, 4, 5, 6, 7, 8 or 9 amino acid substitutions. In some embodiments, the human IL-15 protein of the Fc fusion protein has the amino acid substitution N4D. In some embodiments, the human IL-15 protein of the Fc fusion protein has the amino acid substitution N65D. In some embodiments, the human IL-15 protein of the Fc fusion protein has amino acid substitutions N4D/N65D. In some embodiments, the human IL-15 protein of the Fc fusion protein has amino acid substitutions D30N/E64Q/N65D. The IL-15 protein and

the IL-15Rα protein can have a set of amino acid substitutions selected from the group consisting of E87C : D96/P97/C98; E87C : D96/C97/A98; V49C : S40C; L52C : S40C; E89C : K34C; Q48C : G38C; E53C : L42C; C42S : A37C; and L45C : A37C, respectively.

[00515] In some embodiments, the first protein domain is covalently attached to the N-terminus of the first Fc domain directly and without using the first domain linker and/or the second protein domain is covalently attached to the N-terminus of the second Fc domain directly and without using the second domain linker.

[00516] In some embodiments, the VH and VL of the PD-1 antigen binding domain are selected from the group of pair consisting of 1C11[PD-1]_H3L3 from XENP22553, 1C11[PD-1]_H3.234_L3.144 from XENP25806, 1C11[PD-1]_H3.240_L3.148 from XENP25812, 1C11[PD-1]_H3.241_L3.148 from XENP25813, 1C11[PD-1]_H3.241_L3.92 from XENP25819, 1C11[PD-1]_H3.303_L3.152 from XENP26940, 1C11[PD-1]_H3.329_L3.220 from XENP28026, and 1C11[PD-1]_H3.328_L3.152 from XENP28652. In some embodiments, the VHCDR1, VHCD2, VHCDR3, VLCDR1, VLCDR2, and VLCDR3 of the PD-1 antigen binding domain are selected from the CDRs of the group consisting of 1C11[PD-1]_H3L3 from XENP22553, 1C11[PD-1]_H3.234_L3.144 from XENP25806, 1C11[PD-1]_H3.240_L3.148 from XENP25812, 1C11[PD-1]_H3.241_L3.148 from XENP25813, 1C11[PD-1]_H3.241_L3.92 from XENP25819, 1C11[PD-1]_H3.303_L3.152 from XENP26940, 1C11[PD-1]_H3.329_L3.220 from XENP28026, and 1C11[PD-1]_H3.328_L3.152 from XENP28652. In some embodiments, the sequences for VHCDR1, VHCD2, and VHCDR3 are selected from the sequences depicted in Figures 95A-95J, and the corresponding sequence identifiers. In some embodiments, the sequences for VHCDR1, VHCD2, and VHCDR3 are selected from the sequences depicted in Figures 96A-96F, and the corresponding sequence identifiers.

[00517] In some embodiments, the PD-1-targeted IL-15/Rα-Fc fusion protein comprises an IL-15Rα(sushi) protein fused to IL-15 protein by a variable length linker which is fused to the N-terminus of a first Fc domain of the heterodimeric Fc polypeptide and an anti-PD-1 scFv fused to the N-terminus of a second Fc domain of the heterodimeric Fc polypeptide (see, "scIL-15/Rα x scFv" format and Figure 65A). In some instances, the PD-1-targeted IL-15/Rα-Fc fusion protein is XENP21480. In certain instances, the PD-1-targeted IL-15/Rα-Fc fusion protein is a variant of XENP21480 comprising amino acid substitutions M428L/N434S on each Fc monomer.

[00518] In some embodiments, the PD-1-targeted IL-15/Rα-Fc fusion protein comprises an IL-15Rα(sushi) protein fused to an IL-15 protein by a variable length linker which is fused to the N-terminus of a first Fc domain of the heterodimeric Fc polypeptide and a variable heavy chain (VH) of an anti-PD-1 antibody fused to the N-terminus of a second Fc domain of the heterodimeric Fc polypeptide. A corresponding variable light chain (VL) of the anti-PD-1 antibody is transfected (e.g., introduced) separately and forms an anti-PD-1 Fab with the VH fused to the heterodimeric Fc polypeptide (see, "scIL-15/Rα x Fab" format and Figure 65D). In some instances, the PD-1-targeted IL-15/Rα-Fc fusion protein selected from the group consisting of XENP22022, XENP25849, XENP24535, XENP24536, XENP25850, and XENP25937.

[00519] In some embodiments, the PD-1-targeted IL-15/Rα-Fc fusion protein comprises a variable heavy chain (VH) of an anti-PD-1 antibody fused to the N-terminus of a first Fc domain of the heterodimeric Fc polypeptide and an IL-15Rα(sushi) protein fused to the N-terminus of a second Fc domain of the heterodimeric Fc. A corresponding variable light chain (VL) of the anti-PD-1 antibody can be transfected separately and forms a Fab with the VH fused to the heterodimeric Fc polypeptide. An IL-15 protein can be transfected (e.g., introduced) separately and a non-covalent IL-15/Rα complex forms with the IL-15Rα(sushi) protein fused to the heterodimeric Fc polypeptide (see, "Fab x ncIL-15/Rα" format and Figure 65E). In some instances, the PD-1-targeted IL-15/Rα-Fc fusion protein selected from the group consisting of XENP22112.

[00520] In some embodiments, the PD-1-targeted IL-15/Rα-Fc fusion protein comprises a variable heavy chain (VH) of an anti-PD-1 antibody fused to the N-terminus of a first Fc domain of the heterodimeric Fc polypeptide and an IL-15Rα(sushi) protein comprising one or more engineered cysteine substitutions fused to the N-terminus of a second Fc domain of the heterodimeric Fc. A corresponding variable light chain (VL) of the anti-PD-1 antibody can be transfected (e.g., introduced) separately and forms a Fab with the VH fused to the heterodimeric Fc polypeptide. An IL-15 protein comprising one or more engineered cysteine substitutions can be transfected (e.g., introduced) separately and an IL-15/Rα complex forms via disulfide bonds with the IL-15Rα(sushi) protein fused to the heterodimeric Fc polypeptide (see, "dsIL-15/Rα x Fab" format and Figure 65F). In some instances, the PD-1-targeted IL-15/Rα-Fc fusion protein selected from the group consisting of XENP22641.

[00521] In certain embodiments, the PD-1-targeted IL-15/Rα-Fc fusion protein comprises a first variable heavy chain (VH) of an anti-PD-1 antibody fused to the N-terminus of a first Fc domain of the heterodimeric Fc polypeptide, a second variable heavy chain (VH) of the anti-PD-1 antibody fused to the N-terminus of a second Fc domain of the heterodimeric Fc polypeptide, and an IL-15Rα(sushi) protein fused to the C-terminus of either the first Fc domain or the second Fc domain of the heterodimeric Fc-region. Corresponding variable light chains (VL) of the anti-PD-1 antibody can be transfected (e.g., introduced) to form a first Fab with first variable heavy chain (VH) of the anti-PD-1 antibody and a second Fab with second variable heavy chain (VH) of the anti-PD-1 antibody of the heterodimeric Fc polypeptide. An IL-15 protein can be transfected (e.g., introduced) separately and a non-covalent IL-15/Rα complex forms with the IL-15Rα(sushi) protein fused to the heterodimeric Fc polypeptide (see, “mAb x ncIL-15/Rα” format and Figure 65H). In some instances, the PD-1-targeted IL-15/Rα-Fc fusion protein selected from the group consisting of XENP22642 and XENP22643.

[00522] In certain embodiments, the PD-1-targeted IL-15/Rα-Fc fusion protein comprises a first variable heavy chain (VH) of an anti-PD-1 antibody fused to the N-terminus of a first Fc domain of the heterodimeric Fc polypeptide, a second variable heavy chain (VH) of the anti-PD-1 antibody fused to the N-terminus of a second Fc domain of the heterodimeric Fc polypeptide, and an IL-15Rα(sushi) protein comprising one or more engineered cysteine substitutions fused to the C-terminus of either the first Fc domain or the second Fc domain of the heterodimeric Fc-region. Corresponding variable light chains (VL) of the anti-PD-1 antibody can be transfected (e.g., introduced) to form a first Fab with first variable heavy chain (VH) of the anti-PD-1 antibody and a second Fab with second variable heavy chain (VH) of the anti-PD-1 antibody of the heterodimeric Fc polypeptide. An IL-15 protein comprising one or more engineered cysteine substitutions can be transfected (e.g., introduced) separately and an IL-15/Rα complex forms via disulfide bonds with the IL-15Rα(sushi) protein fused to the heterodimeric Fc polypeptide (see, “mAb x dsIL-15/Rα” format and Figure 65H). In some instances, the PD-1-targeted IL-15/Rα-Fc fusion protein selected from the group consisting of XENP22644 and XENP22645.

[00523] Also provided are nucleic acid compositions encoding the PD-1-targeted IL-15/Rα-Fc fusion protein described herein. In some instances, an expression vector

comprising one or more nucleic acid compositions described herein. In some embodiments, a host cell comprising one or two expression vectors outlined herein is provided.

[00524] Provided herein are exemplary embodiments of PD-1 antigen binding domains (PD-1 ADBs) or anti-PD-1 antibodies that can be used as a PD-1 targeting arm of a PD-1-targeted IL-15/Rα-Fc fusion protein (see, e.g., Example 1).

[00525] Provided herein are PD-1-targeted IL-15/Rα-Fc fusion proteins with one or more engineered amino acid substitutions of the IL-15 protein. In some embodiments, the PD-1-targeted IL-15/Rα-Fc fusion proteins also include one or more engineered cysteine modifications at the IL-15/Rα interface (see, e.g., Example 2). Such PD-1-targeted IL-15/Rα-Fc fusion proteins can induce or promote proliferation of immune cells including NK cells, $CD8^+$ T cells, and $CD4^+$ T cells. Notably, IL-15/Rα-Fc containing fusion proteins that have no linker (e.g., hinge region only) on the IL-15 Fc side demonstrated weaker proliferative activity.

[00526] Provided herein are PD-1-targeted IL-15/Rα-Fc fusion proteins with lower potency, increased pharmacokinetics, and/or increased serum half-life. The PD-1-targeted IL-15/Rα-Fc fusion proteins described herein were engineered to decrease their potency compared to a parental construct (see, Example 2 and the Figures such as but not limited to Figures 44A-44C, 45A-45D, 47A-47B, 51A-51C, 52, 53A-53C, and the like). In some embodiments, one or more amino acid substitutions were introduced into the IL-15/Rα complex and/or in the Fc domain(s) of the heterodimeric Fc fusion protein. In some embodiments, PD-1-targeted IL-15/Rα-Fc fusion proteins with reduced potency compared to a control construct (e.g., a parental construct) have a substantially longer serum half-like. In certain embodiments, the serum half-life increased by 1x, 2x, 3x, 4x, 5x, 6x, 7x, 8x, 9x, 10x, 15x, 20x, 25x or more.

[00527] Provided herein are PD-1-targeted IL-15/Rα-Fc fusion proteins that enhanced GVHD in an animal model (e.g., a human PBMC-engrafted NSG mice) compared to the combination therapy of a control scIL-15/Rα-Fc heterodimeric Fc fusion protein engineered for reduced potency and an anti-PD-1 antibody. Administration of an exemplary PD-1-targeted IL-15/Rα-Fc fusion protein produced a greater effect compared to the combination of IL-15 and PD-1 blockade.

[00528] The PD-1-targeted IL-15/Rα-Fc fusion proteins described herein can induce STAT5 phosphorylation in immune cells including, but not limited to activated lymphocytes, activated T cells (e.g., activated CD4+ T cells and activated CD8+ cells), and activated tumor infiltrating lymphocytes.

[00529] In some embodiments, the PD-1 targeted IL-15/Rα heterodimeric Fc fusion protein is selected from the group consisting of XENP22022, XENP25849, XENP24535, XENP24536, XENP25850, and XENP25937. In certain embodiments, the PD-1 targeted IL-15/Rα-Fc fusion protein is selected from the group consisting XENP25850 and XENP25937.

[00530] In some aspects, provided herein is a pharmaceutical composition comprising an PD-1 targeted IL-15/Rα heterodimeric Fc fusion protein selected from the group consisting of XENP22022, XENP25849, XENP24535, XENP24536, XENP25850, and XENP25937; and a pharmaceutically acceptable carrier. In some embodiments, the PD-1 targeted IL-15/Rα heterodimeric Fc fusion protein is selected from the group consisting of XENP25850, and XENP25937.

[00531] In other aspects, provided herein is a pharmaceutical composition comprising any one of the PD-1 targeted IL-15/Rα heterodimeric Fc fusion proteins described herein and a pharmaceutically acceptable carrier.

[00532] In some aspects, provided herein is a method of treating cancer in a patient in need thereof comprising administering a therapeutically effective amount of any one of the PD-1 targeted IL-15/Rα heterodimeric Fc fusion proteins described herein or any one of the pharmaceutical compositions described herein to said patient.

[00533] In some embodiments, the method also comprises administering a therapeutically effective amount of a checkpoint blockade antibody. In some embodiments, the checkpoint blockade antibody is selected from an anti-PD-1 antibody, an anti-PD-L1 antibody, an anti-TIM3 antibody, an anti-TIGIT antibody, an anti-LAG3 antibody, and an anti-CTLA-4 antibody. In certain embodiments, the anti-PD-1 antibody is nivolumab, pembrolizumab, or pidilizumab. In particular embodiments, the anti-PD-L1 antibody is atezolizumab, avelumab, or durbalumab.

X. **Nucleic Acids of the Invention**

[00534] The invention further provides nucleic acid compositions encoding the PD-1 targeted IL-15/Rα heterodimeric Fc fusion protein of the invention (or, in the case of a monomer Fc domain protein, nucleic acids encoding those as well).

[00535] As will be appreciated by those in the art, the nucleic acid compositions will depend on the format of the PD-1 targeted IL-15/Rα-Fc fusion protein. Thus, for example, when the format requires three amino acid sequences, three nucleic acid sequences can be incorporated into one or more expression vectors for expression. Similarly, some formats only two nucleic acids are needed; again, they can be put into one or two expression vectors.

[00536] As is known in the art, the nucleic acids encoding the components of the invention can be incorporated into expression vectors as is known in the art, and depending on the host cells used to produce the PD-1 targeted IL-15/Rα Fc fusion proteins of the invention. Generally the nucleic acids are operably linked to any number of regulatory elements (promoters, origin of replication, selectable markers, ribosomal binding sites, inducers, etc.). The expression vectors can be extra-chromosomal or integrating vectors.

[00537] The nucleic acids and/or expression vectors of the invention are then transformed into any number of different types of host cells as is well known in the art, including mammalian, bacterial, yeast, insect and/or fungal cells, with mammalian cells (e.g. CHO cells), finding use in many embodiments.

[00538] In some embodiments, nucleic acids encoding each monomer or component of the PD-1 targeted IL-15/Rα-Fc fusion protein, as applicable depending on the format, are each contained within a single expression vector, generally under different or the same promoter controls. In embodiments of particular use in the present invention, each of these two or three nucleic acids are contained on a different expression vector.

[00539] The PD-1 targeted IL-15/Rα heterodimeric Fc fusion protein of the invention are made by culturing host cells comprising the expression vector(s) as is well known in the art. Once produced, traditional fusion protein or antibody purification steps are done, including an ion exchange chromotography step. As discussed herein, having the pIs of the two monomers differ by at least 0.5 can allow separation by ion exchange chromatography or isoelectric focusing, or other methods sensitive to isoelectric point. That is, the inclusion of pI substitutions that alter the isoelectric point (pI) of each monomer so that such that each monomer has a different pI and the heterodimer also has a distinct pI, thus facilitating

isoelectric purification of the heterodimer (e.g., anionic exchange columns, cationic exchange columns). These substitutions also aid in the determination and monitoring of any contaminating homodimers post-purification (e.g., IEF gels, cIEF, and analytical IEX columns).

XI. Biological and Biochemical Functionality of PD-1-Targeted IL-15/Rα-Fc Fusion Proteins

[00540] Generally the PD-1 targeted IL-15/Rα-Fc fusion proteins of the invention are administered to patients with cancer, and efficacy is assessed, in a number of ways as described herein. Thus, while standard assays of efficacy can be run, such as cancer load, size of tumor, evaluation of presence or extent of metastasis, etc., immuno-oncology treatments can be assessed on the basis of immune status evaluations as well. This can be done in a number of ways, including both in vitro and in vivo assays. For example, evaluation of changes in immune status (e.g., presence of ICOS+ CD4+ T cells following ipi treatment) along with "old fashioned" measurements such as tumor burden, size, invasiveness, LN involvement, metastasis, etc. can be done. Thus, any or all of the following can be evaluated: the inhibitory effects of PVRIG on $CD4^+$ T cell activation or proliferation, $CD8^+$ T (CTL) cell activation or proliferation, $CD8^+$ T cell-mediated cytotoxic activity and/or CTL mediated cell depletion, NK cell activity and NK mediated cell depletion, the potentiating effects of PVRIG on Treg cell differentiation and proliferation and Treg- or myeloid derived suppressor cell (MDSC)- mediated immunosuppression or immune tolerance, and/or the effects of PVRIG on proinflammatory cytokine production by immune cells, e.g., IL-2, IFN-γ or TNF-α production by T or other immune cells.

[00541] In some embodiments, assessment of treatment is done by evaluating immune cell proliferation, using for example, CFSE dilution method, Ki67 intracellular staining of immune effector cells, and ^{3}H-thymidine incorporation method,

[00542] In some embodiments, assessment of treatment is done by evaluating the increase in gene expression or increased protein levels of activation-associated markers, including one or more of: CD25, CD69, CD137, ICOS, PD1, GITR, OX40, and cell degranulation measured by surface expression of CD107A.

[00543] In general, gene expression assays are done as is known in the art.

[00544] In general, protein expression measurements are also similarly done as is known in the art.

[00545] In some embodiments, assessment of treatment is done by assessing cytotoxic activity measured by target cell viability detection via estimating numerous cell parameters such as enzyme activity (including protease activity), cell membrane permeability, cell adherence, ATP production, co-enzyme production, and nucleotide uptake activity. Specific examples of these assays include, but are not limited to, Trypan Blue or PI staining, ^{51}Cr or ^{35}S release method, LDH activity, MTT and/or WST assays, Calcein-AM assay, Luminescent based assay, and others.

[00546] In some embodiments, assessment of treatment is done by assessing T cell activity measured by cytokine production, measure either intracellularly in culture supernatant using cytokines including, but not limited to, IFNγ, TNFα, GM-CSF, IL2, IL6, IL4, IL5, IL10, IL13 using well known techniques.

[00547] Accordingly, assessment of treatment can be done using assays that evaluate one or more of the following: (i) increases in immune response, (ii) increases in activation of αβ and/or γδ T cells, (iii) increases in cytotoxic T cell activity, (iv) increases in NK and/or NKT cell activity, (v) alleviation of αβ and/or γδ T-cell suppression, (vi) increases in pro-inflammatory cytokine secretion, (vii) increases in IL-2 secretion; (viii) increases in interferon-γ production, (ix) increases in Th1 response, (x) decreases in Th2 response, (xi) decreases or eliminates cell number and/or activity of at least one of regulatory T cells (Tregs).

A. Assays to Measure Efficacy

[00548] In some embodiments, T cell activation is assessed using a Mixed Lymphocyte Reaction (MLR) assay as is known in the art. An increase in activity indicates immunostimulatory activity. Appropriate increases in activity are outlined below.

[00549] In one embodiment, the signaling pathway assay measures increases or decreases in immune response as measured for an example by phosphorylation or de-phosphorylation of different factors, or by measuring other post translational modifications. An increase in activity indicates immunostimulatory activity. Appropriate increases in activity are outlined below.

[00550] In one embodiment, the signaling pathway assay measures increases or decreases in activation of αβ and/or γδ T cells as measured for an example by cytokine secretion or by proliferation or by changes in expression of activation markers like for an example CD137, CD107a, PD-1, etc. An increase in activity indicates immunostimulatory activity. Appropriate increases in activity are outlined below.

[00551] In one embodiment, the signaling pathway assay measures increases or decreases in cytotoxic T cell activity as measured for an example by direct killing of target cells like for an example cancer cells or by cytokine secretion or by proliferation or by changes in expression of activation markers like for an example CD137, CD107a, PD-1, etc. An increase in activity indicates immunostimulatory activity. Appropriate increases in activity are outlined below.

[00552] In one embodiment, the signaling pathway assay measures increases or decreases in NK and/or NKT cell activity as measured for an example by direct killing of target cells like for an example cancer cells or by cytokine secretion or by changes in expression of activation markers like for an example CD107a, etc. An increase in activity indicates immunostimulatory activity. Appropriate increases in activity are outlined below.

[00553] In one embodiment, the signaling pathway assay measures increases or decreases in αβ and/or γδ T-cell suppression, as measured for an example by cytokine secretion or by proliferation or by changes in expression of activation markers like for an example CD137, CD107a, PD-1, etc. An increase in activity indicates immunostimulatory activity. Appropriate increases in activity are outlined below.

[00554] In one embodiment, the signaling pathway assay measures increases or decreases in pro-inflammatory cytokine secretion as measured for example by ELISA or by Luminex or by Multiplex bead based methods or by intracellular staining and FACS analysis or by Alispot etc. An increase in activity indicates immunostimulatory activity. Appropriate increases in activity are outlined below.

[00555] In one embodiment, the signaling pathway assay measures increases or decreases in IL-2 secretion as measured for example by ELISA or by Luminex or by Multiplex bead based methods or by intracellular staining and FACS analysis or by Alispot etc. An increase in activity indicates immunostimulatory activity. Appropriate increases in activity are outlined below.

[00556] In one embodiment, the signaling pathway assay measures increases or decreases in interferon-γ production as measured for example by ELISA or by Luminex or by Multiplex bead based methods or by intracellular staining and FACS analysis or by Alispot etc. An increase in activity indicates immunostimulatory activity. Appropriate increases in activity are outlined below.

[00557] In one embodiment, the signaling pathway assay measures increases or decreases in Th1 response as measured for an example by cytokine secretion or by changes in expression of activation markers. An increase in activity indicates immunostimulatory activity. Appropriate increases in activity are outlined below.

[00558] In one embodiment, the signaling pathway assay measures increases or decreases in Th2 response as measured for an example by cytokine secretion or by changes in expression of activation markers. An increase in activity indicates immunostimulatory activity. Appropriate increases in activity are outlined below.

[00559] In one embodiment, the signaling pathway assay measures increases or decreases cell number and/or activity of at least one of regulatory T cells (Tregs), as measured for example by flow cytometry or by IHC. A decrease in response indicates immunostimulatory activity. Appropriate decreases are the same as for increases, outlined below.

[00560] In one embodiment, the signaling pathway assay measures increases or decreases in M2 macrophages cell numbers, as measured for example by flow cytometry or by IHC. A decrease in response indicates immunostimulatory activity. Appropriate decreases are the same as for increases, outlined below.

[00561] In one embodiment, the signaling pathway assay measures increases or decreases in M2 macrophage pro-tumorigenic activity, as measured for an example by cytokine secretion or by changes in expression of activation markers. A decrease in response indicates immunostimulatory activity. Appropriate decreases are the same as for increases, outlined below.

[00562] In one embodiment, the signaling pathway assay measures increases or decreases in N2 neutrophils increase, as measured for example by flow cytometry or by IHC. A decrease in response indicates immunostimulatory activity. Appropriate decreases are the same as for increases, outlined below.

[00563] In one embodiment, the signaling pathway assay measures increases or decreases in N2 neutrophils pro-tumorigenic activity, as measured for an example by cytokine secretion or by changes in expression of activation markers. A decrease in response indicates immunostimulatory activity. Appropriate decreases are the same as for increases, outlined below.

[00564] In one embodiment, the signaling pathway assay measures increases or decreases in inhibition of T cell activation, as measured for an example by cytokine secretion or by proliferation or by changes in expression of activation markers like for an example CD137, CD107a, PD1, etc. An increase in activity indicates immunostimulatory activity. Appropriate increases in activity are outlined below.

[00565] In one embodiment, the signaling pathway assay measures increases or decreases in inhibition of CTL activation as measured for an example by direct killing of target cells like for an example cancer cells or by cytokine secretion or by proliferation or by changes in expression of activation markers like for an example CD137, CD107a, PD1, etc. An increase in activity indicates immunostimulatory activity. Appropriate increases in activity are outlined below.

[00566] In one embodiment, the signaling pathway assay measures increases or decreases in αβ and/or γδ T cell exhaustion as measured for an example by changes in expression of activation markers. A decrease in response indicates immunostimulatory activity. Appropriate decreases are the same as for increases, outlined below.

[00567] In one embodiment, the signaling pathway assay measures increases or decreases αβ and/or γδ T cell response as measured for an example by cytokine secretion or by proliferation or by changes in expression of activation markers like for an example CD137, CD107a, PD1, etc. An increase in activity indicates immunostimulatory activity. Appropriate increases in activity are outlined below.

[00568] In one embodiment, the signaling pathway assay measures increases or decreases in stimulation of antigen-specific memory responses as measured for an example by cytokine secretion or by proliferation or by changes in expression of activation markers like for an example CD45RA, CCR7 etc. An increase in activity indicates immunostimulatory activity. Appropriate increases in activity are outlined below. .

[00569] In one embodiment, the signaling pathway assay measures increases or decreases in apoptosis or lysis of cancer cells as measured for an example by cytotoxicity assays such as for an example MTT, Cr release, Calcine AM, or by flow cytometry based assays like for an example CFSE dilution or propidium iodide staining etc. An increase in activity indicates immunostimulatory activity. Appropriate increases in activity are outlined below.

[00570] In one embodiment, the signaling pathway assay measures increases or decreases in stimulation of cytotoxic or cytostatic effect on cancer cells. as measured for an example by cytotoxicity assays such as for an example MTT, Cr release, Calcine AM, or by flow cytometry based assays like for an example CFSE dilution or propidium iodide staining etc. An increase in activity indicates immunostimulatory activity. Appropriate increases in activity are outlined below.

[00571] In one embodiment, the signaling pathway assay measures increases or decreases direct killing of cancer cells as measured for an example by cytotoxicity assays such as for an example MTT, Cr release, Calcine AM, or by flow cytometry based assays like for an example CFSE dilution or propidium iodide staining etc. An increase in activity indicates immunostimulatory activity. Appropriate increases in activity are outlined below.

[00572] In one embodiment, the signaling pathway assay measures increases or decreases Th17 activity as measured for an example by cytokine secretion or by proliferation or by changes in expression of activation markers. An increase in activity indicates immunostimulatory activity. Appropriate increases in activity are outlined below.

[00573] In one embodiment, the signaling pathway assay measures increases or decreases in induction of complement dependent cytotoxicity and/or antibody dependent cell-mediated cytotoxicity, as measured for an example by cytotoxicity assays such as for an example MTT, Cr release, Calcine AM, or by flow cytometry based assays like for an example CFSE dilution or propidium iodide staining etc. An increase in activity indicates immunostimulatory activity. Appropriate increases in activity are outlined below.

[00574] In one embodiment, T cell activation is measured for an example by direct killing of target cells like for an example cancer cells or by cytokine secretion or by proliferation or by changes in expression of activation markers like for an example CD137, CD107a, PD1, etc. For T-cells, increases in proliferation, cell surface markers of activation

(e.g. CD25, CD69, CD137, PD1), cytotoxicity (ability to kill target cells), and cytokine production (e.g. IL-2, IL-4, IL-6, IFNγ, TNF-a, IL-10, IL-17A) would be indicative of immune modulation that would be consistent with enhanced killing of cancer cells.

[00575] In one embodiment, NK cell activation is measured for example by direct killing of target cells like for an example cancer cells or by cytokine secretion or by changes in expression of activation markers like for an example CD107a, etc. For NK cells, increases in proliferation, cytotoxicity (ability to kill target cells and increases CD107a, granzyme, and perforin expression), cytokine production (e.g. IFNγ and TNF), and cell surface receptor expression (e.g. CD25) would be indicative of immune modulation that would be consistent with enhanced killing of cancer cells.

[00576] In one embodiment, γδ T cell activation is measured for example by cytokine secretion or by proliferation or by changes in expression of activation markers.

[00577] In one embodiment, Th1 cell activation is measured for example by cytokine secretion or by changes in expression of activation markers.

[00578] Appropriate increases in activity or response (or decreases, as appropriate as outlined above), are increases of 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95% or 98 to 99% percent over the signal in either a reference sample or in control samples, for example test samples that do not contain an anti-PVRIG antibody of the invention. Similarly, increases of at least one-, two-, three-, four- or five-fold as compared to reference or control samples show efficacy.

XII. **Checkpoint Blockade Antibodies**

[00579] In some embodiments, the PD-1-targeted IL-15/Rα-Fc fusion proteins of the invention described herein are combined with other therapeutic agents including checkpoint blockade antibodies, such as but not limited to, a PD-1 inhibitor, a TIM3 inhibitor, a CTLA4 inhibitor, a PD-L1 inhibitor, a TIGIT inhibitor, a LAG3 inhibitor, or a combination thereof.

A. Anti-PD1 Antibodies

[00580] In some embodiments, a PD-1-targeted IL-15/Rα-Fc fusion protein described herein can be administered to a subject with cancer in combination with a checkpoint blockage antibody, e.g., an anti-PD-1 antibody. In some cases, the anti-PD-1 antibody includes XENP13432 (a bivalent anti-PD-1 mAb based on nivolumab with ablated effector function; amino acid sequence of XENP13432 is depicted in Figure 86. In other cases, the

anti-PD-1 antibody includes XENP25951 (a monovalent anti-PD-1 Fab-Fc based on the PD-1 targeting arm from XENP25850; amino acid sequence of XENP25951 is depicted in Figure 87.

[00581] Exemplary non-limiting anti-PD-1 antibody molecules are disclosed in US 2015/0210769, published on July 30, 2015, entitled "Antibody Molecules to PD-1 and Uses Thereof," incorporated by reference in its entirety.

[00582] In one embodiment, the anti-PD-1 antibody molecule includes at least one or two heavy chain variable domain (optionally including a constant region), at least one or two light chain variable domain (optionally including a constant region), or both, comprising the amino acid sequence of BAP049-Clone-A, BAP049-Clone-B, BAP049-Clone-C, BAP049-Clone-D, or BAP049-Clone-E; or as described in Table 1 of US 2015/0210769, or encoded by the nucleotide sequence in Table 1; or a sequence substantially identical (e.g., at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences. The anti-PD-1 antibody molecule, optionally, comprises a leader sequence from a heavy chain, a light chain, or both, as shown in Table 4 of US 2015/0210769; or a sequence substantially identical thereto.

[00583] In yet another embodiment, the anti-PD-1 antibody molecule includes at least one, two, or three complementarity determining regions (CDRs) from a heavy chain variable region and/or a light chain variable region of an antibody described herein, e.g., an antibody chosen from any of BAP049-hum01, BAP049-hum02, BAP049-hum03, BAP049-hum04, BAP049-hum05, BAP049-hum06, BAP049-hum07, BAP049-hum08, BAP049-hum09, BAP049-hum10, BAP049-hum11, BAP049-hum12, BAP049-hum13, BAP049-hum14, BAP049-hum15, BAP049-hum16, BAP049-Clone-A, BAP049-Clone-B, BAP049-Clone-C, BAP049-Clone-D, or BAP049-Clone-E; or as described in Table 1, or encoded by the nucleotide sequence in Table 1; or a sequence substantially identical (e.g., at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences.

[00584] In yet another embodiment, the anti-PD-1 antibody molecule includes at least one, two, or three CDRs (or collectively all of the CDRs) from a heavy chain variable region comprising an amino acid sequence shown in Table 1 of US 2015/0210769, or encoded by a nucleotide sequence shown in Table 1. In one embodiment, one or more of the CDRs (or collectively all of the CDRs) have one, two, three, four, five, six or more changes, e.g., amino

acid substitutions or deletions, relative to the amino acid sequence shown in Table 1, or encoded by a nucleotide sequence shown in Table 1.

[00585] In yet another embodiment, the anti-PD-1 antibody molecule includes at least one, two, or three CDRs (or collectively all of the CDRs) from a light chain variable region comprising an amino acid sequence shown in Table 1 of US 2015/0210769, or encoded by a nucleotide sequence shown in Table 1. In one embodiment, one or more of the CDRs (or collectively all of the CDRs) have one, two, three, four, five, six or more changes, e.g., amino acid substitutions or deletions, relative to the amino acid sequence shown in Table 1, or encoded by a nucleotide sequence shown in Table 1. In certain embodiments, the anti-PD-1 antibody molecule includes a substitution in a light chain CDR, e.g., one or more substitutions in a CDR1, CDR2 and/or CDR3 of the light chain. In one embodiment, the anti-PD-1 antibody molecule includes a substitution in the light chain CDR3 at position 102 of the light variable region, e.g., a substitution of a cysteine to tyrosine, or a cysteine to serine residue, at position 102 of the light variable region according to Table 1 (e.g., SEQ ID NO:16 or 24 for murine or chimeric, unmodified; or any of SEQ ID NOs:34, 42, 46, 54, 58, 62, 66, 70, 74, or 78 for a modified sequence).

[00586] In another embodiment, the anti-PD-1 antibody molecule includes at least one, two, three, four, five or six CDRs (or collectively all of the CDRs) from a heavy and light chain variable region comprising an amino acid sequence shown in Table 1 of US2015/0210769, or encoded by a nucleotide sequence shown in Table 1. In one embodiment, one or more of the CDRs (or collectively all of the CDRs) have one, two, three, four, five, six or more changes, e.g., amino acid substitutions or deletions, relative to the amino acid sequence shown in Table 1, or encoded by a nucleotide sequence of Table 1.

[00587] In one embodiment, the anti-PD-1 antibody molecule includes:

[00588] (a) a heavy chain variable region (VH) comprising a VHCDR1 amino acid sequence of SEQ ID NO: 4, a VHCDR2 amino acid sequence of SEQ ID NO: 5, and a VHCDR3 amino acid sequence of SEQ ID NO: 3; and a light chain variable region (VL) comprising a VLCDR1 amino acid sequence of SEQ ID NO: 13, a VLCDR2 amino acid sequence of SEQ ID NO: 14, and a VLCDR3 amino acid sequence of SEQ ID NO: 33, each disclosed in Table 1 of US 2015/0210769;

[00589] (b) a VH comprising a VHCDR1 amino acid sequence chosen from SEQ ID NO: 1; a VHCDR2 amino acid sequence of SEQ ID NO: 2; and a VHCDR3 amino acid sequence of SEQ ID NO: 3; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 10, a VLCDR2 amino acid sequence of SEQ ID NO: 11, and a VLCDR3 amino acid sequence of SEQ ID NO: 32, each disclosed in Table 1 of US 2015/0210769;

[00590] (c) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 224, a VHCDR2 amino acid sequence of SEQ ID NO: 5, and a VHCDR3 amino acid sequence of SEQ ID NO: 3; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 13, a VLCDR2 amino acid sequence of SEQ ID NO: 14, and a VLCDR3 amino acid sequence of SEQ ID NO: 33, each disclosed in Table 1 of US 2015/0210769; or

[00591] (d) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 224; a VHCDR2 amino acid sequence of SEQ ID NO: 2; and a VHCDR3 amino acid sequence of SEQ ID NO: 3; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 10, a VLCDR2 amino acid sequence of SEQ ID NO: 11, and a VLCDR3 amino acid sequence of SEQ ID NO: 32, each disclosed in Table 1 of US 2015/0210769.

[00592] In another embodiment, the anti-PD-1 antibody molecule comprises (i) a heavy chain variable region (VH) comprising a VHCDR1 amino acid sequence chosen from SEQ ID NO: 1, SEQ ID NO: 4, or SEQ ID NO: 224; a VHCDR2 amino acid sequence of SEQ ID NO: 2 or SEQ ID NO: 5; and a VHCDR3 amino acid sequence of SEQ ID NO: 3; and (ii) a light chain variable region (VL) comprising a VLCDR1 amino acid sequence of SEQ ID NO: 10 or SEQ ID NO: 13, a VLCDR2 amino acid sequence of SEQ ID NO: 11 or SEQ ID NO: 14, and a VLCDR3 amino acid sequence of SEQ ID NO: 32 or SEQ ID NO: 33, each disclosed in Table 1 of US 2015/0210769.

[00593] In other embodiments, the PD-1 inhibitor is an anti-PD-1 antibody chosen from nivolumab, pembrolizumab, or pidilizumab.

[00594] In some embodiments, the anti-PD-1 antibody is nivolumab. Alternative names for nivolumab include MDX- 1106, MDX-1106-04, ONO-4538, or BMS-936558. In some embodiments, the anti-PD- 1 antibody is nivolumab (CAS Registry Number: 946414-94-4). Nivolumab is a fully human IgG4 monoclonal antibody which specifically blocks PD1. Nivolumab (clone 5C4) and other human monoclonal antibodies that specifically bind to PD1 are disclosed in US 8,008,449 and WO2006/121168. In one embodiment, the inhibitor of

PD-1 is nivolumab, and having a sequence disclosed herein (or a sequence substantially identical or similar thereto, e.g., a sequence at least 85%, 90%, 95% identical or higher to the sequence specified). In some embodiments, the anti-PD-1 antibody is pembrolizumab. Pembrolizumab (also referred to as lambrolizumab, MK-3475, MK03475, SCH-900475 or KEYTRUDA®; Merck) is a humanized IgG4 monoclonal antibody that binds to PD-1. Pembrolizumab and other humanized anti-PD-1 antibodies are disclosed in Hamid, O. *et al.* (2013) *New England Journal of Medicine* 369 (2): 134–44, US 8,354,509 and WO2009/114335.

[00595] In one embodiment, the inhibitor of PD-1 is pembrolizumab disclosed in, *e.g.*, US 8,354,509 and WO 2009/114335, and having a sequence disclosed herein (or a sequence substantially identical or similar thereto, *e.g.*, a sequence at least 85%, 90%, 95% identical or higher to the sequence specified).

[00596] In some embodiments, the anti-PD-1 antibody is pidilizumab. Pidilizumab (CT-011; Cure Tech) is a humanized IgG1k monoclonal antibody that binds to PD1. Pidilizumab and other humanized anti-PD-1 monoclonal antibodies are disclosed in US 8,747,847 and WO2009/101611.

[00597] Other anti-PD1 antibodies include AMP 514 (Amplimmune), among others, *e.g.*, anti-PD1 antibodies disclosed in US 8,609,089, US 2010028330, and/or US 20120114649.

[00598] In some embodiments, the PD-1 inhibitor is an immunoadhesin (e.g., an immunoadhesin comprising an extracellular or PD-1 binding portion of PD-Ll or PD-L2 fused to a constant region (e.g., an Fc region of an immunoglobulin sequence). In some embodiments, the PD-1 inhibitor is AMP-224 (B7-DCIg; Amplimmune; e.g., disclosed in WO2010/027827 and WO2011/066342), is a PD-L2 Fc fusion soluble receptor that blocks the interaction between PD-1 and B7-H1.

[00599] In some embodiments, anti-PD-1 antibodies can be used in combination with a PD-1-targeted IL-15/Rα-Fc fusion protein of the invention. There are several anti-PD-1 antibodies including, but not limited to, two currently FDA approved antibodies, pembrolizumab and nivolizumab, as well as those in clinical testing currently, including, but not limited to, tislelizumab, Sym021, REGN2810 (developed by Rengeneron), JNJ-63723283 (developed by J and J), SHR-1210, pidilizumab, AMP-224, MEDIo680, PDR001 and CT-

001, as well as others outlined in Liu et al., J. Hemat. & Oncol. (2017)10:136, the antibodies therein expressly incorporated by reference.

[00600] In some embodiments, a PD-1-targeted IL-15/Rα-Fc fusion protein described herein can be used in combination with a PD-1 inhibitor (e.g., an anti-PD-1 antibody). In certain embodiments, a PD-1-targeted IL-15/Rα-Fc fusion protein (e.g., XENP25937 and XENP25850) described herein is administered in combination with an anti-PD-1 antibody.

B. Anti-TIM3 Antibodies

[00601] Exemplary non-limiting anti-TIM-3 antibody molecules are disclosed in US 2015/0218274, published on August 6, 2015, entitled "Antibody Molecules to TIM-3 and Uses Thereof," incorporated by reference in its entirety.

[00602] In one embodiment, the anti-TIM-3 antibody molecule includes at least one or two heavy chain variable domain (optionally including a constant region), at least one or two light chain variable domain (optionally including a constant region), or both, comprising the amino acid sequence of ABTIM3, ABTIM3-hum01, ABTIM3-hum02, ABTIM3-hum03, ABTIM3-hum04, ABTIM3-hum05, ABTIM3-hum06, ABTIM3-hum07, ABTIM3-hum08, ABTIM3-hum09, ABTIM3-hum10, ABTIM3-hum11, ABTIM3-hum12, ABTIM3-hum13, ABTIM3-hum14, ABTIM3-hum15, ABTIM3-hum16, ABTIM3-hum17, ABTIM3-hum18, ABTIM3-hum19, ABTIM3-hum20, ABTIM3-hum21, ABTIM3-hum22, ABTIM3-hum23; or as described in Tables 1-4 of US 2015/0218274; or encoded by the nucleotide sequence in Tables 1-4; or a sequence substantially identical (e.g., at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences. The anti-TIM-3 antibody molecule, optionally, comprises a leader sequence from a heavy chain, a light chain, or both, as shown in US 2015/0218274; or a sequence substantially identical thereto.

[00603] In yet another embodiment, the anti-TIM-3 antibody molecule includes at least one, two, or three complementarity determining regions (CDRs) from a heavy chain variable region and/or a light chain variable region of an antibody described herein, e.g., an antibody chosen from any of ABTIM3, ABTIM3-hum01, ABTIM3-hum02, ABTIM3-hum03, ABTIM3-hum04, ABTIM3-hum05, ABTIM3-hum06, ABTIM3-hum07, ABTIM3-hum08, ABTIM3-hum09, ABTIM3-hum10, ABTIM3-hum11, ABTIM3-hum12, ABTIM3-hum13, ABTIM3-hum14, ABTIM3-hum15, ABTIM3-hum16, ABTIM3-hum17, ABTIM3-hum18, ABTIM3-hum19, ABTIM3-hum20, ABTIM3-hum21, ABTIM3-hum22, ABTIM3-hum23; or

as described in Tables 1-4 of US 2015/0218274; or encoded by the nucleotide sequence in Tables 1-4; or a sequence substantially identical (e.g., at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences.

[00604] In yet another embodiment, the anti-TIM-3 antibody molecule includes at least one, two, or three CDRs (or collectively all of the CDRs) from a heavy chain variable region comprising an amino acid sequence shown in Tables 1-4 of US 2015/0218274, or encoded by a nucleotide sequence shown in Tables 1-4. In one embodiment, one or more of the CDRs (or collectively all of the CDRs) have one, two, three, four, five, six or more changes, e.g., amino acid substitutions or deletions, relative to the amino acid sequence shown in Tables 1-4, or encoded by a nucleotide sequence shown in Table 1-4.

[00605] In yet another embodiment, the anti- TIM-3 antibody molecule includes at least one, two, or three CDRs (or collectively all of the CDRs) from a light chain variable region comprising an amino acid sequence shown in Tables 1-4 of US 2015/0218274, or encoded by a nucleotide sequence shown in Tables 1-4. In one embodiment, one or more of the CDRs (or collectively all of the CDRs) have one, two, three, four, five, six or more changes, e.g., amino acid substitutions or deletions, relative to the amino acid sequence shown in Tables 1-4, or encoded by a nucleotide sequence shown in Tables 1-4. In certain embodiments, the anti-TIM-3 antibody molecule includes a substitution in a light chain CDR, e.g., one or more substitutions in a CDR1, CDR2 and/or CDR3 of the light chain.

[00606] In another embodiment, the anti-TIM-3 antibody molecule includes at least one, two, three, four, five or six CDRs (or collectively all of the CDRs) from a heavy and light chain variable region comprising an amino acid sequence shown in Tables 1-4 of US 2015/0218274, or encoded by a nucleotide sequence shown in Tables 1-4. In one embodiment, one or more of the CDRs (or collectively all of the CDRs) have one, two, three, four, five, six or more changes, e.g., amino acid substitutions or deletions, relative to the amino acid sequence shown in Tables 1-4, or encoded by a nucleotide sequence shown in Tables 1-4.

[00607] In one embodiment, the anti-TIM-3 antibody molecule includes:

(a) a heavy chain variable region (VH) comprising a VHCDR1 amino acid sequence chosen from SEQ ID NO: 9; a VHCDR2 amino acid sequence of SEQ ID NO: 10; and a VHCDR3 amino acid sequence of SEQ ID NO: 5; and a light chain variable region (VL) comprising a VLCDR1 amino acid sequence of SEQ ID NO: 12, a VLCDR2 amino acid sequence of SEQ ID NO: 13, and a VLCDR3 amino acid sequence of SEQ ID NO: 14, each disclosed in Tables 1-4 of US 2015/0218274;

(b) a VH comprising a VHCDR1 amino acid sequence chosen from SEQ ID NO: 3; a VHCDR2 amino acid sequence of SEQ ID NO: 4; and a VHCDR3 amino acid sequence of SEQ ID NO: 5; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 6, a VLCDR2 amino acid sequence of SEQ ID NO: 7, and a VLCDR3 amino acid sequence of SEQ ID NO: 8, each disclosed in Tables 1-4 of US 2015/0218274;

(c) a VH comprising a VHCDR1 amino acid sequence chosen from SEQ ID NO: 9; a VHCDR2 amino acid sequence of SEQ ID NO: 25; and a VHCDR3 amino acid sequence of SEQ ID NO: 5; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 12, a VLCDR2 amino acid sequence of SEQ ID NO: 13, and a VLCDR3 amino acid sequence of SEQ ID NO: 14, each disclosed in Tables 1-4 of US 2015/0218274;

(d) a VH comprising a VHCDR1 amino acid sequence chosen from SEQ ID NO: 3; a VHCDR2 amino acid sequence of SEQ ID NO: 24; and a VHCDR3 amino acid sequence of SEQ ID NO: 5; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 6, a VLCDR2 amino acid sequence of SEQ ID NO: 7, and a VLCDR3 amino acid sequence of SEQ ID NO: 8, each disclosed in Tables 1-4 of US 2015/0218274;

(e) a VH comprising a VHCDR1 amino acid sequence chosen from SEQ ID NO: 9; a VHCDR2 amino acid sequence of SEQ ID NO: 31; and a VHCDR3 amino acid sequence of SEQ ID NO: 5; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 12, a VLCDR2 amino acid sequence of SEQ ID NO: 13, and a VLCDR3 amino acid sequence of SEQ ID NO: 14, each disclosed in Tables 1-4 of US 2015/0218274; or

(f) a VH comprising a VHCDR1 amino acid sequence chosen from SEQ ID NO: 3; a VHCDR2 amino acid sequence of SEQ ID NO: 30; and a VHCDR3 amino acid sequence of SEQ ID NO: 5; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 6, a VLCDR2 amino acid sequence of SEQ ID NO: 7, and a VLCDR3 amino acid sequence of SEQ ID NO: 8, each disclosed in Tables 1-4 of US 2015/0218274.

[00608] Exemplary anti-TIM-3 antibodies are disclosed in U.S. Patent No.: 8,552,156, WO 2011/155607, EP 2581113 and U.S Publication No.: 2014/044728.

[00609] In some embodiments, anti-TIM-3 antibodies can be used in combination with a PD-1-targeted IL-15/Rα-Fc fusion protein of the invention. There are several TIM-3 antibodies in clinical development, including, but not limited to, MBG453 and TSR-022.

[00610] In some embodiments, a PD-1-targeted IL-15/Rα-Fc fusion protein described herein can be used in combination with a TIM-3 inhibitor (e.g., an anti-TIM3 antibody). In certain embodiments, a PD-1-targeted IL-15/Rα-Fc fusion protein (e.g., XENP25937 and XENP25850) described herein is administered in combination with an anti-TIM3 antibody.

C. Anti-CTLA4 Antibodies

[00611] Exemplary anti-CTLA4 antibodies include tremelimumab (IgG2 monoclonal antibody available from Pfizer, formerly known as ticilimumab, CP-675,206); and dim (CTLA-4 antibody, also known as MDX-010, CAS No. 477202-00-9). Other exemplary anti-CTLA-4 antibodies are disclosed, *e.g.,* in U.S. Pat. No. 5,811,097.

[00612] In one embodiment, the anti-CTLA4 antibody is ipilimumab disclosed in, *e.g.*, US 5,811,097, US 7,605,238, WO00/32231 and WO97/20574, and having a sequence disclosed herein (or a sequence substantially identical or similar thereto, *e.g.*, a sequence at least 85%, 90%, 95% identical or higher to the sequence specified).

[00613] In one embodiment, the anti-CTLA4 antibody is tremelimumab disclosed in, *e.g.*, US6,682,736 and WO00/37504, and having a sequence disclosed herein (or a sequence substantially identical or similar thereto, *e.g.*, a sequence at least 85%, 90%, 95% identical or higher to the sequence specified).

[00614] In some embodiments, anti-CTLA-4 antibodies can be used in combination with a PD-1-targeted IL-15/Rα-Fc fusion protein of the invention. Thus, suitable anti-CTLA-4 antibodies for use in combination therapies as outlined herein include, but are not limited to, one currently FDA approved antibody ipilimumab, and several more in development, including CP-675,206 and AGEN-1884.

[00615] In some embodiments, PD-1-targeted IL-15/Rα-Fc fusion protein described herein can be used in combination with a CTLA-4 inhibitor (e.g., an anti-CTLA-4 antibody). In certain embodiments, a PD-1-targeted IL-15/Rα-Fc fusion protein (e.g., XENP25937 and XENP25850) described herein is administered in combination with an anti-CTLA-4 antibody.

D. Anti-PD-L1 Antibodies

[00616] Exemplary non-limiting anti-PD-L1 antibody molecules are disclosed in US 2016/0108123, published on April 21, 2016, entitled "Antibody Molecules to PD-L1 and Uses Thereof," incorporated by reference in its entirety.

[00617] In one embodiment, the anti-PD-L1 antibody molecule includes at least one or two heavy chain variable domain (optionally including a constant region), at least one or two light chain variable domain (optionally including a constant region), or both, comprising the amino acid sequence of any of BAP058-hum01, BAP058-hum02, BAP058-hum03, BAP058-hum04, BAP058-hum05, BAP058-hum06, BAP058-hum07, BAP058-hum08, BAP058-hum09, BAP058-hum10, BAP058-hum11, BAP058-hum12, BAP058-hum13, BAP058-hum14, BAP058-hum15, BAP058-hum16, BAP058-hum17, BAP058-Clone-K, BAP058-Clone-L, BAP058-Clone-M, BAP058-Clone-N, or BAP058-Clone-O; or as described in Table 1 of US 2016/0108123, or encoded by the nucleotide sequence in Table 1; or a sequence substantially identical (e.g., at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences.

[00618] In yet another embodiment, the anti-PD-L1 antibody molecule includes at least one, two, or three complementarity determining regions (CDRs) from a heavy chain variable region and/or a light chain variable region of an antibody described herein, e.g., an antibody chosen from any of BAP058-hum01, BAP058-hum02, BAP058-hum03, BAP058-hum04, BAP058-hum05, BAP058-hum06, BAP058-hum07, BAP058-hum08, BAP058-hum09, BAP058-hum10, BAP058-hum11, BAP058-hum12, BAP058-hum13, BAP058-hum14, BAP058-hum15, BAP058-hum16, BAP058-hum17, BAP058-Clone-K, BAP058-Clone-L, BAP058-Clone-M, BAP058-Clone-N, or BAP058-Clone-O; or as described in Table 1 of US 2016/0108123, or encoded by the nucleotide sequence in Table 1; or a sequence substantially identical (e.g., at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences.

[00619] In yet another embodiment, the anti-PD-L1 antibody molecule includes at least one, two, or three CDRs (or collectively all of the CDRs) from a heavy chain variable region comprising an amino acid sequence shown in Table 1 of US 2016/0108123, or encoded by a nucleotide sequence shown in Table 1. In one embodiment, one or more of the CDRs (or collectively all of the CDRs) have one, two, three, four, five, six or more changes, e.g., amino

acid substitutions or deletions, relative to the amino acid sequence shown in Table 1, or encoded by a nucleotide sequence shown in Table 1.

[00620] In yet another embodiment, the anti-PD-L1 antibody molecule includes at least one, two, or three CDRs (or collectively all of the CDRs) from a light chain variable region comprising an amino acid sequence shown in Table 1 of US 2016/0108123, or encoded by a nucleotide sequence shown in Table 1. In one embodiment, one or more of the CDRs (or collectively all of the CDRs) have one, two, three, four, five, six or more changes, e.g., amino acid substitutions or deletions, relative to the amino acid sequence shown in Table 1, or encoded by a nucleotide sequence shown in Table 1. In certain embodiments, the anti-PD-L1 antibody molecule includes a substitution in a light chain CDR, e.g., one or more substitutions in a CDR1, CDR2 and/or CDR3 of the light chain.

[00621] In another embodiment, the anti-PD-L1 antibody molecule includes at least one, two, three, four, five or six CDRs (or collectively all of the CDRs) from a heavy and light chain variable region comprising an amino acid sequence shown in Table 1, or encoded by a nucleotide sequence shown in Table 1 of US 2016/0108123. In one embodiment, one or more of the CDRs (or collectively all of the CDRs) have one, two, three, four, five, six or more changes, e.g., amino acid substitutions or deletions, relative to the amino acid sequence shown in Table 1, or encoded by a nucleotide sequence shown in Table 1.

[00622] In one embodiment, the anti-PD-L1 antibody molecule includes:

(i) a heavy chain variable region (VH) including a VHCDR1 amino acid sequence chosen from SEQ ID NO: 1, SEQ ID NO: 4 or SEQ ID NO: 195; a VHCDR2 amino acid sequence of SEQ ID NO: 2; and a VHCDR3 amino acid sequence of SEQ ID NO: 3, each disclosed in Table 1 of US 2016/0108123; and

(ii) a light chain variable region (VL) including a VLCDR1 amino acid sequence of SEQ ID NO: 9, a VLCDR2 amino acid sequence of SEQ ID NO: 10, and a VLCDR3 amino acid sequence of SEQ ID NO: 11, each disclosed in Table 1 of US 2016/0108123.

[00623] In another embodiment, the anti-PD-L1 antibody molecule includes:

(i) a heavy chain variable region (VH) including a VHCDR1 amino acid sequence chosen from SEQ ID NO: 1, SEQ ID NO: 4 or SEQ ID NO: 195; a VHCDR2 amino acid sequence of SEQ ID NO: 5, and a VHCDR3 amino acid sequence of SEQ ID NO: 3, each disclosed in Table 1 of US 2016/0108123; and

(ii) a light chain variable region (VL) including a VLCDR1 amino acid sequence of SEQ ID NO: 12, a VLCDR2 amino acid sequence of SEQ ID NO: 13, and a VLCDR3 amino acid sequence of SEQ ID NO: 14, each disclosed in Table 1 of US 2016/0108123.

[00624] In one embodiment, the anti-PD-L1 antibody molecule comprises the VHCDR1 amino acid sequence of SEQ ID NO: 1. In another embodiment, the anti-PD-L1 antibody molecule comprises the VHCDR1 amino acid sequence of SEQ ID NO: 4. In yet another embodiment, the anti-PD-L1 antibody molecule comprises the VHCDR1 amino acid sequence of SEQ ID NO: 195, each disclosed in Table 1 of US 2016/0108123.

[00625] In some embodiments, the PD-L1 inhibitor is an antibody molecule. In some embodiments, the anti-PD-Ll inhibitor is chosen from YW243.55.S70, MPDL3280A, MEDI-4736, MSB-0010718C, MDX-1105, atezolizumab, durbalumab, avelumab, or BMS936559.

[00626] In some embodiments, the anti-PD-L1 antibody is atezolizumab. Atezolizumab (also referred to as MPDL3280A and Atezo®; Roche) is a monoclonal antibody that binds to PD-L1. Atezolizumab and other humanized anti-PD-L1 antibodies are disclosed in US 8,217,149, and having a sequence disclosed herein (or a sequence substantially identical or similar thereto, e.g., a sequence at least 85%, 90%, 95% identical or higher to the sequence specified).

[00627] In some embodiments, the anti-PD-L1 antibody is avelumab. Avelumab (also referred to as A09-246-2; Merck Serono) is a monoclonal antibody that binds to PD-L1. Avelumab and other humanized anti-PD-L1 antibodies are disclosed in US 9,324,298 and WO2013/079174, and having a sequence disclosed herein (or a sequence substantially identical or similar thereto, e.g., a sequence at least 85%, 90%, 95% identical or higher to the sequence specified).

[00628] In some embodiments, the anti-PD-L1 antibody is durvalumab. Durvalumab (also referred to as MEDI4736; AstraZeneca) is a monoclonal antibody that binds to PD-L1. Durvalumab and other humanized anti-PD-L1 antibodies are disclosed in US 8,779,108, and having a sequence disclosed herein (or a sequence substantially identical or similar thereto, e.g., a sequence at least 85%, 90%, 95% identical or higher to the sequence specified).

[00629] In some embodiments, the anti-PD-L1 antibody is BMS-936559. BMS-936559 (also referred to as MDX-1105; BMS) is a monoclonal antibody that binds to PD-L1. BMS-936559 and other humanized anti-PD-L1 antibodies are disclosed in US 7,943,743 and

WO2007005874, and having a sequence disclosed herein (or a sequence substantially identical or similar thereto, e.g., a sequence at least 85%, 90%, 95% identical or higher to the sequence specified).

[00630] In some embodiments, anti-PD-L1 antibodies can be used in combination with an PD-1-targeted IL-15/Rα-Fc fusion protein of the invention. There are several anti-PD-L1 antibodies including three currently FDA approved antibodies, atezolizumab, avelumab, durvalumab, as well as those in clinical testing currently, including, but not limited to, LY33000054 and CS1001, as well as others outlined in Liu et al., J. Hemat. & Oncol. (2017)10:136, the antibodies therein expressly incorporated by reference.

[00631] In some embodiments, an PD-1-targeted IL-15/Rα-Fc fusion protein described herein can be used in combination with a PD-L1 inhibitor (e.g., an anti-PD-L1 antibody). In certain embodiments, an PD-1-targeted IL-15/Rα-Fc fusion protein (e.g., XENP25937 and XENP25850) described herein is administered in combination with an anti-PD-L1 antibody.

[00632] In some embodiments, an PD-1-targeted IL-15/Rα-Fc fusion protein described herein can be used in combination with a PD-L1 or PD-L2 inhibitor (e.g., an anti-PD-L1 antibody).

E. Anti-TIGIT Antibodies

[00633] In some embodiments, the anti-TIGIT antibody is OMP-313M32. OMP-313M32 (OncoMed Pharmaceuticals) is a monoclonal antibody that binds to TIGIT. OMP-313M32 and other humanized anti- TIGIT antibodies are disclosed in US20160376365 and WO2016191643, and having a sequence disclosed herein (or a sequence substantially identical or similar thereto, e.g., a sequence at least 85%, 90%, 95% identical or higher to the sequence specified).

[00634] In some embodiments, the anti-TIGIT antibody is BMS-986207. BMS-986207 (also referred to as ONO-4686; Bristol-Myers Squibb) is a monoclonal antibody that binds to TIGIT. BMS-986207 and other humanized anti- TIGIT antibodies are disclosed in US20160176963 and WO2016106302, and having a sequence disclosed herein (or a sequence substantially identical or similar thereto, e.g., a sequence at least 85%, 90%, 95% identical or higher to the sequence specified).

[00635] In some embodiments, the anti-TIGIT antibody is MTIG7192. MTIG7192 (Genentech) is a monoclonal antibody that binds to TIGIT. MTIG7192 and other humanized

anti- TIGIT antibodies are disclosed in US2017088613, WO2017053748, and WO2016011264, and having a sequence disclosed herein (or a sequence substantially identical or similar thereto, e.g., a sequence at least 85%, 90%, 95% identical or higher to the sequence specified).

[00636] In some embodiments, anti-TIGIT antibodies can be used in combination with an PD-1-targeted IL-15/Rα-Fc fusion protein of the invention. There are several TIGIT antibodies in clinical development, BMS-986207, OMP-313M32 and MTIG7192A.

[00637] In some embodiments, an PD-1-targeted IL-15/Rα-Fc fusion protein described herein can be used in combination with a TIGIT inhibitor (e.g., an anti-TIGIT antibody). In certain embodiments, an PD-1-targeted IL-15/Rα-Fc fusion protein (e.g., XENP25937 and XENP25850) described herein is administered in combination with an anti-TIGIT antibody.

F. Anti-LAG-3 Antibodies

[00638] Exemplary non-limiting anti- LAG-3 antibody molecules are disclosed in US 2015/0259420 published on September 17, 2015, entitled "Antibody Molecules to LAG-3 and Uses Thereof," incorporated by reference in its entirety.

[00639] In one embodiment, the anti-LAG-3 antibody molecule includes at least one or two heavy chain variable domain (optionally including a constant region), at least one or two light chain variable domain (optionally including a constant region), or both, comprising the amino acid sequence of any of BAP050-hum01, BAP050-hum02, BAP050-hum03, BAP050-hum04, BAP050-hum05, BAP050-hum06, BAP050-hum07, BAP050-hum08, BAP050-hum09, BAP050-hum10, BAP050-hum11, BAP050-hum12, BAP050-hum13, BAP050-hum14, BAP050-hum15, BAP050-hum16, BAP050-hum17, BAP050-hum18, BAP050-hum19, BAP050-hum20, huBAP050(Ser) (e.g., BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum03-Ser, BAP050-hum04-Ser, BAP050-hum05-Ser, BAP050-hum06-Ser, BAP050-hum07-Ser, BAP050-hum08-Ser, BAP050-hum09-Ser, BAP050-hum10-Ser, BAP050-hum11-Ser, BAP050-hum12-Ser, BAP050-hum13-Ser, BAP050-hum14-Ser, BAP050-hum15-Ser, BAP050-hum18-Ser, BAP050-hum19-Ser, or BAP050-hum20-Ser), BAP050-Clone-F, BAP050-Clone-G, BAP050-Clone-H, BAP050-Clone-I, or BAP050-Clone-J; or as described in Table 1 of US 2015/0259420, or encoded by the nucleotide sequence in Table 1; or a sequence substantially identical (e.g., at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences.

[00640] In yet another embodiment, the anti- LAG-3 antibody molecule includes at least one, two, or three complementarity determining regions (CDRs) from a heavy chain variable region and/or a light chain variable region of an antibody described herein, e.g., an antibody chosen from any of BAP050-hum01, BAP050-hum02, BAP050-hum03, BAP050-hum04, BAP050-hum05, BAP050-hum06, BAP050-hum07, BAP050-hum08, BAP050-hum09, BAP050-hum10, BAP050-hum11, BAP050-hum12, BAP050-hum13, BAP050-hum14, BAP050-hum15, BAP050-hum16, BAP050-hum17, BAP050-hum18, BAP050-hum19, BAP050-hum20, huBAP050(Ser) (e.g., BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum03-Ser, BAP050-hum04-Ser, BAP050-hum05-Ser, BAP050-hum06-Ser, BAP050-hum07-Ser, BAP050-hum08-Ser, BAP050-hum09-Ser, BAP050-hum10-Ser, BAP050-hum11-Ser, BAP050-hum12-Ser, BAP050-hum13-Ser, BAP050-hum14-Ser, BAP050-hum15-Ser, BAP050-hum18-Ser, BAP050-hum19-Ser, or BAP050-hum20-Ser), BAP050-Clone-F, BAP050-Clone-G, BAP050-Clone-H, BAP050-Clone-I, or BAP050-Clone-J; or as described in Table 1 of US 2015/0259420, or encoded by the nucleotide sequence in Table 1; or a sequence substantially identical (e.g., at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences.

[00641] In yet another embodiment, the anti- LAG-3 antibody molecule includes at least one, two, or three CDRs (or collectively all of the CDRs) from a heavy chain variable region comprising an amino acid sequence shown in Table 1 of US 2015/0259420, or encoded by a nucleotide sequence shown in Table 1. In one embodiment, one or more of the CDRs (or collectively all of the CDRs) have one, two, three, four, five, six or more changes, e.g., amino acid substitutions or deletions, relative to the amino acid sequence shown in Table 1, or encoded by a nucleotide sequence shown in Table 1.

[00642] In yet another embodiment, the anti-LAG-3 antibody molecule includes at least one, two, or three CDRs (or collectively all of the CDRs) from a light chain variable region comprising an amino acid sequence shown in Table 1 of US 2015/0259420, or encoded by a nucleotide sequence shown in Table 1. In one embodiment, one or more of the CDRs (or collectively all of the CDRs) have one, two, three, four, five, six or more changes, e.g., amino acid substitutions or deletions, relative to the amino acid sequence shown in Table 1, or encoded by a nucleotide sequence shown in Table 1. In certain embodiments, the anti-PD-L1 antibody molecule includes a substitution in a light chain CDR, e.g., one or more substitutions in a CDR1, CDR2 and/or CDR3 of the light chain.

[00643] In another embodiment, the anti- LAG-3 antibody molecule includes at least one, two, three, four, five or six CDRs (or collectively all of the CDRs) from a heavy and light chain variable region comprising an amino acid sequence shown in Table 1, or encoded by a nucleotide sequence shown in Table 1 of US 2015/0259420. In one embodiment, one or more of the CDRs (or collectively all of the CDRs) have one, two, three, four, five, six or more changes, e.g., amino acid substitutions or deletions, relative to the amino acid sequence shown in Table 1, or encoded by a nucleotide sequence shown in Table 1.

[00644] In one embodiment, the anti- LAG-3 antibody molecule includes:

(i) a heavy chain variable region (VH) including a VHCDR1 amino acid sequence chosen from SEQ ID NO: 1, SEQ ID NO: 4 or SEQ ID NO: 286; a VHCDR2 amino acid sequence of SEQ ID NO: 2; and a VHCDR3 amino acid sequence of SEQ ID NO: 3, each disclosed in Table 1 of US 2015/0259420; and

(ii) a light chain variable region (VL) including a VLCDR1 amino acid sequence of SEQ ID NO: 10, a VLCDR2 amino acid sequence of SEQ ID NO: 11, and a VLCDR3 amino acid sequence of SEQ ID NO: 12, each disclosed in Table 1 of US 2015/0259420.

[00645] In another embodiment, the anti-LAG-3 antibody molecule includes:

(i) a heavy chain variable region (VH) including a VHCDR1 amino acid sequence chosen from SEQ ID NO: 1, SEQ ID NO: 4 or SEQ ID NO: 286; a VHCDR2 amino acid sequence of SEQ ID NO: 5, and a VHCDR3 amino acid sequence of SEQ ID NO: 3, each disclosed in Table 1 of US 2015/0259420; and

(ii) a light chain variable region (VL) including a VLCDR1 amino acid sequence of SEQ ID NO: 13, a VLCDR2 amino acid sequence of SEQ ID NO: 14, and a VLCDR3 amino acid sequence of SEQ ID NO: 15, each disclosed in Table 1 of US 2015/0259420.

[00646] In one embodiment, the anti-LAG-3 antibody molecule comprises the VHCDR1 amino acid sequence of SEQ ID NO: 1. In another embodiment, the anti-LAG-3 antibody molecule comprises the VHCDR1 amino acid sequence of SEQ ID NO: 4. In yet another embodiment, the anti-LAG-3 antibody molecule comprises the VHCDR1 amino acid sequence of SEQ ID NO: 286, each disclosed in Table 1 of US 2015/0259420.

[00647] In some embodiments, the anti-LAG-3 antibody is BMS-986016. BMS-986016 (also referred to as BMS986016; Bristol-Myers Squibb) is a monoclonal antibody that binds

to LAG-3. BMS-986016 and other humanized anti-LAG-3 antibodies are disclosed in US 2011/0150892, WO2010/019570, and WO2014/008218.

[00648] In some embodiments, the anti-LAG3 antibody is LAG525. LAG525 (also referred to as IMP701; Novartis) is a monoclonal antibody that binds to LAG3. LAG525 and other humanized anti-LAG3 antibodies are disclosed in US 9,244,059 and WO2008132601, and having a sequence disclosed herein (or a sequence substantially identical or similar thereto, e.g., a sequence at least 85%, 90%, 95% identical or higher to the sequence specified).

[00649] Other exemplary anti-LAG-3 antibodies are disclosed, *e.g.*, in US2011150892 and US2018066054.

[00650] In some embodiments, anti-LAG-3 antibodies can be used in combination with a PD-1-targeted IL-15/Rα-Fc fusion protein of the invention. There are several anti-LAG-3 antibodies in clinical development including REGN3767, by Regeneron and TSR-033 (Tesaro).

[00651] In some embodiments, a PD-1-targeted IL-15/Rα-Fc fusion protein described herein can be used in combination with a LAG- inhibitor (e.g., an anti-LAG-3 antibody). In certain embodiments, an PD-1-targeted IL-15/Rα-Fc fusion protein (e.g., XENP25937 and XENP25850) described herein is administered in combination with an anti-LAG3 antibody.

XIII. **Combination Therapy**

[00652] In some aspects, the PD-1-targeted IL-15/Rα-Fc fusion proteins described herein is administered in combination with another therapeutic agent. Administered "in combination", as used herein, means that two (or more) different treatments are delivered to the subject during the course of the subject's affliction with the disorder, e.g., the two or more treatments are delivered after the subject has been diagnosed with the disorder and before the disorder has been cured or eliminated or treatment has ceased for other reasons. In some embodiments, the delivery of one treatment is still occurring when the delivery of the second begins, so that there is overlap in terms of administration. This is sometimes referred to herein as "simultaneous" or "concurrent delivery". In other embodiments, the delivery of one treatment ends before the delivery of the other treatment begins. In some embodiments of either case, the treatment is more effective because of combined administration. For example, the second treatment is more effective, e.g., an equivalent effect is seen with less of the

second treatment, or the second treatment reduces symptoms to a greater extent, than would be seen if the second treatment were administered in the absence of the first treatment, or the analogous situation is seen with the first treatment. In some embodiments, delivery is such that the reduction in a symptom, or other parameter related to the disorder is greater than what would be observed with one treatment delivered in the absence of the other. The effect of the two treatments can be partially additive, wholly additive, or greater than additive. The delivery can be such that an effect of the first treatment delivered is still detectable when the second is delivered.

[00653] The PD-1-targeted IL-15/Rα-Fc fusion protein (such as but not limited to XENP25937 and XENP25850) described herein and the at least one additional therapeutic agent can be administered simultaneously, in the same or in separate compositions, or sequentially. For sequential administration, the PD-1-targeted IL-15/Rα-Fc fusion protein described herein can be administered first, and the additional agent can be administered second, or the order of administration can be reversed.

[00654] The PD-1-targeted IL-15/Rα-Fc fusion protein described herein and/or other therapeutic agents, procedures or modalities can be administered during periods of active disorder, or during a period of remission or less active disease. The PD-1-targeted IL-15/Rα-Fc fusion protein can be administered before the other treatment, concurrently with the treatment, post-treatment, or during remission of the disorder.

[00655] When administered in combination, the PD-1-targeted IL-15/Rα-Fc fusion protein (such as, but not limited to, XENP25937 and XENP25850) and the additional agent (e.g., second or third agent), or all, can be administered in an amount or dose that is lower or the same than the amount or dosage of each agent used individually, e.g., as a monotherapy. In some embodiments, the administered amount or dosage of PD-1-targeted IL-15/Rα-Fc fusion protein, the additional agent (e.g., second or third agent), or all, is lower (e.g., at least 20%, at least 30%, at least 40%, or at least 50%) than the amount or dosage of each agent used individually, e.g., as a monotherapy. In other embodiments, the amount or dosage of the PD-1-targeted IL-15/Rα-Fc fusion protein, the additional agent (e.g., second or third agent), or all, that results in a desired effect (e.g., treatment of cancer) is lower (e.g., at least 20%, at least 30%, at least 40%, or at least 50% lower) than the amount or dosage of each agent used individually, e.g., as a monotherapy, required to achieve the same therapeutic effect.

[00656] In further aspects, a PD-1-targeted IL-15/Rα-Fc fusion protein (such as, but not limited to, XENP25937 and XENP25850) described herein may be used in a treatment regimen in combination with chemotherapy, radiation, immunosuppressive agents, such as cyclosporin, azathioprine, methotrexate, mycophenolate, and FK506, antibodies directed against checkpoint inhibitors, or other immunoablative agents such as CAMPATH, other antibody therapies, cytoxan, fludarabine, cyclosporin, FK506, rapamycin, mycophenolic acid, steroids, FR90165, cytokines, and irradiation. peptide vaccine, such as that described in Izumoto et al. 2008 J Neurosurg 108:963-971.

[00657] In certain instances, compounds of the present invention are combined with other therapeutic agents, such as other anti-cancer agents, anti-allergic agents, anti-nausea agents (or anti-emetics), pain relievers, cytoprotective agents, and combinations thereof.

[00658] In one embodiment, a PD-1-targeted IL-15/Rα-Fc fusion protein (such as, but not limited to, XENP25937 and XENP25850) described herein can be used in combination with a chemotherapeutic agent. Exemplary chemotherapeutic agents include an anthracycline (e.g., idarubicin, daunorubicin, doxorubicin (e.g., liposomal doxorubicin)), an anthracenedione derivative (e.g., mitoxantrone), a vinca alkaloid (e.g., vinblastine, vincristine, vindesine, vinorelbine), an alkylating agent (e.g., cyclophosphamide, dacarbazine, melphalan, ifosfamide, temozolomide), an immune cell antibody (e.g., alemtuzamab, gemtuzumab, rituximab, ofatumumab, tositumomab, brentuximab), an antimetabolite (including, e.g., folic acid antagonists, cytarabine, pyrimidine analogs, purine analogs and adenosine deaminase inhibitors (e.g., fludarabine)), an mTOR inhibitor, a TNFR glucocorticoid induced TNFR related protein (GITR) agonist, a proteasome inhibitor (e.g., aclacinomycin A, gliotoxin or bortezomib), an immunomodulator such as thalidomide or a thalidomide derivative (e.g., lenalidomide), a kinase inhibitor such as ibrutinib (e.g., Imbruvica), a corticosteroid (e.g., dexamethasone, prednisone), and CVP (a combination of cyclophosphamide, vincristine, and prednisone), CHOP (a combination of cyclophosphamide, hydroxydaunorubicin, Oncovin® (vincristine), and prednisone) with or without etoposide (e.g., VP-16), a combination of cyclophosphamide and pentostatin, a combination of chlorambucil and prednisone, a combination of fludarabine and cyclophosphamide, or another agent such as mechlorethamine hydrochloride (e.g. Mustargen), doxorubicin (Adriamycin®), methotrexate, oxaliplatin, or cytarabine (ara-C).

[00659] General chemotherapeutic agents considered for use in combination therapies include anastrozole (Arimidex®), bicalutamide (Casodex®), bleomycin sulfate (Blenoxane®), busulfan (Myleran®), busulfan injection (Busulfex®), capecitabine (Xeloda®), N4-pentoxycarbonyl-5-deoxy-5-fluorocytidine, carboplatin (Paraplatin®), carmustine (BiCNU®), chlorambucil (Leukeran®), cisplatin (Platinol®), cladribine (Leustatin®), cyclophosphamide (Cytoxan® or Neosar®), cytarabine, cytosine arabinoside (Cytosar-U®), cytarabine liposome injection (DepoCyt®), dacarbazine (DTIC-Dome®), dactinomycin (Actinomycin D, Cosmegan), daunorubicin hydrochloride (Cerubidine®), daunorubicin citrate liposome injection (DaunoXome®), dexamethasone, docetaxel (Taxotere®), doxorubicin hydrochloride (Adriamycin®, Rubex®), etoposide (Vepesid®), fludarabine phosphate (Fludara®), 5-fluorouracil (Adrucil®, Efudex®), flutamide (Eulexin®), tezacitibine, Gemcitabine (difluorodeoxycitidine), hydroxyurea (Hydrea®), Idarubicin (Idamycin®), ifosfamide (IFEX®), irinotecan (Camptosar®), L-asparaginase (ELSPAR®), leucovorin calcium, melphalan (Alkeran®), 6-mercaptopurine (Purinethol®), methotrexate (Folex®), mitoxantrone (Novantrone®), mylotarg, paclitaxel (Taxol®), phoenix (Yttrium90/MX-DTPA), pentostatin, polifeprosan 20 with carmustine implant (Gliadel®), tamoxifen citrate (Nolvadex®), teniposide (Vumon®), 6-thioguanine, thiotepa, tirapazamine (Tirazone®), topotecan hydrochloride for injection (Hycamptin®), vinblastine (Velban®), vincristine (Oncovin®), and vinorelbine (Navelbine®).

XIV. **Treatments**

[00660] Once made, the compositions of the invention find use in a number of oncology applications, by treating cancer, generally by promoting T cell activation (e.g., T cells are no longer suppressed) with the binding of the heterodimeric Fc fusion proteins of the invention.

[00661] Accordingly, the PD-1-targeted IL-15/Rα-Fc fusion protein compositions of the invention find use in the treatment of these cancers.

A. PD-1-targeted IL-15/Rα-Fc Fusion Proteins Compositions for *In Vivo* Administration

[00662] Formulations of the antibodies used in accordance with the present invention are prepared for storage by mixing an antibody having the desired degree of purity with optional pharmaceutically acceptable carriers, excipients or stabilizers (as generally outlined in Remington's Pharmaceutical Sciences 16th edition, Osol, A. Ed. [1980]), in the form of

lyophilized formulations or aqueous solutions. Acceptable carriers, buffers, excipients, or stabilizers are nontoxic to recipients at the dosages and concentrations employed, and include buffers such as phosphate, citrate, and other organic acids; antioxidants including ascorbic acid and methionine; preservatives (such as octadecyldimethylbenzyl ammonium chloride; hexamethonium chloride; benzalkonium chloride, benzethonium chloride; phenol, butyl or benzyl alcohol; alkyl parabens such as methyl or propyl paraben; catechol; resorcinol; cyclohexanol; 3-pentanol; and m-cresol); low molecular weight (less than about 10 residues) polypeptides; proteins, such as serum albumin, gelatin, or immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidone; amino acids such as glycine, glutamine, asparagine, histidine, arginine, or lysine; monosaccharides, disaccharides, and other carbohydrates including glucose, mannose, or dextrins; chelating agents such as EDTA; sugars such as sucrose, mannitol, trehalose or sorbitol; salt-forming counter-ions such as sodium; metal complexes (e.g., Zn-protein complexes); and/or non-ionic surfactants such as TWEEN™, PLURONICS™ or polyethylene glycol (PEG).

B. Administrative Modalities

[00663] The PD-1-targeted IL-15/Rα-Fc fusion proteins disclosed herein and chemotherapeutic agents of the invention are administered to a subject, in accord with known methods, such as intravenous administration as a bolus or by continuous infusion over a period of time.

C. Treatment Modalities

[00664] In the methods of the invention, therapy is used to provide a positive therapeutic response with respect to a disease or condition. By “positive therapeutic response” is intended an improvement in the disease or condition, and/or an improvement in the symptoms associated with the disease or condition. For example, a positive therapeutic response would refer to one or more of the following improvements in the disease: (1) a reduction in the number of neoplastic cells; (2) an increase in neoplastic cell death; (3) inhibition of neoplastic cell survival; (5) inhibition (i.e., slowing to some extent, preferably halting) of tumor growth; (6) an increased patient survival rate; and (7) some relief from one or more symptoms associated with the disease or condition.

[00665] Positive therapeutic responses in any given disease or condition can be determined by standardized response criteria specific to that disease or condition. Tumor response can be assessed for changes in tumor morphology (i.e., overall tumor burden, tumor

size, and the like) using screening techniques such as magnetic resonance imaging (MRI) scan, x-radiographic imaging, computed tomographic (CT) scan, bone scan imaging, endoscopy, and tumor biopsy sampling including bone marrow aspiration (BMA) and counting of tumor cells in the circulation.

[00666] In addition to these positive therapeutic responses, the subject undergoing therapy may experience the beneficial effect of an improvement in the symptoms associated with the disease.

[00667] Treatment according to the present invention includes a “therapeutically effective amount” of the medicaments used. A “therapeutically effective amount” refers to an amount effective, at dosages and for periods of time necessary, to achieve a desired therapeutic result.

[00668] A therapeutically effective amount may vary according to factors such as the disease state, age, sex, and weight of the individual, and the ability of the medicaments to elicit a desired response in the individual. A therapeutically effective amount is also one in which any toxic or detrimental effects of the antibody or antibody portion are outweighed by the therapeutically beneficial effects.

[00669] A “therapeutically effective amount” for tumor therapy may also be measured by its ability to stabilize the progression of disease. The ability of a compound to inhibit cancer may be evaluated in an animal model system predictive of efficacy in human tumors.

[00670] Alternatively, this property of a composition may be evaluated by examining the ability of the compound to inhibit cell growth or to induce apoptosis by in vitro assays known to the skilled practitioner. A therapeutically effective amount of a therapeutic compound may decrease tumor size, or otherwise ameliorate symptoms in a subject. One of ordinary skill in the art would be able to determine such amounts based on such factors as the subject’s size, the severity of the subject’s symptoms, and the particular composition or route of administration selected.

[00671] Dosage regimens are adjusted to provide the optimum desired response (e.g., a therapeutic response). For example, a single bolus may be administered, several divided doses may be administered over time or the dose may be proportionally reduced or increased as indicated by the exigencies of the therapeutic situation. Parenteral compositions may be formulated in dosage unit form for ease of administration and uniformity of dosage. Dosage

unit form as used herein refers to physically discrete units suited as unitary dosages for the subjects to be treated; each unit contains a predetermined quantity of active compound calculated to produce the desired therapeutic effect in association with the required pharmaceutical carrier.

[00672] The specification for the dosage unit forms of the present invention are dictated by and directly dependent on (a) the unique characteristics of the active compound and the particular therapeutic effect to be achieved, and (b) the limitations inherent in the art of compounding such an active compound for the treatment of sensitivity in individuals.

[00673] The efficient dosages and the dosage regimens for the PD-1-targeted IL-15/Rα-Fc fusion proteins used in the present invention depend on the disease or condition to be treated and may be determined by the persons skilled in the art.

[00674] An exemplary, non-limiting range for a therapeutically effective amount of an PD-1-targeted IL-15/Rα-Fc fusion protein used in the present invention is about 0.1-100 mg/kg.

[00675] All cited references are herein expressly incorporated by reference in their entirety.

[00676] Whereas particular embodiments of the invention have been described above for purposes of illustration, it will be appreciated by those skilled in the art that numerous variations of the details may be made without departing from the invention as described in the appended claims.

EXAMPLES

[00677] Examples are provided below to illustrate the present invention. These examples are not meant to constrain the present invention to any particular application or theory of operation. For all constant region positions discussed in the present invention, numbering is according to the EU index as in Kabat (Kabat et al., 1991, Sequences of Proteins of Immunological Interest, 5th Ed., United States Public Health Service, National Institutes of Health, Bethesda, entirely incorporated by reference). Those skilled in the art of antibodies will appreciate that this convention consists of nonsequential numbering in specific regions of an immunoglobulin sequence, enabling a normalized reference to conserved positions in immunoglobulin families. Accordingly, the positions of any given

immunoglobulin as defined by the EU index will not necessarily correspond to its sequential sequence.

[00678] General and specific scientific techniques are outlined in US Publications 2015/0307629, 2014/0288275 and WO2014/145806, all of which are expressly incorporated by reference in their entirety and particularly for the techniques outlined therein. Examples 1 and 2 from U.S. Ser. No. 62,416, 087, filed on November 1, 2016 are expressly incorporated by reference in their entirety, including the corresponding figures.

XV. Example 1: Anti-PD-1 ABDs

A. 1A: Illustrative anti-PD-1 ABDs

[00679] Examples of antigen-binding domains which bind PD-1 were described in WO 2017/218707, herein incorporated by reference, for example, illustrative sequences of variable domains for which are depicted in Figure 14. Additional non-limiting examples of PD-1 ABDs which may find use in the PD-1-targeted IL-15/Rα-Fc fusion proteins of the invention are depicted in Figure 15.

B. 1B: Generation of anti-PD-1 clone 1C11

1. 1B(a): Generation and screening of anti-PD-1 hybridoma

[00680] To develop additional PD-1 targeting arms PD-1 targeted IL-15/Rα-Fc fusion proteins of the invention, monoclonal antibodies were first generated by hybridoma technology through ImmunoPrecise Antibodies Ltd., through their Standard Method and Rapid Prime Method. For the Standard Method, antigen(s) was injected into 3 BALB/c mice. 7-10 days before being sacrificed for hybridoma generation, the immunized mice received an antigen boost. Antibody titer was evaluated by ELISA on the antigen and the best responding mice are chosen for fusion. A final antigen boost was given 4 days prior to fusion. Lymphocytes from the mice were pooled, purified then fused with SP2/0 myeloma cells. Fused cells were grown on HAT selective Single-Step cloning media for 10-12 days at which point the hybridomas were ready for screening. For the Rapid Prime method, antigen(s) was injected into 3 BALB/c mice. After 19 days, lymphocytes from all the mice were pooled, purified then fused with SP2/0 myeloma cells. Fused cells were grown on HAT selective Single-Step cloning media for 10-12 days at which point the hybridomas were ready for screening. Antigen(s) used were mouse Fc fusion of human PD-1 (huPD-1-mFc), mouse Fc

fusion of cyno PD-1 (cynoPD-1-mFc), His-tagged human PD-1 (huPD-1-His), His-tagged cyno PD-1 (cynoPD-1-His) or mixtures thereof.

[00681] Anti-PD-1 hybridoma clones generated as described above were subject to two rounds of screening using Octet, a BioLayer Interferometry (BLI)-based method. Experimental steps for Octet generally included the following: Immobilization (capture of ligand or test article onto a biosensor); Association (dipping of ligand- or test article-coated biosensors into wells containing serial dilutions of the corresponding test article or ligand); and Dissociation (returning of biosensors to well containing buffer) in order to determine the affinity of the test articles. A reference well containing buffer alone was also included in the method for background correction during data processing.

[00682] For the first round, anti-mouse Fc (AMC) biosensors were used to capture the clones with dips into 500 nM of bivalent human and cyno PD-1-Fc-His. For the second round, clones identified in the first round that were positive for both human and cyno PD-1 were captured onto AMC biosensors and dipped into 500 nM monovalent human and cyno PD-1-His.

2. 1B(b): Characterization of clone 1C11

[00683] One hybridoma clone identified in Example 1B(a) was clone 1C11. DNA encoding the VH and VL of hybridoma clone 1C11 were generated by gene synthesis and subcloned using standard molecular biology techniques into expression vector pTT5 containing human IgG1 constant region with E233P/L234V/L235A/G236del/S267K substitutions to generate XENP21575, sequences for which are depicted in Figure 16.

1B(b)(i): PD-L1 blocking with clone 1C11

[00684] Blocking of checkpoint receptor/ligand interaction is necessary for T cell activation. The blocking ability of XENP21575 was investigated in a cell binding assay. HEK293T cells transfected to express PD-1 were incubated with XENP21575, as well as control antibodies. Following incubation, a murine Fc fusion of PD-L1 was added and allowed to incubate. Binding of PD-L1-mFc to HEK293T cells was detected with an anti-murine IgG secondary antibody, data for which are depicted in Figure 17.

1B(b)(ii): T cell surface binding of clone 1C11

[00685] Binding of anti-PD-1 clone 1C11 to T cells was measured in an SEB-stimulated PBMC assay. Staphylococcal Enterotoxin B (SEB) is a superantigen that causes T cell activation and proliferation in a manner similar to that achieved by activation via the T cell receptor (TCR), including expression of checkpoint receptors such as PD-1. Human PBMCs were stimulated with 100 ng/mL for 3 days. Following stimulation, PBMCs were incubated with the indicated test articles at indicated concentrations at 4°C for 30 min. PBMCs were stained with anti-CD3-FITC (UCHT1) and APC labeled antibody for human immunoglobulin κ light chain. The binding of the test articles to T cells as indicated by APC MFI on FITC+ cells is depicted in Figure 18.

1B(b)(iii): T cell activation by clone 1C11

[00686] T cell activation by clone 1C11, as indicated by cytokine secretion, was investigated in an SEB-stimulated PBMC assay. Human PBMCs were stimulated with 500 ng/mL SEB for 2 days. Cells were then washed twice in culture medium and stimulated with 500 ng/mL SEB in combination with indicated amounts of indicated test articles for 24 hours. Supernatants were then assayed for IL-2 and IFNγ by cells, data for which are depicted in Figures 19A-19B.

3. 1B(c): Humanization of clone 1C11

[00687] Clone 1C11 humanized using string content optimization (see, e.g., U.S. Patent No. 7,657,380, issued on February 2, 2010). DNA encoding the heavy and light chains were generated by gene synthesis and subcloned using standard molecular biology techniques into the expression vector pTT5. Sequences for illustrative humanized variants of clone 1C11 in bivalent antibody format are depicted in Figures 20A-20C.

[00688] The affinity of XENP22553 was determined using Octet as generally described in Example 1B(a). In particular, anti-human Fc (AHC) biosensors were used to capture the test article with dips into multiple concentrations of histidine-tagged PD-1. The affinity result and corresponding sensorgram are depicted in Figure 21.

XVI. Example 2: IL-15/Rα-Fc

A. 2A: Engineering IL-15 Rα-Fc fusion proteins

[00689] In order to address the short half-life of IL-15/IL-15Rα heterodimers, we generated the IL-15/IL-15Rα(sushi) complex as a Fc fusion (hereon referred to as "IL-15/Rα-Fc fusion proteins") with the goal of facilitating production and promoting FcRn-mediated recycling of the complex and prolonging half-life.

[00690] Plasmids coding for IL-15 or IL-15Rα sushi domain were constructed by standard gene synthesis, followed by subcloning into a pTT5 expression vector containing Fc fusion partners (e.g., constant regions as depicted in Figure 8A- Figure 8F). Cartoon schematics of illustrative IL-15/Rα-Fc fusion protein formats are depicted in Figure 22A-22 Figure G.

[00691] Illustrative proteins of the IL-15/Rα-heteroFc format (Figure 22A) include XENP20818 and XENP21475, sequences for which are depicted in Figure 23. An illustrative proteins of the scIL-15/Rα-Fc format (Figure 22B) is XENP21478, sequences for which are depicted in Figure 24. Illustrative proteins of the ncIL-15/Rα-Fc format (Figure 22C) include XENP21479, XENP22366, and XENP24348 sequences for which are depicted in Figures 25A-25B. An illustrative protein of the bivalent ncIL-15/Rα-Fc format (Figure 22D) is XENP21978, sequences for which are depicted in Figure 26. Sequences for an illustrative protein of the bivalent scIL-15/Rα-Fc format (Figure 22E) are depicted in Figure 27. An illustrative protein of the Fc-ncIL-15/Rα format (Figure 22F) is XENP22637, sequences for which are depicted in Figure 28. Sequences for an illustrative protein of the Fc-scIL-15/Rα format (Figure 22G) are depicted in Figure 29.

[00692] Proteins were produced by transient transfection in HEK293E cells and were purified by a two-step purification process comprising protein A chromatography (GE Healthcare) and anion exchange chromatography (HiTrapQ 5 mL column with a 5-40% gradient of 50 mM Tris pH 8.5 and 50 mM Tris pH 8.5 with 1 M NaCl).

[00693] IL-15/Rα-Fc fusion proteins in the various formats as described above were tested in a cell proliferation assay. Human PBMCs were treated with the test articles at the indicated concentrations. 4 days after treatment, the PBMCs were stained with anti-CD8-FITC (RPA-T8), anti-CD4-PerCP/Cy5.5 (OKT4), anti-CD27-PE (M-T271), anti-CD56-BV421 (5.1H11), anti-CD16-BV421 (3G8), and anti-CD45RA-BV605 (Hi100) to gate for the following cell types: CD4+ T cells, CD8+ T cells, and NK cells (CD56+/CD16+). Ki67 is

a protein strictly associated with cell proliferation, and staining for intracellular Ki67 was performed using anti-Ki67-APC (Ki-67) and Foxp3/Transcription Factor Staining Buffer Set (Thermo Fisher Scientific, Waltham, Mass.). The percentage of Ki67 on the above cell types was measured using FACS (depicted in Figures 30A-30C and 31A-31C). The various IL-15/Rα-Fc fusion proteins induced strong proliferation of CD8+ T cells and NK cells. Notably, differences in proliferative activity were dependent on the linker length on the IL-15-Fc side. In particular, constructs having no linker (hinge only), including XENP21471, XENP21474, and XENP21475, demonstrated weaker proliferative activity.

B. 2B: IL-15/Rα-Fc fusion proteins with engineered disulfide bonds

[00694] To further improve stability and prolong the half-life of IL-15/Rα-Fc fusion proteins, we engineered disulfide bonds into the IL-15/Rα interface. By examining the crystal structure of the IL-15/Rα complex, as well as by modeling using Molecular Operating Environment (MOE; Chemical Computing Group, Montreal, Quebec, Canada) software, we predicted residues at the IL-15/Rα interface that may be substituted with cysteine in order to form covalent disulfide bonds, as depicted in Figure 32. Additionally, up to three amino acids following the sushi domain in IL-15Rα were added to the C-terminus of IL-15Rα(sushi) as a scaffold for engineering cysteines (illustrative sequences for which are depicted in Figure 33). Sequences for illustrative IL-15 and IL-15Rα(sushi) variants engineered with cysteines are respectively depicted in Figure 34 and Figure 35.

[00695] Plasmids coding for IL-15 or IL-15Rα(sushi) were constructed by standard gene synthesis, followed by subcloning into a pTT5 expression vector containing Fc fusion partners (e.g., constant regions as depicted in Figures 11A-11C). Residues identified as described above were substituted with cysteines by standard mutagenesis techniques. Cartoon schematics of IL-15/Rα-Fc fusion proteins with engineered disulfide bonds are depicted in Figure 36A- Figure 36D.

[00696] Illustrative proteins of the dsIL-15/Rα-heteroFc format (Figure 36A) include XENP22013, XENP22014, XENP22015, and XENP22017, sequences for which are depicted in Figure 37A-37B. Illustrative proteins of the dsIL-15/Rα-Fc format (Figure 36B) include XENP22357, XENP22358, XENP22359, XENP22684, and XENP22361, sequences for which are depicted in Figures 38A-38B. Illustrative protein of the bivalent dsIL-15/Rα-Fc format (Figure 36C) include XENP22634, XENP22635, and XENP22636, sequences for

which are depicted in Figure 39. Illustrative proteins of the Fc-dsIL-15/Rα format (Figure 36D) include XENP22639 and XENP22640, sequences for which are depicted in Figure 40.

[00697] Proteins were produced by transient transfection in HEK293E cells and were purified by a two-step purification process comprising protein A chromatography (GE Healthcare) and anion exchange chromatography (HiTrapQ 5 mL column with a 5-40% gradient of 50 mM Tris pH 8.5 and 50 mM Tris pH 8.5 with 1 M NaCl).

[00698] After the proteins were purified, they were characterized by capillary isoelectric focusing (CEF) for purity and homogeneity. CEF was performed using LabChip GXII Touch HT (PerkinElmer, Waltham, Mass.) using Protein Express Assay LabChip and Protein Express Assay Reagent Kit carried out using the manufacturer's instructions. Samples were run in duplicate, one under reducing (with dithiothreitol) and the other under non-reducing conditions. Many of the disulfide bonds were correctly formed as indicated by denaturing non-reducing CEF, where the larger molecular weight of the covalent complex can be seen when compared to the controls without engineered disulfide bonds (Figure 41).

[00699] The proteins were then tested in a cell proliferation assay. IL-15/Rα-Fc fusion proteins (with or without engineered disulfide bonds) or controls were incubated with PBMCs for 4 days. Following incubation, PBMCs were stained with anti-CD4-PerCP/Cy5.5 (RPA-T4), anti-CD8-FITC (RPA-T8), anti-CD45RA-BV510 (HI100), anti-CD16-BV421 (3G8), anti-CD56-BV421 (HCD56), anti-CD27-PE (O323), and anti-Ki67-APC (Ki-67) to mark various cell populations and analyzed by FACS as generally described in Example 2A. Proliferation of NK cells, CD4+ T cells, and CD8+ T cells as indicated by Ki67 expression are depicted in Figures 42A-42C. Each of the IL-15/Rα-Fc fusion proteins and the IL-15 control induced strong proliferation of NK cells, CD8+ T cells, and CD4+ T cells.

C. 2C: IL-15/Rα-Fc fusion proteins engineered for lower potency and increased PK and half-life

[00700] In order to further improve PK and prolong half-life, we reasoned that decreasing the potency of IL-15 would decrease the antigen sink, and thus, increase the half-life. By examining the crystal structure of the IL-15:IL-2Rß and IL-15:common gamma chain interfaces, as well as by modeling using MOE software, we predicted residues at these interfaces that may be substituted in order to reduce potency. Figure 43 depicts a structural model of the IL-15:receptor complexes showing locations of the predicted residues where we

engineered isosteric substitutions (in order to reduce the risk of immunogenicity). Sequences for illustrative IL-15 variants engineered for reduced potency are depicted in Figure 44A-Figure 44C.

[00701] Plasmids coding for IL-15 or IL-15Rα(sushi) were constructed by standard gene synthesis, followed by subcloning into a pTT5 expression vector containing Fc fusion partners (e.g., constant regions as depicted in Figure 11). Substitutions identified as described above were incorporated by standard mutagenesis techniques. Sequences for illustrative IL-15/Rα-Fc fusion proteins of the "IL-15/Rα-heteroFc" format engineered for reduced potency are depicted in Figure 45A- Figure 45D. Sequences for illustrative IL-15/Rα-Fc fusion proteins of the "scIL-15/Rα-Fc" format engineered for reduced potency are depicted in Figures 46A-46C. Sequences for illustrative IL-15/Rα-Fc fusion proteins of the "ncIL-15/Rα-Fc" format engineered for reduced potency are depicted in Figure 47A- Figure 47B. Sequences for illustrative ncIL-15/Rα heterodimers engineered for reduced potency are depicted in Figure 48. Sequences for an illustrative IL-15/Rα-Fc fusion protein of the "bivalent ncIL-15/Rα-Fc" format engineered for reduced potency are depicted in Figure 49. Sequences for illustrative IL-15/Rα-Fc fusion proteins of the "dsIL-15/Rα-Fc" format engineered for reduced potency are depicted in Figure 50. Proteins were produced by transient transfection in HEK293E cells and were purified by a two-step purification process comprising protein A chromatography (GE Healthcare) and anion exchange chromatography (HiTrapQ 5 mL column with a 5-40% gradient of 50 mM Tris pH 8.5 and 50 mM Tris pH 8.5 with 1 M NaCl).

D. 2C(a): In vitro activity of variant IL-15/Rα-Fc fusion proteins engineered for decreased potency

[00702] The variant IL-15/Rα-Fc fusion proteins were tested in a number of cell proliferation assays.

[00703] In a first cell proliferation assay, IL-15/Rα-Fc fusion proteins (with or without engineered substitutions) or control were incubated with PBMCs for 4 days. Following incubation, PBMCs were stained with anti-CD4-Evolve605 (SK-3), anti-CD8-PerCP/Cy5.5 (RPA-T8), anti-CD45RA-APC/Cy7 (HI100), anti-CD16-eFluor450 (CB16), anti-CD56-eFluor450 (TULY56), anti-CD3-FITC (OKT3), and anti-Ki67-APC (Ki-67) to mark various cell populations and analyzed by FACS as generally described in Example 2A. Proliferation

of NK cells, CD8+ T cells, and CD4+ T cells as indicated by Ki67 expression are depicted in Figure 51A-Figure 51C and 52. Most of the IL-15/Rα-Fc fusion proteins induced proliferation of each cell population; however, activity varied depending on the particular engineered substitutions.

[00704] In a second cell proliferation assay, IL-15/Rα-Fc fusion proteins (with or without engineered substitutions) were incubated with PBMCs for 3 days. Following incubation, PBMCs were stained with anti-CD3-FITC (OKT3), anti-CD4-Evolve604 (SK-3), anti-CD8-PerCP/Cy5.5 (RPA-T8), anti-CD16-eFluor450 (CB16), anti-CD56-eFluor450 (TULY56), anti-CD27-PE (O323), anti-CD45RA-APC/Cy7 (HI100) and anti-Ki67-APC (20Raj1) antibodies to mark various cell populations. Figures 53A-53C and 54A-54C depict selection of various cell populations following incubation with XENP22821 by FACS. Lymphocytes were first gated on the basis of side scatter (SSC) and forward scatter (FSC) (Figure 53A). Lymphocytes were then gated based on CD3 expression (Figure 53B). Cells negative for CD3 expression were further gated based on CD16 expression to identify NK cells (CD16+) (Figure 53C). CD3+ T cells were further gated based on CD4 and CD8 expression to identify CD4+ T cells, CD8+ T cells, and γδ T cells (CD3+CD4-CD8-) (Figure 54A). The CD4+ and CD8+ T cells were gated for CD45RA expression as shown respectively in Figure 54B- Figure 54C. Finally, the proliferation of the various cell populations were determined based on percentage Ki67 expression, and the data are shown in Figure 56A- Figure 56D. NK and CD8+ T cells are more sensitive than CD4+ T cells to IL-15/Rα-Fc fusion proteins, and as above, proliferative activity varied depending on the particular engineered substitutions. Figure 56D shows the fold change in EC50 of various IL-15/Rα-Fc fusion proteins relative to control XENP20818. Figure 55A and B further depict the activation of lymphocytes following treatment with IL-15/Rα-Fc fusion proteins by gating for the expression of CD69 and CD25 (T cell activation markers) before and after incubation of PBMCs with XENP22821.

[00705] In a third experiment, additional variant IL-15/Rα-Fc fusion proteins were incubated with human PBMCs for 3 days at 37°C. Following incubation, PBMCs were stained with anti-CD3-FITC (OKT3), anti-CD4-SB600 (SK-3), anti-CD8-PerCP/Cy5.5 (RPA-T8), anti-CD45RA-APC/Cy7 (HI100), anti-CD16-eFluor450 (CB16), anti-CD25-PE (M-A251), and anti-Ki67-APC (Ki-67) to mark various cell populations and analyzed by FACS as generally described in Example 2A. Proliferation of CD8+ (CD45RA-) T cells,

CD4+ (CD45RA-) T cells, γδ T cells, and NK cells as indicated by Ki67 expression are depicted in Figure 57A- Figure 57D.

[00706] In a fourth experiment, human PBMCs were incubated with the additional IL-15/Rα-Fc variants at the indicated concentrations for 3 days. Following incubation, PBMCs were stained with anti-CD3-FITC (OKT3), anti-CD4 (SB600), anti-CD8-PerCP/Cy5.5 (RPA-T8), anti-CD16-eFluor450 (CB16), anti-CD25-PE (M-A251), anti-CD45RA-APC/Cy7 (HI100), and anti-Ki67-APC (Ki67) and analyzed by FACS as generally described in Example 2A. Percentage of Ki67 on CD8+ T cells, CD4+ T cells and NK cells following treatment are depicted in Figure 58A- Figure 58C.

[00707] In a fifth experiment, variant IL-15/Rα-Fc fusion proteins were incubated with human PBMCs for 3 days at 37oC. Following incubation, cells were stained with anti-CD3-PE (OKT3), anti-CD4-FITC (RPA-T4), anti-CD8α-BV510 (SK1), anti-CD8ß-APC (2ST8.5H7), anti-CD16-BV421 (3G8), anti-CD25-PerCP/Cy5.5 (M-A251), anti-CD45RA-APC/Cy7 (HI100), anti-CD56-BV605 (NCAM16.2), and anti-Ki67-PE/Cy7 (Ki-67) and analyzed by FACS as generally described in Example 2A. Percentage of Ki67 on CD8+ T cells, CD4+ T cells, γδ T cells, and NK cells are depicted in Figure 59A- Figure 59E.

[00708] In a sixth experiment, variant IL-15/Rα-Fc fusion proteins were incubated with human PBMCs for 3 days at 37oC. Following incubation, cells were stained with anti-CD3-PE (OKT3), anti-CD4-FITC (RPA-T4), anti-CD8α-BV510 (SK1), anti-CD8ß-APC (SIDI8BEE), anti-CD16-BV421 (3G8), anti-CD25-PerCP/Cy5.5 (M-A251), anti-CD45RA-APC/Cy7 (HI100), anti-CD56-BV605 (NCAM16.2), and anti-Ki67-PE/Cy7 (Ki-67) and analyzed by FACS as generally described in Example 2A. Percentage of Ki67 on CD8+ T cells, CD4+ T cells, γδ T cells, and NK cells are depicted in Figure 60A- Figure 60E.

[00709] In a seventh experiment, variant IL-15/Rα-Fc fusion proteins were incubated with human PBMCs at the indicated concentrations for 3 days at 37oC. Following incubation, PBMCs were stained with anti-CD3-PE (OKT3), anti-CD4-FITC (RPA-T4), anti-CD8-APC (RPA-T8), anti-CD16-BV605 (3G8), anti-CD25-PerCP/Cy5.5 (M-A251), anti-CD45RA-APC/Fire750 (HI100) and anti-Ki67-PE/Cy7 (Ki-67) and analyzed by FACS as generally described in Example 2A. Percentage Ki67 on CD8+ T cells, CD4+ T cells, γδ T cells and NK (CD16+) cells are depicted in Figures 61A-61D. The data show that the ncIL-15/Rα-Fc

fusion protein XENP21479 is the most potent inducer of CD8+ T cell, CD4+ T cell, NK (CD16+) cell, and γδ T cell proliferation. Each of the scIL-15/Rα-Fc fusion proteins were less potent than XENP21479 in inducing proliferation, but differences were dependent on both the linker length, as well as the particular engineered substitutions.

[00710] In an eighth experiment, variant IL-15/Rα-Fc fusion proteins were incubated with human PBMCs at the indicated concentrations for 3 days at 37°C. Following incubation, PBMCs were stained with anti-CD3-PE (OKT3), anti-CD4-FITC (RPA-T4), anti-CD8-APC (RPA-T8), anti-CD16-BV605 (3G8), anti-CD25-PerCP/Cy5.5 (M-A251), anti-CD45RA-APC/Fire750 (HI100) and anti-Ki67-PE/Cy7 (Ki-67) and analyzed by FACS as generally described in Example 2A. Percentage Ki67 on CD8+ T cells, CD4+ T cells, γδ T cells and NK (CD16+) cells are respectively depicted in Figures 62A-62D. As above, the data show that the ncIL-15/Rα-Fc fusion protein XENP21479 is the most potent inducer of CD8+ T cell, CD4+ T cell, NK (CD16+) cell, and γδ T cell proliferation. Notably, introduction of Q108E substitution into the ncIL-15/Rα-Fc format (XENP24349) drastically reduces its proliferative activity in comparison to wildtype (XENP21479).

E. 2C(b): PK of IL-15/Rα-Fc fusion proteins engineered for reduced potency

[00711] In order to investigate if IL-15/Rα-Fc fusion proteins engineered for reduced potency had improved half-life and PK, we examined these variants in a PK study in C57BL/6 mice. Two cohorts of mice (5 mice per test article per cohort) were dosed with 0.1 mg/kg of the indicated test articles via IV-TV on Day 0. Serum was collected 60 minutes after dosing and then on Days 2, 4, and 7 for Cohort 1 and Days 1, 3, and 8 for Cohort 2. Serum levels of IL-15/Rα-Fc fusion proteins were determined using anti-IL-15 and anti-IL-15Rα antibodies in a sandwich ELISA. The results are depicted in Figure 63. Figure 64 depicts the correlation between potency and half-life of the test articles. Variants with reduced potency demonstrated substantially longer half-life. Notably, half-life was improved up to almost 9 days (see XENP22821 and XENP22822), as compared to 0.5 days for the wild-type control XENP20818.

XVII. Example 3: PD-1-targeted IL-15/Rα-Fc fusions

A. 3A: Generation and physical characterization of PD-1-targeted IL-15/Rα-Fc fusions

[00712] Plasmids coding for IL-15, IL-15Rα sushi domain, or the anti-PD-1 variable regions were constructed by standard gene synthesis, followed by subcloning into a pTT5 expression vector containing Fc fusion partners (e.g., constant regions as depicted in Figure 12). Cartoon schematics of illustrative PD-1-targeted IL-15/Rα-Fc fusions are depicted in Figure 65A- Figure 65K.

[00713] The "scIL-15/Rα x scFv" format (Figure 65A) comprises IL-15Rα(sushi) fused to IL-15 by a variable length linker (termed "scIL-15/Rα") which is then fused to the N-terminus of a heterodimeric Fc-region, with an scFv fused to the other side of the heterodimeric Fc. Sequences for illustrative proteins of this format are depicted in Figure 66.

[00714] The "scFv x ncIL-15/Rα" format (Figure 65B) comprises an scFv fused to the N-terminus of a heterodimeric Fc-region, with IL-15Rα(sushi) fused to the other side of the heterodimeric Fc, while IL-15 is transfected separately so that a non-covalent IL-15/Rα complex is formed. Sequences for illustrative proteins of this format are depicted in Figure 67.

[00715] The "scFv x dsIL-15/Rα" format (Figure 65C) is the same as the "scFv x ncIL-15/Rα" format, but wherein IL-15Rα(sushi) and IL-15 are covalently linked as a result of engineered cysteines. Sequences for illustrative proteins of this format are depicted in Figure 68.

[00716] The "scIL-15/Rα x Fab" format (Figure 65D) comprises IL-15Rα(sushi) fused to IL-15 by a variable length linker (termed "scIL-15/Rα") which is then fused to the N-terminus of a heterodimeric Fc-region, with a variable heavy chain (VH) fused to the other side of the heterodimeric Fc, while a corresponding light chain is transfected separately so as to form a Fab with the VH. Sequences for illustrative proteins of this format are depicted in Figure 69A- Figure 69D.

[00717] The "ncIL-15/Rα x Fab" format (Figure 65E) comprises a VH fused to the N-terminus of a heterodimeric Fc-region, with IL-15Rα(sushi) fused to the other side of the heterodimeric Fc, while a corresponding light chain is transfected separately so as to form a Fab with the VH, and while IL-15 is transfected separately so that a non-covalent IL-15/Rα complex is formed. Sequences for illustrative proteins of this format are depicted in Figure 70.

[00718] The “dsIL-15/Rα x Fab” format (Figure 65F) is the same as the “ncIL-15/Rα x Fab” format, but wherein IL-15Rα(sushi) and IL-15 are covalently linked as a result of engineered cysteines. Sequences for illustrative proteins of this format are depicted in Figure 71.

[00719] The “mAb-scIL-15/Rα” format (Figure 65G) comprises VH fused to the N-terminus of a first and a second heterodimeric Fc, with IL-15 is fused to IL-15Rα(sushi) which is then further fused to the C-terminus of one of the heterodimeric Fc-region, while corresponding light chains are transfected separately so as to form Fabs with the VHs. Sequences for illustrative proteins of this format are depicted in Figure 72.

[00720] The “mAb-ncIL-15/Rα” format (Figure 65H) comprises VH fused to the N-terminus of a first and a second heterodimeric Fc, with IL-15Rα(sushi) fused to the C-terminus of one of the heterodimeric Fc-region, while corresponding light chains are transfected separately so as to form Fabs with the VHs, and while and while IL-15 is transfected separately so that a non-covalent IL-15/Rα complex is formed. Sequences for illustrative proteins of this format are depicted in Figure 73.

[00721] The “mAb-dsIL-15/Rα” format (Figure 65I) is the same as the “mAb-ncIL-15/Rα” format, but wherein IL-15Rα(sushi) and IL-15 are covalently linked as a result of engineered cysteines. Sequences for illustrative proteins of this format are depicted in Figure 74.

[00722] The “central-IL-15/Rα” format (Figure 65J) comprises a VH recombinantly fused to the N-terminus of IL-15 which is then further fused to one side of a heterodimeric Fc and a VH recombinantly fused to the N-terminus of IL-15Rα(sushi) which is then further fused to the other side of the heterodimeric Fc, while corresponding light chains are transfected separately so as to form Fabs with the VHs. Sequences for illustrative proteins of this format are depicted in Figure 75.

[00723] The “central-scIL-15/Rα” format (Figure 65K) comprises a VH fused to the N-terminus of IL-15Rα(sushi) which is fused to IL-15 which is then further fused to one side of a heterodimeric Fc and a VH fused to the other side of the heterodimeric Fc, while corresponding light chains are transfected separately so as to form Fabs with the VHs.

Sequences for illustrative PD-1 targeted IL-15/Rα-Fc fusion proteins of this format are depicted in Figure 76.

[00724] PD-1-targeted IL-15/Rα-Fc fusion proteins were characterized by size-exclusion chromatography (SEC) and capillary isoelectric focusing (CEF) for purity and homogeneity.

[00725] The proteins were analyzed using SEC to measure their size (i.e., hydrodynamic volume) and determine the native-like behavior of the purified samples. The analysis was performed on an Agilent 1200 high-performance liquid chromatography (HPLC) system. Samples were injected onto a Superdex™ 200 10/300 GL column (GE Healthcare Life Sciences) at 1.0 mL/min using 1 x PBS, pH 7.4 as the mobile phase at 4°C for 25 minutes with UV detection wavelength at 280 nM. Analysis was performed using Agilent OpenLab Chromatography Data System (CDS) ChemStation Edition AIC version C.01.07. Chromatogram for an illustrative PD-1 targeted IL-15/Rα-Fc fusion protein XENP21480 in the IL-15/Rα x scFv format is shown in Figure 77B.

[00726] The proteins were analyzed electrophoretically via CEF using LabChip GXII Touch HT (PerkinElmer, Waltham, Mass.) using Protein Express Assay LabChip and Protein Express Assay Reagent Kit carried out using the manufacturer's instructions. Samples were run in duplicate, one under reducing (with dithiothreitol) and the other under non-reducing conditions. Gel image for XENP21480 is shown in Figure 77C.

[00727] Affinity screens of the heterodimeric Fc-fusion proteins for IL-2Rß and PD-1 were performed using Octet as generally described in Example 1B(a). In a first screen, anti-human Fc (AHC) biosensors were used to capture the test articles and then dipped into multiple concentration of IL-2Rß (R&D Systems, Minneapolis, Minn.) or histidine-tagged PD-1 for KD determination. The affinity result and corresponding sensorgrams for XENP21480 are depicted in Figure 77D- Figure 77E. In a second screen, a HIS1K biosensors were used to capture either histidine-tagged IL-2Rß:common gamma chain complex-Fc fusion or histidine-tagged PD-1-Fc fusion and then dipped into 2 different batches of XENP25850, sensorgrams for which are depicted in Figure 78A- Figure 78B.

[00728] Stability of the heterodimeric Fc-fusion proteins were evaluated using Differential Scanning Fluorimetry (DSF). DSF experiments were performed using a Bio-Rad

CFX Connect Real-Time PCR Detection System. Proteins were mixed with SYPRO Orange fluorescent dye and diluted to 0.2 mg/mL in PBS. The final concentration of SYPRO Orange was 10X. After an initial 10 minute incubation period at 25°C, proteins were heated from 25 to 95°C using a heating rate of 1°C/min. A fluorescence measurement was taken every 30 sec. Melting temperatures (Tm) were calculated using the instrument software. The stability result and corresponding melting curve for XENP21480 are depicted in Figure 77F.

B. 3B: Activity of PD-1-targeted IL-15/Rα-Fc fusions in cell proliferation assays

[00729] An illustrative PD-1-targeted IL-15/Rα-Fc fusion protein XENP21480 and controls were tested in a cell proliferation assay. Human PBMCs were treated with the test articles at the indicated concentrations. 4 days after treatment, the PBMCs were stained with anti-CD8-FITC (RPA-T8), anti-CD4-PerCP/Cy5.5 (OKT4), anti-CD27-PE (M-T271), anti-CD56-BV421 (5.1H11), anti-CD16-BV421 (3G8), and anti-CD45RA-BV605 (Hi100) to gate for the following cell types: CD4+ T cells, CD8+ T cells, and NK cells (CD56+/CD16+). Ki67 is a protein strictly associated with cells proliferation, and staining for intracellular Ki67 was performed using anti-Ki67-APC (Ki-67) and Foxp3/Transcription Factor Staining Buffer Set (Thermo Fisher Scientific, Waltham, Mass.). The percentage of Ki67 on the above cell types was measured using FACS (depicted in Figure 79A-Figure 79C).

C. 3C: Activity of PD-1-targeted IL-15/Rα-Fc fusion proteins in an SEB-stimulated PBMC assay

[00730] Human PBMCs from multiple donors were stimulated with 10 ng/mL of SEB for 72 hours in combination with 20 μg/mL of an PD-1-targeted IL-15/Rα-Fc fusion or controls. After treatment, supernatant was collected and assayed for IL-2, data for which is depicted in Figure 80.

D. 3D: PD-1-targeted IL-15/Rα-Fc fusions enhance engraftment and disease activity in human PBMC-engrafted NSG mice

[00731] An illustrative PD-1-targeted IL-15/Rα-Fc fusion protein was evaluated in a Graft-versus-Host Disease (GVHD) model conducted in NSG (NOD-SCID-gamma) immunodeficient mice. When the NSG mice are injected with human PBMCs, the human PBMCs develop an autoimmune response against mouse cells. Treatment of NSG mice injected with human PBMCs followed with PD-1-targeted IL-15/Rα-Fc fusions proliferate the engrafted T cells and enhances engraftment.

[00732] In a first study, 10 million human PBMCs were engrafted into NSG mice via IV-OSP on Day -8 followed by dosing with the indicated test articles at the indicated concentrations on Day 0. IFNγ levels and human CD45+ lymphocytes, CD8+ T cell and CD4+ T cell counts were measured at Days 4, 7, and 11. Figure 81 depicts IFNγ levels in mice serum on Days 4, 7, and 11. Figure 82A- Figure 82C respectively depict CD8+ T cell counts on Days 4, 7, and 11. Figure 83A- Figure 83C respectively depict CD4+ T cell counts on Days 4, 7, and 11. Figure 84A- Figure 84C respectively depict CD45+ cell counts on Days 4, 7, and 11. Body weight of the mice were also measured on Days 4, 7, and 11 and depicted as percentage of initial body weight in Figure 85A- Figure 85C.

[00733] In a second study, 10 million human PBMCs were engrafted into NSG mice via IV-OSP on Day -7 followed by dosing with the following test articles at the indicated concentrations on Days 0 and 19: XENP16432 (a bivalent anti-PD-1 mAb with ablated effector function based on nivolumab; sequences depicted in Figure 86; 3.0 mg/kg), XENP24050 (0.61 mg/kg), XENP25951 (a monovalent anti-PD-1 Fab-Fc based on the PD-1 targeting arm from XENP25850; sequence depicted in Figure 87; 0.82 mg/kg), XENP24050 in combination with XENP25951 (0.61 and 0.82 mg/kg respectively), and XENP25850 (1.0 mg/kg). Cell counts were measured at Day 4, 7, and 11, and are depicted in Figure 88- Figure 91 respectively for CD45+ cells, CD3+ cells, CD4+ cells, and CD8+ cells. The data show that the PD-1-targeted IL-15/Rα-Fc fusion increased CD45+, CD3+, CD4+, and CD8+ cell counts by Day 7 indicating enhanced GVHD. Notably, XENP25850 enhanced GVHD to a much greater extent than XENP24050 in combination with XENP25951, indicating that the enhanced GVHD is attributable to PD-1 targeting of the IL-15/Rα-Fc fusion rather than merely a combined effect of IL-15 and PD-1 blockade.

E. 3E: PD-1-targeted IL-15/Rα-Fc fusion proteins of the invention preferentially expand activated lymphocytes

[00734] Following binding of cytokines to their receptors, Janus kinases (JAKs) associated with the receptors phosphorylate STAT proteins which then translocate into the nucleus to regulate further downstream processes. Therefore, phosphorylation of STAT proteins (in particular, STAT5, which include STAT5a and STAT5b) is one of the earliest signaling events triggered by IL-15 binding to its receptors. Accordingly, the ability of the PD-1-targeted IL-15/Rα-Fc fusions to induce STAT5 phosphorylation in various cell types was investigated.

[00735] For this experiment, both fresh and activated PBMCs were used. Activated PBMCs, used as surrogates for activated lymphocytes in the tumor environment, were prepared by stimulating fresh PBMCs with 100 ng/mL plate-bound anti-CD3 (OKT3) for 2 days. Fresh and activated PBMCs were incubated with the following test articles at the indicated concentrations for 15 minutes at 37oC: XENP20818 (WT IL-15/Rα-Fc), XENP24050 (an illustrative reduced potency IL-15/Rα-Fc), and XENP25850 (an illustrative PD-1-targeted IL-15/Rα-Fc fusion). To gate for various cell populations following incubation, PBMCs were stained with anti-CD3-BUV395 (UCHT1), anti-CD4-BV605 (RPA-T4), and anti-CD8-Alexa700 (SK1) for 30-45 minutes at room temperature. Cells were washed and incubated with pre-chilled (-20°C) 90% methanol for 20-60 minutes. After methanol incubation, cells were washed again and stained with anti-CD25-BV421 (M-A251), anti-CD45RA-BV510 (HI100), and anti-pSTAT5-Alexa647 (pY687) to mark various cell populations and STAT5 phosphorylation. Data depicting induction of STAT5 phosphorylation on various CD8+ and CD4+ T cell populations are depicted in Figure 92A-Figure 92H. Notably, the data show that the PD-1-targeted IL-15/Rα-Fc fusion protein (XENP25850) demonstrated increased effect on T cells from activated PBMCs (due to increased PD-1 expression) while maintaining minimal and in some cases reduced effect on T cells from fresh PBMCs in comparison to the equivalent non-targeted reduced potency IL-15/Rα-Fc fusion (XENP24050). This suggests that, in a clinical setting, the PD-1-targeted IL-15/Rα-Fc fusions will be selective for activated tumor-infiltrating lymphocytes in the tumor environment that have higher PD-1 expression.

XVIII. Example 4: PD-1-targeted IL-15/Rα-Fc fusions with tuned PD-1 Affinity

A. 4A: Affinity-engineering PD-1-targeting arm

[00736] Next, we sought to optimize the affinity of the PD-1-targeting arm. We generated libraries of variants based on the variable regions of anti-PD-1 clone 1C11 humanized variant H3L3 (as in XENP22553) in the context of scFvs (sequences for which are depicted in Figure 93A-Figure 93T), in the context of bivalent mAbs (sequences for which are depicted in Figure 94A-Figure 94AP), and in the context of variable heavy and variable light chains (sequences for which are depicted respectively in Figure 95A-Figure 95J and Figure 96A-Figure 96F).

[00737] To determine the affinity of the variants from the scFv library, the variable regions from the scFvs were formatted as Fabs in a bivalent IgG1 with

E233P/L234V/L235A/G236del/S267K substitutions. DNA encoding the heavy and light chains were generated by gene synthesis and subcloned using standard molecular biology techniques into pTT5 expression vector containing IgG1 constant regions, and transiently transfected into HEK293E cells. Affinity screens of supernatant were performed using Octet. Anti-human Fc (AHC) biosensors were used to capture 1:2 dilutions of each supernatant to a density of 2.0 nm, and dipped into PD-1-His for KD determination. Affinity results are depicted in Figure 97A-Figure 97Q.

[00738] Affinity screen of variants from the bivalent mAb library were also performed in a number of experiments using Octet as described above, results for which are depicted in Figure 98-Figure 104.

[00739] Affinity screen of variants based on combinations of variable heavy and variable light chain variants formatted in bivalent IgG1 format were also performed in a couple of experiments using Octet as described above, results for which are depicted in Figure 105A-Figure 105E and Figure 106.

[00740] Affinity screen of selected 1C11 variants (as well as control mAbs based on nivolumab (XENP16432) and pembrolizumab (XENP21461)) were also determined using Biacore, a surface plasmon resonance (SPR)-based technology. Experimental steps for Biacore generally included the following: Immobilization (capture of ligand onto a sensor chip); Association (flowing of various concentrations of analyte over sensor chip); and Dissociation (flowing buffer over the sensor chips) in order to determine the affinity of the test articles. A reference flow with buffer alone was also included in the method for background correction during data processing. Binding affinities and kinetic rate constants were obtained by analyzing the processed data using a 1:1 binding model. In particular, anti-PD-1 mAbs were captured onto Protein A sensor chips, and then multiple concentrations of histidine-tagged human PD-1 or histidine tagged cyno PD-1 were flowed over the sensor chips. The resulting dissociation constants (KD) are depicted in Figure 107.

[00741] Finally, we investigated T cell surface binding of affinity optimized 1C11 variants. Binding of affinity optimized 1C11 variants to T cells was measured in an SEB-stimulated PBMC assay. Human PBMCs were stimulated with 500 ng/mL SEB for 3 days. Following stimulation, PBMCs were incubated with the indicated test articles at indicated concentrations 30 min. PBMCs were stained with anti-CD3-FITC (UCHT1) and A647

labeled antibody for human Fc. The binding of the test articles to T cells as indicated by A647 MFI on FITC+ cells is depicted in Figure 108.

B. 4B: Activity of PD-1-targeted IL-15/Rα-Fc fusions correlate with PD-1 affinity

[00742] We engineered and produced illustrative PD-1-targeted IL-15/Rα-Fc fusions comprising affinity-engineered PD-1-targeting arms as generally described in Example 3A, sequences for which are depicted in Figure 109A-Figure 109D, and investigated their activity.

[00743] Human PBMCs were stimulated for 48 hours with 500 ng/ml plate-bound anti-CD3 (OKT3) and then labeled with CFSE and incubated with the following test articles for 4 days at 37oC: XENP25850 (PD-1-targeted IL-15/Rα-Fc fusion based on 1C11_H3L3); XENP29159 (PD-1-targeted IL-15/Rα-Fc fusion based on affinity-matured 1C11_H3.329_L3.220); XENP24306 (control untargeted IL-15(D30N/E64Q/N65D)/Rα-Fc fusion having D30N/E64Q/N65D IL-15 variant); and XENP26007 (control RSV-targeted IL-15/Rα-Fc fusion having N4D/N65D IL-15 variant). Cells were stained with the following antibodies: anti-LAG-3-PE (3DS223H), anti-CD8-PerCP-Cy5.5 (SK1), anti-CD3-PE-Cy7 (OKT3), anti-CD45RO-APC-Fire750 (UCHL1), anti-HLA-DR-Alexa700 (L243), anti-CD16-BV605 (3G6), anti-CD56-BV605 (HCD56), anti-CD25-BV711 (M-A251), anti-CD45RA-BV785 (HI100), anti-CD4-BUV395 (SK3), and Zombie Aqua-BV510 and analyzed by flow for various cell populations.

[00744] We investigated the proliferation of various T cell and NK cell populations based on CFSE dilution (Zombie Aqua to exclude dead cells), data for which are depicted in Figure 110A-Figure 110B, Figure 111A-Figure 111B, Figure 112A-Figure 112B, Figure 113A-Figure 113B, Figure 114A-Figure 114B, Figure 115A-Figure 115B. The data show that PD-1-targeted IL-15/Rα-Fc fusions are much more potent in inducing proliferation of CD4+ T cells in comparison to untargeted IL-15(D30N/E64Q/N65D)/Rα-Fc fusion (as well as control RSV-targeted IL-15/Rα-Fc fusion). Notably, the PD-1-targeted IL-15/Rα-Fc fusions preferentially targets memory T cells, suggesting that in a clinical setting, the PD-1-targeted IL-15/Rα-Fc fusions will be selective for activated tumor-infiltrating lymphocytes in the tumor environment.

[00745] We also investigated the activation of various T cell populations based on expression of CD25 (a late stage T cell activation marker) and HLA-DR (another activation marker), data for which are depicted in Figure 116A-Figure 116D, Figure 117A-Figure 117D, and Figure 118A-Figure 118D. The data show that PD-1-targeted IL-15/Rα-Fc fusions generally appear more potent in inducing activation of the various T cell populations in comparison to untargeted IL-15(D30N/E64Q/N65D)/Rα-Fc fusion (as well as control RSV-targeted IL-15/Rα-Fc fusion).

[00746] Collectively, the data show that activity of the PD-1-targeted IL-15/Rα-Fc fusions correlate with PD-1 affinity. For example, as shown in Figure 110A-Figure 110D, XENP29159 (having an affinity-enhanced PD-1-targeting arm) induces proliferation of both CD8+ and CD4+ T cells more potently than does XENP25850.

XIX. Example 5: PD-1-targeted IL-15/Rα-Fc fusions with tuned IL-15 Potency

A. 5A: IL-15(D30N/N65D) variant

[00747] In a study investigating the pharmacokinetics of IL-15-Fc potency variants with Xtend, cynomolgus monkeys were administered a first single intravenous (i.v.) dose of XENP22853 (WT IL-15/Rα-heteroFc with Xtend; sequences depicted in Figure 119), XENP24306 (IL-15(D30N/E64Q/N65D)/Rα-heteroFc with Xtend; sequences depicted in Figure 122), XENP24113 (IL-15(N4D/N65D)/Rα-heteroFc with Xtend; sequences depicted in Figure 120), and XENP24294 (scIL-15(N4D/N65D)/Rα-Fc with Xtend; sequences depicted in Figure 121) at varying concentrations.

[00748] Figure 123 depicts the serum concentration of the test articles over time following the first dose. As expected, incorporating potency variants in addition to Xtend substitution (as in XENP24306 and XENP24113) greatly improves the pharmacokinetics of IL-15-Fc fusions (in comparison to XENP22583). Unexpectedly, however, IL-15/Rα-heteroFc fusion XENP24113 and scIL-15/Rα-Fc fusion XENP24294 (which have the same IL-15(N4D/N65D) potency variant) demonstrated reduced pharmacokinetics in comparison to XENP24306. This suggests that the reduced pharmacokinetics was due to the particular IL-15 potency variant rather than the format of the IL-15-Fc fusion. While a decrease in pharmacokinetics for XENP24113 and XENP24294 was expected on the basis of previous findings which demonstrated that the IL-15-Fc fusions having IL-15(N4D/N65D) variant had greater in vitro potency than IL-15-Fc fusions having the IL-15(D30N/E64Q/N65D) variant, the decrease in pharmacokinetics was unexpectedly disproportionate to the increase in

potency. Accordingly, we sought to identify alternative IL-15 potency variants for use in the LAG-3-targeted IL-15-Fc fusions of the invention.

[00749] We noted that IL-15(N4D/N65D) has both its substitutions at the IL-15 interface responsible for binding to CD122, while IL-15(D30N/E64Q/N65D) has two substitutions (E64Q and N65D) at IL-15:CD122 interface; and one substitution (D30N) at the IL-15 interface responsible for binding to CD132. Accordingly, we reasoned that the modification at the IL-15:CD132 interface may contribute to the superior pharmacokinetics observed for XENP24306. Notably, we found that scIL-15/Rα-Fc fusions comprising IL-15(N4D/N65D) variant and IL-15(D30N/N65D) variant demonstrated very similar potency in vitro, as depicted in Figure 125. In view of the above, we conceived illustrative PD-1-targeted IL-15-Fc fusion comprising the IL-15(D30N/N65D) variants, sequences for which are depicted in Figure 126A-Figure 126D. We also generated a control RSV-targeted IL-15/Rα-Fc fusion protein XENP29481 with IL-15(D30N/N65D) variant, sequences for which are depicted in Figure 129A- Figure 129B.

B. 5B: IL-15(D30N/E64Q/N65D) variant

[00750] Although the PD-1-targeted IL-15/Rα-Fc fusions were designed with the aim to be targeted to the tumor environment via the PD-1-targeting arm, the cytokine moiety is still capable of signaling before reaching the tumor site and may contribute to systemic toxicity. Accordingly, we sought to further reduce the IL-15 potency by constructing PD-1-targeted IL-15/Rα-Fc fusions with IL-15(D30N/E64Q/N65D) variant, which as illustrated in Example 2C has drastically reduced activity and in Figure 125. Sequences for illustrative PD-1-targeted IL-15/Rα-Fc fusions comprising IL-15(D30N/E64Q/N65D) variant are depicted in Figure 127A-Figure 127D. Additionally, we constructed XENP30432, a RSV-targeted IL-15/Rα-Fc fusion comprising IL-15(D30N/E64Q/N65D) variant (sequences for which are depicted in Figure 129A-Figure 129B), to act as a surrogate for investigating the behavior of PD-1-targeted IL-15/Rα-Fc fusions comprising IL-15(D30N/E64Q/N65D) variant outside of the tumor environment.

WHAT IS CLAIMED IS:

1. A PD-1 targeted IL-15/Rα heterodimeric Fc fusion protein comprising:

a) a first monomer comprising, from N- to C-terminal:

i) an IL-15 receptor alpha (IL-15Rα) sushi domain;

ii) a first domain linker,

iii) a variant IL-15 domain, and

iv) a second domain linker, and

v) a first variant Fc domain comprising CH2-CH3; and

b) a second monomer comprising, from N- to C-terminal: a heavy chain comprising VH-CH1-hinge-CH2-CH3, wherein said CH2-CH3 is a second variant Fc domain; and

c) a light chain comprising VL-CL;

wherein said VH and VL form an antigen binding domain that binds human PD-1 and have sequences selected from the pairs consisting of 1C11[PD-1]_H3L3 from XENP22553(SEQ ID NOS:186-187), 1C11[PD-1]_H3.234_L3.144 from XENP25806 (SEQ ID NOS:578-579), 1C11[PD-1]_H3.240_L3.148 from XENP25812 (SEQ ID NO:584), 1C11[PD-1]_H3.241_L3.148 from XENP25813 (SEQ ID NO:585), 1C11[PD-1]_H3.241_L3.92 from XENP25819 (SEQ ID NO:591), 1C11[PD-1]_H3.303_L3.152 from XENP26940 (SEQ ID NOS:642 and 1103), 1C11[PD-1]_H3.329_L3.220 from XENP28026 (SEQ ID NOS:708 and 1169), and 1C11[PD-1]_H3.328_L3.152 from XENP28652 (SEQ ID NOS:719 and 1180); and

wherein said first variant and said second variant Fc domains have a set of amino acid substitutions selected from the group consisting of S267K/L368D/K370S : S267K/LS364K/E357Q; S364K/E357Q : L368D/K370S; L368D/K370S : S364K; L368E/K370S : S364K; T411E/K360E/Q362E : D401K; L368D/K370S : S364K/E357L; L368D/K370S : S364K/E357Q; and K370S : S364K/E357Q, respectively and according to EU numbering.

2. The heterodimeric Fc fusion protein according to claim 1, wherein said first variant Fc domain and/or said second variant Fc domain have amino acid substitutions comprising Q295E/N384D/Q418E/N421D, according to EU numbering.

3. The heterodimeric Fc fusion protein according to claim 1 or 2, wherein said first variant and said variant second Fc domains each have amino acid substitutions selected from the group consisting of G236R/L328R, E233P/L234V/L235A/G236del/S239K, E233P/L234V/L235A/G236del/S267K, E233P/L234V/L235A/G236del/S239K/A327G, E233P/L234V/L235A/G236del/S267K/A327G and E233P/L234V/L235A/G236del, according to EU numbering.

4. The heterodimeric Fc fusion protein according to any one of claims 1 to 3, wherein said first variant and said second variant Fc domains each have amino acid substitution M428L/N434S, according to EU numbering.

5. The heterodimeric Fc fusion protein according to any one of claims 1 to 4, wherein said variant IL-15 domain comprises the amino acid sequence of SEQ ID NO:2.

6. The heterodimeric Fc fusion protein according to any one of claims 1 to 5 wherein said variant IL-15 domain comprises the amino acid sequence of SEQ ID NO:2 and amino acid substitutions selected from the group consisting of N4D/N65D, D30N/N65D, and D30N/E64Q/N65D.

7. The heterodimeric Fc fusion protein according to any one of claims 1 to 5, wherein said IL-15Rα sushi domain comprises the amino acid sequence of SEQ ID NO:4.

8. The heterodimeric Fc fusion protein according to any one of claims 1 to 7, selected from the group consisting of XENP29482 set forth in SEQ ID NOS 925, 926, and 1216, XENP25937 set forth in SEQ ID NOS: 70-372, and any one depicted in Figure 126A (SEQ ID NOS:925-929), Figure 126B (SEQ ID NOS:930-935), Figure 126C (SEQ ID NOS:936-941), Figure 126D (SEQ ID NOS:942-947), Figure 127A (SEQ ID NOS:948-953), Figure 127B (SEQ ID NOS:954-959), Figure 127C (SEQ ID NOS:960-965), Figure 127D (SEQ ID NOS:966-971), Figure 128A (SEQ ID NOS:972-977), Figure 128B (SEQ ID NOS:978-983), Figure 128C (SEQ ID NOS:984-989), Figure 128D (SEQ ID NOS:990-995),

Figure 128E (SEQ ID NOS:996-1001), Figure 128F (SEQ ID NOS:1002-1007), Figure 128G (SEQ ID NOS:1008-1013), Figure 128H (SEQ ID NOS:1014-1019), Figure 128I (SEQ ID NOS:1020-1025), Figure 128J (SEQ ID NOS:1026-1031), Figure 128K (SEQ ID NOS:1032-1035), Figure 128L (SEQ ID NOS:1036-1041).

9. A nucleic acid composition comprising:

a) a first nucleic acid encoding the first monomer of the heterodimeric Fc fusion protein according to any one of claims 1 to 8;

b) a second nucleic acid encoding the second monomer of the heterodimeric Fc fusion protein according to any one of claims 1 to 8; and

c) a third nucleic acid encoding the light chain of the heterodimeric Fc fusion protein according to any one of claims 1 to 8, respectively.

10. An expression vector composition comprising:

a) a first expression vector comprising said first nucleic acid of claim 9;

b) a second expression vector comprising said second nucleic acid of claim 9; and

c) a third expression vector comprising said third nucleic acid of claim 9.

11. A host cell comprising the nucleic acid composition of claim 9 or the expression vector composition of claim 10.

12. A method of producing a PD-1 targeted IL-15/Rα heterodimeric Fc fusion protein according to any one of claims 1 to 8 comprising: culturing the host cell of claim 11 under suitable conditions, wherein said heterodimeric Fc fusion protein is expressed; and recovering said protein.

13. A PD-1 targeted IL-15/Rα heterodimeric Fc fusion protein selected from the group consisting of XENP29482 set forth in SEQ ID NOS:925, 926, and 1216, XENP25937 set forth in SEQ ID NOS:370-372, and any one depicted in Figure 126A (SEQ ID NOS:925-929), Figure 126B (SEQ ID NOS:930-935), Figure 126C (SEQ ID NOS:936-941), Figure 126D (SEQ ID NOS:942-947), Figure 127A (SEQ ID NOS:948-953), Figure 127B (SEQ ID NOS:954-959), Figure 127C (SEQ ID NOS:960-965), Figure 127D (SEQ ID

NOS:966-971), Figure 128A (SEQ ID NOS:972-977), Figure 128B (SEQ ID NOS:978-983), Figure 128C (SEQ ID NOS:984-989), Figure 128D (SEQ ID NOS:990-995), Figure 128E (SEQ ID NOS:996-1001), Figure 128F (SEQ ID NOS:1002-1007), Figure 128G (SEQ ID NOS:1008-1013), Figure 128H (SEQ ID NOS:1014-1019), Figure 128I (SEQ ID NOS:1020-1025), Figure 128J (SEQ ID NOS:1026-1031), Figure 128K (SEQ ID NOS:1032-1035), Figure 128L (SEQ ID NOS:1036-1041).

14. A method of treating cancer in a patient in need thereof comprising administering a therapeutically effective amount of a PD-1 targeted IL-15/Rα heterodimeric Fc fusion protein according to any one of claims 1 to 8 and 13 to said patient.

15. The method of claim 14, further comprising administering a therapeutically effective amount of a checkpoint blockade antibody.

16. The method according to claim 15, wherein said checkpoint blockade antibody is selected from the group consisting of an anti-PD-1 antibody, an anti-PD-L1 antibody, an anti-TIM3 antibody, an anti-TIGIT antibody, an anti-LAG3 antibody, and an anti-CTLA-4 antibody.

17. The method according to claim 16, wherein said anti-PD-L1 antibody is atezolizumab, avelumab, or durbalumab.

Figure 1

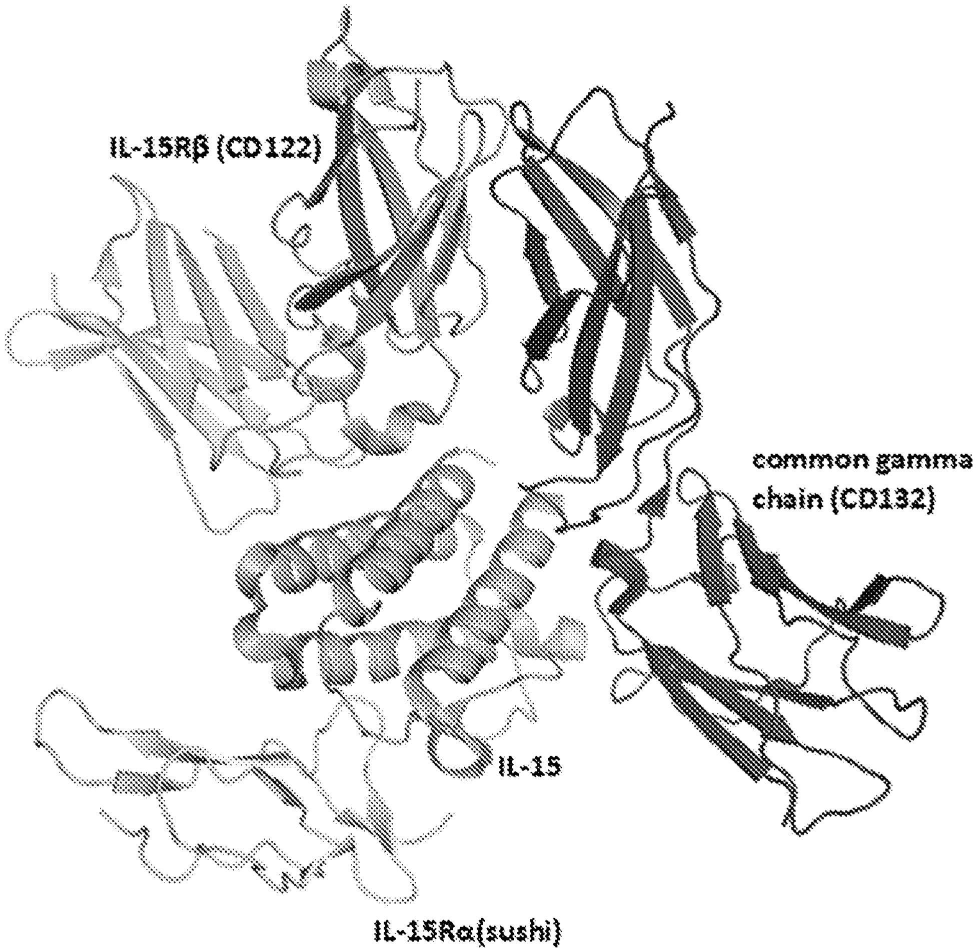


Figure 2

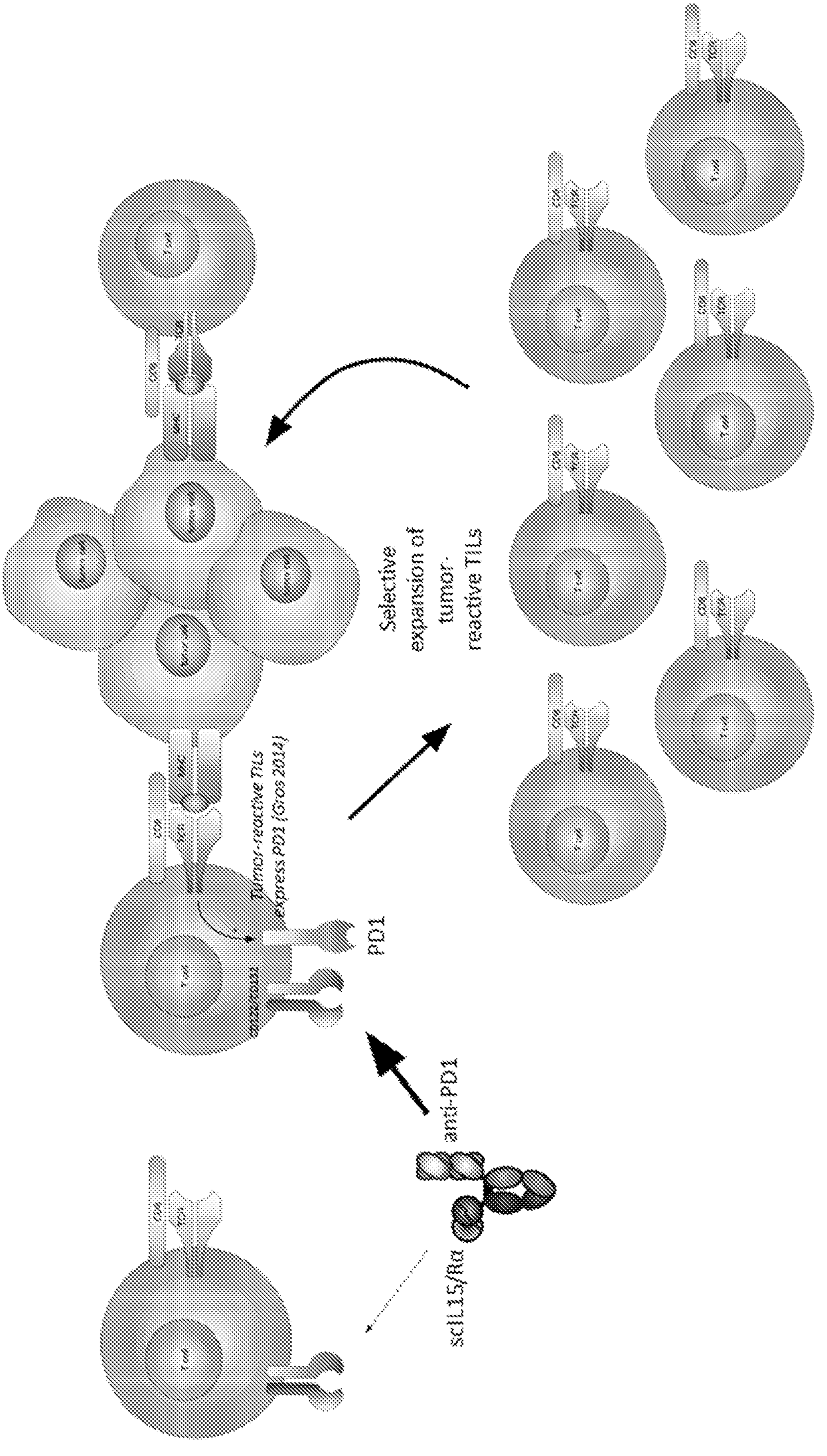

scIL15/Rα
anti-PD1
PD1
Tumor-reactive TILs express PD1 (Gros 2014)
Selective expansion of tumor-reactive TILs

Figure 3A

Human IL-15 precursor sequence

>sp|P40933 SEQ ID NO:5
MRISKPHLRSISIQCYLCLLLNSHFLTEAGIHVFILGCFSAGLPKTEANWVNVISDLKKIEDLIQSMHIDATLYT
ESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVENLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQS
FVHIVQMFINTS

Human IL-15 mature form sequence

>sp|P40933|49-162 SEQ ID NO:6
NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVENLIILANNSLS
SNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS

Human IL-15Rα sequence

>sp|Q13261 SEQ ID NO:7
MAPRRARGCRTLGLPALLLLLLLRPPATRGITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTEC
VLNKATNVAHWTTPSLKCIRDPALVHQRPAPPSTVTTAGVTPQPESLSPSGKEPAASSPSSNNTAATTAAIVPGS
QLMPSKSPSTGTTEISSHESSHGTPSQTTAKNWELTASASHQPPGVYPQGHSDTTVAISTSTVLLCGLSAVSLLA
CYLKSRQTPPLASVEMEAMEALPVTWGTSSRDEDLENCSHHL

Human IL-15Rα, extracellular domain

>sp|Q13261|31-205 SEQ ID NO:8
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIRDPALVHQRPA
PPSTVTTAGVTPQPESLSPSGKEPAASSPSSNNTAATTAAIVPGSQLMPSKSPSTGTTEISSHESSHGTPSQTTA
KNWELTASASHQPPGVYPQGHSDTT

Human IL-15Rα, sushi domain

>sp|Q13261|31-95 SEQ ID NO:9
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR

Human IL-15Rß sequence

>sp|P14784 SEQ ID NO:10
MAAPALSWRLPLLILLLPLATSWASAAVNGTSQFTCFYNSRANISCVWSQDGALQDTSCQVHAWPDRRRWNQTCE
LLPVSQASWACNLILGAPDSQKLTTVDIVTLRVLCREGVRWRVMAIQDFKPFENLRLMAPISLQVVHVETHRCNI
SWEISQASHYFERHLEFEARTLSPGHTWEEAPLLTLKQKQEWICLETLTPDTQYEFQVRVKPLQGEFTTWSPWSQ
PLAFRTKPAALGKDTIPWLGHLLVGLSGAFGFIILVYLLINCRNTGPWLKKVLKCNTPDPSKFFSQLSSEHGGDV
QKWLSSPFPSSSFSPGGLAPEISPLEVLERDKVTQLLLQQDKVPEPASLSSNHSLTSCFTNQGYFFFHLPDALEI
EACQVYFTYDPYSEEDPDEGVAGAPTGSSPQPLQPLSGEDDAYCTFPSRDDLLLFSPSLLGGPSPPSTAPGGSGA
GEERMPPSLQERVPRDWDPQPLGPPTPGVPDLVDFQPPPELVLREAGEEVPDAGPREGVSFPWSRPPGQGEFRAL
NARLPLNTDAYLSLQELQGQDPTHLV

Human IL-15Rß, extracellular domain

>sp|P14784|27-240 SEQ ID NO:11
AVNGTSQFTCFYNSRANISCVWSQDGALQDTSCQVHAWPDRRRWNQTCELLPVSQASWACNLILGAPDSQKLTTV
DIVTLRVLCREGVRWRVMAIQDFKPFENLRLMAPISLQVVHVETHRCNISWEISQASHYFERHLEFEARTLSPGH
TWEEAPLLTLKQKQEWICLETLTPDTQYEFQVRVKPLQGEFTTWSPWSQPLAFRTKPAALGKDT

Figure 3B

Human common gamma chain sequence

>sp|P31785 SEQ ID NO:12
MLKPSLPFTSLLFLQLPLLGVGLNTTILTPNGNEDTTADFFLTTMPTDSLSVSTLPLPEVQCFVFNVEYMNCTWN
SSSEPQPTNLTLHYWYKNSDNDKVQKCSHYLFSEEITSGCQLQKKEIHLYQTFVVQLQDPREPRRQATQMLKLQN
LVIPWAPENLTLHKLSESQLELNWNNRFLNHCLEHLVQYRTDWDHSWTEQSVDYRHKFSLPSVDGQKRYTFRVRS
RFNPLCGSAQHWSEWSHPIHWGSNTSKENPFLFALEAVVISVGSMGLIISLLCVYFWLERTMPRIPTLKNLEDLV
TEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPPKGGALGEGPGASPCNQHSPYWAPPCYTLKPET

Human common gamma chain, extracellular domain

>sp|P31785|23-262 SEQ ID NO:13
LNTTILTPNGNEDTTADFFLTTMPTDSLSVSTLPLPEVQCFVFNVEYMNCTWNSSSEPQPTNLTLHYWYKNSDND
KVQKCSHYLFSEEITSGCQLQKKEIHLYQTFVVQLQDPREPRRQATQMLKLQNLVIPWAPENLTLHKLSESQLEL
NWNNRFLNHCLEHLVQYRTDWDHSWTEQSVDYRHKFSLPSVDGQKRYTFRVRSRFNPLCGSAQHWSEWSHPIHWG
SNTSKENPFLFALEA

Figure 4A

Monomer 1	Monomer 2
F405A	T394F
S364D	Y349K
S364E	L368K
S364E	Y349K
S364F	K370G
S364H	Y349K
S364H	Y349T
S364Y	K370G
T411K	K370E
V397S/F405A	T394F
K370R/T411K	K370E/T411E
L351E/S364D	Y349K/L351K
L351E/S364E	Y349K/L351K
L351E/T366D	L351K/T366K
P395T/V397S/F405A	T394F
S364D/K370G	S364Y/K370R
S364D/T394F	Y349K/F405A
S364E/F405A	Y349K/T394F
S364E/F405S	Y349K/T394Y
S364E/T411E	Y349K/D401K
S364H/D401K	Y349T/T411E
S364H/F405A	Y349T/T394F
S364H/T394F	Y349T/F405A
Y349C/S364E	Y349K/S354C
L351E/S364D/F405A	Y349K/L351K/T394F
L351K/S364H/D401K	Y349T/L351E/T411E
S364E/T411E/F405A	Y349K/T394F/D401K
S364H/D401K/F405A	Y349T/T394F/T411E
S364H/F405A/T411E	Y349T/T394F/D401K

Figure 4B

Monomer 1	Monomer 2
K370E/T411D	T411K
L368E/K409E	L368K
Y349T/T394F/S354C	S364H/F405A/Y349C
T411E	D401K
T411E	D401R/T411R
Q347E/K360E	Q347R
L368E	S364K
L368E/K370S	S364K
L368E/K370T	S364K
L368E/D401R	S364K
L368E/D401N	S364K
L368E	E357S/S364K
L368E	S364K/K409E
L368E	S364K/K409V
L368D	S364K
L368D/K370S	S364K
L368D/K370S	S364K/E357L
L368D/K370S	S364K/E357Q
T411E/K360E/Q362E	D401K
K370S	S364K
L368E/K370S	S364K/E357Q
K370S	S364K/E357Q
T411E/K360D	D401K
T411E/K360E	D401K
T411E/Q362E	D401K
T411E/N390D	D401K
T411E	D401K/Q347K
T411E	D401K/Q347R
T411E/K360D/Q362E	D401K

Figure 4C

Monomer 1	Monomer 2
T411E/K360E/N390D	D401K
T411E/Q362E/N390D	D401K
T411E/Q347R	D401K/K360D
T411E/Q347R	D401K/K360E
T411E/K360	D401K/Q347K
T411E/K360D	D401K/Q347R
T411E/K360E	D401K/Q347K
T411E/K360E	D401K/Q347R
T411E/S364K	D401K/K370S
T411E/K370S	D401K/S364K
Q347E	E357Q
Q347E	E357Q/Q362K
K360D/Q362E	Q347R
K360D/Q362E	D401K
K360D/Q362E	Q347R/D401K
K360E/Q362E	Q347R
K360E/Q362E	D401K
K360E/Q362E	Q347R/D401K
Q362E/N390D	D401K
Q347E/K360D	D401N
K360D	Q347R/N390K
K360D	N390K/D401N
K360E	Y349H
K370S/Q347E	S364K
K370S/E357L	S364K
K370S/E357Q	S364K
K370S/Q347E/E357L	S364K
K370S/Q347E/E357Q	S364K

Figure 4D

Monomer 1	Monomer 2
L368D/K370S/Q347E	S364K
L368D/K370S/E357L	S364K
L368D/K370S/E357Q	S364K
L368D/K370S/Q347E/E357L	S364K
L368D/K370S/Q347E/E357Q	S364K
L368E/K370S/Q347E	S364K
L368E/K370S/E357L	S364K
L368E/K370S/E357Q	S364K
L368E/K370S/Q347E/E357L	S364K
L368E/K370S/Q347E/E357Q	S364K
L368D/K370T/Q347E	S364K
L368D/K370T/E357L	S364K
L368D/K370T/E357Q	S364K
L368D/K370T/Q347E/E357L	S364K
L368D/K370T/Q347E/E357Q	S364K
L368E/K370T/Q347E	S364K
L368E/K370T/E357L	S364K
L368E/K370T/E357Q	S364K
L368E/K370T/Q347E/E357L	S364K
L368E/K370T/Q347E/E357Q	S364K
T411E/Q362E	D401K/T411K
T411E/N390D	D401K/T411K
T411E/Q362E	D401R/T411R
T411E/N390D	D401R/T411R
Y407T	T366Y
F405A	T394W
T366Y/F405A	T394W/Y407T
Y407A	T366W
T366S/L368A/Y407V	T366W
T366S/L368A/Y407V/Y349C	T366W/S354C

Figure 4E

Monomer 1	Monomer 2
K392D/K409D	E356K/D399K
K370D/K392D/K409D	E356K/E357K/D399K
I199T/N203D/K247Q/R355Q/N384S/K392N/V397M/Q419E/K447_	Q196K/I199T/P217R/P228R/N276K
I199T/N203D/K247Q/R355Q/N384S/K392N/V397M/Q419E/K447_	Q196K/I199T/N276K
K247Q/R355Q/N384S/K392N/V397M/Q419E/K447_	P217R/P228R/N276K
K247Q/R355Q/N384S/K392N/V397M/Q419E/K447_	N276K
N384S/K392N/V397M/Q419E	N276K
D221E/P228E/L368E	D221R/P228R/K409R
C220E/P228E/L368E	C220R/E224R/P228R/K409R
F405L	K409R
T366I/K392M/T394W	F405A/Y407V
T366V/K409F	L351Y/Y407A
T366A/K392E/K409F/T411E	D399R/S400R/Y407A
L351K	L351E
I199T/N203D/K247Q/R355Q/Q419E/K447_	Q196K/I199T/P217R/P228R/N276K
I199T/N203D/K247Q/R355Q/Q419E/K447_	Q196K/I199T/N276K
K247Q/R355Q/Q419E/K447_	P217R/P228R/N276K
K247Q/R355Q/Q419E/K447_	N276K
I199T/N203D/K274Q/R355Q/N384S/K392N/V397M/Q419E/K447_	
N208D/Q295E/N384D/Q418E/N421D	
N208D/Q295E/Q418E/N421D	
Q196K/I199T/P217R/P228R/N276K	
Q196K/I199T/N276K	
K274Q/R355Q/N384S/K392N/V397M/Q419E/K447_	
Q295E/N384D/Q418E/N421D	
Q295E/Q418E/N421D	
P217R/P228R/N276K	
N276K	
E269Q/E272Q/E283Q/E357Q	
E269Q/E272Q/E283Q	
E269Q/E272Q	
E269Q/E283Q	
E272Q/E283Q	
E269Q	

Figure 5

Variant constant region	**Substitutions**
pI_ISO(-)	I199T/N203D/K274Q/R355Q/N384S/K392N/V397M/Q419E/K447_
pI_ISO(-)-Fc only	K274Q/R355Q/N384S/K392N/V397M/Q419E/K447_
pI_(-)_isosteric A	N208D/Q295E/N384D/Q418E/N421D
pI_(-)_isosteric A-Fc only	Q295E/N384D/Q418E/N421D
pI_(-)_isosteric_B	N208D/Q295E/Q418E/N421D
pI_(-)_isosteric_B-Fc only	Q295E/Q418E/N421D
pI_ISO(+RR)	Q196K/I199T/P217R/P228R/N276K
pI_ISO(+RR)-Fc only	P217R/P228R/N276K
pI_ISO(+)	Q196K/I199T/N276K
pI_ISO(+)-Fc only	N276K
pI_(+)_isosteric_A	E269Q/E272Q/E283Q/E357Q
pI_(+)_isosteric_B	E269Q/E272Q/E283Q
pI_(+)_isosteric_E269Q/E272Q	E269Q/E272Q
pI_(+)_isosteric_E269Q/E283Q	E269Q/E283Q
pI_(+)_isosteric_E272Q/E283Q	E272Q/E283Q
pI_(+)_isosteric_E269Q	E269Q

Figure 6

Ablation Variants

G236R
S239G
S239K
S239Q
S239R
V266D
S267K
S267R
H268K
E269R
299R
299K
K322A
A327G
A327L
A327N
A327Q
L328E
P329K
A330L
A330S/P331S
I332K
I332R
V266D/A327Q
V266D/P329K
S267R/A327Q
S267R/P329K
G236R/L328R
E233P/L234V/L235A/G236_/S239K
E233P/L234V/L235A/G236_/S267K
E233P/L234V/L235A/G236_/S239K/A327G
E233P/L234V/L235A/G236_/S267K/A327G
E233P/L234V/L235A/G236_
S239K/S267K
267K/P329K

Figure 7A

IL-15-Fc monomer (-)	IL-15Rα(sushi)-Fc monomer (+)
C220S	C220S
Heterodimer pI variants L368D/K370S	Heterodimer pI variants S364K/E357Q
Isosteric pI substitutions Q295E/N384D/Q418E/N421D	
FcKO E233P/L234V/L235A/G236_/S267K	FcKO E233P/L234V/L235A/G236_/S267K
±M428L/N434S	±M428L/N434S

Figure 7B

scIL-15/Rα-Fc monomer (-)	empty-Fc monomer (+)
C220S	C220S
Heterodimer pI variants L368D/K370S	Heterodimer pI variants S364K/E357Q
Isosteric pI substitutions Q295E/N384D/Q418E/N421D	
FcKO E233P/L234V/L235A/G236_/S267K	FcKO E233P/L234V/L235A/G236_/S267K
±M428L/N434S	±M428L/N434S

Figure 7C

empty-Fc monomer (-)	IL-15Rα(sushi)-Fc monomer (+)
C220S	C220S
Heterodimer pI variants L368D/K370S	Heterodimer pI variants S364K/E357Q
Isosteric pI substitutions Q295E/N384D/Q418E/N421D	
FcKO E233P/L234V/L235A/G236_/S267K	FcKO E233P/L234V/L235A/G236_/S267K
±M428L/N434S	±M428L/N434S

Figure 7D

IL-15Rα(sushi)-Fc Chain 1	IL-15Rα(sushi)-Fc Chain 2
C220S	C220S
FcKO E233P/L234V/L235A/G236_/S267K	FcKO E233P/L234V/L235A/G236_/S267K
±M428L/N434S	±M428L/N434S

Figure 7E

Fc-IL-15Rα(sushi) (-)	IL-15Rα(sushi)-Fc monomer (+)
C220S	C220S
Heterodimer pI variants L368D/K370S	Heterodimer pI variants S364K/E357Q
	Isosteric pI substitutions P217R/P228R/N276K
FcKO E233P/L234V/L235A/G236_/S267K	FcKO E233P/L234V/L235A/G236_/S267K
±M428L/N434S	±M428L/N434S

Figure 8A

scIL-15/Rα-Fc monomer (-)	**scFv-Fc monomer (+)**
C220S	C220S
Heterodimer pI variants L368D/K370S	Heterodimer pI variants S364K/E357Q
Isosteric pI substitutions Q295E/N384D/Q418E/N421D	
FcKO E233P/L234V/L235A/G236_/S267K	FcKO E233P/L234V/L235A/G236_/S267K
±M428L/N434S	±M428L/N434S

Figure 8B

scFv-Fc monomer (-)	**IL-15Rα(sushi)-Fc monomer (+)**
C220S	C220S
Heterodimer pI variants L368D/K370S	Heterodimer pI variants S364K/E357Q
Isosteric pI substitutions Q295E/N384D/Q418E/N421D	
FcKO E233P/L234V/L235A/G236_/S267K	FcKO E233P/L234V/L235A/G236_/S267K
±M428L/N434S	±M428L/N434S

Figure 8C

scIL-15/Rα-Fc monomer (-)	**Heavy Chain (+)**
C220S	
Heterodimer pI variants L368D/K370S	Heterodimer pI variants S364K/E357Q
Isosteric pI substitutions Q295E/N384D/Q418E/N421D	
FcKO E233P/L234V/L235A/G236_/S267K	FcKO E233P/L234V/L235A/G236_/S267K
±M428L/N434S	±M428L/N434S

Figure 8D

Heavy Chain (-)	**IL-15Rα(sushi)-Fc monomer (+)**
	C220S
Heterodimer pI variants L368D/K370S	Heterodimer pI variants S364K/E357Q
Isosteric pI substitutions N208D/Q295E/N384D/Q418E/N421D	
FcKO E233P/L234V/L235A/G236_/S267K	FcKO E233P/L234V/L235A/G236_/S267K
±M428L/N434S	±M428L/N434S

Figure 8E

Heavy Chain-IL-15Rα(sushi) (-)	**Heavy Chain (+)**
Heterodimer pI variants L368D/K370S	Heterodimer pI variants S364K/E357Q
Isosteric pI substitutions N208D/Q295E/N384D/Q418E/N421D	Isosteric pI subsitutions Q196K/I199T/P217R/P228R/N276K
FcKO E233P/L234V/L235A/G236_/S267K	FcKO E233P/L234V/L235A/G236_/S267K
±M428L/N434S	±M428L/N434S

Figure 8F

Heavy Chain (-)	**Heavy Chain-IL-15Rα(sushi) (+)**
Heterodimer pI variants L368D/K370S	Heterodimer pI variants S364K/E357Q
Isosteric pI substitutions N208D/Q295E/N384D/Q418E/N421D	Isosteric pI subsitutions Q196K/I199T/P217R/P228R/N276K
FcKO E233P/L234V/L235A/G236_/S267K	FcKO E233P/L234V/L235A/G236_/S267K
±M428L/N434S	±M428L/N434S

Figure 9

Name	Sequence	SEQ ID NO:
$(GGGGS)_1$ or GGGGS	GGGGS	14
$(GGGGS)_2$	GGGGSGGGGS	15
$(GGGGS)_3$	GGGGSGGGGSGGGGS	16
$(GGGGS)_4$	GGGGSGGGGSGGGGSGGGGS	17
$(GGGGS)_5$	GGGGSGGGGSGGGGSGGGGSGGGGS	18
$(GGGGS)_6$	GGGGSGGGGSGGGGSGGGGSGGGGSGGGGS	19
$(GGGGS)_7$	GGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGS	20
30AA-linker	DPALVHQRPAPPGGGGSGGGGSGGGGSGGG	21
$(GKPGS)_1$ or GKPGS	GKPGS	22
$(GKPGS)_5$	GKPGSGKPGSGKPGSGKPGSGKPGS	23
$(GKPGS)_6$	GKPGSGKPGSGKPGSGKPGSGKPGSGKPGS	24
$(GGGES)_1$ or GGGES	GGGES	25

Figure 10

Positive Charged scFv Linkers

Name	Sequence	Length	Charge	SEQ ID NO:
Gly-Ser 15	GGGGSGGGGSGGGGS	15	0	26
Whitlow linker	GSTSGSGKPGSGEGSTKG	18	+1	27
6paxA_1 (+A)	IRPRAIGGSKPRVA	14	+4	28
+B	GKGGSGKGGSGKGGS	15	+3	29
+C	GGKGSGGKGSGGKGS	15	+3	30
+D	GGGKSGGGKSGGGKS	15	+3	31
+E	GKGKSGKGKSGKGKS	15	+6	32
+F	GGGKSGGKGSGKGGS	15	+3	33
+G	GKPGSGKPGSGKPGS	15	+3	34
+H	GKPGSGKPGSGKPGSGKPGS	20	+4	35
+I	GKGKSGKGKSGKGKSGKGKS	20	+8	36

Negative Charged scFv Linkers

Name	Sequence	Length	Charge	SEQ ID NO:
Gly-Ser 20	GGGGSGGGGSGGGGSGGGGS	20	0	37
3hsc_2 (-A)	STAGDTHLGGEDFD	14	-4	38
-B	GEGGSGEGGSGEGGS	15	-3	39
-C	GGEGSGGEGSGGEGS	15	-3	40
-D	GGGESGGGESGGGES	15	-3	41
-E	GEGESGEGESGEGES	15	-6	42
-F	GGGESGGEGSGEGGS	15	-3	43
-G	GEGESGEGESGEGESGEGES	20	-8	44

Additional scFv Linkers

GGGGSGGGGSGGGGS	SEQ ID NO:45
GGGGSGGGGSGGGGSGGGGS	SEQ ID NO:46
GSTSGSGKPGSGEGSTKG	SEQ ID NO:47
PRGASKSGSASQTGSAPGS	SEQ ID NO:48
GTAAAGAGAAGGAAAGAAG	SEQ ID NO:49
GTSGSSGSGSGGSGSGGGG	SEQ ID NO:50
GKPGSGKPGSGKPGSGKPGS	SEQ ID NO:51

Figure 11A

IL-15/Rα-Fc Backbone 1

>IL-15/Rα-Fc monomer 1 (SEQ ID NO:52)
EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKP
REEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSL
SLSPGK

>IL-15/Rα-Fc monomer 2 (SEQ ID NO:53)
EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKP
REEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLT
CDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSL
SLSPGK

IL-15/Rα-Fc Backbone 2

>IL-15/Rα-Fc monomer 1 (SEQ ID NO:54)
EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKP
REEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVKLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSL
SLSPGK

>IL-15/Rα-Fc monomer 2 (SEQ ID NO:55)
EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKP
REEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLT
CDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSL
SLSPGK

IL-15/Rα-Fc Backbone 3

>IL-15/Rα-Fc monomer 1 (SEQ ID NO:56)
EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKP
REEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVKLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSL
SLSPGK

>IL-15/Rα-Fc monomer 2 (SEQ ID NO:57)
EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKP
REEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLT
CEVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSL
SLSPGK

IL-15/Rα-Fc Backbone 4

>IL-15/Rα-Fc monomer 1 (SEQ ID NO:58)
EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKP
REEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSKGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSL
SLSPGK

>IL-15/Rα-Fc monomer 2 (SEQ ID NO:59)
EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKP
REEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTENEVSLT
CLVKGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLEVDKSRWEQGDVFSCSVMHEALHNHYTQKSL
SLSPGK

Figure 11B

IL-15/Rα-Fc Backbone 5

>IL-15/Rα-Fc monomer 1 (SEQ ID NO:60)
EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKP
REEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDQLTKNQVKLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSL
SLSPGK

>IL-15/Rα-Fc monomer 2 (SEQ ID NO:61)
EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKP
REEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLT
CDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSL
SLSPGK

IL-15/Rα-Fc Backbone 6

>IL-15/Rα-Fc monomer 1 (SEQ ID NO:62)
EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKP
REEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSL
SLSPGK

>IL-15/Rα-Fc monomer 2 (SEQ ID NO:63)
EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKP
REEEYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLT
CDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSL
SLSPGK

IL-15/Rα-Fc Backbone 7

>IL-15/Rα-Fc monomer 1 (SEQ ID NO:64)
EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKP
REEQYSSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSL
SLSPGK

>IL-15/Rα-Fc monomer 2 (SEQ ID NO:65)
EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKP
REEEYSSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLT
CDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSL
SLSPGK

IL-15/Rα-Fc Backbone 8

>IL-15/Rα-Fc monomer 1 (SEQ ID NO:66)
ESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPRE
EQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEQMTKNQVKLTCL
VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSL
SLGK

>IL-15/Rα-Fc monomer 2 (SEQ ID NO:67)
ESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPRE
EEFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCD
VSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWEEGDVFSCSVMHEALHNHYTQKSLSL
SLGK

Figure 11C

IL-15/Rα-Fc Backbone 9

>IL-15/Rα-Fc monomer 1 (SEQ ID NO:68)
ERKCCVECPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVQFNWYVDGVEVHNAKTKPREE
QFNSTFRVVSVLTVVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTKGQPREPQVYTLPPSREQMTKNQVKLTCLV
KGFYPSDIAVEWESNGQPENNYKTTPPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS
PGK

>IL-15/Rα-Fc monomer 2 (SEQ ID NO:69)
ERKCCVECPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVQFNWYVDGVEVHNAKTKPREE
EFNSTFRVVSVLTVVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTKGQPREPQVYTLPPSREEMTKNQVSLTCDV
SGFYPSDIAVEWESDGQPENNYKTTPPMLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLS
PGK

IL-15/Rα-Fc Backbone 10

>IL-15/Rα-Fc monomer 1 (SEQ ID NO:70)
ERKCCVECPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVQFNWYVDGVEVHNAKTKPREE
QFNSTFRVVSVLTVVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTKGQPREPQVYTLPPSREQMTKNQVKLTCLV
KGFYPSDIAVEWESNGQPENNYKTTPPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS
PGK

>IL-15/Rα-Fc monomer 2 (SEQ ID NO:71)
ERKCCVECPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVQFNWYVDGVEVHNAKTKPREE
EFNSTFRVVSVLTVVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTKGQPREPQVYTLPPSREEMTKNQVSLTCDV
SGFYPSDIAVEWESDGQPENNYKTTPPMLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLS
PGK

IL-15/Rα-Fc Backbone 11

>IL-15/Rα-Fc monomer 1 (SEQ ID NO:72)
EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKP
REEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKSL
SLSPGK

>IL-15/Rα-Fc monomer 2 (SEQ ID NO:73)
EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKP
REEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLT
CDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVLHEALHSHYTQKSL
SLSPGK

IL-15/Rα-Fc Backbone 12

>IL-15/Rα-Fc monomer 1 (SEQ ID NO:74)
EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKP
REEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSL
SLSPGK

>IL-15/Rα-Fc monomer 2 (SEQ ID NO:75)
EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKP
REEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSL
SLSPGK

Figure 11D

IL-15/Rα-Fc Backbone 13

>IL-15/Rα-Fc monomer 1 (SEQ ID NO:76)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKP
REEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLT
CDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSL
SLSPGK

>IL-15/Rα-Fc monomer 2 (SEQ ID NO:77)

ERKSSDKTHTCPRCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFKWYVDGVEVHNAKTKP
REEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSL
SLSPGK

Figure 12

IL-15/Rα x anti-PD-1 Backbone 1

>Chain 1 (SEQ ID NO:78)
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPS
NTKVDKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNS
TYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPE
NNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>Chain 2 (SEQ ID NO:79)
EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVL
TVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPP
VLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

IL-15/Rα x anti-PD-1 Backbone 2

>Chain 1 (SEQ ID NO:80)
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPS
DTKVDKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNS
TYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

>Chain 2 (SEQ ID NO:81)
EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVL
TVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPP
VLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

IL-15/Rα x anti-PD-1 Backbone 3

>Chain 1 (SEQ ID NO:82)
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPS
DTKVDKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNS
TYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPE
NNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

>Chain 2 (SEQ ID NO:83)
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVNHKPS
NTKVDKKVERKSCDKTHTCPRCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFKWYVDGVEVHNAKTKPREEQYNS
TYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPE
NNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Figure 13

Constant Light Chain – Kappa SEQ ID NO:84
RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVT
HQGLSSPVTKSFNRGEC

Constant Light Chain – Lambda SEQ ID NO:85
GQPKAAPSVTLFPPSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTTPSKQSNNKYAASSYLSLT
PEQWKSHRSYSCQVTHEGSTVEKTVAPTECS

Figure 14

>1G6_H1L1 Variable Heavy SEQ ID NO:86
EVQLVESGGGLVKPGGSLRLSCAASGFTFSNYWMNWVRQAPGKGLEWVGEIRLKSNNYATHYAEPVKGRFTISRD
DSKSTVYLQMNSLKTEDTAVYYCTRYYGNYGGYFDVWGAGTLVTVSS

>1G6_H1L1 Variable Light SEQ ID NO:87
SIVMTQSPATLSVSPGERATLSCRASQSVSNDVAWYQQKPGQSPRLLINYASHRYTGVPDRFTGSGYGTEFTLTI
SSLQSEDFAVYFCQQDYSSPRTFGGGTKVEIK

>1G6_H1.279_L1.194 Variable Heavy SEQ ID NO:88
EVQLVESGGGLVKPGGSLRLSCVASGFTFSNYWMNWVRQAPGKGLEWVAEIRLYSNNYATHYAESVKGRFTISRD
DSKSTLYLQMNNLKTEDTGVYYCTRYYGNYGGYFDVWGRGTLVTVSS

>1G6_H1.279_L1.194 Variable Light SEQ ID NO:89
EIVLTQSPATLSASPGERVTLTCRASQSVGNDVAWYQQKPGQAPRLLINYASHRYTGVPDRFTGSGYGTEFTLTI
SSVQSEDFGVYYCQQDFSSPRTFGGGTKVEIK

Figure 15A

>pembrolizumab[PD-1] Variable Heavy SEQ ID NO:90
QVQLVQSGVEVKKPGASVKVSCKASGYTFTNYYMYWVRQAPGQGLEWMGGINPSNGGTNFNEKFKNRVTLTTDSS
TTTAYMELKSLQFDDTAVYYCARRDYRFDMGFDYWGQGTTVTVSS

>pembrolizumab[PD-1] Variable Light SEQ ID NO:91
EIVLTQSPATLSLSPGERATLSCRASKGVSTSGYSYLHWYQQKPGQAPRLLIYLASYLESGVPARFSGSGSGTDF
TLTISSLEPEDFAVYYCQHSRDLPLTFGGGTKVEIK

>nivolumab[PD-1] Variable Heavy SEQ ID NO:92
QVQLVESGGGVVQPGRSLRLDCKASGITFSNSGMHWVRQAPGKGLEWVAVIWYDGSKRYYADSVKGRFTISRDNS
KNTLFLQMNSLRAEDTAVYYCATNDDYWGQGTLVTVSS

>nivolumab[PD-1] Variable Light SEQ ID NO:93
EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASNRATGIPARFSGSGSGTDFTLTI
SSLEPEDFAVYYCQQSSNWPRTFGQGTKVEIK

>pidilizumab[PD-1] Variable Heavy SEQ ID NO:94
QVQLVQSGSELKKPGASVKISCKASGYTFTNYGMNWVRQAPGQGLQWMGWINTDSGESTYAEEFKGRFVFSLDTS
VNTAYLQITSLTAEDTGMYFCVRVGYDALDYWGQGTLVTVSS

>pidilizumab[PD-1] Variable Light SEQ ID NO:95
EIVLTQSPSSLSASVGDRVTITCSARSSVSYMHWFQQKPGKAPKLWIYRTSNLASGVPSRFSGSGSGTSYCLTIN
SLQPEDFATYYCQQRSSFPLTFGGGTKLEIK

>MK-3475[PD-1] Variable Heavy SEQ ID NO:96
QVQLVQSGVEVKKPGASVKVSCKASGYTFTNYYMYWVRQAPGQGLEWMGGINPSNGGTNFNEKFKNRVTLTTDSS
TTTAYMELKSLQFDDTAVYYCARRDYRFDMGFDYWGQGTTVTVSS

>MK-3475[PD-1] Variable Light SEQ ID NO:97
EIVLTQSPATLSLSPGERATLSCRASKGVSTSGYSYLHWYQQKPGQAPRLLIYLASYLESGVPARFSGSGSGTDF
TLTISSLEPEDFAVYYCQHSRDLPLTFGGGTKVEIK

>BAP049 Clone E[PD-1] Variable Heavy SEQ ID NO:98
EVQLVQSGAEVKKPGESLRISCKGSGYTFTTYWMHWVRQATGQGLEWMGNIYPGTGGSNFDEKFKNRVTITADKS
TSTAYMELSSLRSEDTAVYYCTRWTTGTGAYWGQGTTVTVSS

>BAP049 Clone E[PD-1] Variable Light SEQ ID NO:99
EIVLTQSPATLSLSPGERATLSCKSSQSLLDSGNQKNFLTWYQQKPGQAPRLLIYWASTRESGVPSRFSGSGSGT
DFTFTISSLEAEDAATYYCQNDYSYPYTFGQGTKVEIK

>BAP049 Clone B[PD-1] Variable Heavy SEQ ID NO:100
EVQLVQSGAEVKKPGESLRISCKGSGYTFTTYWMHWVRQATGQGLEWMGNIYPGTGGSNFDEKFKNRVTITADKS
TSTAYMELSSLRSEDTAVYYCTRWTTGTGAYWGQGTTVTVSS

>BAP049 Clone B[PD-1] Variable Light SEQ ID NO:101
EIVLTQSPATLSLSPGERATLSCKSSQSLLDSGNQKNFLTWYQQKPGKAPKLLIYWASTRESGVPSRFSGSGSGT
DFTFTISSLQPEDIATYYCQNDYSYPYTFGQGTKVEIK

>H7798N[PD-1] Variable Heavy SEQ ID NO:102
EVQLLESGGVLVQPGGSLRLSCAASGFTFSNFGMTWVRQAPGKGLEWVSGISGGGRDTYFADSVKGRFTISRDNS
KNTLYLQMNSLKGEDTAVYYCVKWGNIYFDYWGQGTLVTVSS

Figure 15B

>H7709N[PD-1] Variable Light SEQ ID NO:103
DIQMTQSPSSLSASVGDSITITCRASLSINTFLNWYQQKPGKAPNLLIYAASSLHGGVPSRFSGSGSGTDFTLTI
RTLQPEDFATYYCQQSSNTPFTFGPGTVVDFR

>h1H3 Var 6[PD-1] Variable Heavy SEQ ID NO:104
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMHWVRQAPGKGLEWVAYISSGSYTIYYADSVKGRFTISRDNA
KNTLYLQMSSLRAEDTAVYYCARRGYGSFYEYYFDYWGQGTTVTVSS

>h1H3 Var 6[PD-1] Variable Light SEQ ID NO:105
QIVLTQSPATLSLSPGERATLSCSASSSVSYMYWYQQKPGQAPRLLIYLTSNRATGIPARFSGSGSGTDYTLTIS
SLEPEDFAVYYCQQWSSNPFTFGQGTKLEIK

>APE2058[PD-1] Variable Heavy SEQ ID NO:106
EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYDMSWVRQAPGKGLEWVSTISGGGSYTYYQDSVKGRFTISRDNS
KNTLYLQMNSLRAEDTAVYYCASPYYAMDYWGQGTTVTVSSA

>APE2058[PD-1] Variable Light SEQ ID NO:107
DIQLTQSPSFLSAYVGDRVTITCKASQDVGTAVAWYQQKPGKAPKLLIYWASTLHTGVPSRFSGSGSGTEFTLTI
SSLQPEDFATYYCQHYSSYPWTFGQGTKLEIKR

>H005-1[PD-1] Variable Heavy SEQ ID NO:108
EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYMMSWVRQAPGKGLEWVATISGGGANTYYPDSVKGRFTISRDNA
KNSLYLQMNSLRAEDTAVYYCARQLYYFDYWGQGTTVTVSS

>H005-1[PD-1] Variable Light SEQ ID NO:109
DIQMTQSPSSLSASVGDRVTITCLASQTIGTWLTWYQQKPGKAPKLLIYTATSLADGVPSRFSGSGSGTDFTLTI
SSLQPEDFATYYCQQVYSIPWTFGGGTKVEIK

>317-4B6[PD-1] Variable Heavy SEQ ID NO:110
QVQLQESGPGLVKPSETLSLTCTVSGFSLTSYGVHWIRQPPGKGLEWIGVIYADGSTNYNPSLKSRVTISKDTSK
NQVSLKLSSVTAADTAVYYCARAYGNYWYIDVWGQGTTVTVSS

>317-4B6[PD-1] Variable Light SEQ ID NO:111
DIVMTQSPDSLAVSLGERATINCKSSESVSNDVAWYQQKPGQPPKLLINYAFHRFTGVPDRFSGSGYGTDFTLTI
SSLQAEDVAVYYCHQAYSSPYTFGQGTKLEIK

>326-4A3[PD-1] Variable Heavy SEQ ID NO:112
QVQLVQSGSELKKPGASVKVSCKASGYTFTNYGMNWVRQAPGQGLKWMGWINNNNAEPTYAQDFRGRFVFSLDTS
ASTAYLQISSLKTEDTAVYYCARDVMDYWGQGTLVTVSS

>326-4A3[PD-1] Variable Light SEQ ID NO:113
DIVLTQSPASLAVSPGQRATITCRASESVDNYGYSFMHWYQQKPGQPPKLLIYRASNLESGVPARFSGSGSGTDF
TLTINPVEAEDTANYYCQQSKEYPTFGGGTKVEIK

>hPD-1 mAb 7 (1.2)[PD-1] Variable Heavy SEQ ID NO:114
QVQLVQSGAEVKKPGASVKVSCKASGYSFTSYWMNWVRQAPGQGLEWIGVIHPSDSETWLDQKFKDRVTITVDKS
TSTAYMELSSLRSEDTAVYYCAREHYGTSPFAYWGQGTLVTVSS

>hPD-1 mAb 7 (1.2)[PD-1] Variable Light SEQ ID NO:115
EIVLTQSPATLSLSPGERATLSCRASESVDNYGMSFMNWFQQKPGQPPKLLIHAASNQGSGVPSRFSGSGSGTDF
TLTISSLEPEDFAVYFCQQSKEVPYTFGGGTKVEIK

Figure 15C

>Clone 38[PD-1] Variable Heavy SEQ ID NO:116
QGQLVQSGAEVKKPGASVKVSCKASGYTFTDYEMHWVRQAPIHGLEWIGVIESETGGTAYNQKFKGRVTITADKS
TSTAYMELSSLRSEDTAVYYCAREGITTVATTYYWYFDVWGQGTTVTVSS

>Clone 38[PD-1] Variable Light SEQ ID NO:117
DVVMTQSPLSLPVTLGQPASISCRSSQSIVHSNGNTYLEWYLQKPGQSPQLLIYKVSNRFSGVPDRFSGSGSGTD
FTLKISRVEAEDVGVYYCFQGSHVPLTFGQGTKLEIK

>Clone 39[PD-1] Variable Heavy SEQ ID NO:118
QGQLVQSGAEVKKPGASVKVSCKASGYTFTDYEMHWVRQAPGQGLEWMGVIESETGGTAYNQKFKGRAKITADKS
TSTAYMELSSLRSEDTAVYYCTREGITTVATTYYWYFDVWGQGTTVTVSS

>Clone 39[PD-1] Variable Light SEQ ID NO:119
DVVMTQSPLSLPVTLGQPASISCRSSQSIVHSNGNTYLEWYLQKPGQSPQLLIYKVSNRFSGVPDRFSGSGSGTD
FTLKISRVEAEDVGVYYCFQGSHVPLTFGQGTKLEIK

>Clone 41[PD-1] Variable Heavy SEQ ID NO:120
QGQLVQSGAEVKKPGASVKVSCKASGYTFTDYEMHWVRQAPGQGLEWMGVIESETGGTAYNQKFQGRVTLTADKS
SSTAYMELSSLRSEDTAVYYCTREGITTVATTYYWYFDVWGQGTLVTVSS

>Clone 41[PD-1] Variable Light SEQ ID NO:121
DVVMTQSPLSLPVTLGQPASISCRSSQSIVHSNGNTYLEWYLQKPGQSPQLLIYKVSNRFSGVPDRFSGSGSGTD
FTLKISRVEAEDVGVYYCFQGSHVPLTFGQGTKLEIK

>Clone 48[PD-1] Variable Heavy SEQ ID NO:122
QGQLVQSGAEVKKPGASVKVSCKASGYTFTDYEMHWVRQAPGQGLEWMGVIESETGGTAYNQKFKGRAKITADKS
TSTAYMELSSLRSEDTAVYYCTREGITTVATTYYWYFDVWGQGTTVTVSS

>Clone 48[PD-1] Variable Light SEQ ID NO:123
DVVMTQSPLSLPVTLGQPASISCRSSQSIVHSNGNTYLEWYLQKPGQSPRLLIYKVSNRFSGVPDRFSGSGSGTD
FTLKISRVEAEDVGVYYCFQGSHVPLTFGQGTKLEIK

>PD1-17[PD-1] Variable Heavy SEQ ID NO:124
QVQLQESGPGVVKPSGTLSLTCAISGGSIGSGGSIRSTRWWSWVRQSPGKGLEWIGEIYHSGSTNYNPSLKSRVT
ISLDKSRNHFSLRLNSVTAADTAVYYCARQDYGDSGDWYFDLWGKGTMVTVSS

>PD1-17[PD-1] Variable Light SEQ ID NO:125
NFMLTQPHSVSESPGKTVTISCTRSSGSIASNSVQWYQQRPGSSPTTVIYEDNQRPSGVPDRFSGSIDSSSNSAS
LTVSGLKTEDEADYYCQSSDSSAVVFGSGTKLTVL

>PD1-28[PD-1] Variable Heavy SEQ ID NO:126
EVQLVQSGAEVKKPGASVKVSCKASGYRFTSYGISWVRQAPGQGLEWMGWISAYNGNTNYAQKLQGRVTMTTDTS
TNTAYMELRSLRSDDTAVYYCARDADYSSGSGYWGQGTLVTVSS

>PD1-28[PD-1] Variable Light SEQ ID NO:127
SYELTQPPSVSVSPGQTARITCSGDALPKQYAYWYQQKPGQAPVMVIYKDTERPSGIPERFSGSSSGTKVTLTIS
GVQAEDEADYYCQSADNSITYRVFGGGTKVTVL

>PD1-33[PD-1] Variable Heavy SEQ ID NO:128
QVQLVQSGAEVKKPGASVRVSCKASGYTLTSYYIHWVRQAPGQGLEWMGIINPRGATISYAQKFQGRVTMTRDTS
TSTVYMELRNLKSEDTALYYCATAGIYGFDFDYWGRGTLVTVSS

Figure 15D

>PD1-33[PD-1] Variable Light SEQ ID NO:129
QSALTQPASVSGSPGQSITISCTGTSNDVGGYNYVSWYQHHPGKAPKLIIYDVTNRPSGVSDRFSGSKSGNTASL
TISGLLAEDEGDYYCSSYTIVTNFEVLFGGGTKLTV

>PD1-35[PD-1] Variable Heavy SEQ ID NO:130
QVQLQESGPGLVKPSQTLSLTCTVSGGSISSGAYYWSWIRQHPGKGLEWIGYIYYNGNTYYNPSLRSLVTISVDA
SKNQFSLKLSSVTAADTAVYYCARASDYVWGGYRYMDAFDIWGRGTLITVSS

>PD1-35[PD-1] Variable Light SEQ ID NO:131
QSVLTQPPSASGTPGQRVTISCSGSNSNIGSNSVNWYQQLPGTAPKLLIYGNNQRPSGVPDRFSGSKSGTSASLA
ISGLQSENEADYYCAAWDDSLNGPVFGRGTKVTVLGE

>LOPD180[PD-1] Variable Heavy SEQ ID NO:132
QVQLQESGPGLVKPSQTLSLTCTVSGGSISSGAYYWSWIRQHPGKGLEWIGYIYYNGNTYYNPSLRSRVTISVDT
SKNQFSLKLSSVTAADTAVYYCVRASDYVWGGYHYFDAFDLWGRGTLVTVSS

>LOPD180[PD-1] Variable Light SEQ ID NO:133
QSVLTQPPSASGTPGQRVTISCSGSNSNIGSNSVNWYQQLPGTAPKLLIYGNNQRPSGVPDRFSGSKSGTSASLA
ISGLQSEDEADYYCAAWDDSLNGPVFGGGTKVTVL

>Ab948[PD-1] Variable Heavy SEQ ID NO:134
EVQLQESGPGLVKPSQTLSLTCTVTGYSITSDYAWNWIRQPPGKKLEWMGYINYSGSTSYNPSLKSRVTISRDTS
KNQFSLKLSSVTAADTAVYYCARWIGSSAWYFDVWGQGTLVTVS

>Ab948[PD-1] Variable Light SEQ ID NO:135
DVLMTQTPLSLSVTPGQPASISCRSGQNIVHSNGNTYLEWYLQKPGQSPKLLIYKVSNRFFGVPDRISGSGSGTD
FTLKISRVEAEDVGVYFCFQGSHVPFTFGQGTKLEIK

>humanized EH-12.2H7[PD-1] Variable Heavy SEQ ID NO:136
QVQLVQSGHEVKQPGASVKMSCKASGYSFTSSWIHWVRQAPGQGLEWIGYIYPSTGFTEYNQKFKDRATLTADKS
TSTAYMELSSLRSEDTAVYYCARWRDSSGYHAMDYWGQGTLVTVSS

>humanized EH-12.2H7[PD-1] Variable Light SEQ ID NO:137
EIVLTQSPATLSLSPGQRLTISCRASQSVSTSGYSYMHWYQQKPDQSPKLLIKFGSNLESGIPARFSGSGSGTDF
TLTISSLEPEDFATYYCQHSWEIPYTFGQGTKLEIK

>RG1H10[PD-1] Variable Heavy SEQ ID NO:138
QVQLVQSGSELKKPGASVKISCKASGYIFSDNGVNWVRQAPGQGLEWMGWINTKIGNPTYAQGFTGRFVFSLDTS
ISTTYLQISSLQAGDTAVYYCAREHDYYYGMDVWGQGTTVTVSS

>RG1H10[PD-1] Variable Light SEQ ID NO:139
QSALTQPPSASGSPGQSVTISCTGTSSDVGGYNYVSWYQHHPGKAPKLMIYEVSKRPSGVPDRFSGSKSAITASL
TISGLLTEDEADYYCSAWDDSLNADVFGGGTKVTVL

>RG1H10-H2A-22-1S[PD-1] Variable Heavy SEQ ID NO:140
QVQLVQSGSELKKPGASVKISCKASGYIFSDNGVNWVRQAPGQGLEWMGWINTKDGNPTYAQGFTGRFVFSLDTS
ISTTYLQISSLQAGDTAVYYCAREHDYYYGMDVWGQGTTVTVSS

>RG1H10-H2A-22-1S[PD-1] Variable Light SEQ ID NO:141
QSALTQPPSASGSPGQSVTISCTGTSSDVGGYNYVSWYQHHPGKAPKLMIYEVSKRPSGVPDRFSGSKSAITASL
TISGLLTEDEADYYCSAWDDSLNADVFGGGTKVTVL

Figure 15E

>RG1H10-H2A-27-2S[PD-1] Variable Heavy SEQ ID NO:145
QVQLVQSGSELKKPGASVKISCKASGYIFSDNGVNWVRQAPGQGLEWMGWINTKTGNPTYAQGFTGRFVFSLDTS
ISTTYLQISSLQAGDTAVYYCAREHDYYYGMDVWGQGTTVTVSS

>RG1H10-H2A-27-2S[PD-1] Variable Light SEQ ID NO:146
QSALTQPPSASGSPGQSVTISCTGTSSDVGGYNYVSWYQHHPGKAPKLMIYEVSKRPSGVPDRFSGSKSAITASL
TISGLLTEDEADYYCSAWDDSLNADVFGGGTKVTVL

>RG1H10-3C[PD-1] Variable Heavy SEQ ID NO:147
QVQLVQSGSELKKPGASVKISCKASGYTFSDNGVNWVRQAPGQGLEWMGWINTKDGNPTYAQGFTGRFVFSLDTS
ISTTYLQISSLQAGDTAVYYCAREHDYYYGMDVWGQGTTVTVSS

>RG1H10-3C[PD-1] Variable Light SEQ ID NO:148
QSALTQPPSASGSPGQSVTISCTGTSSDVGGYNYVSWYQHHPGKAPKLMIYEVSKRPSGVPDRFSGSKSAITASL
TISGLLTEDEADYYCSAWDDSLNADVFGGGTKVTVL

>RG1H10-16C[PD-1] Variable Heavy SEQ ID NO:149
QVQLVQSGSELKKPGASVKISCKASGYTFSDNGVNWVRQAPGQGLEWMGWINTKTGNPTYAQGFTGRFVFSLDTS
ISTTYLQISSLQAGDTAVYYCAREHDYYYGMDVWGQGTTVTVS

>RG1H10-16C[PD-1] Variable Light SEQ ID NO:150
QSALTQPPSASGSPGQSVTISCTGTSSDVGGYNYVSWYQHHPGKAPKLMIYEVSKRPSGVPDRFSGSKSAITASL
TISGLLTEDEADYYCSAWDDSLNADVFGGGTKVTVL

>RG1H10-17C[PD-1] Variable Heavy SEQ ID NO:151
QVQLVQSGSELKKPGASVKISCKASGYKFSDNGVNWVRQAPGQGLEWMGWINTKSGNPTYAQGFTGRFVFSLDTS
ISTTYLQISSLQAGDTAVYYCAREHDYYYGMDVWGQGTTVTVSS

>RG1H10-17C[PD-1] Variable Light SEQ ID NO:152
QSALTQPPSASGSPGQSVTISCTGTSSDVGGYNYVSWYQHHPGKAPKLMIYEVSKRPSGVPDRFSGSKSAITASL
TISGLLTEDEADYYCSAWDDSLNADVFGGGTKVTVL

>RG1H10-19C[PD-1] Variable Heavy SEQ ID NO:153
QVQLVQSGSELKKPGASVKISCKASGYKFSDNGVNWVRQAPGQGLEWMGWINTKTGNPTYAQGFTGRFVFSLDTS
ISTTYLQISSLQAGDTAVYYCAREHDYYYGMDVWGQGTTVTVSS

>RG1H10-19C[PD-1] Variable Light SEQ ID NO:154
QSALTQPPSASGSPGQSVTISCTGTSSDVGGYNYVSWYQHHPGKAPKLMIYEVSKRPSGVPDRFSGSKSAITASL
TISGLLTEDEADYYCSAWDDSLNADVFGGGTKVTVL

>RG1H10-21C[PD-1] Variable Heavy SEQ ID NO:155
QVQLVQSGSELKKPGASVKISCKASGYTFSDNGVNWVRQAPGQGLEWMGWINTKSGNPTYAQGFTGRFVFSLDTS
ISTTYLQISSLQAGDTAVYYCAREHDYYYGMDVWGQGTTVTVSS

>RG1H10-21C[PD-1] Variable Light SEQ ID NO:156
QSALTQPPSASGSPGQSVTISCTGTSSDVGGYNYVSWYQHHPGKAPKLMIYEVSKRPSGVPDRFSGSKSAITASL
TISGLLTEDEADYYCSAWDDSLNADVFGGGTKVTVL

Figure 15F

>RG1H10-23C2[PD-1] Variable Heavy SEQ ID NO:157
QVQLVQSGSELKKPGASVKISCKASGYKFSDNGVNWVRQAPGQGLEWMGWINTKDGNPTYAQGFTGRFVFSLDTS
ISTTYLQISSLQAGDTAVYYCAREHDYYYGMDVWGQGTTVTVSS

>RG1H10-23C2[PD-1] Variable Light SEQ ID NO:158
QSALTQPPSASGSPGQSVTISCTGTSSDVGGYNYVSWYQHHPGKAPKLMIYEVSKRPSGVPDRFSGSKSAITASL
TISGLLTEDEADYYCSAWDDSLNADVFGGGTKVTVL

>mAb7[PD-1] Variable Heavy SEQ ID NO:159
QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYWINWVRQAPGQGLEWMGNIYPGSSLTNYNEKFKNRVTMTRDTS
TSTVYMELSSLRSEDTAVYYCARLSTGTFAYWGQGTLVTVSS

>mAb7[PD-1] Variable Light SEQ ID NO:160
DIVMTQSPDSLAVSLGERATINCKSSQSLWDSGNQKNFLTWYQQKPGQPPKLLIYWTSYRESGVPDRFSGSGSGT
DFTLTISSLQAEDVAVYYCQNDYFYPHTFGGGTKVEIK

>PD1AB-6[PD-1] Variable Heavy SEQ ID NO:161
EVQLVQSGAEVKKPGATVKISCKASGFNIKDTYMHWVQQAPGKGLEWMGRIDPANGDRKYDPKFQGRVTITADTS
TDTAYMELSSLRSEDTAVYYCARSGPVYYYGSSYVMDYWGQGTTVTVSS

>PD1AB-6[PD-1] Variable Light SEQ ID NO:162
DIVMTQSPDSLAVSLGERATINCKSGQSVLYSSNQKNFLAWYQQKPGQPPKLLIYWASTRESGVPDRFSGSGSGT
DFTLTISSLQAEDVAVYYCHQYLYSWTFGQGTKLEIKR

Figure 16

XENP021575 1C11[PD-1]_H0L0_IgG1_PVA_/S267K Heavy Chain SEQ ID NO:163
QIQLVQSGPELKKPGETVKISCRASGYTFT**HYGMN**WVKQAPGKGLKWMG**WINTYTGEPTYADDFKG**RFAFSLETSASTAYLQINNLKNED
TATYFCAR**DYYGSSPY**WGQGTTLTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGL
YSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHED
PEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

XENP021575 1C11[PD-1]_H0L0_IgG1_PVA_/S267K Light Chain SEQ ID NO:164
DVLMTQTPLSLPVSLGDQASISC**RSSQSIVHSNGNTYLE**WYLQKPGQSPKLLIY**KVSNRFS**GVPDRFSGSGSGTDFTLKISRVEAEDLGV
YYC**FQGSHVPNT**FGGGTKLEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYS
LSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 17

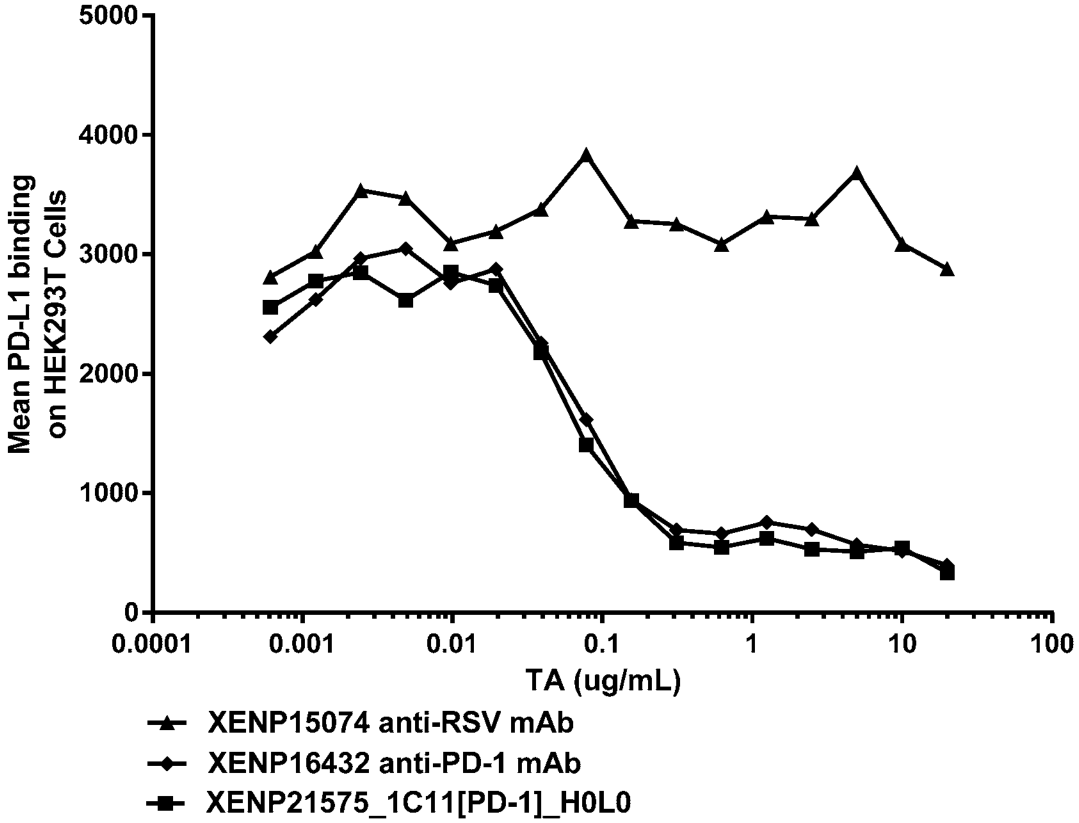

Mean PD-L1 binding on HEK293T Cells
5000
4000
3000
2000
1000
0
0.0001
0.001
0.01
0.1
1
10
100
TA (ug/mL)
XENP15074 anti-RSV mAb
XENP16432 anti-PD-1 mAb
XENP21575_1C11[PD-1]_H0L0

Figure 18

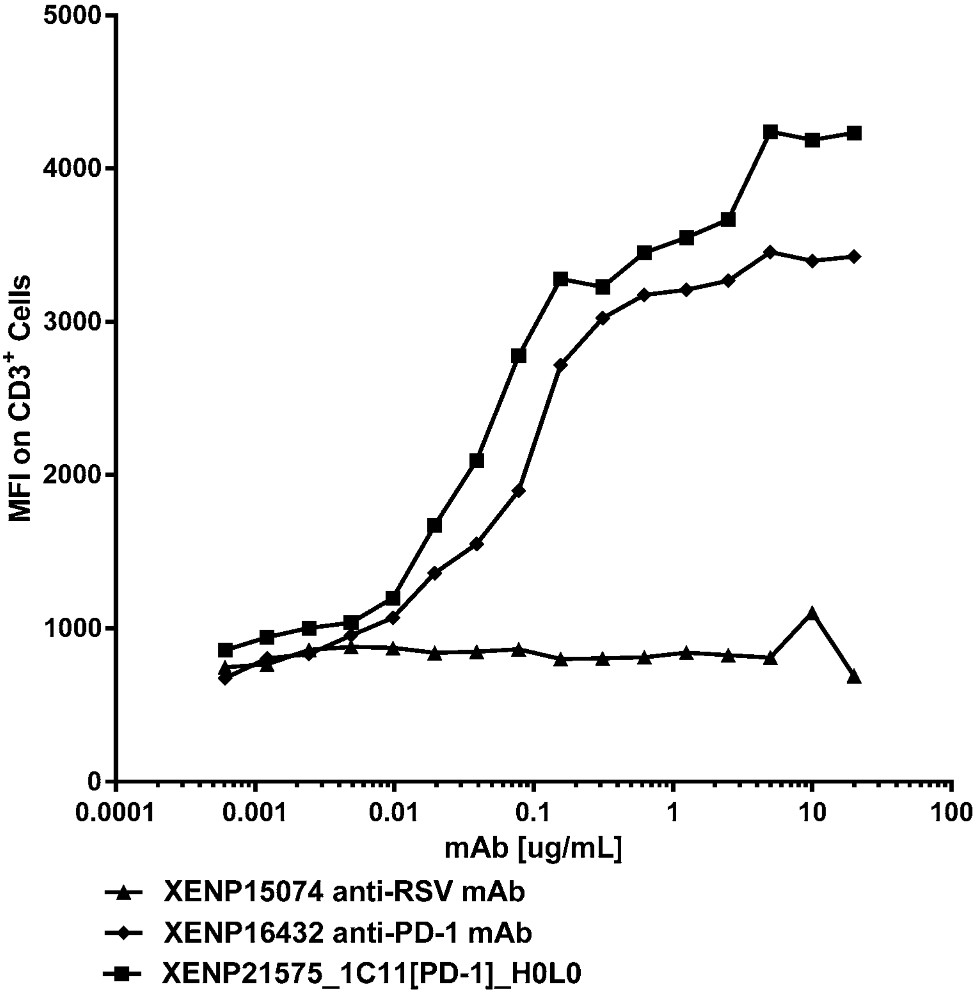

5000
4000
3000
2000
1000
0
MFI on CD3$^+$ Cells
0.0001
0.001
0.01
0.1
1
10
100
mAb [ug/mL]
XENP15074 anti-RSV mAb
XENP16432 anti-PD-1 mAb
XENP21575_1C11[PD-1]_H0L0

Figure 19A

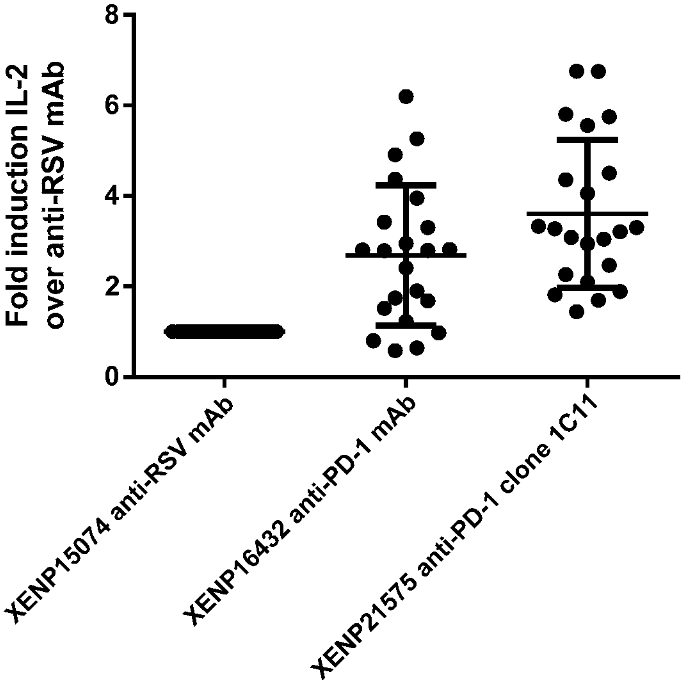


Figure 19B

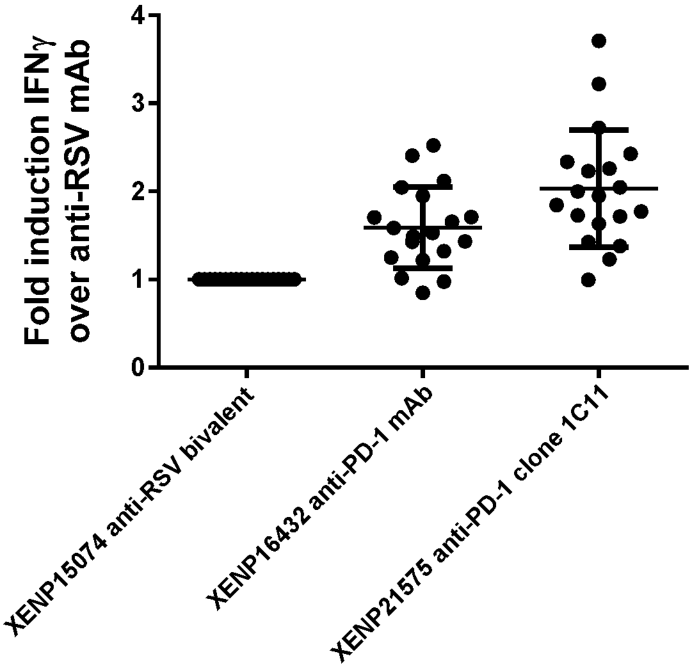


Figure 20A

>XENP022543 1C11[PD-1]_H1L1_IgG1_PVA_/S267K Heavy Chain SEQ ID NO:166
QIQLVQSGAEVKKPGASVKVSCKASGYTFT**HYGMN**WVRQAPGQGLEWMG**WINTYTGEPTYADKFQG**RVTMTLDTS
TSTAYMELSSLRSEDTAVYFCAR**DYYGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP022543 1C11[PD-1]_H1L1_IgG1_PVA_/S267K Light Chain SEQ ID NO:167
DVLMTQSPLSLPVTPGEPASISC**RSSQSIVHSNGNTYLE**WYLQKPGQSPQLLIY**KVSNRFS**GVPDRFSGSGSGTD
FTLKISRVEAEDVGVYYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP022544 1C11[PD-1]_H2L1_IgG1_PVA_/S267K Heavy Chain SEQ ID NO:168
EIQLLESGGGLVQPGGSLRLSCAASGYTFT**HYGMN**WVRQAPGKGLEWVS**WINTYTGEPTYADSVKG**RFTISLDTS
KSTAYLQMNSLRAEDTAVYFCAR**DYYGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP022544 1C11[PD-1]_H2L1_IgG1_PVA_/S267K Light Chain SEQ ID NO:169
DVLMTQSPLSLPVTPGEPASISC**RSSQSIVHSNGNTYLE**WYLQKPGQSPQLLIY**KVSNRFS**GVPDRFSGSGSGTD
FTLKISRVEAEDVGVYYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP022545 1C11[PD-1]_H3L1_IgG1_PVA_/S267K Heavy Chain SEQ ID NO:170
QIQLVQSGSELKKPGASVKVSCKASGYTFT**HYGMN**WVRQAPGQGLEWMG**WINTYTGEPTYADGFTG**RFVFSLDTS
VSTAYLQISSLKAEDTAVYFCAR**DYYGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP022545 1C11[PD-1]_H3L1_IgG1_PVA_/S267K Light Chain SEQ ID NO:171
DVLMTQSPLSLPVTPGEPASISC**RSSQSIVHSNGNTYLE**WYLQKPGQSPQLLIY**KVSNRFS**GVPDRFSGSGSGTD
FTLKISRVEAEDVGVYYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP022546 1C11[PD-1]_H4L1_IgG1_PVA_/S267K Heavy Chain SEQ ID NO:172
EVQLLESGGGLVQPGGSLRLSCAASGYTFT**HYGMN**WVRQAPGKGLEWVS**WINTYTGEPTYADSVKG**RFTISLDTS
KSTAYLQMNSLRAEDTAVYYCAR**DYYGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP022546 1C11[PD-1]_H4L1_IgG1_PVA_/S267K Light Chain SEQ ID NO:173
DVLMTQSPLSLPVTPGEPASISC**RSSQSIVHSNGNTYLE**WYLQKPGQSPQLLIY**KVSNRFS**GVPDRFSGSGSGTD
FTLKISRVEAEDVGVYYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 20B

>XENP022547 1C11[PD-1]_H1L2_IgG1_PVA_/S267K Heavy Chain SEQ ID NO:174
QIQLVQSGAEVKKPGASVKVSCKASGYTFT**HYGMN**WVRQAPGQGLEWMG**WINTYTGEPTYADKFQG**RVTMTLDTS
TSTAYMELSSLRSEDTAVYFCAR**DYYGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP022547 1C11[PD-1]_H1L2_IgG1_PVA_/S267K Light Chain SEQ ID NO:175
DVLMTQSPLSLPVTLGQPASISC**RSSQSIVHSNGNTYLE**WYQQRPGQSPRLLIY**KVSNRFS**GVPDRFSGSGSGTD
FTLKISRVEAEDVGVYYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP022548 1C11[PD-1]_H2L2_IgG1_PVA_/S267K Heavy Chain SEQ ID NO:176
EIQLLESGGGLVQPGGSLRLSCAASGYTFT**HYGMN**WVRQAPGKGLEWVS**WINTYTGEPTYADSVKG**RFTISLDTS
KSTAYLQMNSLRAEDTAVYFCAR**DYYGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP022548 1C11[PD-1]_H2L2_IgG1_PVA_/S267K Light Chain SEQ ID NO:177
DVLMTQSPLSLPVTLGQPASISC**RSSQSIVHSNGNTYLE**WYQQRPGQSPRLLIY**KVSNRFS**GVPDRFSGSGSGTD
FTLKISRVEAEDVGVYYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP022549 1C11[PD-1]_H3L2_IgG1_PVA_/S267K Heavy Chain SEQ ID NO:178
QIQLVQSGSELKKPGASVKVSCKASGYTFT**HYGMN**WVRQAPGQGLEWMG**WINTYTGEPTYADGFTG**RFVFSLDTS
VSTAYLQISSLKAEDTAVYFCAR**DYYGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP022549 1C11[PD-1]_H3L2_IgG1_PVA_/S267K Light Chain SEQ ID NO:179
DVLMTQSPLSLPVTLGQPASISC**RSSQSIVHSNGNTYLE**WYQQRPGQSPRLLIY**KVSNRFS**GVPDRFSGSGSGTD
FTLKISRVEAEDVGVYYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP022550 1C11[PD-1]_H4L2_IgG1_PVA_/S267K Heavy Chain SEQ ID NO:180
EVQLLESGGGLVQPGGSLRLSCAASGYTFT**HYGMN**WVRQAPGKGLEWVS**WINTYTGEPTYADSVKG**RFTISLDTS
KSTAYLQMNSLRAEDTAVYYCAR**DYYGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP022550 1C11[PD-1]_H4L2_IgG1_PVA_/S267K Light Chain SEQ ID NO:181
DVLMTQSPLSLPVTLGQPASISC**RSSQSIVHSNGNTYLE**WYQQRPGQSPRLLIY**KVSNRFS**GVPDRFSGSGSGTD
FTLKISRVEAEDVGVYYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 20C

>XENP022551 1C11[PD-1]_H1L3_IgG1_PVA_/S267K Heavy Chain SEQ ID NO:182
QIQLVQSGAEVKKPGASVKVSCKASGYTFT**HYGMN**WVRQAPGQGLEWMG**WINTYTGEPTYADKFQG**RVTMTLDTS
TSTAYMELSSLRSEDTAVYFCAR**DYYGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP022551 1C11[PD-1]_H1L3_IgG1_PVA_/S267K Light Chain SEQ ID NO:183
DVLMTQSPDSLAVSLGERATINC**KSSQSIVHSNGNTYLE**WYQQKPGQSPKLLIY**KVSNRFS**GVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP022552 1C11[PD-1]_H2L3_IgG1_PVA_/S267K Heavy Chain SEQ ID NO:184
EIQLLESGGGLVQPGGSLRLSCAASGYTFT**HYGMN**WVRQAPGKGLEWVS**WINTYTGEPTYADSVKG**RFTISLDTS
KSTAYLQMNSLRAEDTAVYFCAR**DYYGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP022552 1C11[PD-1]_H2L3_IgG1_PVA_/S267K Light Chain SEQ ID NO:185
DVLMTQSPDSLAVSLGERATINC**KSSQSIVHSNGNTYLE**WYQQKPGQSPKLLIY**KVSNRFS**GVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

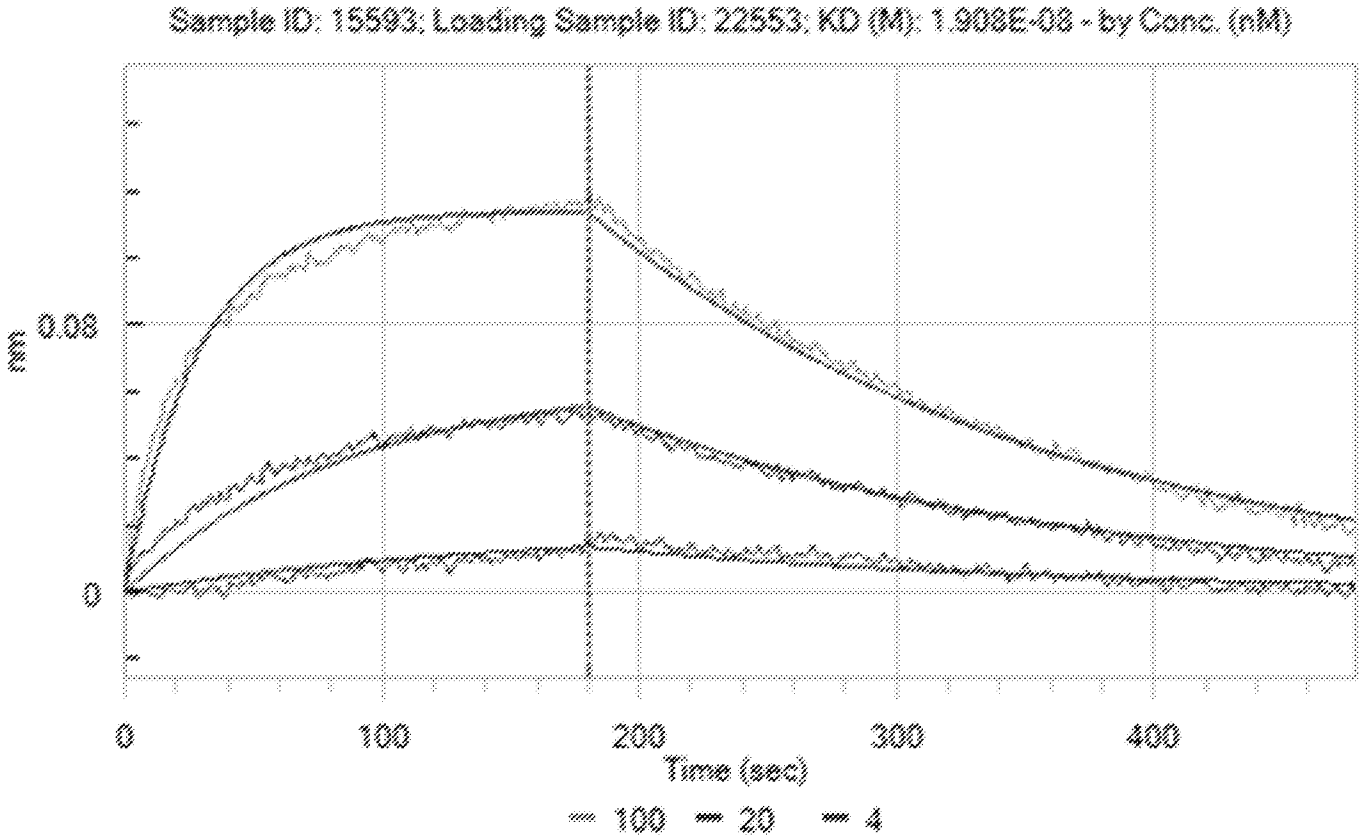
>XENP022553 1C11[PD-1]_H3L3_IgG1_PVA_/S267K Heavy Chain SEQ ID NO:186
QIQLVQSGSELKKPGASVKVSCKASGYTFT**HYGMN**WVRQAPGQGLEWMG**WINTYTGEPTYADGFTG**RFVFSLDTS
VSTAYLQISSLKAEDTAVYFCAR**DYYGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP022553 1C11[PD-1]_H3L3_IgG1_PVA_/S267K Light Chain SEQ ID NO:187
DVLMTQSPDSLAVSLGERATINC**KSSQSIVHSNGNTYLE**WYQQKPGQSPKLLIY**KVSNRFS**GVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP022554 1C11[PD-1]_H4L3_IgG1_PVA_/S267K Heavy Chain SEQ ID NO:188
EVQLLESGGGLVQPGGSLRLSCAASGYTFT**HYGMN**WVRQAPGKGLEWVS**WINTYTGEPTYADSVKG**RFTISLDTS
KSTAYLQMNSLRAEDTAVYYCAR**DYYGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP022554 1C11[PD-1]_H4L3_IgG1_PVA_/S267K Light Chain SEQ ID NO:189
DVLMTQSPDSLAVSLGERATINC**KSSQSIVHSNGNTYLE**WYQQKPGQSPKLLIY**KVSNRFS**GVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 21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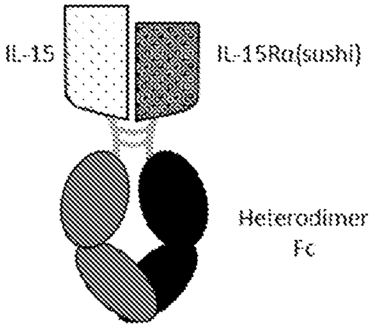
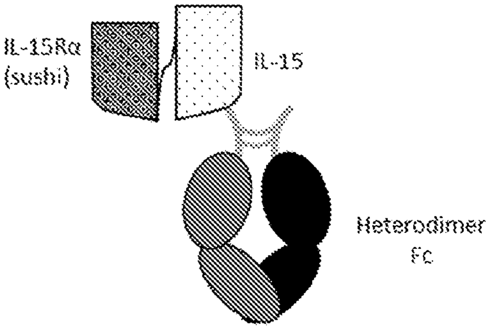
nm
0.08
0
0
100
200
300
400
Time (sec)
100
20
4

Figure 22A



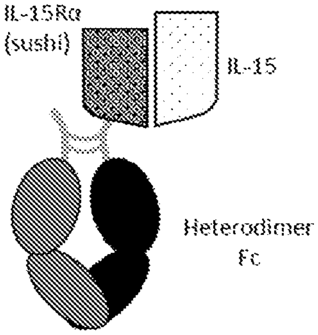
IL-15/Rα-heteroFc
Example: XENP20818

Figure 22B



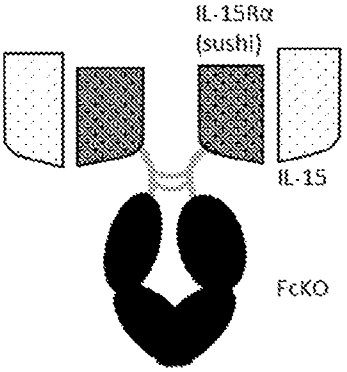
scIL-15/Rα-Fc
Example: XENP21478

Figure 22C



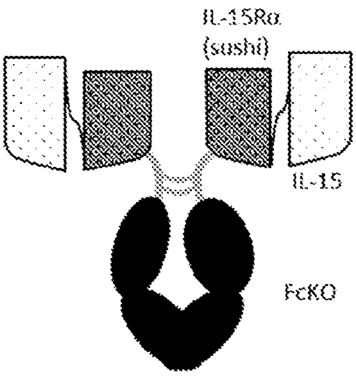
ncIL-15/Rα-Fc
Example: XENP21479

Figure 22D



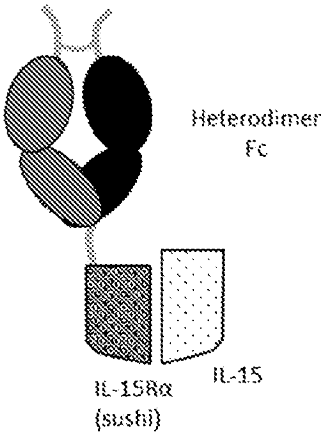
Bivalent ncIL-15/Rα-Fc
Example: XENP21978

Figure 22E



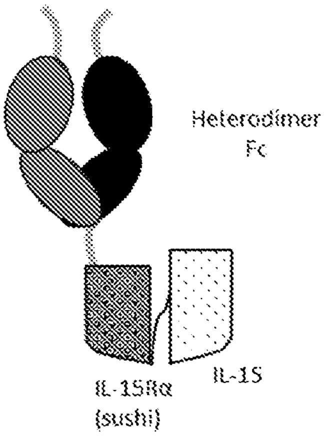
Bivalent scIL-15/Rα-Fc

Figure 22F



Fc-ncIL-15/Rα
Example: XENP22637

Figure 22G



Fc-scIL-15/Rα

Figure 23

>XENP20818 – human IL15-(GGGGS)$_1$ x human IL15Rα(Sushi)-(GGGGS)$_1$ Fc heterodimer

Chain 1 - human_IL15_(GGGGS)$_1$_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (15902) SEQ ID NO:190
NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVENLIILANNSLS
SNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/GGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPP
KPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYK
CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTP
PVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 - human_IL15Rα(Sushi)_(GGGGS)$_1$_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q (15908) SEQ ID NO:191
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGS/EPK
SSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREE
QYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLV
KGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS
PGK

>XENP21475 – human IL15 x human IL15Rα(Sushi) Fc heterodimer

Chain 1 - human_IL15-Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (16479) SEQ ID NO:192
NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVENLIILANNSLS
SNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTL
MISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK
ALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSD
GSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 - human_IL15Rα(Sushi)-Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q (16481) SEQ ID NO:193
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/EPKSSDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Figure 24

>XENP21478 – human IL15Rα(Sushi)-(GGGGS)$_6$-human IL15(single-chain) Fc heterodimer

Chain 1 - human_IL15Rα(sushi)_(GGGGS)$_6$-human_IL15-Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (16478) SEQ ID NO:194

ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGG
SGGGGSGGGGSGGGGSGGGGS/NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLE
SGDASIHDTVENLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPP
CPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVS
VLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAV
EWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 - empty-Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q (8924) SEQ ID NO:195

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKP
REEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSL
SLSPGK

Figure 25A

>XENP21479 – empty-Fc-IL15(non-covalent)-human_IL15Rα(Sushi) Fc heterodimer

Chain 1 - human_IL15_no_tag (16484) SEQ ID NO:196
NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVENLIILANNSLS
SNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS

Chain 2 - empty-Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (8793) SEQ ID NO:197
EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKP
REEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLT
CDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSL
SLSPGK

Chain 3 - human_IL15Rα(Sushi)-Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q (16481) SEQ ID NO:198
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/EPKSSDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP022366 – empty-Fc-IL15(non-covalent)-human_IL15Ra(sushi)_(GGGGS)1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

Chain 1 - human_IL15_no_tag (16484) SEQ ID NO:199
NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVENLIILANNSLS
SNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS

Chain 2 - empty-Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (8793) SEQ ID NO:200
EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKP
REEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLT
CDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSL
SLSPGK

Chain 3 - human_IL15Ra(Sushi)_(GGGGS)1_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q (15908) SEQ ID NO:201
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGS/EPK
SSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREE
QYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLV
KGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS
PGK

Figure 25B

>XENP024348 IL15(non-covalent)-human_IL15Ra(Sushi)_empty-Fc_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

Chain 1 – IL15 WT SEQ ID NO:202
NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVENLIILANNSLS
SNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS

Chain 2 – human_IL15Ra(Sushi)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S SEQ ID NO:203
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/EPKSSDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPS
DIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 3 – empty_ Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q SEQ ID NO:204
EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKP
REEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSL
SLSPGK

Figure 26

>XENP021978 – human_IL15(non-covalent)-human_IL15Ra(Sushi)_Fc(216)_IgG1_C220S/PVA_/S267K

Chain 1 - human_IL15Ra(Sushi)-Fc(216)_IgG1_C220S/PVA_/S267K (17023) SEQ ID NO:205
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/EPKSSDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 - human_IL15_no_tag (16484) SEQ ID NO:206
NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVENLIILANNSLS
SNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS

Figure 27

human_IL15(single-chain)-human_IL15Ra(Sushi)_Fc(216)_IgG1_C220S/PVA_/S267K SEQ ID NO:207

NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVENLIILANNSLS
SNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/GGGGS/ITCPPPMSVEHADIWVKSYSLYSRERYIC
NSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMIS
RTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALP
APIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSF
FLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Figure 28

>XENP022637 – empty-Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S_(GGGGS)2_IL15Ra(Sushi)_IL15(non-covalent)_IgG1_ISO(+RR)_C220S/PVA_/S267K/S364K/E357Q

Chain 1 - empty-Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S_(GGGGS)2_IL15Ra(Sushi) (17603) SEQ ID NO:208
EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKP
REEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLT
CDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSL
SLSPGK/GGGGSGGGGS/ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWT
TPSLKCIR

Chain 2 - empty-Fc(216)_IgG1_ISO(+RR)_C220S/PVA_/S267K/S364K/E357Q (8927) SEQ ID NO:209
ERKSSDKTHTCPRCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFKWYVDGVEVHNAKTKP
REEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSL
SLSPGK

Chain 3 - human_IL15_no_tag (16484) SEQ ID NO:210
NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVENLIILANNSLS
SNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS

Figure 29

empty-Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S_(GGGGS)2_IL15Ra(Sushi)_IL15(single-chain)_IgG1_ISO(+RR)_C220S/PVA_/S267K/S364K/E357Q

Chain 1 - empty-Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S_(GGGGS)2_IL15Ra(Sushi)_IL15(single-chain) SEQ ID NO:211
EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKP
REEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLT
CDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSL
SLSPGK/GGGGSGGGGS/ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWT
TPSLKCIR/GGGGS/NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIH
DTVENLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS

Chain 2 - empty-Fc(216)_IgG1_ISO(+RR)_C220S/PVA_/S267K/S364K/E357Q (8927) SEQ ID NO:212
ERKSSDKTHTCPRCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFKWYVDGVEVHNAKTKP
REEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSL
SLSPGK

Figure 30A

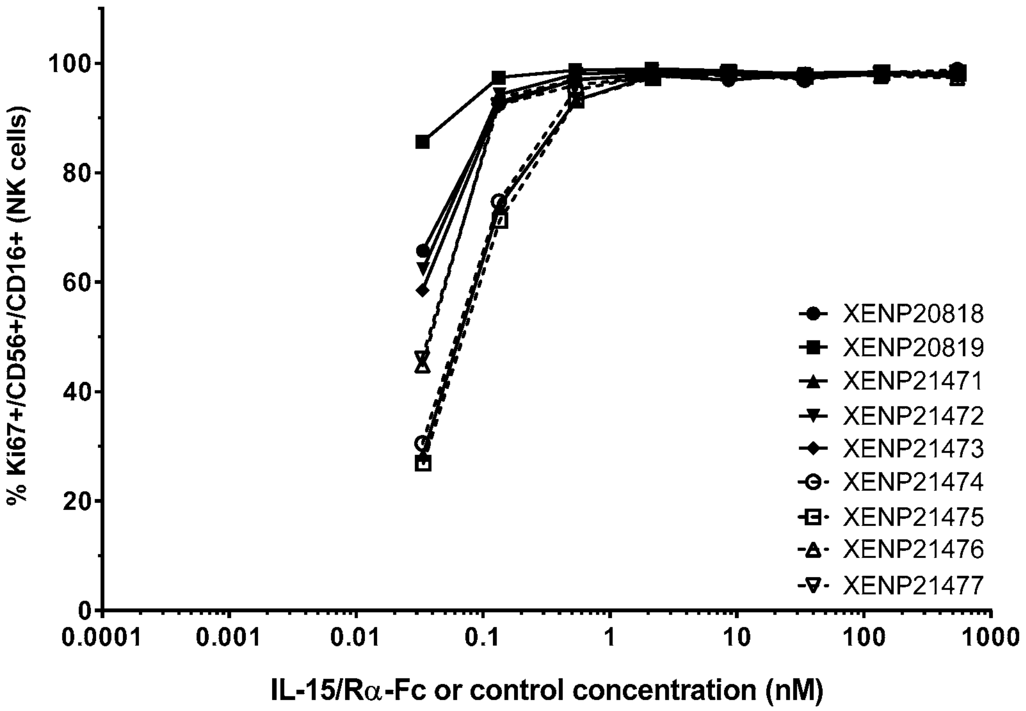


Figure 30B

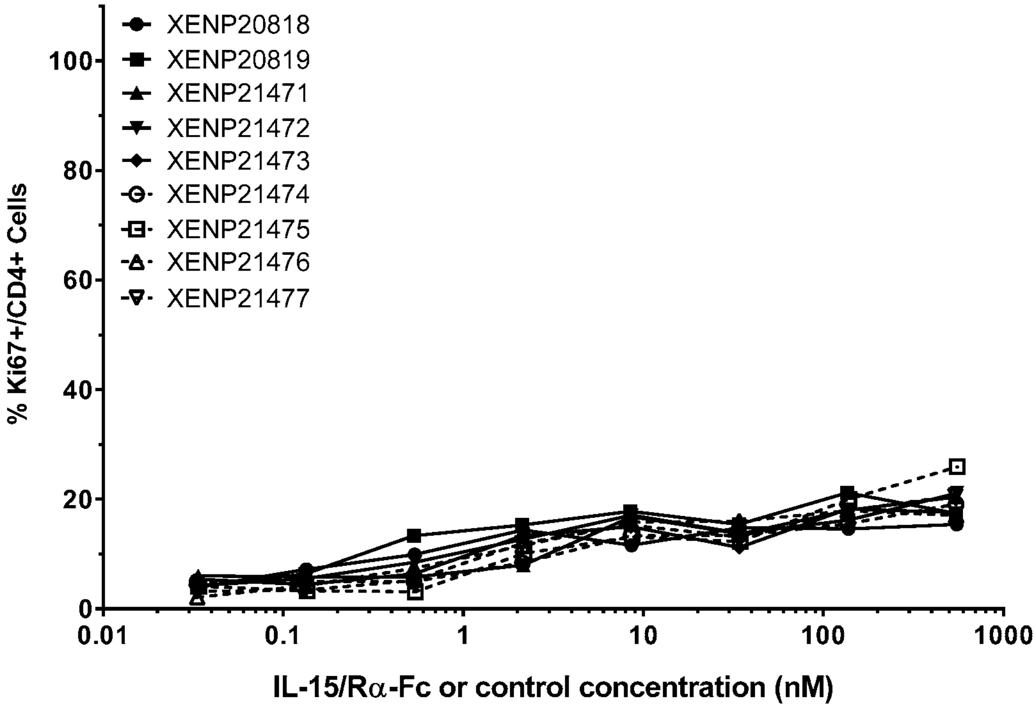
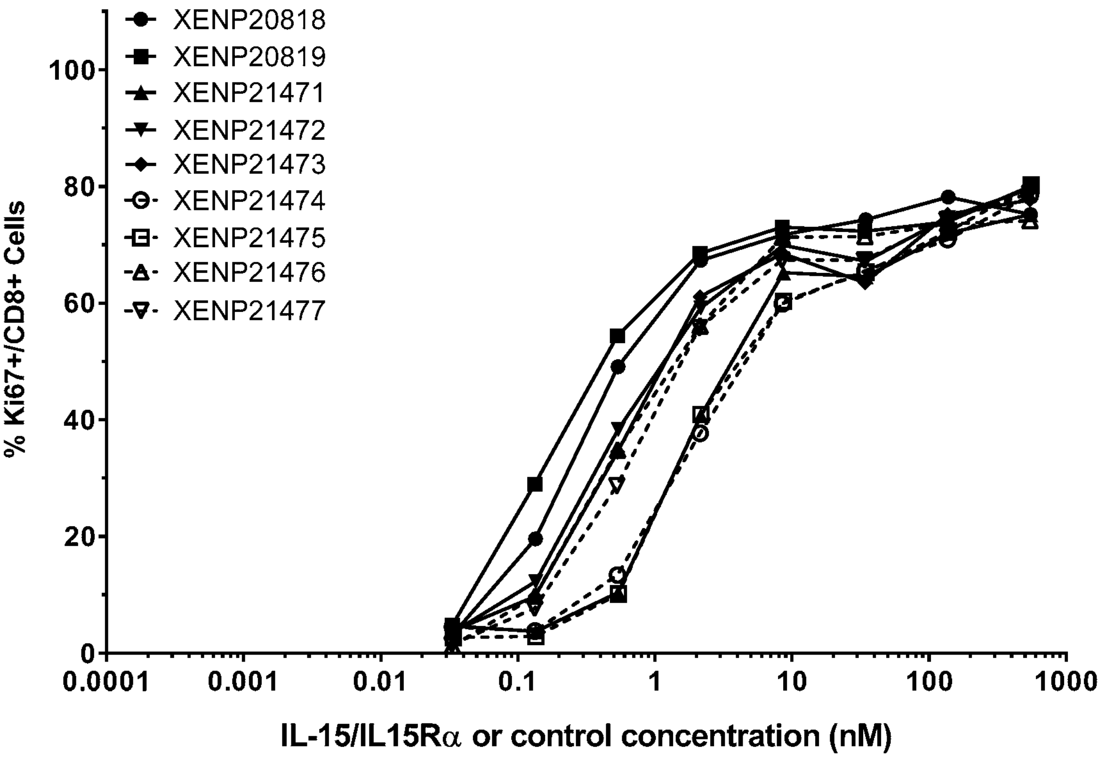


Figure 30C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-■- XENP20819
-▲- XENP21471
-▼- XENP21472
-◆- XENP21473
-○- XENP21474
-□- XENP21475
-△- XENP21476
-▽- XENP21477
% Ki67+/CD8+ Cells
100
80
60
40
20
0
0.0001
0.001
0.01
0.1
1
10
100
1000
IL-15/IL15Rα or control concentration (nM)

Figure 31A

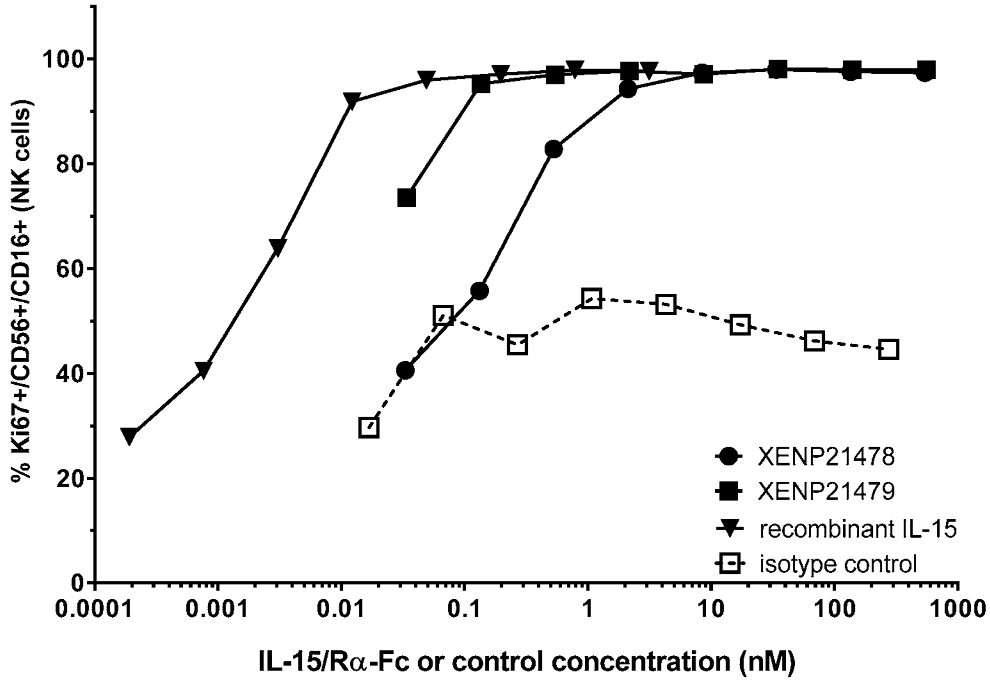


Figure 31B

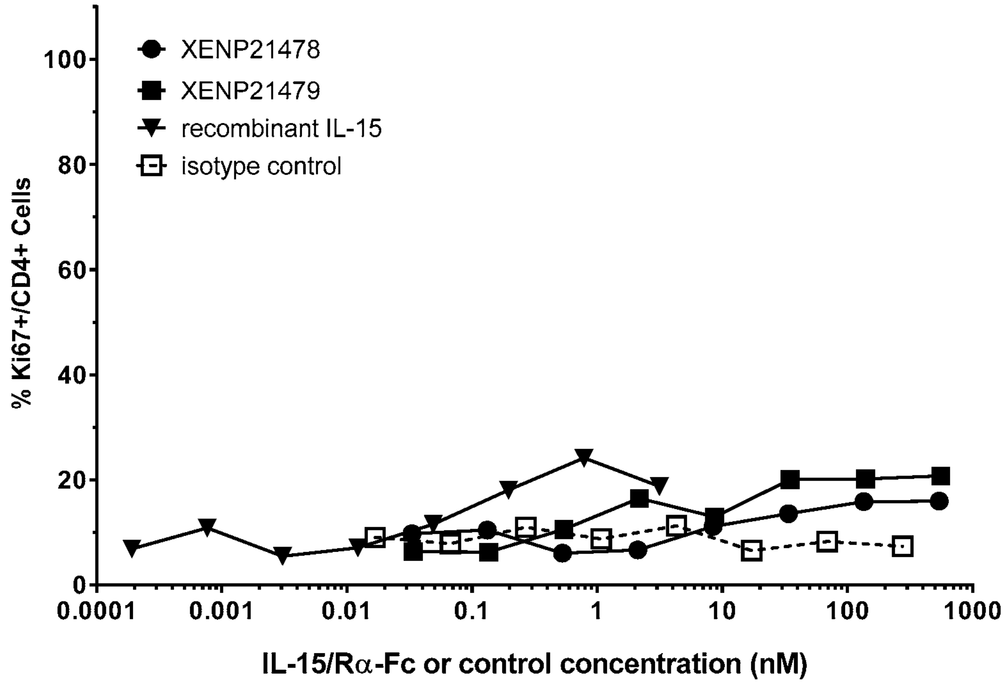


Figure 31C

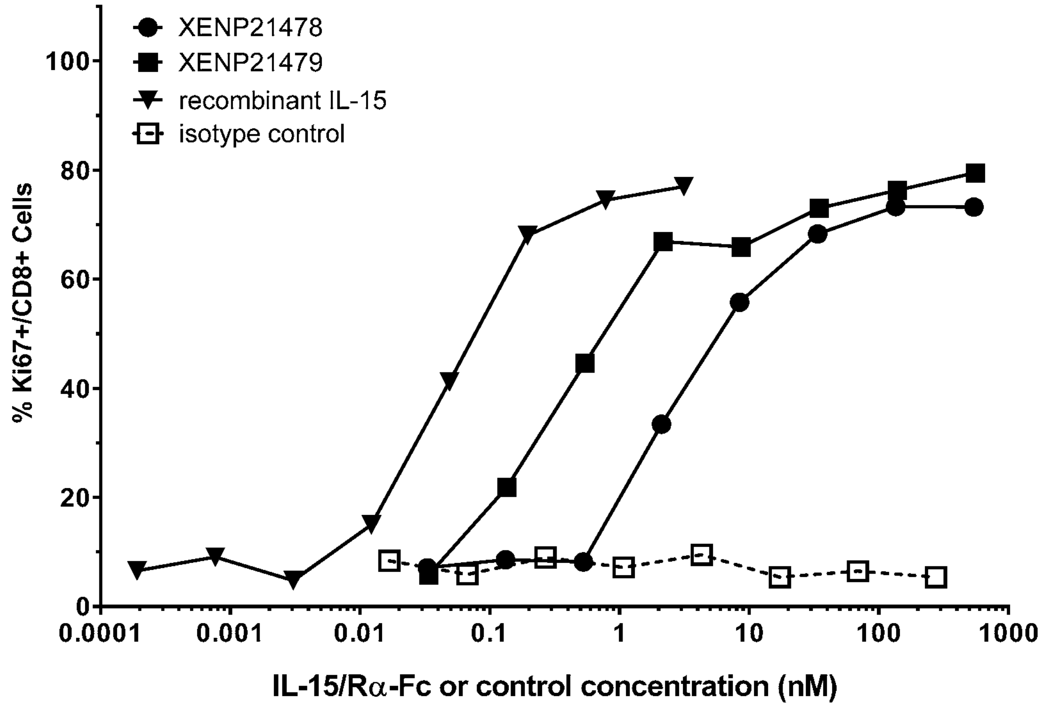

XENP21478
XENP21479
recombinant IL-15
isotype control
% Ki67+/CD8+ Cells
0
20
40
60
80
100
0.0001
0.001
0.01
0.1
1
10
100
1000
IL-15/Rα-Fc or control concentration (nM)

Figure 32

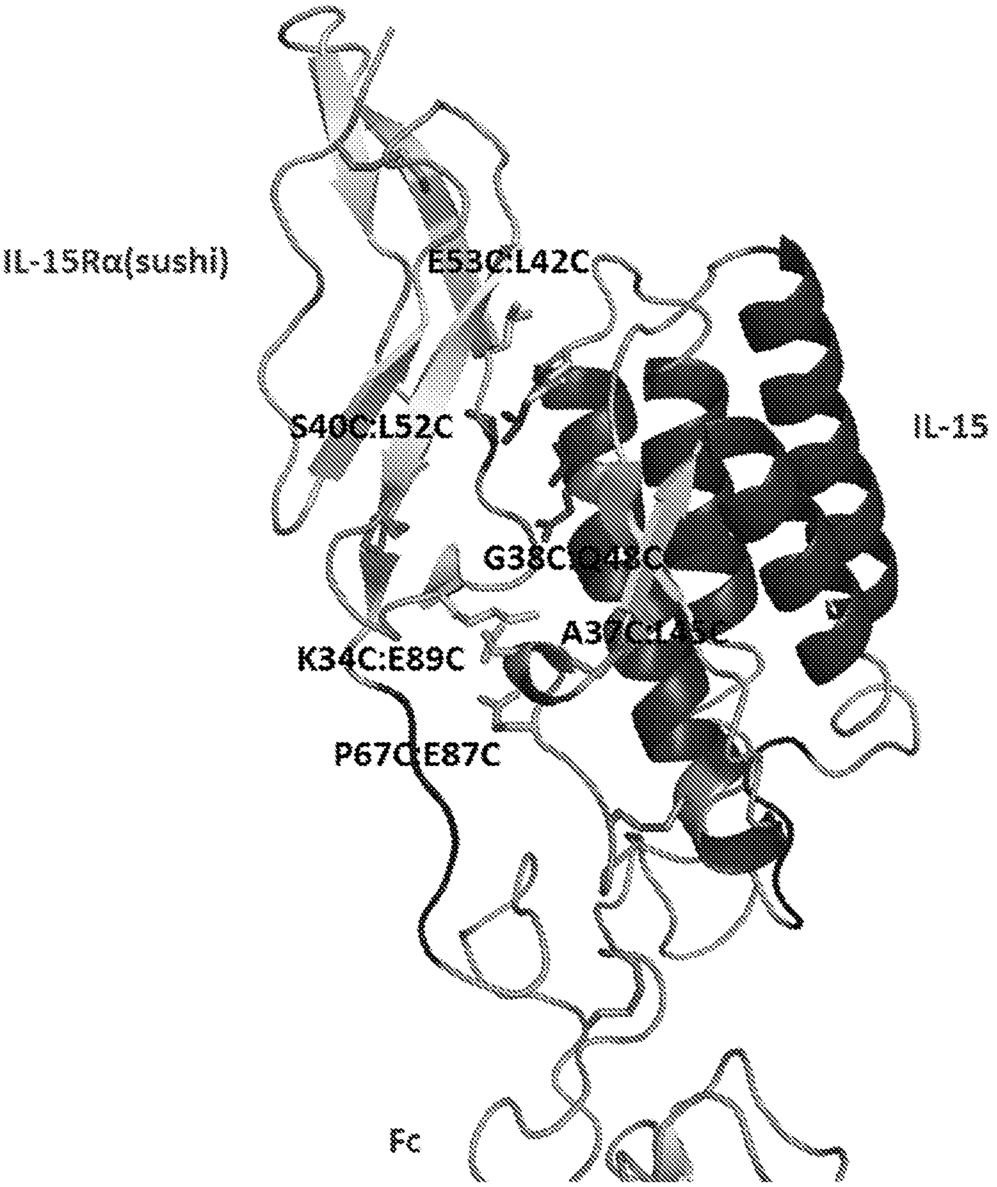

IL-15Rα(sushi)
E53C:L42C
S40C:L52C
IL-15
G38C:Q48C
A37C:L45C
K34C:E89C
P67C:E87C
Fc

Figure 33

IL-15Rα(sushi-D96) SEQ ID NO:213
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIRD

IL-15Rα(sushi-D96/P97) SEQ ID NO:214
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIRDP

IL-15Rα(sushi-D96/P97/A98) SEQ ID NO:215
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIRDPA

Figure 34

IL-15(E87C) SEQ ID NO:216
NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVENLIILANNSLS
SNGNVTESGCKCCEELEEKNIKEFLQSFVHIVQMFINTS

IL-15(V49C) SEQ ID NO:217
NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQCISLESGDASIHDTVENLIILANNSLS
SNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS

IL-15(L52C) SEQ ID NO:218
NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISCESGDASIHDTVENLIILANNSLS
SNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS

IL-15(E89C) SEQ ID NO:219
NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVENLIILANNSLS
SNGNVTESGCKECCELEEKNIKEFLQSFVHIVQMFINTS

IL-15(Q48C) SEQ ID NO:220
NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELCVISLESGDASIHDTVENLIILANNSLS
SNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS

IL-15(E53C) SEQ ID NO:221
NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLCSGDASIHDTVENLIILANNSLS
SNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS

IL-15(C42S) SEQ ID NO:222
NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKSFLLELQVISLESGDASIHDTVENLIILANNSLS
SNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS

IL-15(L45C) SEQ ID NO:223
NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLCELQVISLESGDASIHDTVENLIILANNSLS
SNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS

Figure 35

IL-15Rα(sushi-D96/C97) SEQ ID NO:224
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIRDC

IL-15Rα(sushi-D96/P97/C98) SEQ ID NO:225
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIRDPC

IL-15Rα(sushi-D96/C97/A98) SEQ ID NO:226
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIRDCA

IL-15Rα(sushi-S40C) SEQ ID NO:227
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTCSLTECVLNKATNVAHWTTPSLKCIR

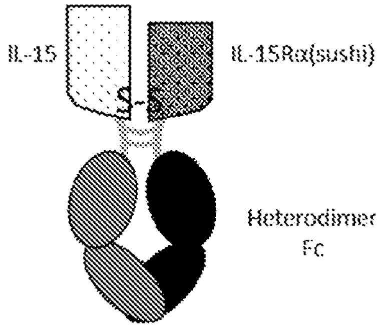
IL-15Rα(sushi-K34C) SEQ ID NO:228
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFCRKAGTSSLTECVLNKATNVAHWTTPSLKCIR

IL-15Rα(sushi-G38C) SEQ ID NO:229
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKACTSSLTECVLNKATNVAHWTTPSLKCIR

IL-15Rα(sushi-L42C) SEQ ID NO:230
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSCTECVLNKATNVAHWTTPSLKCIR

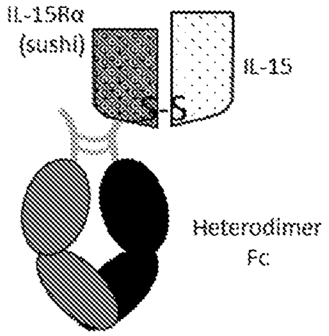
IL-15Rα(sushi-A37C) SEQ ID NO:231
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKCGTSSLTECVLNKATNVAHWTTPSLKCIR

Figure 36A



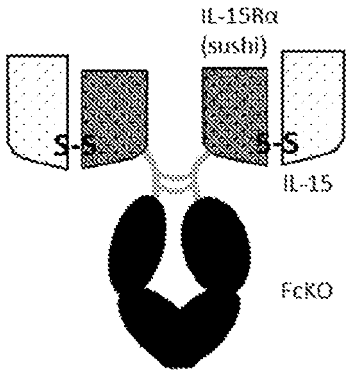
dsIL-15/Rα-heteroFc
Example: XENP22013

Figure 36B



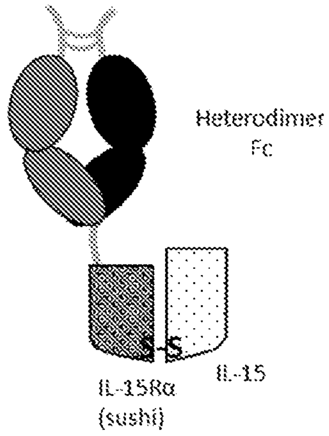
dsIL-15/Rα-Fc
Example: XENP22357

Figure 36C



Bivalent dsIL-15/Rα-Fc
Example: XENP22634

Figure 36D



Fc-dsIL-15/Rα
Example: XENP22639

Figure 37A

>XENP022013 human_IL15_E87C_(GGGGS)1-human_IL15Ra(Sushi-D96/C97)_(GGGGS)1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

Chain 1 - human_IL15_E87C_(GGGGS)1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S SEQ ID NO:232
NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVENLIILANNSLSSNGNVTESGCKCCEE
LEEKNIKEFLQSFVHIVQMFINTS/GGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKF
NWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSL
TCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 - human_IL15Ra(Sushi-D96/C97)_(GGGGS)1_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q SEQ ID NO:233
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIRDC/GGGGS/EPKSSDKTHTCPPCPA
PPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCK
VSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTV
DKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP022014 human_IL15_E87C_(GGGGS)1-human_IL15Ra(Sushi-D96/P97/C98)_(GGGGS)1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

Chain 1 - human_IL15_E87C_(GGGGS)1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S SEQ ID NO:234
NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVENLIILANNSLSSNGNVTESGCKCCEE
LEEKNIKEFLQSFVHIVQMFINTS/GGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKF
NWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSL
TCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 - human_IL15Ra(Sushi-D96/P97/C98)_(GGGGS)1_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q SEQ ID NO:235
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIRDPC/GGGGS/EPKSSDKTHTCPPCP
APPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKC
KVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLT
VDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP022015 human_IL15_E87C_(GGGGS)1-human_IL15Ra(Sushi-D96/C97/A98)_(GGGGS)1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

Chain 1 - human_IL15_E87C_(GGGGS)1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S SEQ ID NO:236
NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVENLIILANNSLSSNGNVTESGCKCCEE
LEEKNIKEFLQSFVHIVQMFINTS/GGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKF
NWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSL
TCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 - human_IL15Ra(Sushi-D96/C97/A98)_(GGGGS)1_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q SEQ ID NO:237
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIRDCA/GGGGS/EPKSSDKTHTCPPCP
APPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKC
KVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLT
VDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Figure 37B

>XENP022017 human_IL15_L52C_(GGGGS)1-human_IL15Ra(Sushi-S40C)_(GGGGS)1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

Chain 1 – human_IL15_L52C_(GGGGS)1-_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S SEQ ID NO:238

NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISCESGDASIHDTVENLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/GGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 – human_IL15Ra(Sushi-S40C)_(GGGGS)1_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q SEQ ID NO:239

ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTCSLTECVLNKATNVAHWTTPSLKCIR/GGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Figure 38A

>XENP022358 – empty-Fc-IL15_E87C-human_IL15Ra(Sushi-D96/P97/C98)_(GGGGS)1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

Chain 1 - human_IL15_E87C_no_tag (17074) SEQ ID NO:240
NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVENLIILANNSLS
SNGNVTESGCKCCEELEEKNIKEFLQSFVHIVQMFINTS

Chain 2 - empty-Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (8793) SEQ ID NO:241
EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKP
REEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLT
CDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSL
SLSPGK

Chain 3 - human_IL15Ra(Sushi-D96/P97/C98)_(GGGGS)1_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q (17039) SEQ ID NO:242
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIRDPC/GGGGS/
EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKP
REEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSL
SLSPGK

>XENP022359 – empty-Fc-IL15_E87C-human_IL15Ra(Sushi-D96/C97/A98)_(GGGGS)1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

Chain 1 - human_IL15_E87C_no_tag (17074) SEQ ID NO:243
NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVENLIILANNSLS
SNGNVTESGCKCCEELEEKNIKEFLQSFVHIVQMFINTS

Chain 2 - empty-Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (8793) SEQ ID NO:244
EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKP
REEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLT
CDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSL
SLSPGK

Chain 3 - human_IL15Ra(Sushi-D96/C97/A98)_(GGGGS)1_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q (17040) SEQ ID NO:245
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIRDCA/GGGGS/
EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKP
REEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSL
SLSPGK

Figure 38B

>XENP022361 – empty-Fc-IL15_L52C-human_IL15Ra(Sushi-S40C)_(GGGGS)1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

Chain 1 - human_IL15_L52C_no_tag (17072) SEQ ID NO:246

NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISCESGDASIHDTVENLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS

Chain 2 - empty-Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (8793) SEQ ID NO:247

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 3 - human_IL15Ra(Sushi-S40C)_(GGGGS)1_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q (17044) SEQ ID NO:248

ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTCSLTECVLNKATNVAHWTTPSLKCIR/GGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP022684 empty-Fc-IL15_E87C-human_IL15Ra(Sushi-D96/C97/A98)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

Chain 1 – IL15_E87C SEQ ID NO:249

NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVENLIILANNSLSSNGNVTESGCKCCEELEEKNIKEFLQSFVHIVQMFINTS

Chain 2 - IL15Ra(Sushi-D96/C97/A98)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S SEQ ID NO:250

ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIRDCA/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Figure 39

>XENP022634 – human_IL15(E87C)-human_IL15Ra(Sushi-D96/C97)_Fc(216)_IgG1_C220S/PVA_/S267K

Chain 1 - human_IL15Ra(Sushi-D96/C97)-Fc(216)_IgG1_C220S/PVA_/S267K (17581) SEQ ID NO:251
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIRDC/EPKSSDK
THTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNS
TYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFY
PSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 - human_IL15_E87C_no_tag (17074) SEQ ID NO:252
NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVENLIILANNSLS
SNGNVTESGCKCCEELEEKNIKEFLQSFVHIVQMFINTS

>XENP022635 – human_IL15(E87C)-human_IL15Ra(Sushi-D96/C97/A98)_Fc(216)_IgG1_C220S/PVA_/S267K

Chain 1 - human_IL15Ra(Sushi-D96/C97/A98)-Fc(216)_IgG1_C220S/PVA_/S267K (17582) SEQ ID NO:253
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIRDCA/EPKSSD
KTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYN
STYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGF
YPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 - human_IL15_E87C_no_tag (17074) SEQ ID NO:254
NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVENLIILANNSLS
SNGNVTESGCKCCEELEEKNIKEFLQSFVHIVQMFINTS

>XENP022636 – human_IL15(L52C)-human_IL15Ra(Sushi-S40C)_Fc(216)_IgG1_C220S/PVA_/S267K

Chain 1 - human_IL15Ra(Sushi-S40C)-Fc(216)_IgG1_C220S/PVA_/S267K (17583) SEQ ID NO:255
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTCSLTECVLNKATNVAHWTTPSLKCIR/EPKSSDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 - human_IL15_L52C_no_tag (17072) SEQ ID NO:256
NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISCESGDASIHDTVENLIILANNSLS
SNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS

Figure 40

>XENP022639 – empty-Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S_(GGGGS)2_IL15Ra(Sushi-D96/C97)_IL15(E87C)_IgG1_ISO(+RR)_C220S/PVA_/S267K/S364K/E357Q

Chain 1 - empty-Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S_(GGGGS)2_IL15Ra(Sushi-D96/C97) (17605) SEQ ID NO:257
EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKP
REEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLT
CDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSL
SLSPGK/GGGGSGGGGS/ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWT
TPSLKCIRDC

Chain 2 - empty-Fc(216)_IgG1_ISO(+RR)_C220S/PVA_/S267K/S364K/E357Q (8927) SEQ ID NO:258
ERKSSDKTHTCPRCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFKWYVDGVEVHNAKTKP
REEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSL
SLSPGK

Chain 3 - human_IL15_E87C_no_tag (17074) SEQ ID NO:259
NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVENLIILANNSLS
SNGNVTESGCKCCEELEEKNIKEFLQSFVHIVQMFINTS

>XENP022640 empty-Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S_IgG1_ISO(+RR)_C220S/PVA_/S267K/S364K/E357Q_(GGGGS)2_IL15Ra(Sushi-D96/C97)_IL15(E87C)

Chain 1 – IL15 SEQ ID NO:260
NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVENLIILANNSLSSNGNVTESGCKCCEE
LEEKNIKEFLQSFVHIVQMFINTS

Chain 2 – empty_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S SEQ ID NO:261
EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVL
TVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPP
VLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Figure 41

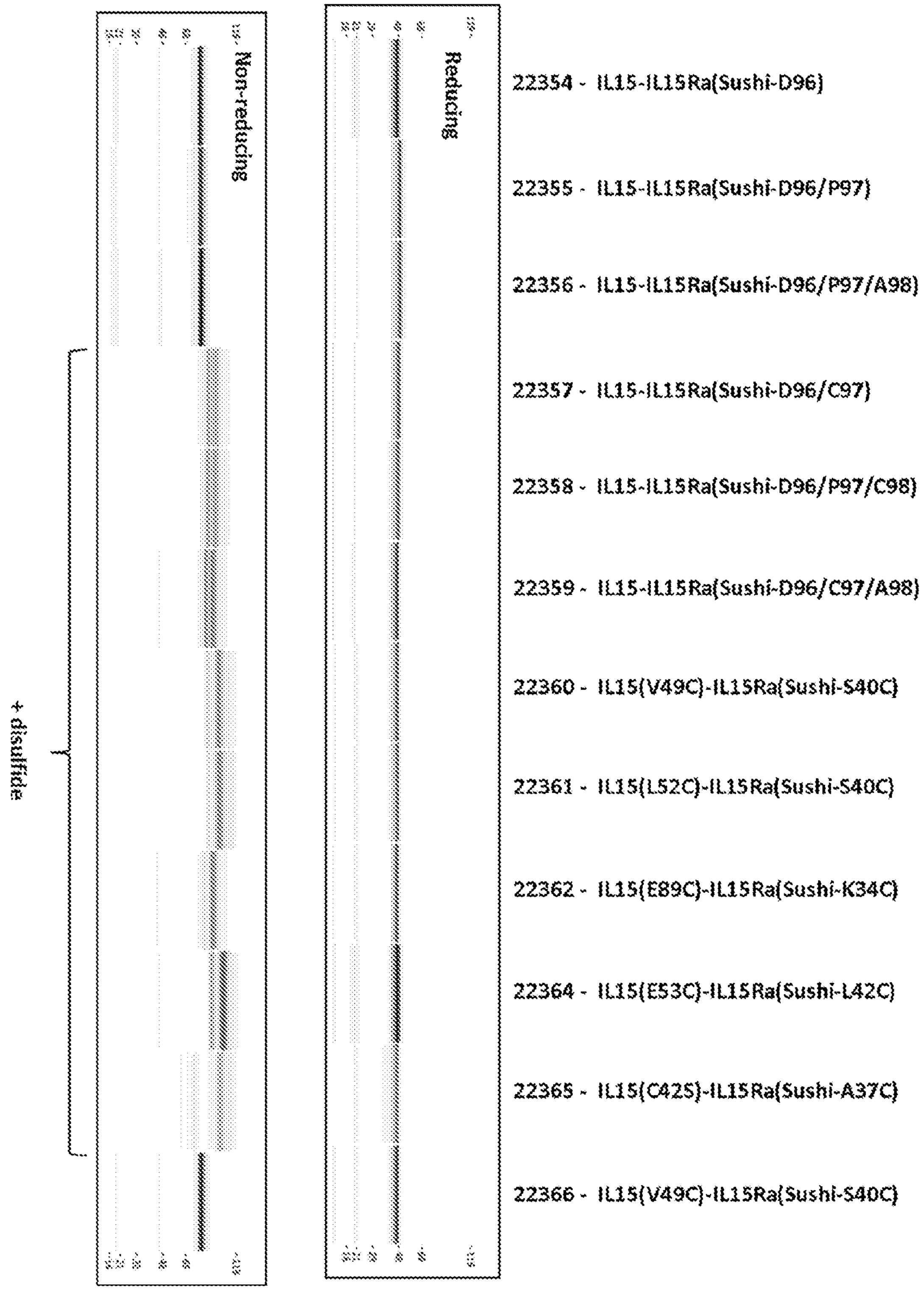

Non-reducing
Reducing
+ disulfide
22354 - IL15-IL15Ra(Sushi-D96)
22355 - IL15-IL15Ra(Sushi-D96/P97)
22356 - IL15-IL15Ra(Sushi-D96/P97/A98)
22357 - IL15-IL15Ra(Sushi-D96/C97)
22358 - IL15-IL15Ra(Sushi-D96/P97/C98)
22359 - IL15-IL15Ra(Sushi-D96/C97/A98)
22360 - IL15(V49C)-IL15Ra(Sushi-S40C)
22361 - IL15(L52C)-IL15Ra(Sushi-S40C)
22362 - IL15(E89C)-IL15Ra(Sushi-K34C)
22364 - IL15(E53C)-IL15Ra(Sushi-L42C)
22365 - IL15(C42S)-IL15Ra(Sushi-A37C)
22366 - IL15(V49C)-IL15Ra(Sushi-S40C)

Figure 42A

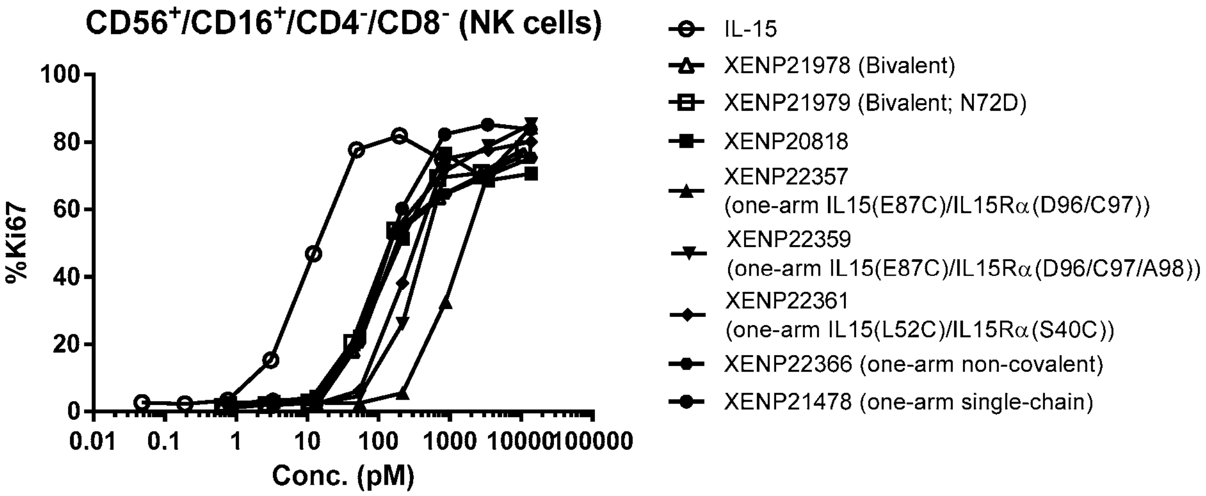


Figure 42B

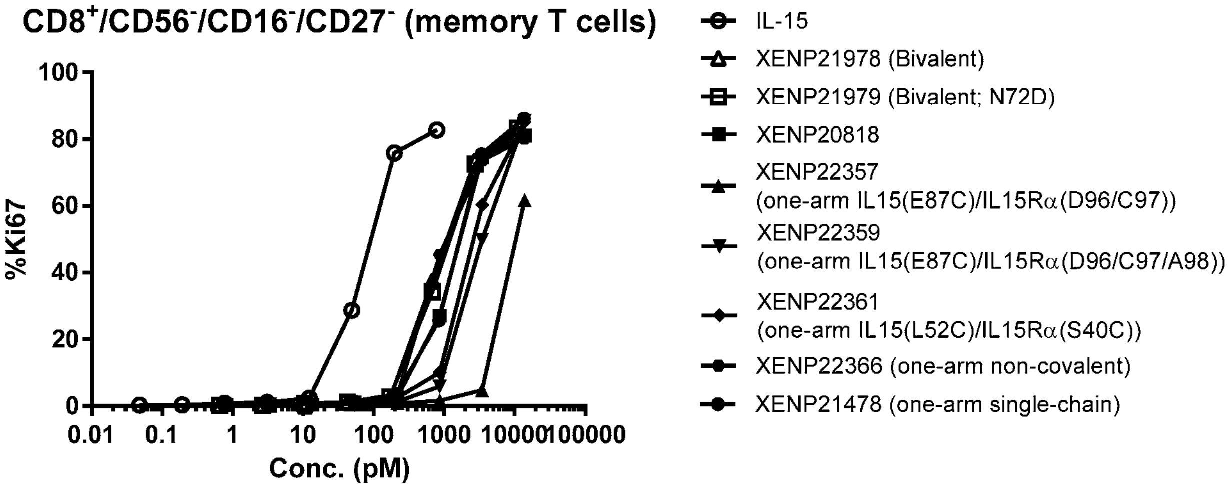
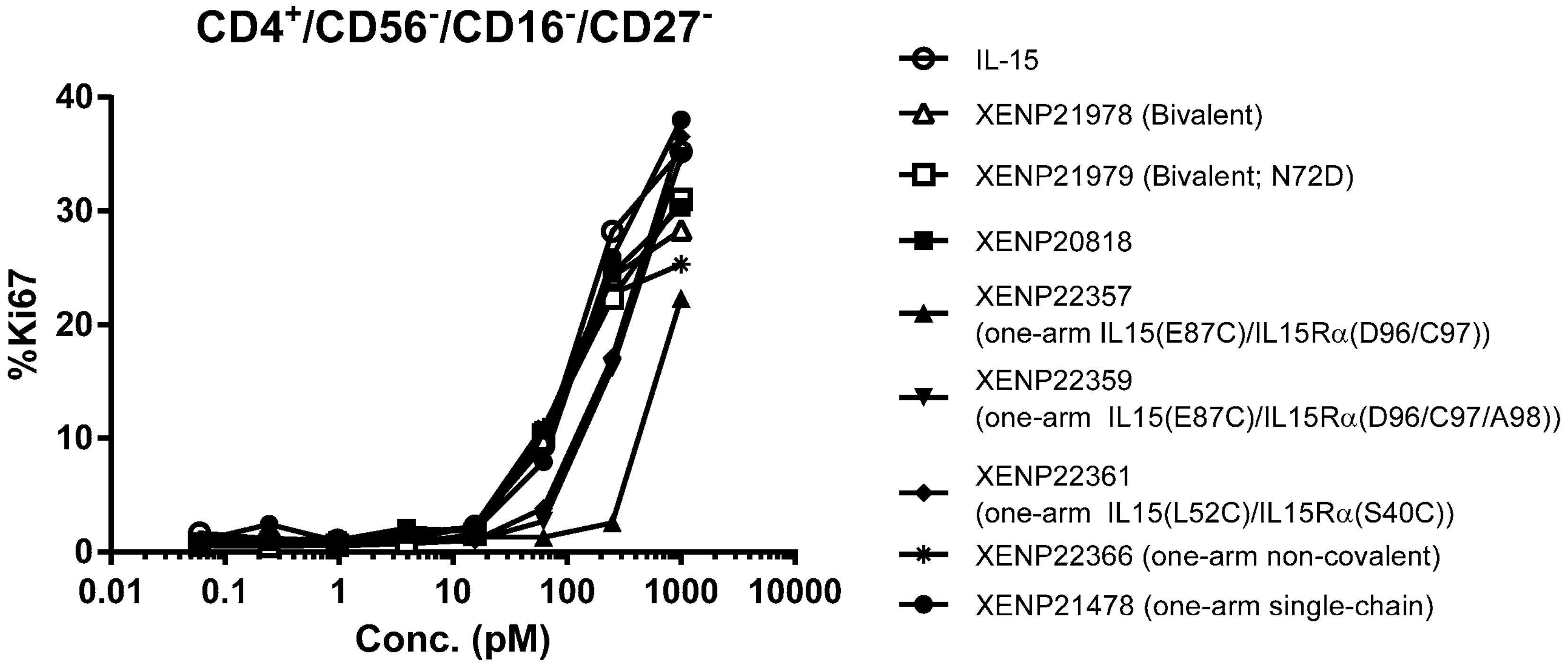


Figure 42C



CD4$^+$/CD56$^-$/CD16$^-$/CD27$^-$

Figure 43

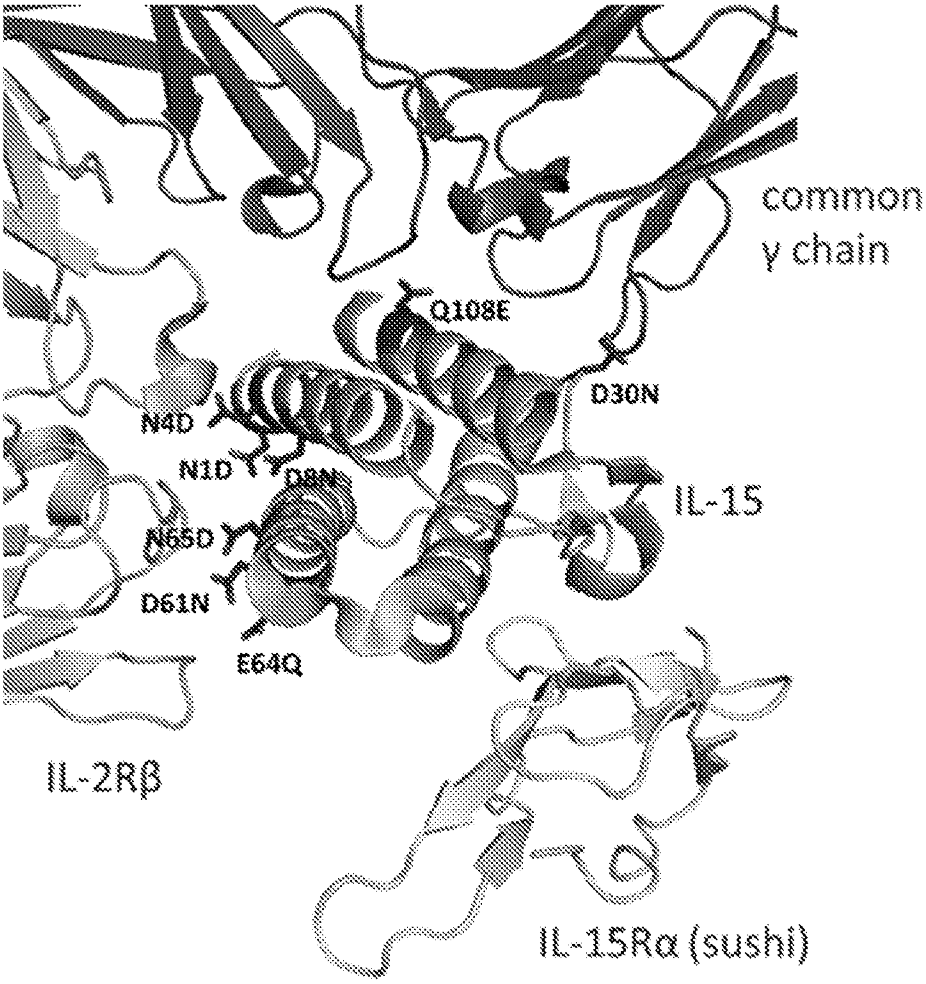

common
γ chain
Q108E
D30N
N4D
N1D
D8N
N65D
D61N
E64Q
IL-15
IL-2Rβ
IL-15Rα (sushi)

Figure 44A

N1D (SEQ ID NO:262)
DWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVENLIILANNSLSSNGNVTESGCKECEE
LEEKNIKEFLQSFVHIVQMFINTS

N4D (SEQ ID NO:263)
NWVDVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVENLIILANNSLSSNGNVTESGCKECEE
LEEKNIKEFLQSFVHIVQMFINTS

D8N (SEQ ID NO:264)
NWVNVISNLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVENLIILANNSLSSNGNVTESGCKECEE
LEEKNIKEFLQSFVHIVQMFINTS

D30N (SEQ ID NO:265)
NWVNVISDLKKIEDLIQSMHIDATLYTESNVHPSCKVTAMKCFLLELQVISLESGDASIHDTVENLIILANNSLSSNGNVTESGCKECEE
LEEKNIKEFLQSFVHIVQMFINTS

D61N (SEQ ID NO:266)
NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHNTVENLIILANNSLSSNGNVTESGCKECEE
LEEKNIKEFLQSFVHIVQMFINTS

E64Q (SEQ ID NO:267)
NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVQNLIILANNSLSSNGNVTESGCKECEE
LEEKNIKEFLQSFVHIVQMFINTS

N65D (SEQ ID NO:268)
NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVEDLIILANNSLSSNGNVTESGCKECEE
LEEKNIKEFLQSFVHIVQMFINTS

Q108E (SEQ ID NO:269)
NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVENLIILANNSLSSNGNVTESGCKECEE
LEEKNIKEFLQSFVHIVEMFINTS

N1D/D61N (SEQ ID NO:270)
DWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHNTVENLIILANNSLSSNGNVTESGCKECEE
LEEKNIKEFLQSFVHIVQMFINTS

N1D/E64Q (SEQ ID NO:271)
DWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVQNLIILANNSLSSNGNVTESGCKECEE
LEEKNIKEFLQSFVHIVQMFINTS

N4D/D61N (SEQ ID NO:272)
NWVDVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHNTVENLIILANNSLSSNGNVTESGCKECEE
LEEKNIKEFLQSFVHIVQMFINTS

N4D/E64Q (SEQ ID NO:273)
NWVDVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVQNLIILANNSLSSNGNVTESGCKECEE
LEEKNIKEFLQSFVHIVQMFINTS

D8N/D61N (SEQ ID NO:274)
NWVNVISNLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHNTVENLIILANNSLSSNGNVTESGCKECEE
LEEKNIKEFLQSFVHIVQMFINTS

Figure 44B

D8N/E64Q (SEQ ID NO:275)
NWVNVISNLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVQNLIILANNSLSSNGNVTESGCKECEE
LEEKNIKEFLQSFVHIVQMFINTS

D61N/E64Q (SEQ ID NO:276)
NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHNTVQNLIILANNSLSSNGNVTESGCKECEE
LEEKNIKEFLQSFVHIVQMFINTS

E64Q/Q108E (SEQ ID NO:277)
NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVQNLIILANNSLSSNGNVTESGCKECEE
LEEKNIKEFLQSFVHIVEMFINTS

N1D/N4D/D8N (SEQ ID NO:278)
DWVDVISNLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVENLIILANNSLSSNGNVTESGCKECEE
LEEKNIKEFLQSFVHIVQMFINTS

D61N/E64Q/N65D (SEQ ID NO:279)
NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHNTVQDLIILANNSLSSNGNVTESGCKECEE
LEEKNIKEFLQSFVHIVQMFINTS

N1D/D61N/E64Q/Q108E (SEQ ID NO:280)
DWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHNTVQNLIILANNSLSSNGNVTESGCKECEE
LEEKNIKEFLQSFVHIVEMFINTS

N4D/D61N/E64Q/Q108E (SEQ ID NO:281)
NWVDVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHNTVQNLIILANNSLSSNGNVTESGCKECEE
LEEKNIKEFLQSFVHIVEMFINTS

N1D/N65D (SEQ ID NO:282)
DWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVEDLIILANNSLSSNGNVTESGCKECEE
LEEKNIKEFLQSFVHIVQMFINTS

N1D/Q108E (SEQ ID NO:283)
DWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVENLIILANNSLSSNGNVTESGCKECEE
LEEKNIKEFLQSFVHIVEMFINTS

N4D/N65D (SEQ ID NO:284)
NWVDVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVEDLIILANNSLSSNGNVTESGCKECEE
LEEKNIKEFLQSFVHIVQMFINTS

D30N/N65D (SEQ ID NO:285)
NWVNVISDLKKIEDLIQSMHIDATLYTESNVHPSCKVTAMKCFLLELQVISLESGDASIHDTVEDLIILANNSLSSNGNVTESGCKECEE
LEEKNIKEFLQSFVHIVQMFINTS

D30N/Q108E (SEQ ID NO:286)
NWVNVISDLKKIEDLIQSMHIDATLYTESNVHPSCKVTAMKCFLLELQVISLESGDASIHDTVENLIILANNSLSSNGNVTESGCKECEE
LEEKNIKEFLQSFVHIVEMFINTS

N65D/Q108E (SEQ ID NO:287)
NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVEDLIILANNSLSSNGNVTESGCKECEE
LEEKNIKEFLQSFVHIVEMFINTS

Figure 44C

E64Q/N65D (SEQ ID NO:288)

NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVQDLIILANNSLSSNGNVTESGCKECEE
LEEKNIKEFLQSFVHIVQMFINTS

N1D/N4D/N65D (SEQ ID NO:289)

DWVDVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVEDLIILANNSLSSNGNVTESGCKECEE
LEEKNIKEFLQSFVHIVQMFINTS

D30N/E64Q/N65D (SEQ ID NO:290)

NWVNVISDLKKIEDLIQSMHIDATLYTESNVHPSCKVTAMKCFLLELQVISLESGDASIHDTVQDLIILANNSLSSNGNVTESGCKECEE
LEEKNIKEFLQSFVHIVQMFINTS

N4D/D61N/N65D (SEQ ID NO:291)

NWVDVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHNTVEDLIILANNSLSSNGNVTESGCKECEE
LEEKNIKEFLQSFVHIVQMFINTS

Figure 45A

>XENP022821 - human_IL15_N65D_(GGGGS)$_1$-human_IL15Rα(Sushi)_(GGGGS)$_1$_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

Chain 1 - human_IL15_N65D_(GGGGS)$_1$ (17692) SEQ ID NO:292
NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVEDLIIILANNSLS
SNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/GGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPP
KPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYK
CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTP
PVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 - human_IL15Rα(Sushi)_(GGGGS)$_1$_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q (15908)
SEQ ID NO:293
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGS/EPK
SSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREE
QYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLV
KGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS
PGK

>XENP022822 - human_IL15_Q108E_(GGGGS)$_1$-human_IL15Rα(Sushi)_(GGGGS)$_1$_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

Chain 1 - human_IL15_Q108E_(GGGGS)$_1$ (17693) SEQ ID NO:294
NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVENLIIILANNSLS
SNGNVTESGCKECEELEEKNIKEFLQSFVHIVEMFINTS/GGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPP
KPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYK
CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTP
PVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 - human_IL15Rα(Sushi)_(GGGGS)$_1$_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q (15908)
SEQ ID NO:295
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGS/EPK
SSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREE
QYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLV
KGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS
PGK

>XENP023554 - human_IL15_N1D/N65D_(GGGGS)1-human_IL15Ra(Sushi)_(GGGGS)1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

Chain 1 - human_IL15_N1D/N65D_(GGGGS)1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (18783) SEQ ID NO:296
DWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVEDLIIILANNSLS
SNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/GGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPP
KPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYK
CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTP
PVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 - human_IL15Ra(Sushi)_(GGGGS)1_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q (15908) SEQ ID NO:297
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGS/EPK
SSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREE
QYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLV
KGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS
PGK

Figure 45B

>XENP023557 - human_IL15_N4D/N65D_(GGGGS)1-human_IL15Ra(Sushi)_(GGGGS)1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

Chain 1 - human_IL15_N4D/N65D_(GGGGS)1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (18786) SEQ ID NO:298
NWVDVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVEDLIILANNSLS
SNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/GGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPP
KPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYK
CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTP
PVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 - human_IL15Ra(Sushi)_(GGGGS)1_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q (15908) SEQ ID NO:299
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGS/EPK
SSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREE
QYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLV
KGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS
PGK

>XENP023561 human_IL15_N65D/Q108E_(GGGGS)1-human_IL15Ra(Sushi)_(GGGGS)1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

Chain 1 - human_IL15_N65D/Q108E_(GGGGS)1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S SEQ ID NO:300
NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVEDLIILANNSLS
SNGNVTESGCKECEELEEKNIKEFLQSFVHIVEMFINTS/GGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPP
KPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYK
CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTP
PVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 - human_IL15Ra(Sushi)_(GGGGS)1_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q SEQ ID NO:301
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGS/EPKSSDKTHTCP
PCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVV
SVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIA
VEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP024018 human_IL15(N65D)-human_IL15Ra(Sushi)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

Chain 1 - human_IL15(N65D)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S SEQ ID NO:302
NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVEDLIILANNSLS
SNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTL
MISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK
ALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSD
GSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 - human_IL15Ra(Sushi)_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q SEQ ID NO:303
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/EPKSSDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Figure 45C

>XENP024019 - human_IL15(Q108E)-human_IL15Ra(Sushi)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

Chain 1 - human_IL15(Q108E)-human_IL15Ra(Sushi)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (19242) SEQ ID NO:304

NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVENLIILANNSLS
SNGNVTESGCKECEELEEKNIKEFLQSFVHIVEMFINTS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTL
MISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK
ALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSD
GSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 - human_IL15Ra(Sushi)_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q (16481) SEQ ID NO:305

ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/EPKSSDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP024045 human_IL15_D30N/E64Q/N65D_(GGGGS)1-human_IL15Rα(Sushi)_(GGGGS)1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

Chain 1 – human_IL15_D30N/E64Q/N65D_(GGGGS)1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S SEQ ID NO:306

NWVNVISDLKKIEDLIQSMHIDATLYTESNVHPSCKVTAMKCFLLELQVISLESGDASIHDTVQDLIILANNSLS
SNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/GGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPP
KPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYK
CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTP
PVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 – human_IL15Rα(Sushi)_(GGGGS)1_ Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q SEQ ID NO:307

ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGS/EPK
SSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREE
QYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLV
KGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS
PGK

>XENP024051 human_IL15_N1D/N65D-human_IL15Rα(Sushi)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

Chain 1 – human_IL15_N1D/N65D-human_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S SEQ ID NO:308

DWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVEDLIILANNSLS
SNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTL
MISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK
ALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSD
GSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 – human_IL15Rα(Sushi)_ Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q SEQ ID NO:309

ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/EPKSSDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Figure 45D

>XENP024052 human_IL15_N4D/N65D-human_IL15Rα(Sushi)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

Chain 1 – human_IL15_N4D/N65D-human_ Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S SEQ ID NO:310
NWVDVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVEDLIILANNSLS
SNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTL
MISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK
ALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSD
GSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 – human_IL15Rα(Sushi)_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q SEQ ID NO:311
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/EPKSSDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Figure 46A

>XENP024015 human_IL15Ra(sushi)_(GGGGS)5-human_IL15(Q108E;single-chain)-empty-Fc_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

Chain 1 - human_IL15Ra(sushi)_(GGGGS)5-human_IL15(Q108E;single-chain) _Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S SEQ ID NO:312
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGG
SGGGGSGGGGSGGGGS/NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDAS
IHDTVENLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVEMFINTS/EPKSSDKTHTCPPCPAPP
VAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESD
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 – empty_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q SEQ ID NO:313
EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKP
REEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSL
SLSPGK

>XENP024050 human_IL15Ra(sushi)_(GGGGS)5-human_IL15_N4D/N65D_(single-chain)-empty-Fc_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

Chain 1 - human_IL15Ra(sushi)_(GGGGS)5-human_IL15_N4D/N65D_(single-chain)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S SEQ ID NO:314
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGG
SGGGGSGGGGSGGGGS/NWVDVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDAS
IHDTVEDLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPP
VAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESD
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 – empty_ Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q SEQ ID NO:315
EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKP
REEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSL
SLSPGK

>XENP024475 human_IL15Ra(sushi)_(GGGGS)6-human_IL15(single-chain;Q108E)-empty-Fc_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

Chain 1 - human_IL15Ra(sushi)_(GGGGS)6-human_IL15(single-chain;Q108E)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S SEQ ID NO:316
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGG
SGGGGSGGGGSGGGGSGGGGS/NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLE
SGDASIHDTVENLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVEMFINTS/EPKSSDKTHTCPP
CPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVS
VLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAV
EWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 – empty_ Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q SEQ ID NO:317
EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKP
REEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSL
SLSPGK

Figure 46B

>XENP024476 human_IL15Ra(sushi)_(GGGGS)6-human_IL15(single-chain;N4D/N65D)-empty-Fc_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

Chain 1 - human_IL15Ra(sushi)_(GGGGS)6-human_IL15(single-chain;N4D/N65D)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S SEQ ID NO:318
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGG
SGGGGSGGGGSGGGGSGGGGS/NWVDVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLE
SGDASIHDTVEDLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPP
CPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVS
VLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAV
EWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 – empty_ Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q SEQ ID NO:319
EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKP
REEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSL
SLSPGK

>XENP024478 human_IL15Ra(sushi)_(GGGGS)7-human_IL15(single-chain;Q108E)-empty-Fc_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

Chain 1 - human_IL15Ra(sushi)_(GGGGS)7-human_IL15(single-chain;Q108E)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S SEQ ID NO:320
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGG
SGGGGSGGGGSGGGGSGGGGSGGGGS/NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQ
VISLESGDASIHDTVENLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVEMFINTS/EPKSSDKT
HTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNST
YRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYP
SDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 – empty_ Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q SEQ ID NO:321
EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKP
REEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSL
SLSPGK

>XENP024479 human_IL15Ra(sushi)_(GGGGS)7-human_IL15(single-chain;N4D/N65D)-empty-Fc_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

Chain 1 - human_IL15Ra(sushi)_(GGGGS)7-human_IL15(single-chain;N4D/N65D)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S SEQ ID NO:322
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGG
SGGGGSGGGGSGGGGSGGGGSGGGGS/NWVDVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQ
VISLESGDASIHDTVEDLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKT
HTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNST
YRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYP
SDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 - empty-Fc_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q SEQ ID NO:323
EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKP
REEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSL
SLSPGK

Figure 46C

>XENP024481 human_IL15Ra(sushi)_(30AA_linker_variant)-human_IL15(single-chain;Q108E)-empty-Fc_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

Chain 1 - human_IL15Ra(sushi)_(30AA_linker_variant)-human_IL15(single-chain;Q108E)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S SEQ ID NO:324
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/DPALVHQRP
APPGGGGSGGGGSGGGGSGGG/NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLE
SGDASIHDTVENLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVEMFINTS/EPKSSDKTHTCPP
CPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVS
VLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAV
EWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 – empty_ Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q SEQ ID NO:325
EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKP
REEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSL
SLSPGK

Figure 47A

>XENP024349 IL15_Q108E_(non-covalent)-human_IL15Rα(Sushi)_empty-Fc_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

Chain 1 – human_IL15Rα(Sushi)_ Isosteric_A_C220S/PVA_/S267K/L368D/K370S SEQ ID NO:326
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/EPKSSDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPS
DIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 – empty- Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q SEQ ID NO:327
EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKP
REEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSL
SLSPGK

Chain 3 – IL15_Q108E_(non-covalent) SEQ ID NO:328
NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVENLIILANNSLS
SNGNVTESGCKECEELEEKNIKEFLQSFVHIVEMFINTS

>XENP024890 IL15_N4D/N65D_(non-covalent)-human_IL15Ra(Sushi)-empty-Fc_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-IgG1_PVA_/S267K/S364K/E357Q

Chain 1 – IL-15_N4D/N65D SEQ ID NO:329
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/EPKSSDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPS
DIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 - human_IL15Ra(Sushi)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S SEQ ID NO:330
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/EPKSSDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPS
DIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 3 – empty_Fc(216)_ IgG1_PVA_/S267K/S364K/E357Q SEQ ID NO:331
EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKP
REEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSL
SLSPGK

Figure 47B

>XENP25138 IL15_D30N/E64Q/N65D_(non-covalent)-empty-Fc_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-IgG1_PVA_/S267K/S364K/E357Q

Chain 1 - IL15_D30N/E64Q/N65D SEQ ID NO:332
NWVNVISDLKKIEDLIQSMHIDATLYTESNVHPSCKVTAMKCFLLELQVISLESGDASIHDTVQDLIILANNSLS
SNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS

Chain 2 - human_IL15Ra(Sushi)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S SEQ ID NO:333
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/EPKSSDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPS
DIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 3 - empty_Fc(216)_ IgG1_PVA_/S267K/S364K/E357Q SEQ ID NO:334
EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKP
REEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSL
SLSPGK

Figure 48

>XENP022801 - human_IL15_N65D(non-covalent)-human_IL15Rα(Sushi)

Chain 1 - human_IL15_N65D(non-covalent) (17672) SEQ ID NO:335
NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVEDLIILANNSLS
SNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS

Chain 2 - human_IL15Rα(Sushi) (17033) SEQ ID NO:336
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR

>XENP022802 - human_IL15_Q108E(non-covalent)-human_IL15Rα(Sushi)

Chain 1 - human_IL15_Q108E(non-covalent) (17673) SEQ ID NO:337
NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVENLIILANNSLS
SNGNVTESGCKECEELEEKNIKEFLQSFVHIVEMFINTS

Chain 2 - human_IL15Rα(Sushi) (17033) SEQ ID NO:338
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR

Figure 49

>XENP024342 human_IL15(non-covalent; Q108E)-human_IL15Rα(Sushi)_Fc(216)_IgG1_C220S/PVA_/S267K

Chain 1 – human_IL15Rα(Sushi) _Fc(216)_IgG1_C220S/PVA_/S267K SEQ ID NO:339
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/EPKSSDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 –human_IL15(non-covalent; Q108E) SEQ ID NO:340
NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVENLIILANNSLS
SNGNVTESGCKECEELEEKNIKEFLQSFVHIVEMFINTS

Figure 50

>XENP023472 empty-Fc-IL15_N65D/E87C-human_IL15Ra(Sushi-D96/C97)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

Chain 1 – empty_ Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S SEQ ID NO:341
EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKP
REEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLT
CDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSL
SLSPGK

Chain 2 - IL15_N65D/E87C SEQ ID NO:342
NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVEDLIILANNSLS
SNGNVTESGCKCCEELEEKNIKEFLQSFVHIVQMFINTS

Chain 3 - IL15Ra(Sushi-D96/C97)_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q SEQ ID NO:343
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIRDC/EPKSSDK
THTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNS
TYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFY
PSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP023473 empty-Fc-IL15_N65D/L52C-human_IL15Ra(Sushi-S40C)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

Chain 1 – empty_ Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S SEQ ID NO:344
EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKP
REEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLT
CDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSL
SLSPGK

Chain 2 - IL15_N65D/L52C SEQ ID NO:345
NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISCESGDASIHDTVEDLIILANNSLS
SNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS

Chain 3 - IL15Ra(Sushi-S40C)_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q SEQ ID NO:346
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTCSLTECVLNKATNVAHWTTPSLKCIR/EPKSSDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Figure 51A

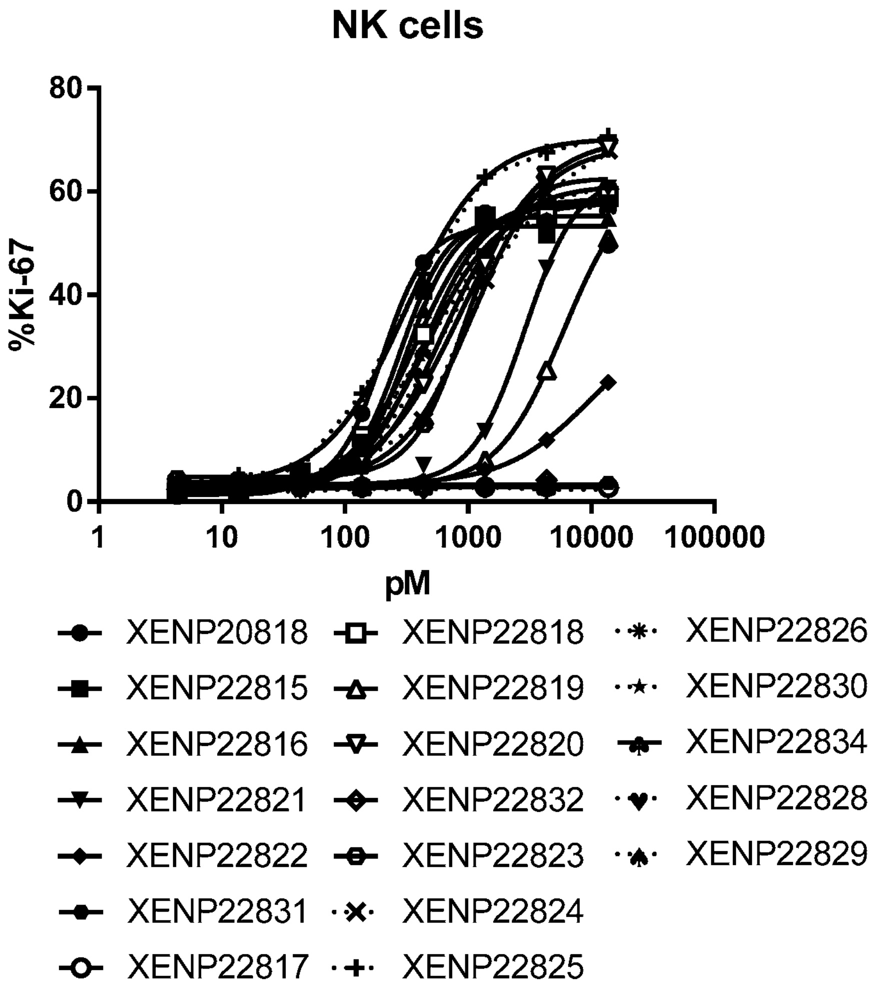

NK cells
%Ki-67
80
60
40
20
0
1
10
100
1000
10000
100000
pM
XENP20818
XENP22815
XENP22816
XENP22821
XENP22822
XENP22831
XENP22817
XENP22818
XENP22819
XENP22820
XENP22832
XENP22823
XENP22824
XENP22825
XENP22826
XENP22830
XENP22834
XENP22828
XENP22829

Figure 51B

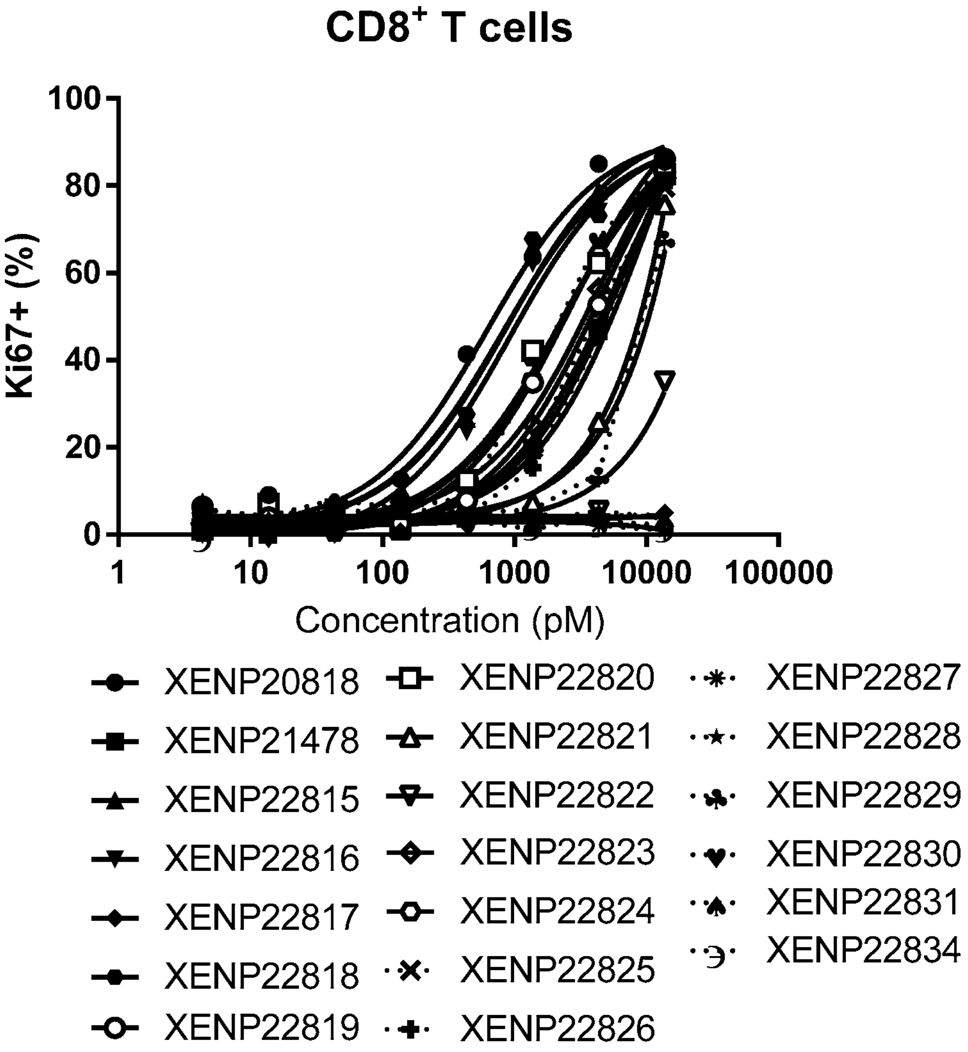

CD8$^+$ T cells
Ki67+ (%)
100
80
60
40
20
0
1
10
100
1000
10000
100000
Concentration (pM)
XENP20818
XENP21478
XENP22815
XENP22816
XENP22817
XENP22818
XENP22819
XENP22820
XENP22821
XENP22822
XENP22823
XENP22824
XENP22825
XENP22826
XENP22827
XENP22828
XENP22829
XENP22830
XENP22831
XENP22834

Figure 51C

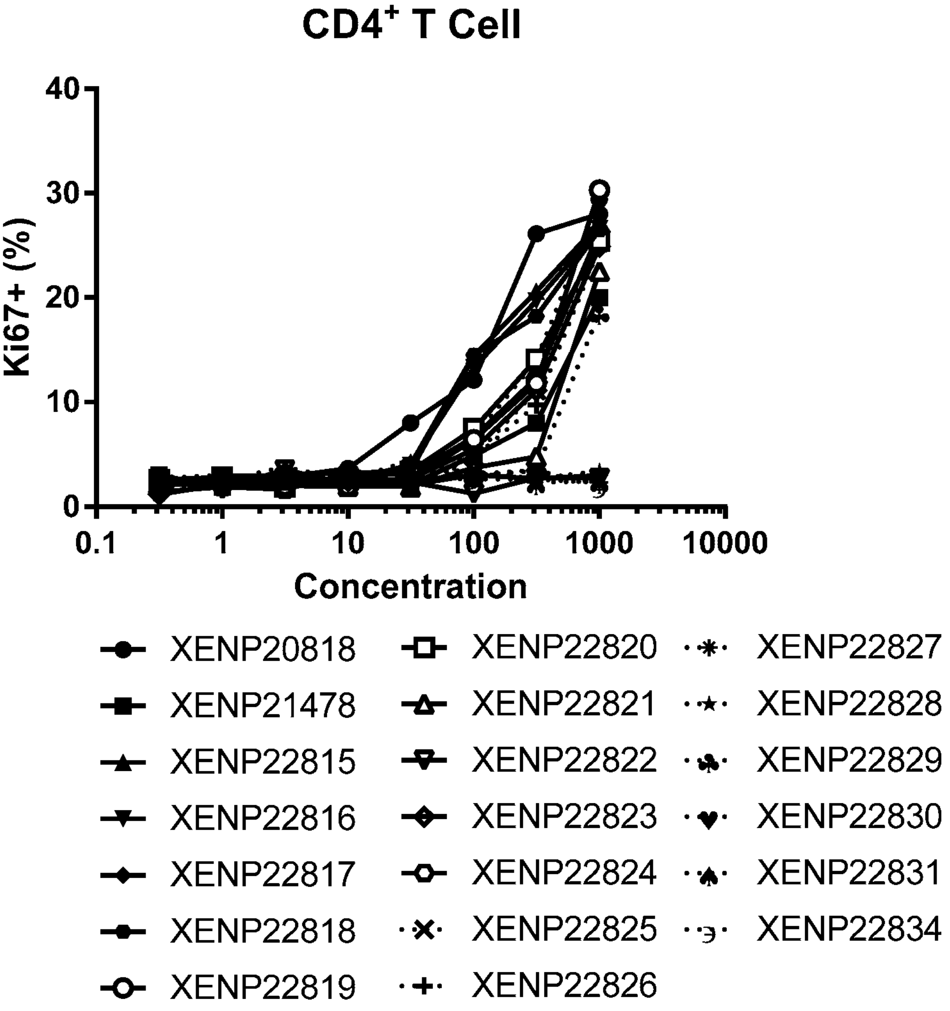

CD4⁺ T Cell
Ki67+ (%)
40
30
20
10
0
0.1
1
10
100
1000
10000
Concentration
XENP20818
XENP21478
XENP22815
XENP22816
XENP22817
XENP22818
XENP22819
XENP22820
XENP22821
XENP22822
XENP22823
XENP22824
XENP22825
XENP22826
XENP22827
XENP22828
XENP22829
XENP22830
XENP22831
XENP22834

Figure 52

XENP	Variant	EC50 pM (NK cells)	Fold reduced (NK cells)	EC50 pM (CD8 T cells)	Fold reduced (CD8 T cells)
20818	WT	200.6		637.1	
21478	single-chain	848.5	4.2	4982.0	7.8
22815	N1D	281.3	1.4	1051.0	1.6
22816	N4D	321.9	1.6	1190.0	1.9
22817	D8N	very weak	very weak	very weak	very weak
22818	D30N	376.3	1.9	1366.0	2.1
22819	D61N	5934.0	29.6	161937.0	>100
22820	E64Q	877.0	4.4	2858.0	4.5
22821	N65D	2883.0	14.4	6928.0	10.9
22822	Q108E	9777.0	48.7	very weak	>100
22823	N1D/D61N	918.0	4.6	4225.0	6.6
22824	N1D/E64Q	1091.0	5.4	4228.0	6.6
22825	N4D/D61N	309.0	1.5	1070.0	1.7
22826	N4D/E64Q	very weak	very weak	very weak	very weak
22827	D8N/D61N	ND	ND	ND	ND
22828	D8N/E64Q	597.7	3.0	1658.0	2.6
22829	D61N/E64Q	458.2	2.3	2115.0	3.3
22830	E64Q/Q108E	436.6	2.2	1815.0	2.8
22831	N1D/N4D/D8N	very weak	very weak	very weak	very weak
22832	D61N/E64Q/N65D	ND	ND	ND	ND
22833	N1D/D61N/E64Q/Q108E	ND	ND	ND	ND
22834	N4D/D61N/E64Q/Q108E	very weak	very weak	very weak	very weak

Figure 53A

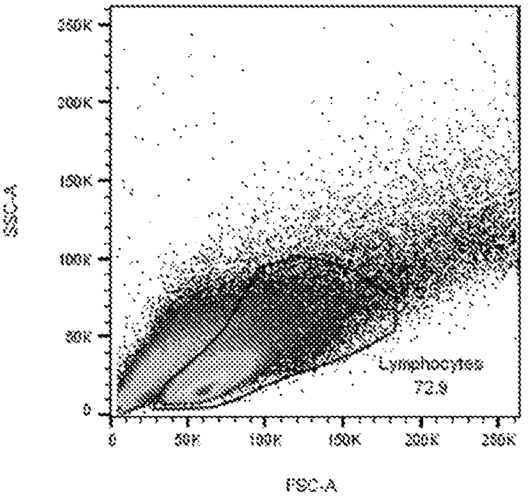


Figure 53B

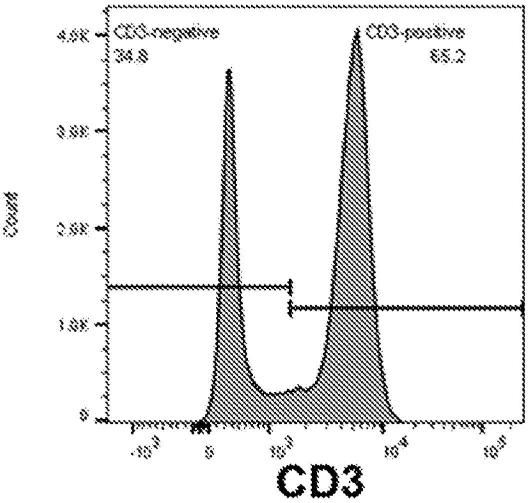


Figure 53C

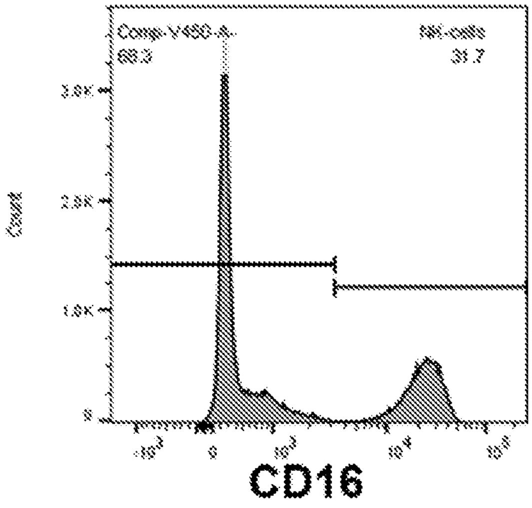


Figure 54A

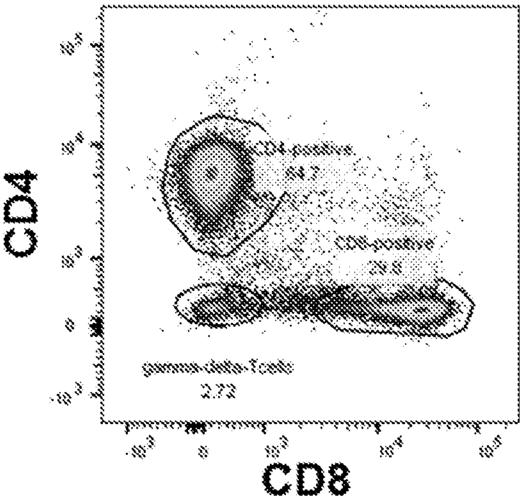


Figure 54B

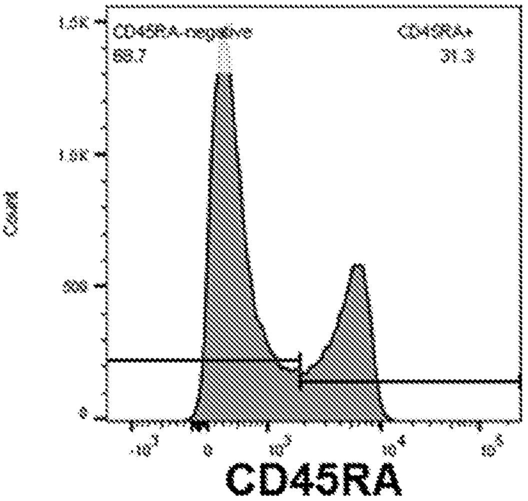


Figure 54C

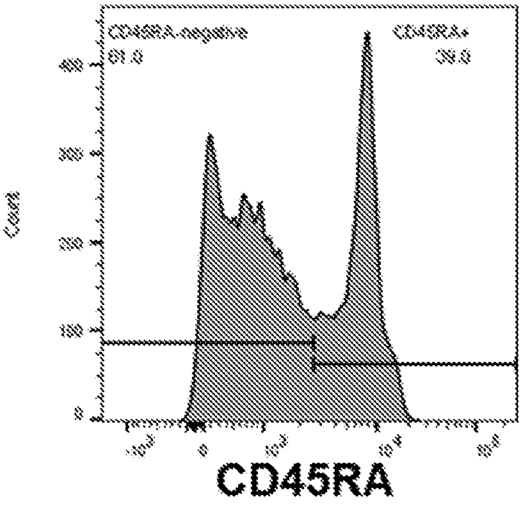


Figure 55A

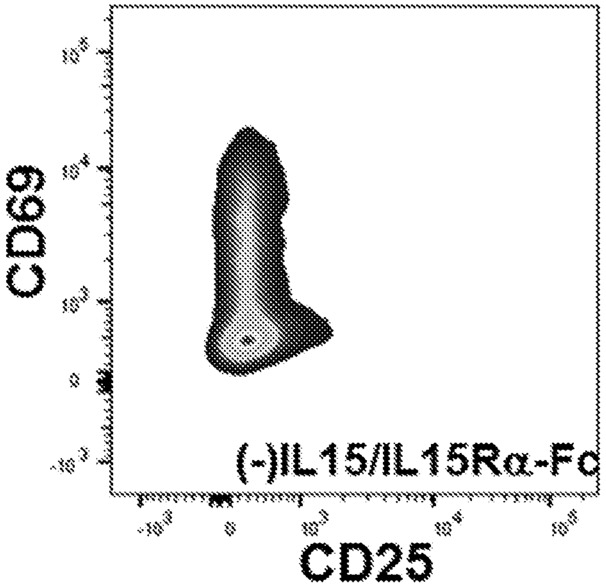


Figure 55B

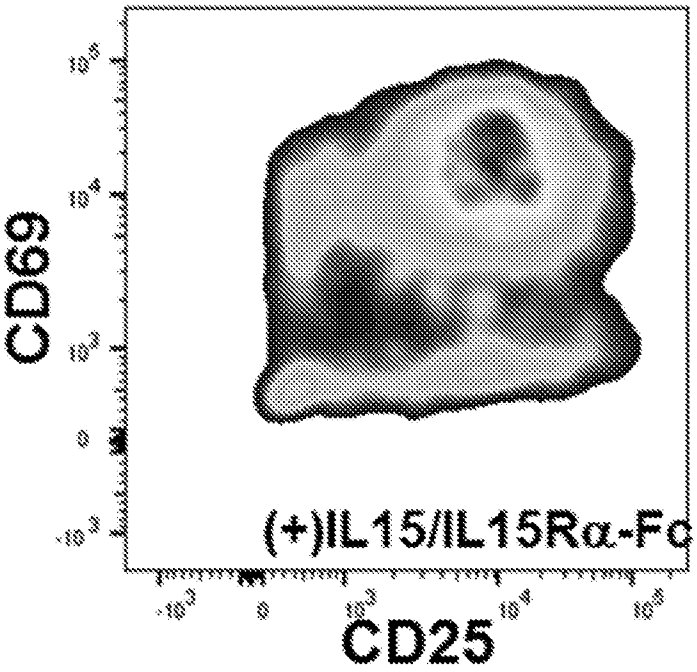


Figure 56A

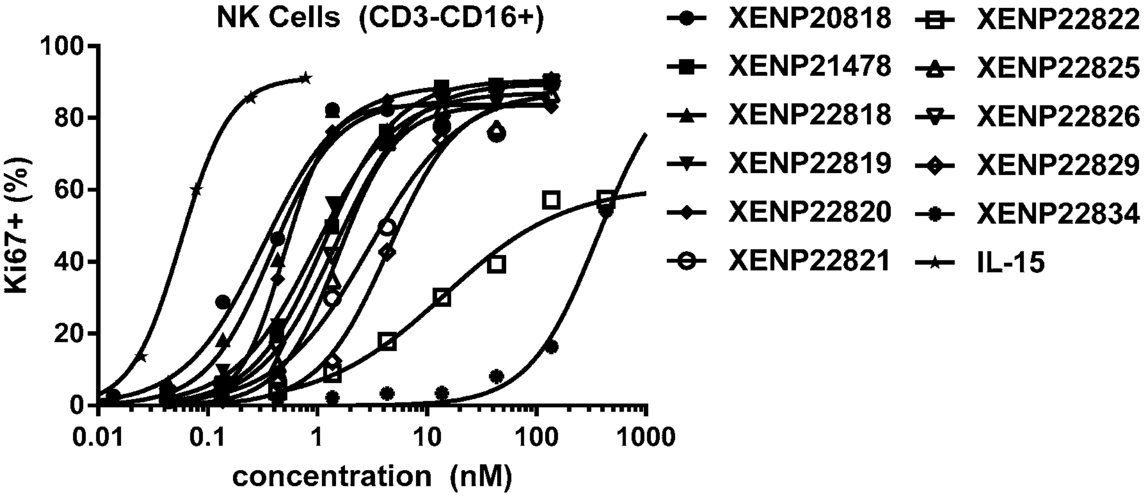


Figure 56B

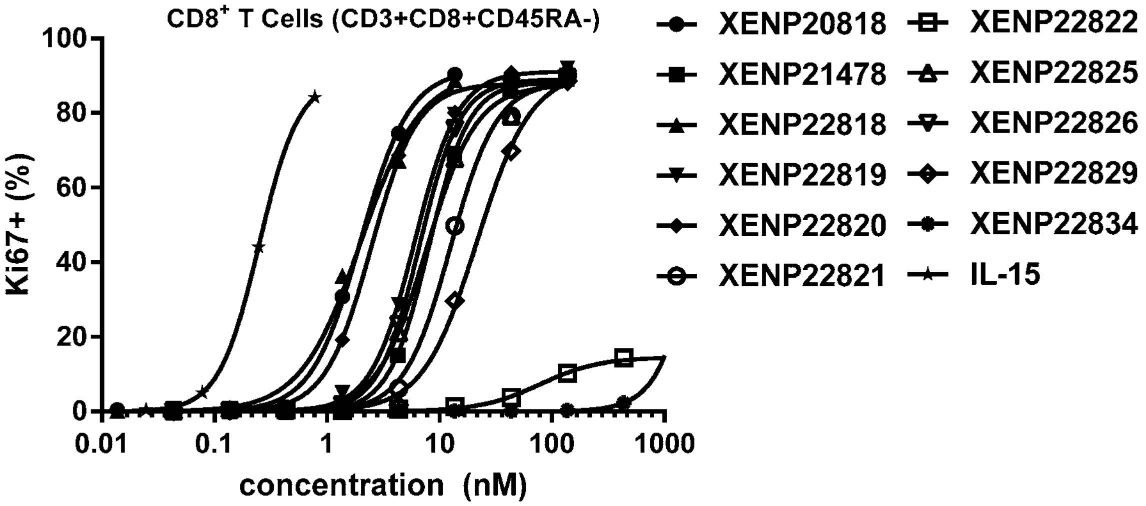


Figure 56C

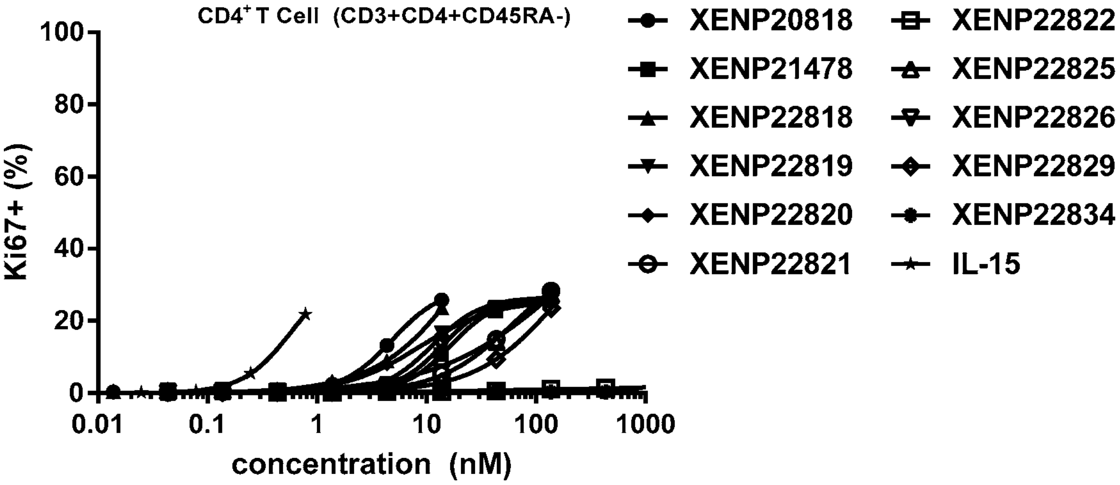

CD4+ T Cell (CD3+CD4+CD45RA-)
Ki67+ (%)
100
80
60
40
20
0
0.01
0.1
1
10
100
1000
concentration (nM)
XENP20818
XENP21478
XENP22818
XENP22819
XENP22820
XENP22821
XENP22822
XENP22825
XENP22826
XENP22829
XENP22834
IL-15

Figure 56D

XENP	EC50 nM (NK cells)	Fold reduced (NK cells)	EC50 nM (CD8 T cells)	Fold reduced (CD8 T cells)	EC50 nM (CD4 T cells)	Fold reduced (CD4 T cells)
20818	0.3223	1.0	2.701	1.0	16.467	1.0
21478	1.116	3.5	11.728	4.3	28.349	1.7
22818	0.4205	1.3	2.829	1.0	40.676	2.5
22819	1.016	3.2	8.254	3.1	18.101	1.1
22820	0.562	1.7	3.918	1.5	10.362	0.6
22821	3.14	9.7	18.706	6.9	112.823	6.9
22822	68.866	213.7	6439.69	2384.2	48.738	3.0
22825	1.769	5.5	12.09	4.5	60.081	3.6
22826	1.448	4.5	9.678	3.6	22.41	1.4
22829	4.839	15.0	29.638	11.0	337.571	20.5
22834	331.293	1027.9	4107.897	1520.9	ND	ND
IL-15	0.05322	0.2	0.3452	0.1	ND	ND

Figure 57A

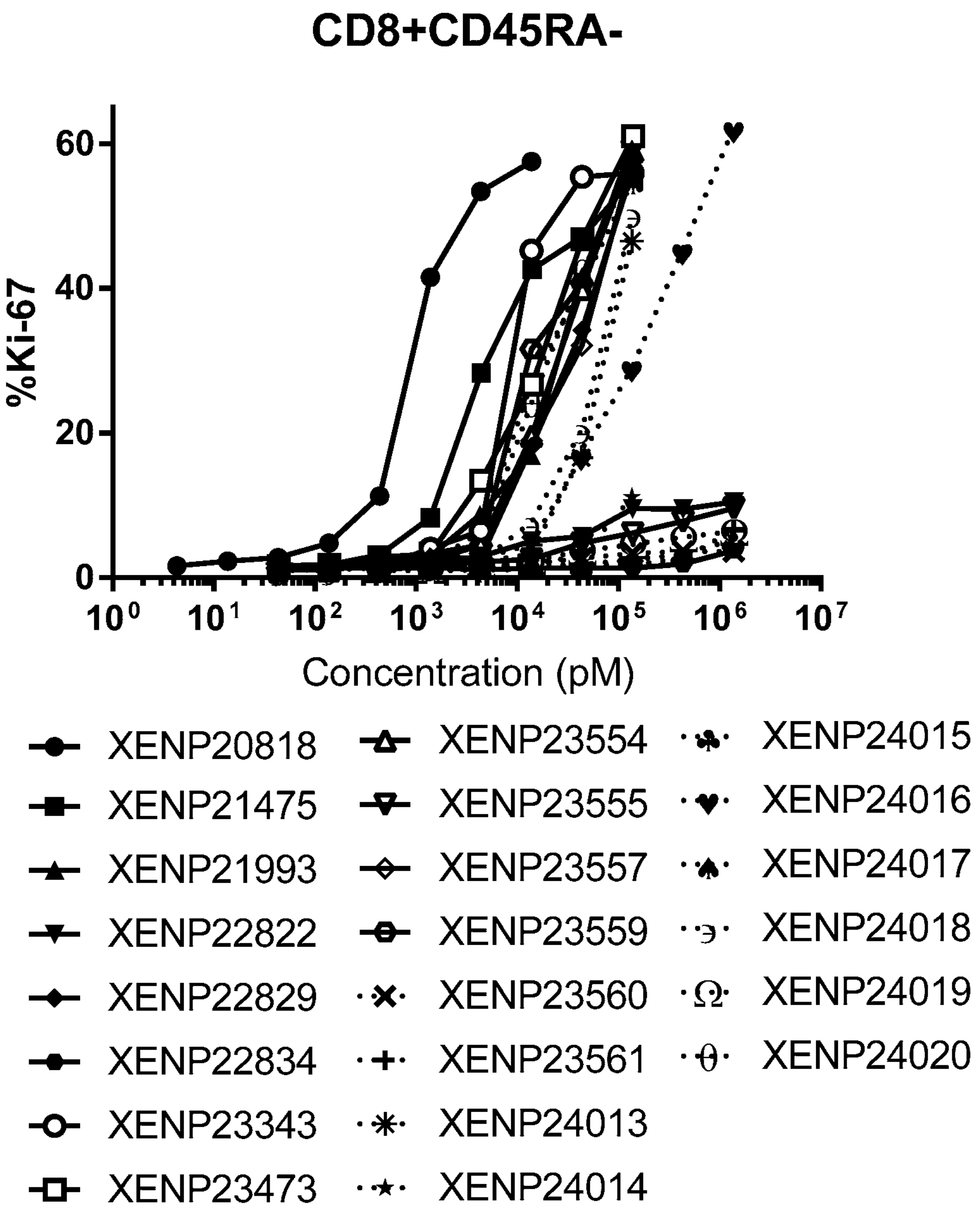

CD8+CD45RA-
%Ki-67
60
40
20
0
10⁰
10¹
10²
10³
10⁴
10⁵
10⁶
10⁷
Concentration (pM)
XENP20818
XENP21475
XENP21993
XENP22822
XENP22829
XENP22834
XENP23343
XENP23473
XENP23554
XENP23555
XENP23557
XENP23559
XENP23560
XENP23561
XENP24013
XENP24014
XENP24015
XENP24016
XENP24017
XENP24018
XENP24019
XENP24020

Figure 57B

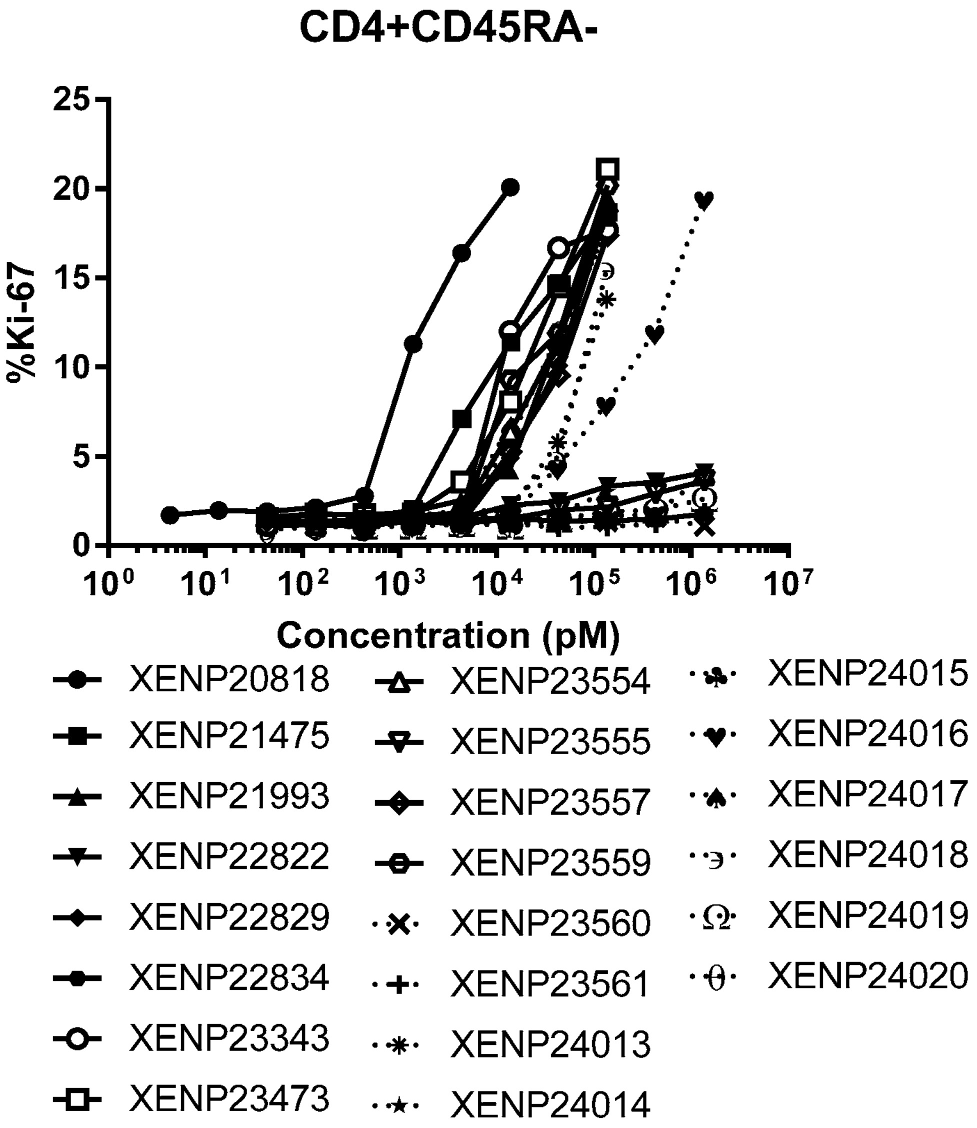

CD4+CD45RA-
%Ki-67
0
5
10
15
20
25
10^0
10^1
10^2
10^3
10^4
10^5
10^6
10^7
Concentration (pM)
XENP20818
XENP21475
XENP21993
XENP22822
XENP22829
XENP22834
XENP23343
XENP23473
XENP23554
XENP23555
XENP23557
XENP23559
XENP23560
XENP23561
XENP24013
XENP24014
XENP24015
XENP24016
XENP24017
XENP24018
XENP24019
XENP24020

Figure 57C

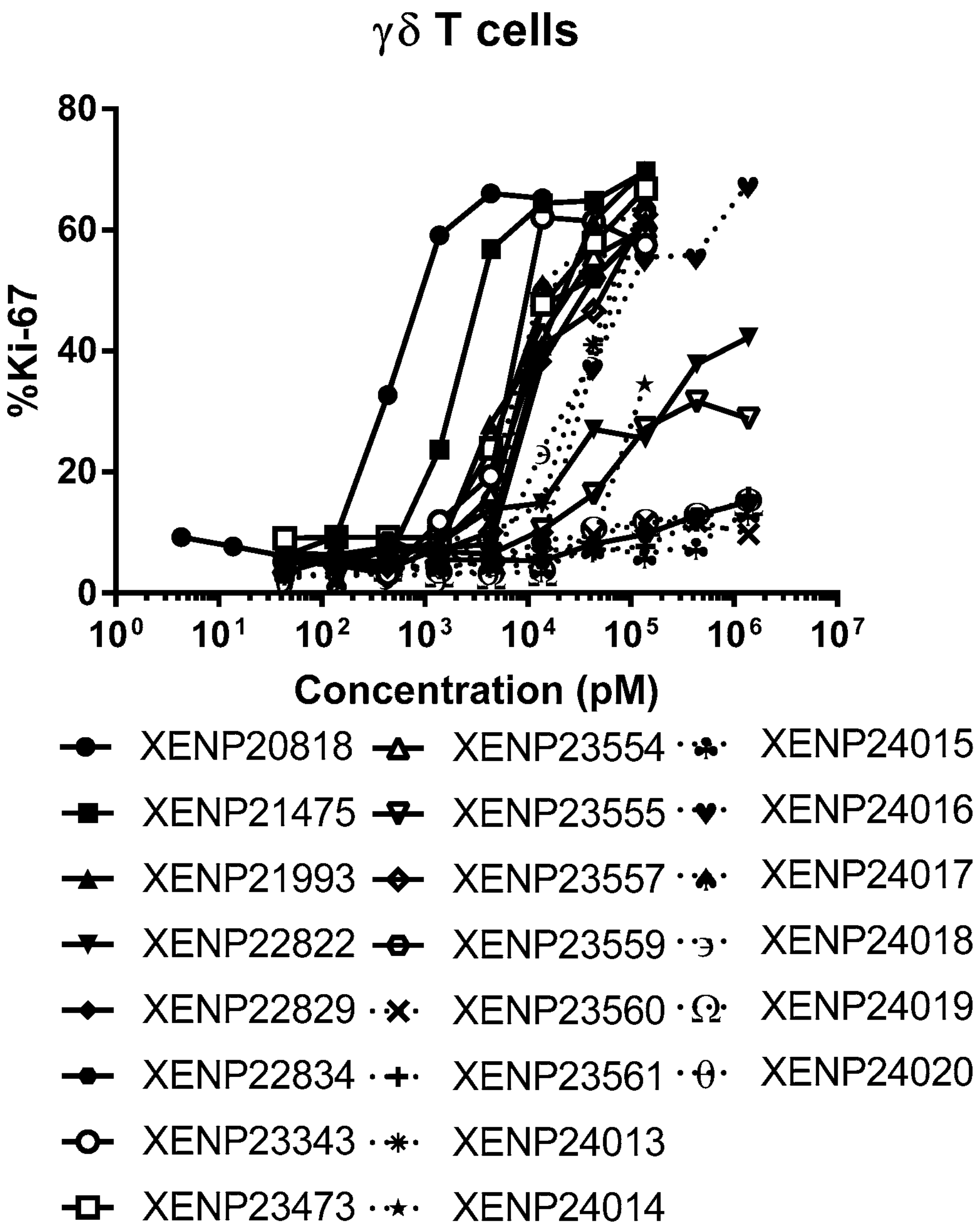

γδ T cells
%Ki-67
0
20
40
60
80
10^0
10^1
10^2
10^3
10^4
10^5
10^6
10^7
Concentration (pM)
XENP20818
XENP21475
XENP21993
XENP22822
XENP22829
XENP22834
XENP23343
XENP23473
XENP23554
XENP23555
XENP23557
XENP23559
XENP23560
XENP23561
XENP24013
XENP24014
XENP24015
XENP24016
XENP24017
XENP24018
XENP24019
XENP24020

Figure 57D

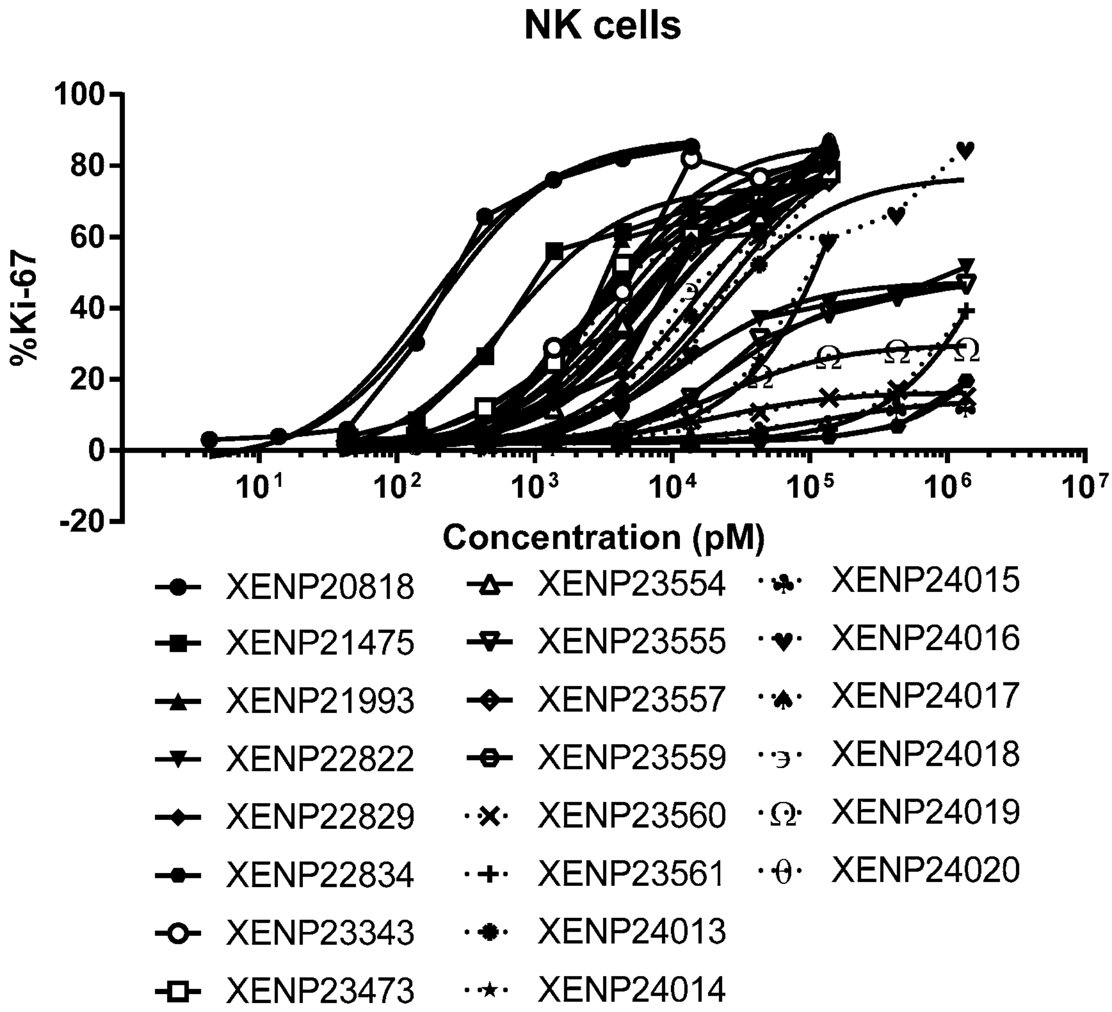

NK cells
%Ki-67
100
80
60
40
20
0
-20
10^1
10^2
10^3
10^4
10^5
10^6
10^7
Concentration (pM)
XENP20818
XENP21475
XENP21993
XENP22822
XENP22829
XENP22834
XENP23343
XENP23473
XENP23554
XENP23555
XENP23557
XENP23559
XENP23560
XENP23561
XENP24013
XENP24014
XENP24015
XENP24016
XENP24017
XENP24018
XENP24019
XENP24020

Figure 58A

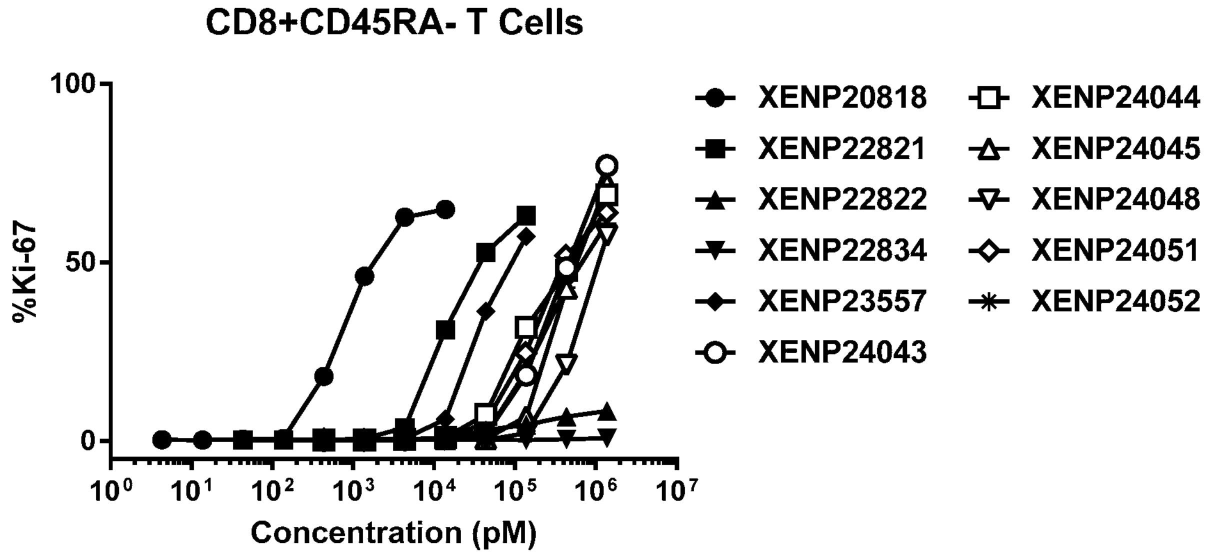


Figure 58B

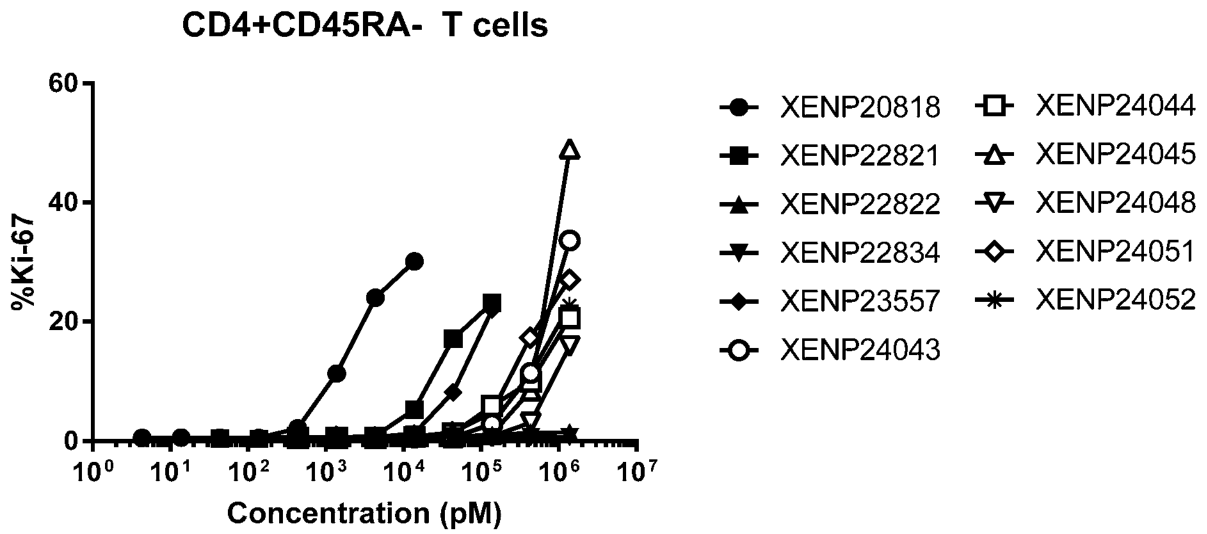


Figure 58C

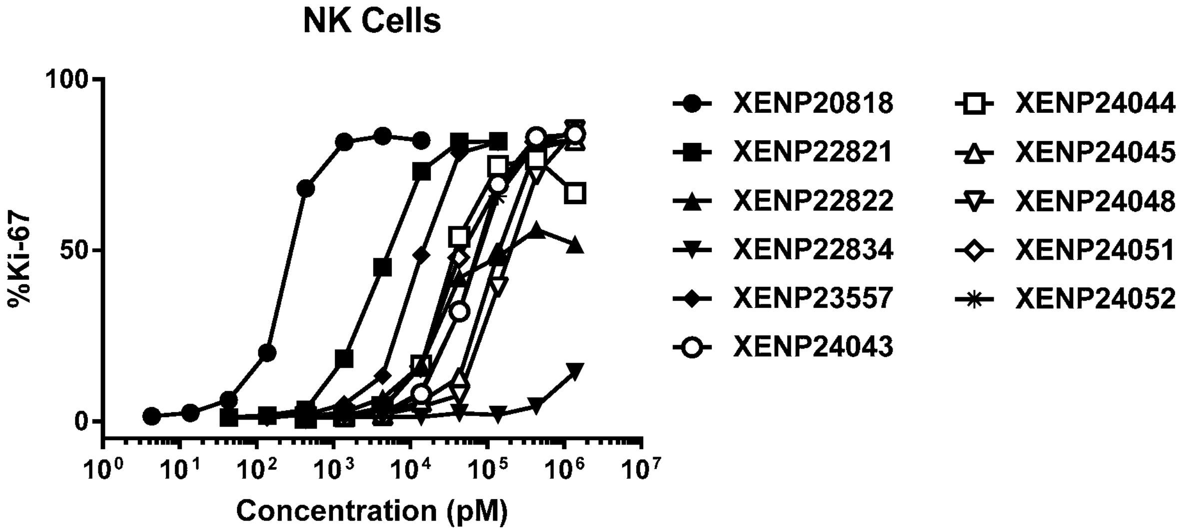

NK Cells
%Ki-67
100
50
0
10^0
10^1
10^2
10^3
10^4
10^5
10^6
10^7
Concentration (pM)
XENP20818
XENP22821
XENP22822
XENP22834
XENP23557
XENP24043
XENP24044
XENP24045
XENP24048
XENP24051
XENP24052

Figure 59A

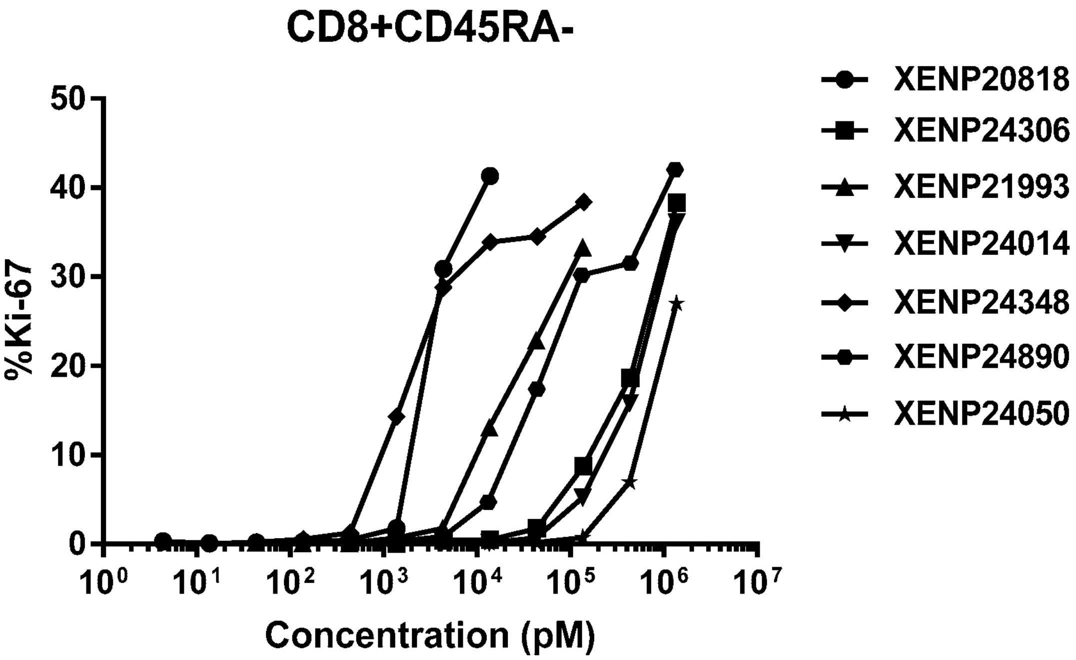


Figure 59B

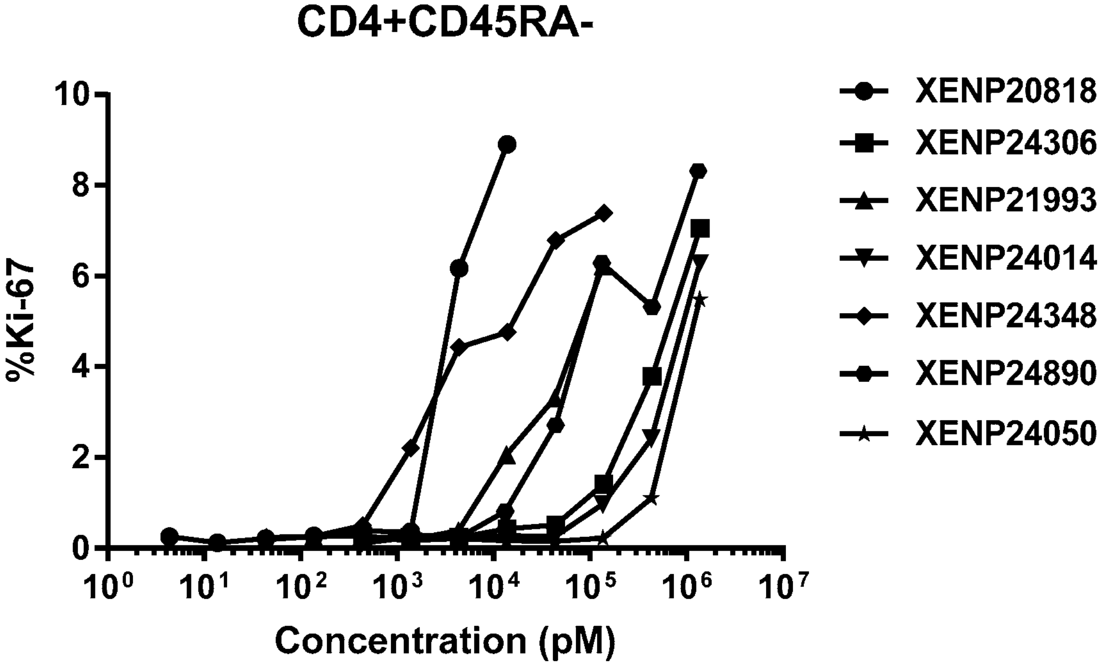


Figure 59C

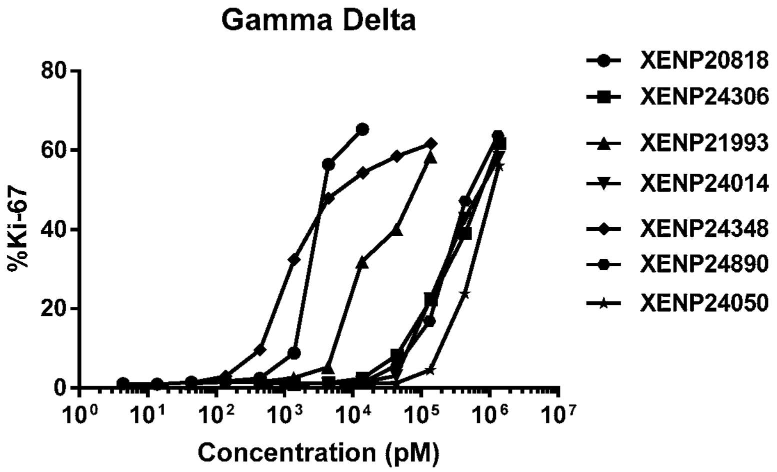


Figure 59D

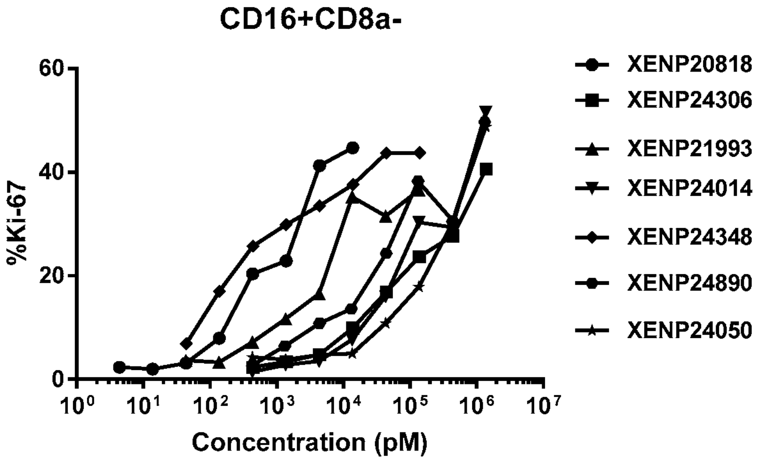


Figure 59E

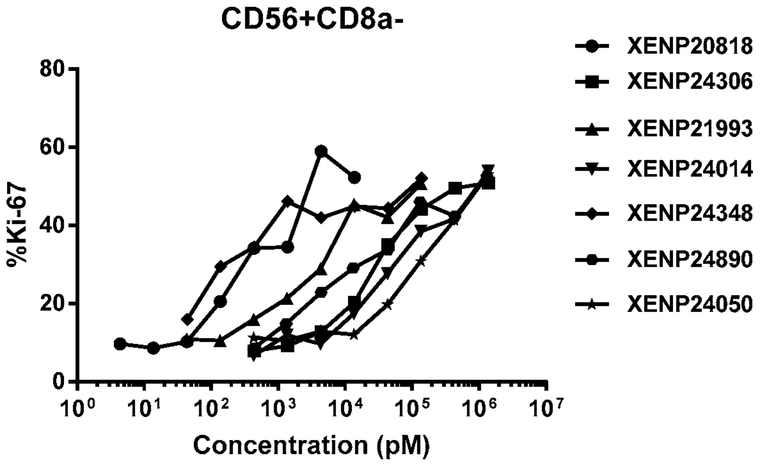


Figure 60A

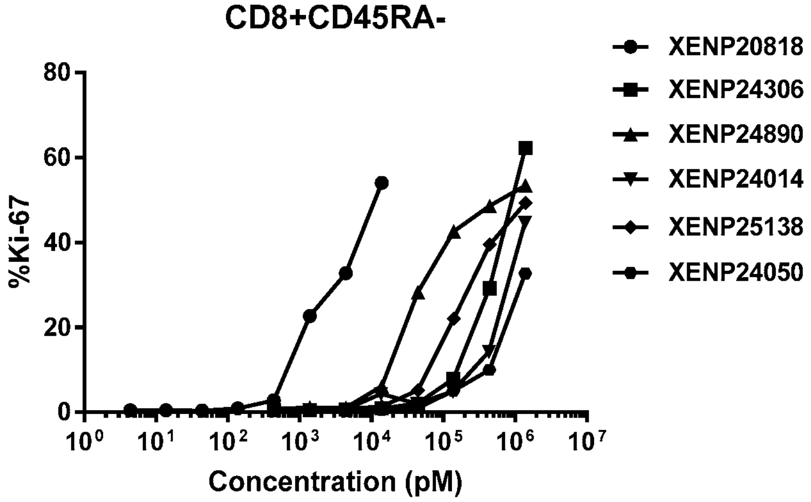


Figure 60B

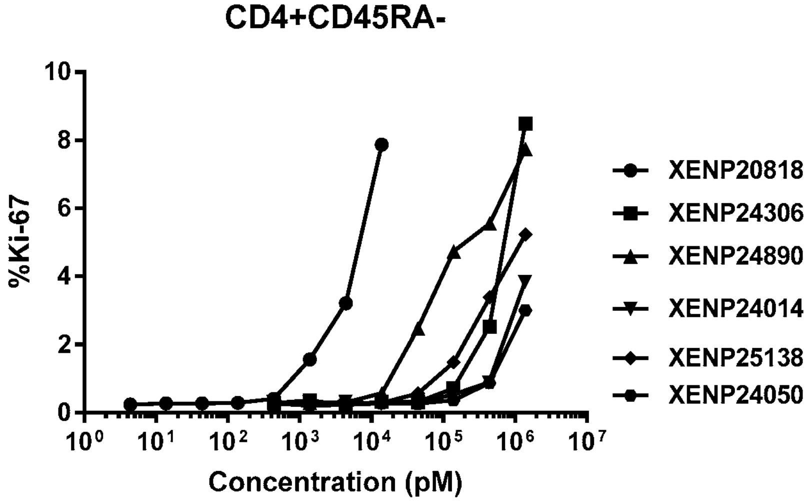


Figure 60C

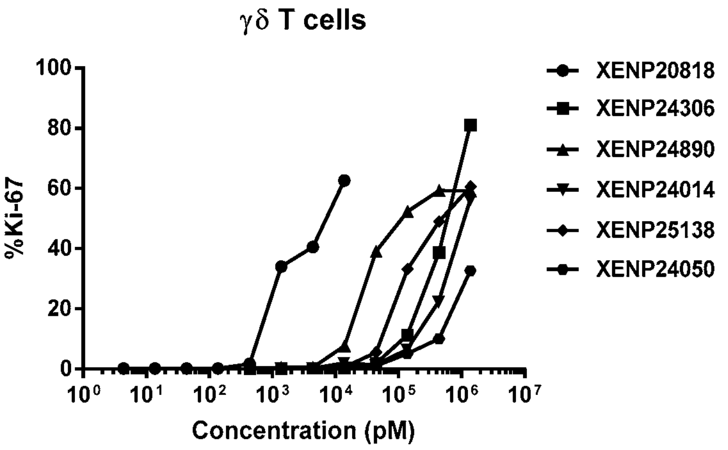


Figure 60D

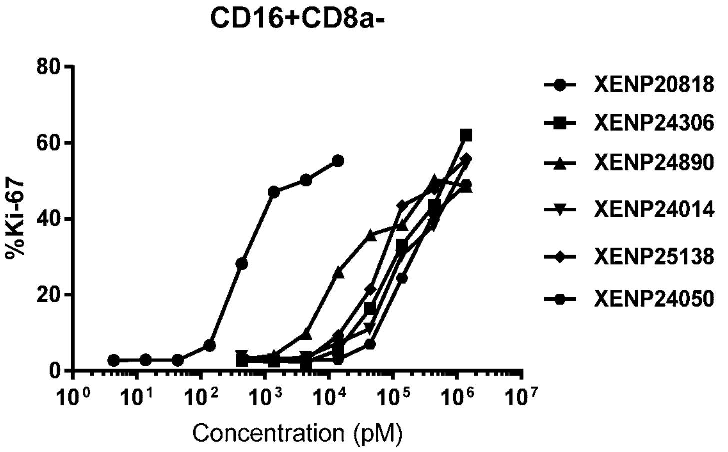


Figure 60E

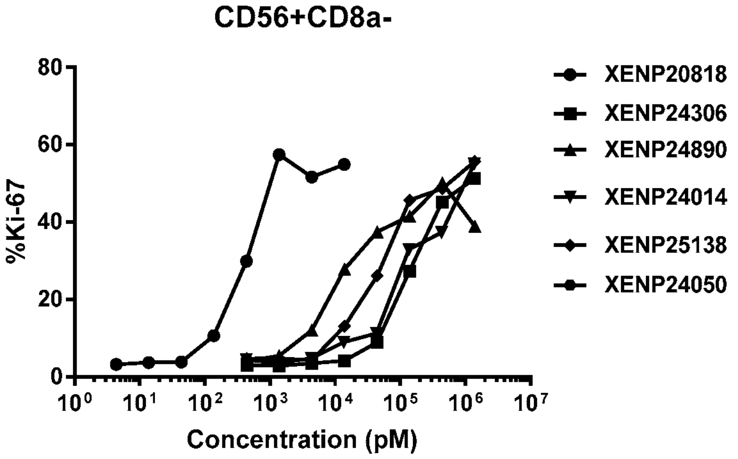


Figure 61A

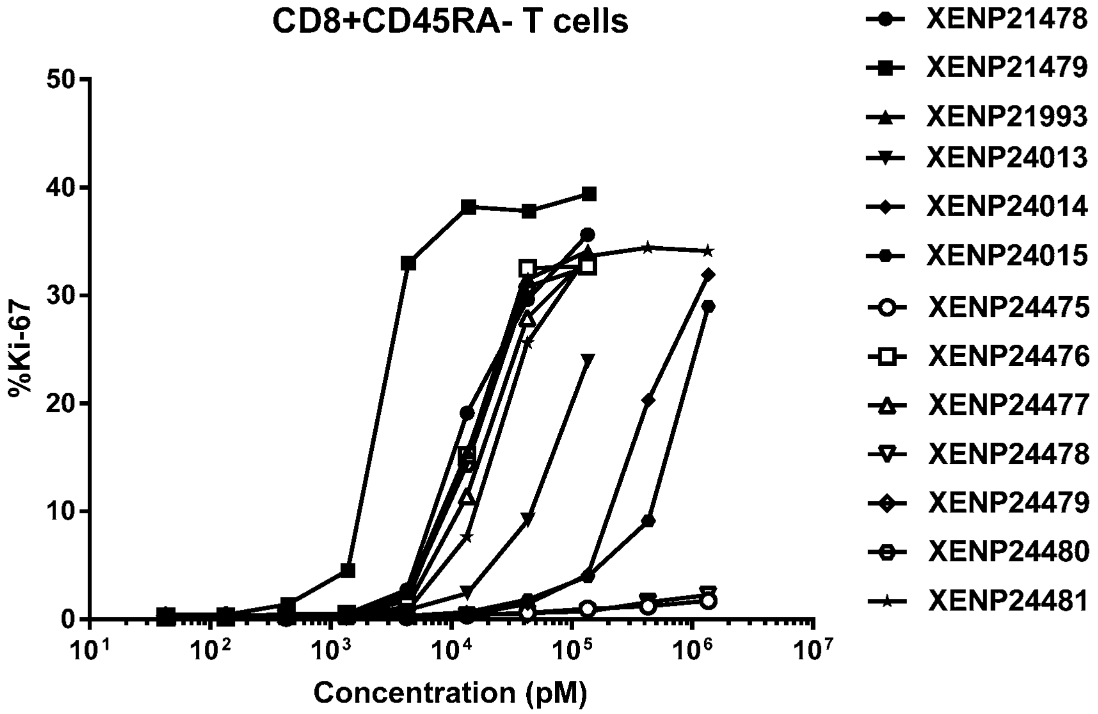

CD8+CD45RA- T cells
%Ki-67
50
40
30
20
10
0
10¹
10²
10³
10⁴
10⁵
10⁶
10⁷
Concentration (pM)
XENP21478
XENP21479
XENP21993
XENP24013
XENP24014
XENP24015
XENP24475
XENP24476
XENP24477
XENP24478
XENP24479
XENP24480
XENP24481

Figure 61B

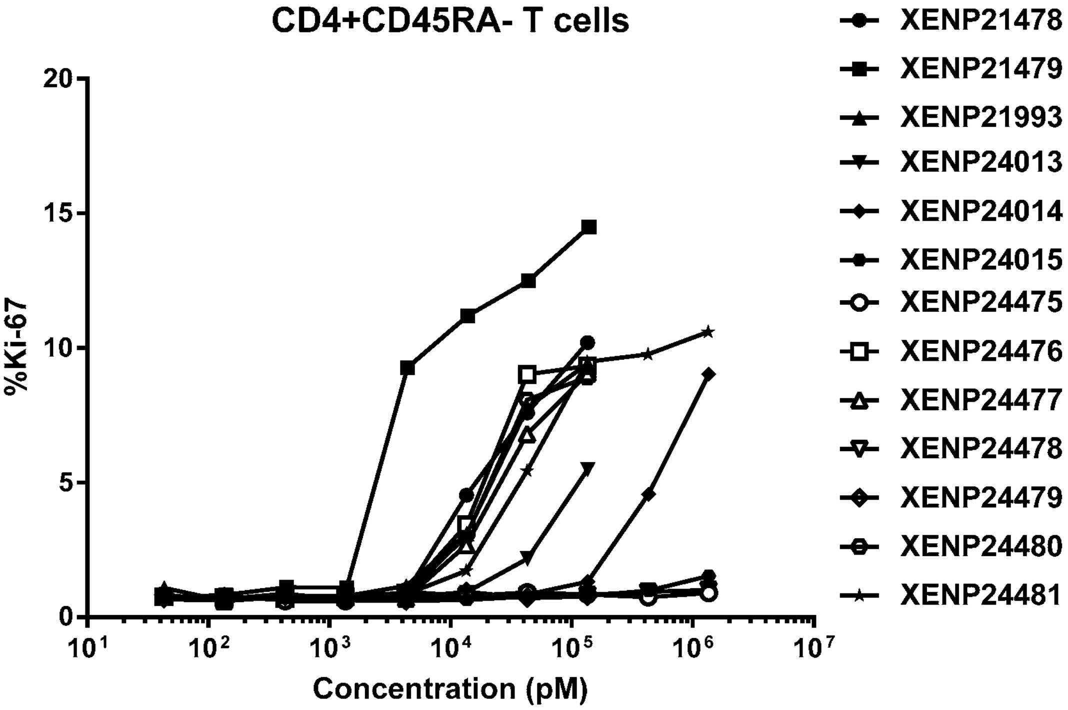

CD4+CD45RA- T cells
%Ki-67
20
15
10
5
0
10^1
10^2
10^3
10^4
10^5
10^6
10^7
Concentration (pM)
XENP21478
XENP21479
XENP21993
XENP24013
XENP24014
XENP24015
XENP24475
XENP24476
XENP24477
XENP24478
XENP24479
XENP24480
XENP24481

Figure 61C

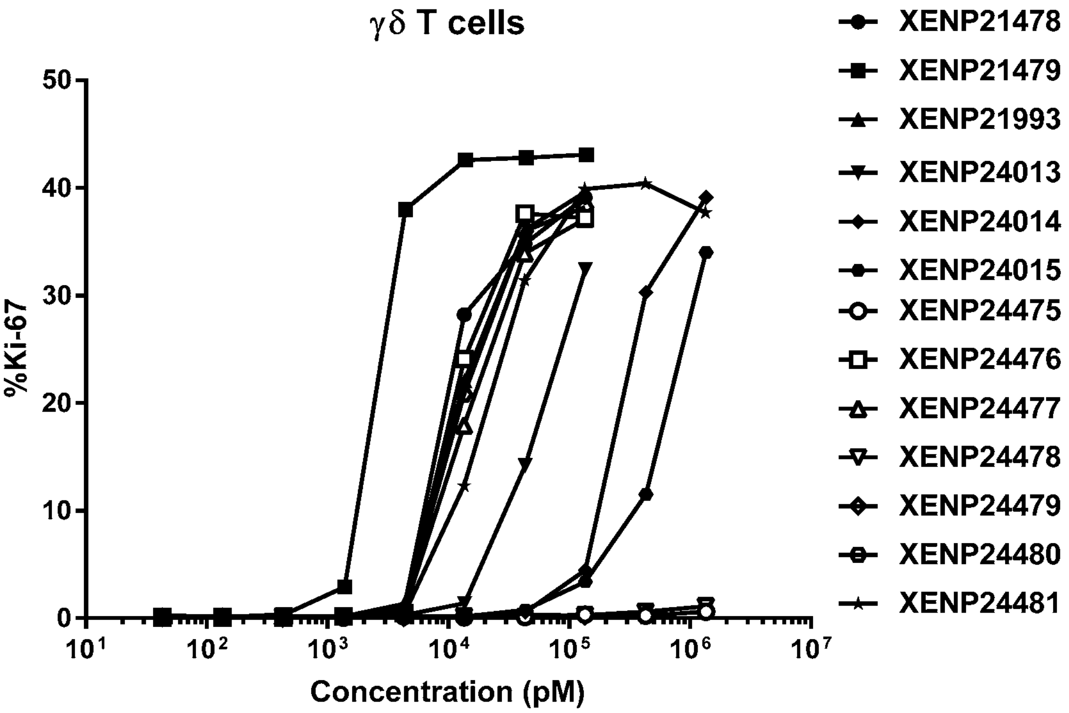

γδ T cells
%Ki-67
0
10
20
30
40
50
10^1
10^2
10^3
10^4
10^5
10^6
10^7
Concentration (pM)
XENP21478
XENP21479
XENP21993
XENP24013
XENP24014
XENP24015
XENP24475
XENP24476
XENP24477
XENP24478
XENP24479
XENP24480
XENP24481

Figure 61D

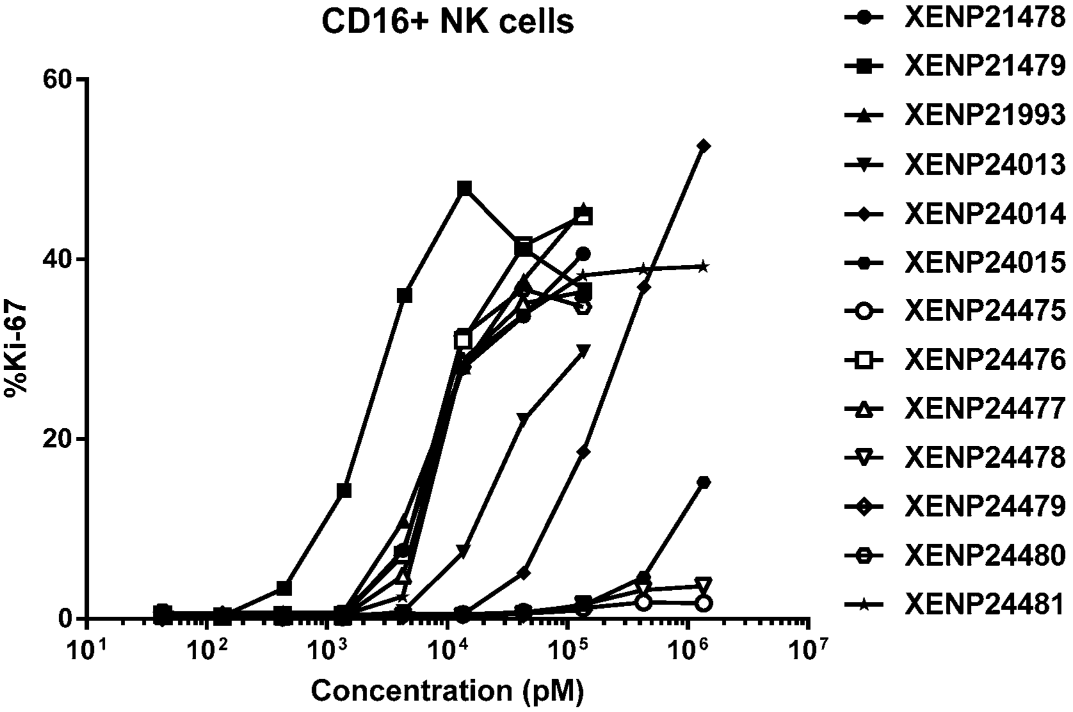

CD16+ NK cells
%Ki-67
60
40
20
0
10¹
10²
10³
10⁴
10⁵
10⁶
10⁷
Concentration (pM)
XENP21478
XENP21479
XENP21993
XENP24013
XENP24014
XENP24015
XENP24475
XENP24476
XENP24477
XENP24478
XENP24479
XENP24480
XENP24481

Figure 62A

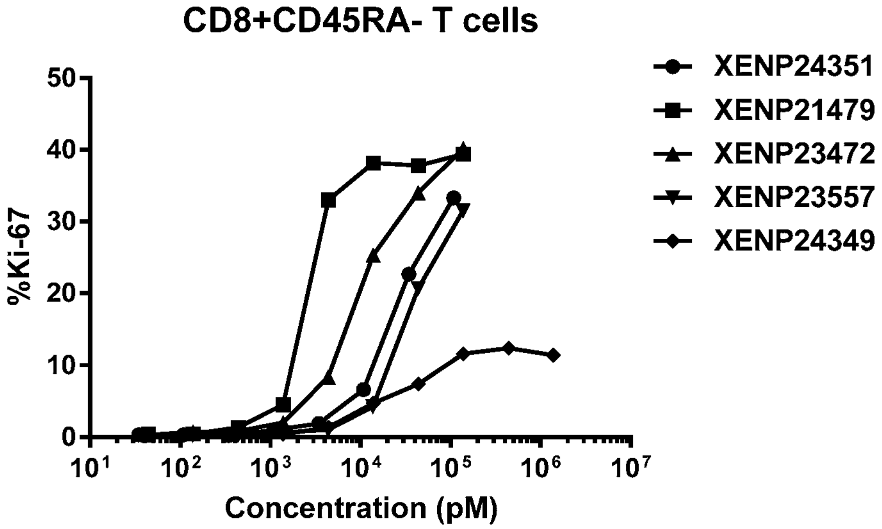


Figure 62B

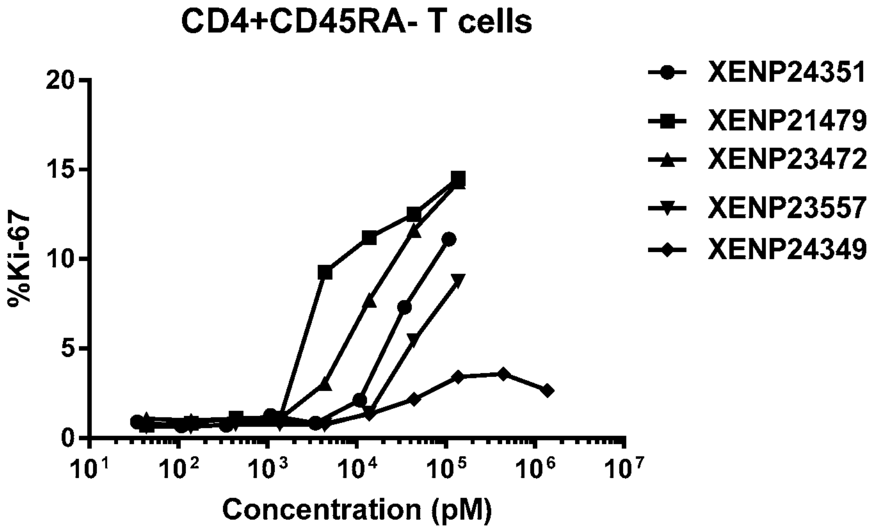


Figure 62C

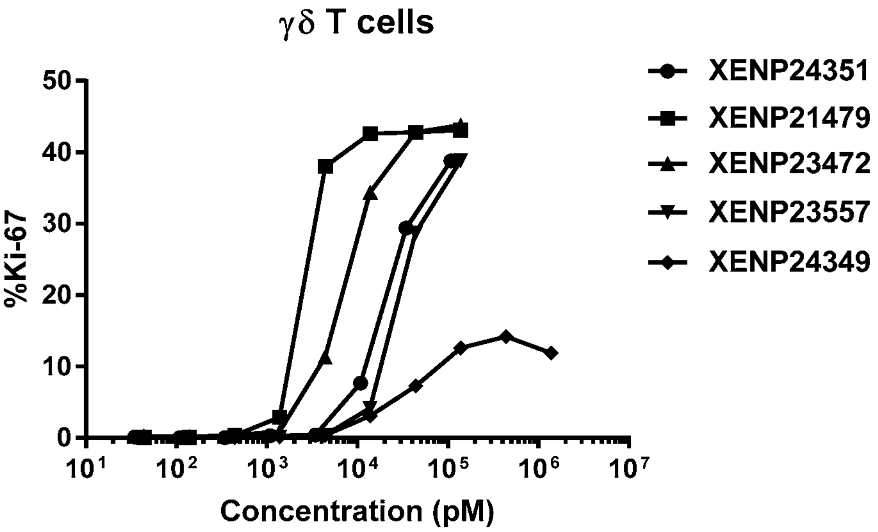


Figure 62D

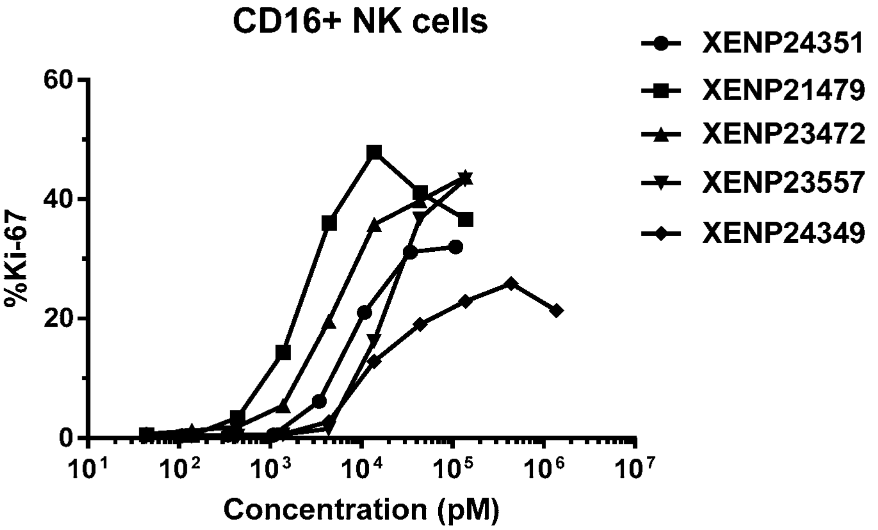


Figure 63

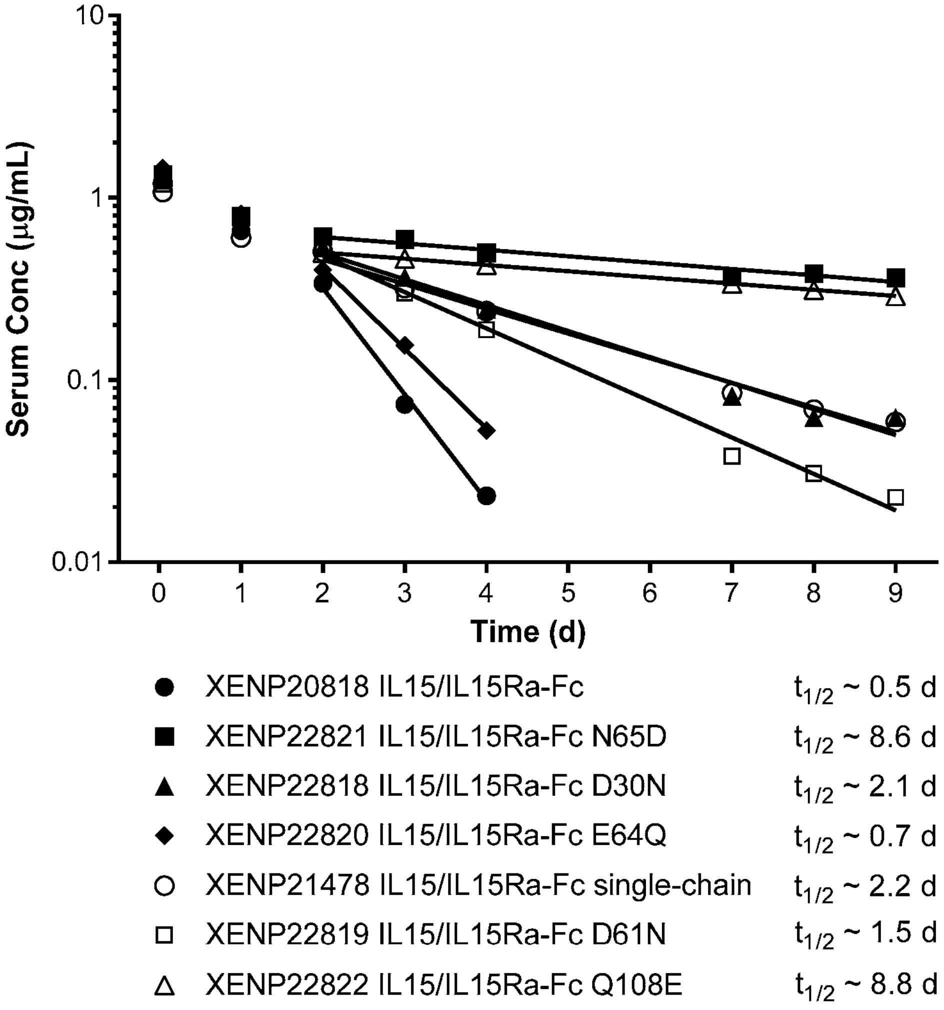

10
1
0.1
0.01
Serum Conc (µg/mL)
0
1
2
3
4
5
6
7
8
9
Time (d)
● XENP20818 IL15/IL15Ra-Fc $t_{1/2}$ ~ 0.5 d
■ XENP22821 IL15/IL15Ra-Fc N65D $t_{1/2}$ ~ 8.6 d
▲ XENP22818 IL15/IL15Ra-Fc D30N $t_{1/2}$ ~ 2.1 d
◆ XENP22820 IL15/IL15Ra-Fc E64Q $t_{1/2}$ ~ 0.7 d
○ XENP21478 IL15/IL15Ra-Fc single-chain $t_{1/2}$ ~ 2.2 d
□ XENP22819 IL15/IL15Ra-Fc D61N $t_{1/2}$ ~ 1.5 d
△ XENP22822 IL15/IL15Ra-Fc Q108E $t_{1/2}$ ~ 8.8 d

Figure 64

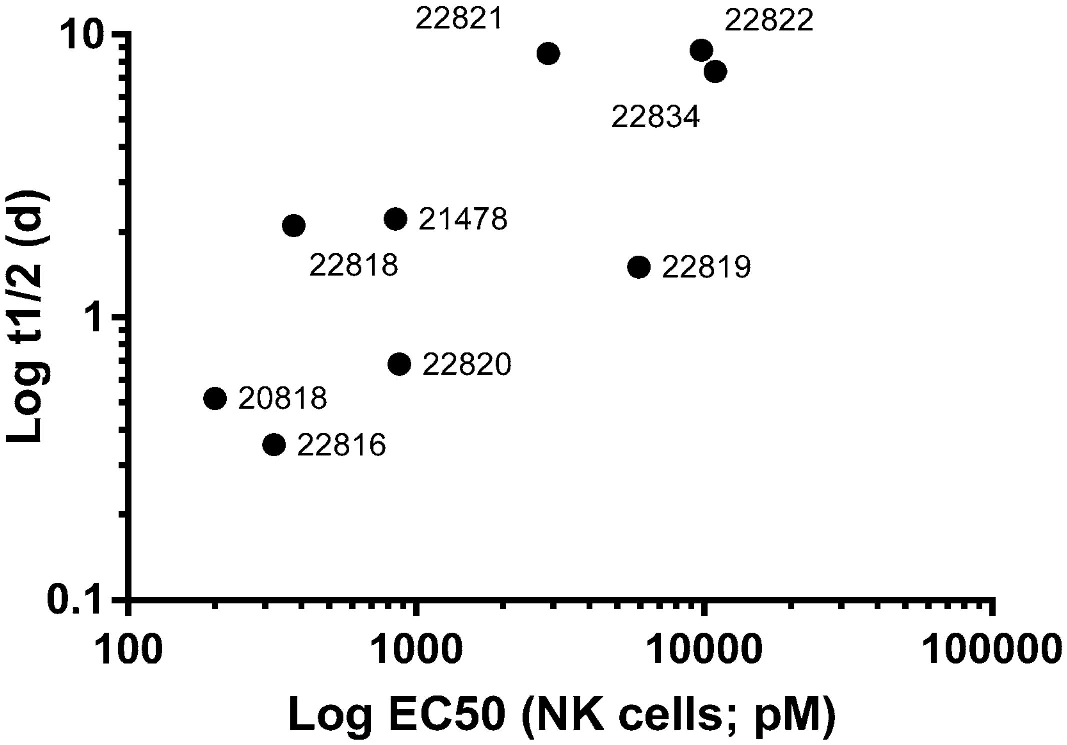
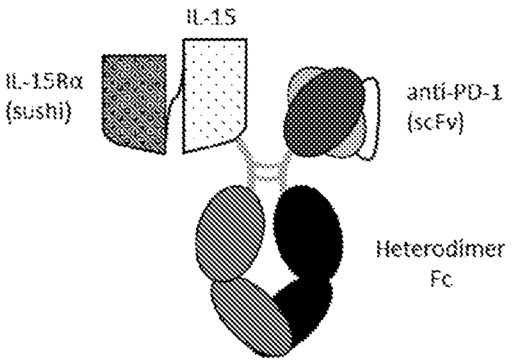
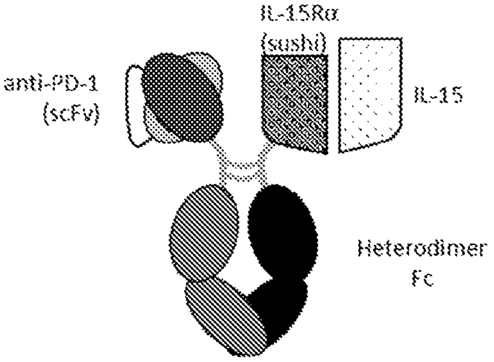

22821
22822
22834
21478
22818
22819
22820
20818
22816
10
1
0.1
Log t1/2 (d)
100
1000
10000
100000
Log EC50 (NK cells; pM)

Figure 65A



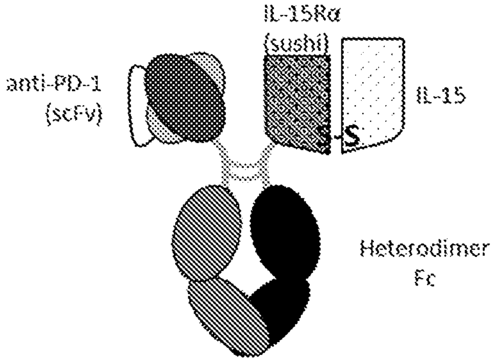
scIL-15/Rα x scFv
Example: XENP21480

Figure 65B



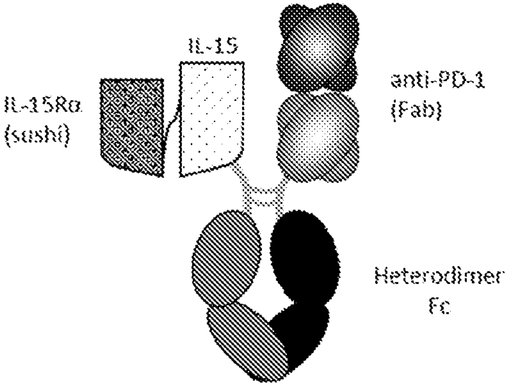
scFv x ncIL-15/Rα

Figure 65C



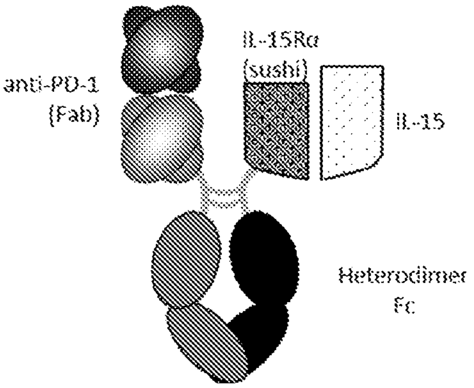
scFv x dsIL-15/Rα

Figure 65D



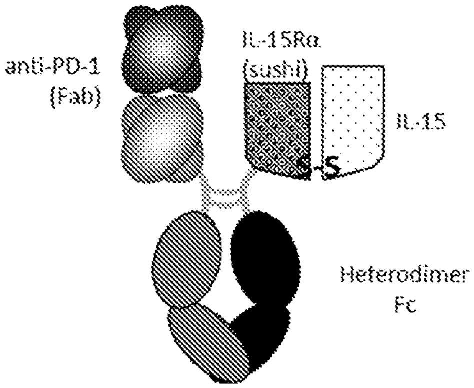
scIL-15/Rα x Fab
Example: XENP22022

Figure 65E



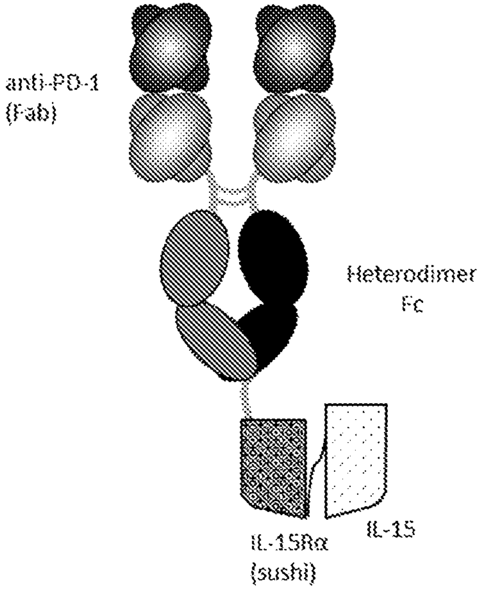
Fab x ncIL-15/Rα
Example: XENP22112

Figure 65F



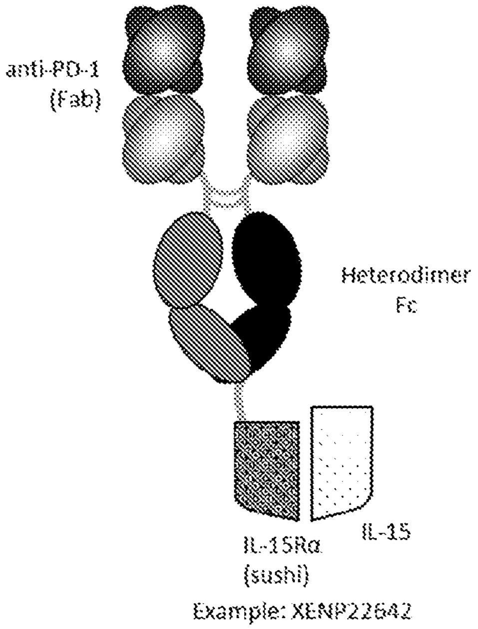
Fab x dsIL-15/Rα
Example: XENP22641

Figure 65G



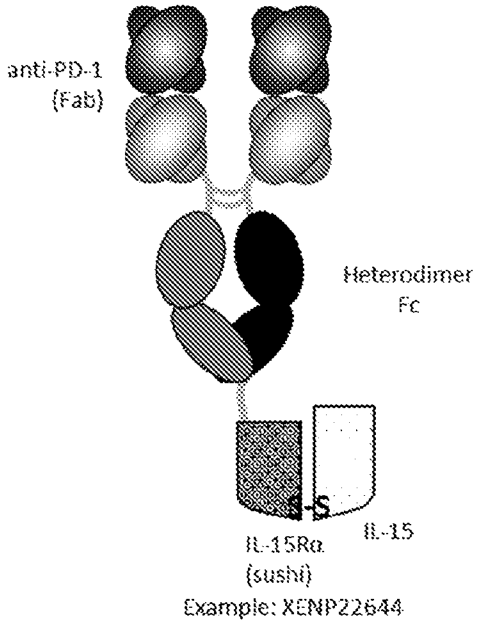
mAb-scIL-15/Rα

Figure 65H



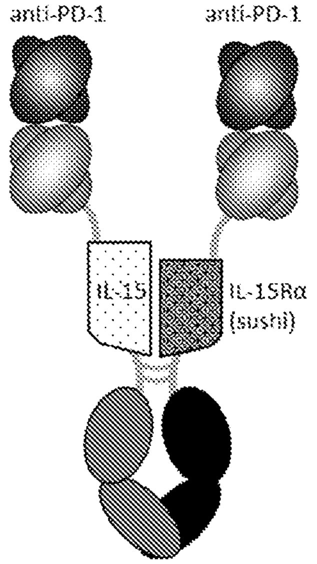
mAb-ncIL-15/Rα
Example: XENP22642

Figure 65I



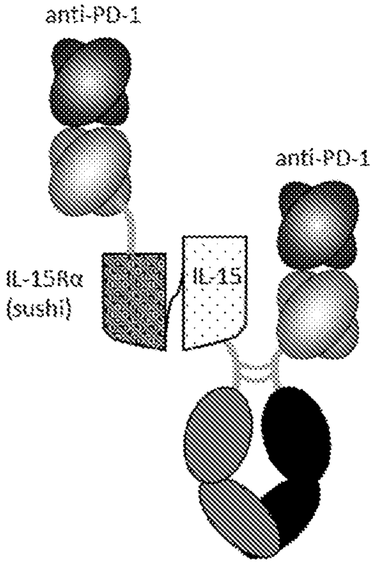
mAb-dsIL-15/Rα
Example: XENP22644

Figure 65J



central-IL-15/Rα

Figure 65K



central-scIL-15/Rα

Figure 66

XENP021480 human_IL15Ra(sushi)_(GGGGS)6-human_IL15(single-chain)-1G6_L1.194_H1.279_scFv(GKPGS)4_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

Chain 1 - human_IL15Ra(sushi)_(GGGGS)6-human_IL15(single-chain)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S SEQ ID NO:347

ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGGSGGGGSGGGGSGGGGSGGGGS/NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVENLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain2 -1G6_L1.194_H1.279_scFv(GKPGS)4_IgG1_C220S/PVA_/S267K/S364K/E357Q SEQ ID NO:348

EIVLTQSPATLSASPGERVTLTC**RASQSVGNDVA**WYQQKPGQAPRLLIN**YASHRYT**GVPDRFTGSGYGTEFTLTISSVQSEDFGVYYC**QQDFSSPRT**FGGGTKVEIK/GKPGSGKPGSGKPGSGKPGS/EVQLVESGGGLVKPGGSLRLSCVASGFTFS**NYWMN**WVRQAPGKGLEWVA**EIRLYSNNYATHYAESVKG**RFTISRDDSKSTLYLQMNNLKTEDTGVYYCTR**YYGNYGGYFDV**WGRGTLVTVSS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Figure 67

1G6_L1.194_H1.279_scFv(GKPGS)4-human_IL15Ra(sushi)_(GGGGS)6-human_IL15(non-covalent)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

Chain 1 – 1G6_L1.194_H1.279_scFv(GKPGS)4_ Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S SEQ ID NO:349

EIVLTQSPATLSASPGERVTLTC**RASQSVGNDVA**WYQQKPGQAPRLLIN**YASHRYT**GVPDRFTGSGYGTEFTLTISSVQSEDFGVYYC**QQDFSSPRT**FGGGTKVEIK/GKPGSGKPGSGKPGSGKPGS/EVQLVESGGGLVKPGGSLRLSCVASGFTFS**NYWMN**WVRQAPGKGLEWVA**EIRLYSNNYATHYAESVKG**RFTISRDDSKSTLYLQMNNLKTEDTGVYYCTR**YYGNYGGYFDV**WGRGTLVTVSS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain2-human_IL15Ra(sushi)_(GGGGS)6_ Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q SEQ ID NO:350

ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGGSGGGGSGGGGSGGGGSGGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Chain3–IL-15 SEQ ID NO:351

NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVENLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS

Figure 68

1G6_L1.194_H1.279_scFv(GKPGS)4-human_IL15Ra(sushi-D96/C97/A98)-human_IL15(E87C)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

Chain 1 – 1G6_L1.194_H1.279_scFv(GKPGS)4_ Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S SEQ ID NO:352
EIVLTQSPATLSASPGERVTLTC**RASQSVGNDVA**WYQQKPGQAPRLLIN**YASHRYT**GVPDRFTGSGYGTEFTLTISSVQSEDFGVYYC**QQ**
DFSSPRTFGGGTKVEIK/GKPGSGKPGSGKPGSGKPGS/EVQLVESGGGLVKPGGSLRLSCVASGFTFS**NYWMN**WVRQAPGKGLEWVA**EI**
RLYSNNYATHYAESVKGRFTISRDDSKSTLYLQMNNLKTEDTGVYYCTR**YYGNYGGYFDV**WGRGTLVTVSS/EPKSSDKTHTCPPCPAPP
VAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVS
NKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDK
SRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain2-human_IL15Ra(sushi-D96/C97/A98)_ Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q SEQ ID NO:353
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIRDCA/EPKSSDKTHTCPPCPAPPVAG
PSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKA
LPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW
QQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Chain3–IL-15(E87C) SEQ ID NO:354
NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVENLIILANNSLSSNGNVTESGCKCCEE
LEEKNIKEFLQSFVHIVQMFINTS

Figure 69A

XENP022022human_IL15Ra(sushi)_(GGGGS)6-human_IL15(single-chain)-1G6_H1.278_L1.188_[PD-1]_Fab_IgG1_pI(-)_Isosteric_A_/PVA_/S267K/L368D/K370S-Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

Chain 1 - human_IL15Ra(sushi)_(GGGGS)6-human_IL15(single-chain)_ IgG1_pI(-)_Isosteric_A_/PVA_/S267K/L368D/K370S SEQ ID NO:355

ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGGSGGGGSGGGGSGGGGSGGGGS/NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVENLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain2-1G6_H1.278 [PD-1]_IgG1_C220S/PVA_/S267K/S364K/E357Q SEQ ID NO:356

EVQLVESGGGLVKPGGSLRLSCVASGFTFS**NYWMN**WVRQAPGKGLEWVA**EIRLYSNNYATHYAESVKG**RFTISRDDSKSTLYLQMNNLKTEDTGVYYCTR**YYGNYGGYFDV**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Chain3-1G6_L1.188[PD-1] SEQ ID NO:357

EIVMTQSPATLSVSPGERVTLTC**RASQSVGNDVA**WYQQKPGQSPRLLIN**YASHRYT**GVPDRFTGSGYGTEFTLTISSVQSEDFAVYFC**QQDFSSPRT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

XENP025849human_IL15Ra(sushi)_(GGGGS)5-human_IL15(single-chain)-1C11[PD-1]_H3L3_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-IgG1_PVA_/S267K/S364K/E357Q

Chain 1 - 1C11[PD-1]_H3_ IgG1_PVA_/S267K/S364K/E357Q SEQ ID NO:358

QIQLVQSGSELKKPGASVKVSCKASGYTFT**HYGMN**WVRQAPGQGLEWMG**WINTYTGEPTYADGFTG**RFVFSLDTSVSTAYLQISSLKAEDTAVYFCAR**DYYGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Chain2-human_IL15Ra(sushi)_(GGGGS)5-human_IL15(single-chain)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S SEQ ID NO:359

ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGGSGGGGSGGGGSGGGGS/NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVENLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain3–1C11[PD-1]_L3 SEQ ID NO:360

DVLMTQSPDSLAVSLGERATINC**KSSQSIVHSNGNTYLE**WYQQKPGQSPKLLIY**KVSNRFS**GVPDRFSGSGSGTDFTLTISSLQAEDVAVYYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 69B

XENP024535human_IL15Ra(sushi)_(GGGGS)5-human_IL15(N65D;single-chain)-1C11[PD-1]_H3L3_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-IgG1_PVA_/S267K/S364K/E357Q

Chain 1 - 1C11[PD-1]_H3_ IgG1_PVA_/S267K/S364K/E357Q SEQ ID NO:361
QIQLVQSGSELKKPGASVKVSCKASGYTFT**HYGMN**WVRQAPGQGLEWMG**WINTYTGEPTYADGFTG**RFVFSLDTSVSTAYLQISSLKAED
TAVYFCAR**DYYGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGL
YSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHED
PEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTK
NQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Chain2-human_IL15Ra(sushi)_(GGGGS)5-human_IL15(N65D;single-chain)_ Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S SEQ ID NO:362
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGGSGGGGSGGGGSGGGG
S/NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVEDLIILANNSLSSNGNVTESGCKEC
EELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYV
DGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDV
SGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain3-1C11[PD-1]_L3 SEQ ID NO:363
DVLMTQSPDSLAVSLGERATINC**KSSQSIVHSNGNTYLE**WYQQKPGQSPKLLIY**KVSNRFS**GVPDRFSGSGSGTDFTLTISSLQAEDVAV
YYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYS
LSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

XENP024536human_IL15Ra(sushi)_(GGGGS)5-human_IL15(Q108E;single-chain)-1C11[PD-1]_H3L3_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-IgG1_PVA_/S267K/S364K/E357Q

Chain1-1C11[PD-1]_H3_ IgG1_PVA_/S267K/S364K/E357Q SEQ ID NO:364
QIQLVQSGSELKKPGASVKVSCKASGYTFT**HYGMN**WVRQAPGQGLEWMG**WINTYTGEPTYADGFTG**RFVFSLDTSVSTAYLQISSLKAED
TAVYFCAR**DYYGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGL
YSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHED
PEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTK
NQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Chain2-human_IL15Ra(sushi)_(GGGGS)5-human_IL15(Q108E;single-chain)_ Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S SEQ ID NO:365
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGGSGGGGSGGGGSGGGG
S/NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVENLIILANNSLSSNGNVTESGCKEC
EELEEKNIKEFLQSFVHIVEMFINTS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYV
DGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDV
SGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain3-1C11[PD-1]_L3 SEQ ID NO:366
DVLMTQSPDSLAVSLGERATINC**KSSQSIVHSNGNTYLE**WYQQKPGQSPKLLIY**KVSNRFS**GVPDRFSGSGSGTDFTLTISSLQAEDVAV
YYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYS
LSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 69C

XENP025850human_IL15Ra(sushi)_(GGGGS)5-human_IL15(N4D/N65D;single-chain)-1C11[PD-1]_H3L3_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-IgG1_PVA_/S267K/S364K/E357Q

Chain 1 - 1C11[PD-1]_H3L3_ IgG1_PVA_/S267K/S364K/E357Q SEQ ID NO:367
QIQLVQSGSELKKPGASVKVSCKASGYTFT**HYGMN**WVRQAPGQGLEWMG**WINTYTGEPTYADGFTG**RFVFSLDTSVSTAYLQISSLKAED
TAVYFCAR**DYYGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGL
YSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHED
PEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTK
NQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Chain2-human_IL15Ra(sushi)_(GGGGS)5-human_IL15(N4D/N65D;single-chain)_ Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S SEQ ID NO:368
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGGSGGGGSGGGGSGGGG
S/NWVDVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVEDLIILANNSLSSNGNVTESGCKEC
EELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYV
DGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDV
SGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain3-1C11[PD-1]_L3 SEQ ID NO:369
DVLMTQSPDSLAVSLGERATINC**KSSQSIVHSNGNTYLE**WYQQKPGQSPKLLIY**KVSNRFS**GVPDRFSGSGSGTDFTLTISSLQAEDVAV
YYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYS
LSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

XENP025937human_IL15Ra(sushi)_(GGGGS)5-human_IL15(N4D/N65D;single-chain)-1C11[PD-1]_H3L3_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S-IgG1_PVA_/S267K/S364K/E357Q/M428L/N434S

Chain 1 - 1C11[PD-1]_H3_ IgG1_PVA_/S267K/S364K/E357Q/M428L/N434S SEQ ID NO:370
QIQLVQSGSELKKPGASVKVSCKASGYTFT**HYGMN**WVRQAPGQGLEWMG**WINTYTGEPTYADGFTG**RFVFSLDTSVSTAYLQISSLKAED
TAVYFCAR**DYYGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGL
YSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHED
PEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTK
NQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKSLSLSPGK

Chain2-human_IL15Ra(sushi)_(GGGGS)5-human_IL15(N4D/N65D;single-chain)_ Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S SEQ ID NO: 371
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGGSGGGGSGGGGSGGGG
S/NWVDVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVEDLIILANNSLSSNGNVTESGCKEC
EELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYV
DGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDV
SGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVLHEALHSHYTQKSLSLSPGK

Chain3-1C11[PD-1]_L3 SEQ ID NO: 372
DVLMTQSPDSLAVSLGERATINC**KSSQSIVHSNGNTYLE**WYQQKPGQSPKLLIY**KVSNRFS**GVPDRFSGSGSGTDFTLTISSLQAEDVAV
YYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYS
LSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 70

XENP0221121G6_H1.278_L1.188_[PD-1]_Fab-IL15(non-covalent)-human_IL15Ra(Sushi)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

Chain 1 – IL-15 SEQ ID NO: 373

NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVENLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS

Chain2–1G6_H1.278[PD-1] _IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S SEQ ID NO: 374

EVQLVESGGGLVKPGGSLRLSCVASGFTFS**NYWMN**WVRQAPGKGLEWVA**EIRLYSNNYATHYAESVKG**RFTISRDDSKSTLYLQMNNLKTEDTGVYYCTR**YYGNYGGYFDV**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain3-human_IL15Ra(Sushi)_Fc(216)_ IgG1_C220S/PVA_/S267K/S364K/E357Q SEQ ID NO: 375

ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Chain4–1G6_L1.188[PD-1] SEQ ID NO: 376

EIVMTQSPATLSVSPGERVTLTC**RASQSVGNDVA**WYQQKPGQSPRLLIN**YASHRYT**GVPDRFTGSGYGTEFTLTISSVQSEDFAVYFC**QQDFSSPRT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 71

XENP0226411G6_H1.278_L1.188_[PD-1]_Fab-IL15(E87C)-human_IL15Ra(Sushi-D96/C97)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

Chain 1 – IL-15(E87C) SEQ ID NO: 377
NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVENLIILANNSLSSNGNVTESGCKCCEE
LEEKNIKEFLQSFVHIVQMFINTS

Chain2–1G6_H1.278_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S SEQ ID NO: 378
EVQLVESGGGLVKPGGSLRLSCVASGFTFS**NYWMN**WVRQAPGKGLEWVA**EIRLYSNNYATHYAESVKG**RFTISRDDSKSTLYLQMNNLKT
EDTGVYYCTR**YYGNYGGYFDV**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVL
QSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVD
VKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSR
EEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSP
GK

Chain3-human_IL15Ra(Sushi-D96/C97)_Fc(216)_ IgG1_C220S/PVA_/S267K/S364K/E357Q SEQ ID NO: 379
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIRDC/EPKSSDKTHTCPPCPAPPVAGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKAL
PAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ
QGNVFSCSVMHEALHNHYTQKSLSLSPGK

Chain4–1G6_L1.188[PD-1] SEQ ID NO: 380
EIVMTQSPATLSVSPGERVTLTC**RASQSVGNDVA**WYQQKPGQSPRLLIN**YASHRYT**GVPDRFTGSGYGTEFTLTISSVQSEDFAVYFC**QQ**
DFSSPRTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTL
TLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 72A

1C11[PD-1]_H3L3_H1L1_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S_(GGGGS)2_IL15Ra(sushi)_(GGGGS)5-IL15(N4D/N65D)

Chain 1 – 1C11[PD-1]_H3_ IgG1_pI(-)_Isosteric_A_PVA_/S267K/L368D/K370S_(GGGGS)2_IL15Ra(sushi)_(GGGGS)5-IL15(N4D/N65D) SEQ ID NO: 381
QIQLVQSGSELKKPGASVKVSCKASGYTFT**HYGMN**WVRQAPGQGLEWMG**WINTYTGEPTYADGFTG**RFVFSLDTSVSTAYLQISSLKAED
TAVYFCAR**DYYGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGL
YSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHED
PEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSP/GGGG
GSGGGGS/ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGGSGGGGSG
GGGSGGGGS/NWVDVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVEDL
IILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS

Chain 2 - 1C11[PD-1]_H3_ IgG1_ PVA_/S267K/S364K/E357Q SEQ ID NO: 382
QIQLVQSGSELKKPGASVKVSCKASGYTFT**HYGMN**WVRQAPGQGLEWMG**WINTYTGEPTYADGFTG**RFVFSLDTSVSTAYLQISSLKAED
TAVYFCAR**DYYGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGL
YSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHED
PEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTK
NQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 3 – 1C11[PD-1]_L3 SEQ ID NO: 383
DVLMTQSPDSLAVSLGERATINC**KSSQSIVHSNGNTYLE**WYQQKPGQSPKLLIY**KVSNRFS**GVPDRFSGSGSGTDFTLTISSLQAEDVAV
YYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYS
LSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

1C11[PD-1]_H3L3_IgG1_pI(-)_Isosteric_A_PVA_/S267K/L368D/K370S_(GGGGS)5_IL15Ra(Sushi)_IL15(single-chain)_IgG1_pI_ISO(+RR)_/PVA_/S267K/S364K/E357Q

Chain1–1C11[PD-1]_H3_IgG1_pI(-)_Isosteric_A_PVA_/S267K/L368D/K370S__(GGGGS)5_IL15Ra(Sushi)_IL15(single-chain) SEQ ID NO: 384
QIQLVQSGSELKKPGASVKVSCKASGYTFT**HYGMN**WVRQAPGQGLEWMG**WINTYTGEPTYADGFTG**RFVFSLDTSVSTAYLQISSLKAED
TAVYFCAR**DYYGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGL
YSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHED
PEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK/GG
GGSGGGGS/ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGGSGGGGS
GGGGSGGGGS/NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVENLIILANNSLSSNGN
VTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS

Chain2-1C11[PD-1]_H3_IgG1_pI_ISO(+RR)_/PVA_/S267K/S364K/E357Q SEQ ID NO: 385
QIQLVQSGSELKKPGASVKVSCKASGYTFT**HYGMN**WVRQAPGQGLEWMG**WINTYTGEPTYADGFTG**RFVFSLDTSVSTAYLQISSLKAED
TAVYFCAR**DYYGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGL
YSLSSVVTVPSSSLGTKTYTCNVNHKPSNTKVDKKVERKSCDKTHTCPRCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHED
PEVKFKWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTK
NQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Chain3–1C11[PD-1]_L3 SEQ ID NO: 386
DVLMTQSPDSLAVSLGERATINC**KSSQSIVHSNGNTYLE**WYQQKPGQSPKLLIY**KVSNRFS**GVPDRFSGSGSGTDFTLTISSLQAEDVAV
YYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYS
LSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 72B

1C11[PD-1]_H3L3_IgG1_pI(-)_Isosteric_A_PVA_/S267K/L368D/K370S_IgG1_pI_ISO(+RR)_/PVA_/S267K/S364K/E357Q_(GGGGS)5_IL15Ra(Sushi)_IL15(single-chain)

Chain1–1C11[PD-1]_H3_IgG1_pI(-)_Isosteric_A_PVA_/S267K/L368D/K370S SEQ ID NO: 387
QIQLVQSGSELKKPGASVKVSCKASGYTFT**HYGMN**WVRQAPGQGLEWMG**WINTYTGEPTYADGFTG**RFVFSLDTSVSTAYLQISSLKAED
TAVYFCAR**DYYGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGL
YSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHED
PEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain2–1C11[PD-1]_H3_IgG1_pI_ISO(+RR)_/PVA_/S267K/S364K/E357Q_(GGGGS)5_IL15Ra(Sushi)_IL15(single-chain) SEQ ID NO: 388
QIQLVQSGSELKKPGASVKVSCKASGYTFT**HYGMN**WVRQAPGQGLEWMG**WINTYTGEPTYADGFTG**RFVFSLDTSVSTAYLQISSLKAED
TAVYFCAR**DYYGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGL
YSLSSVVTVPSSSLGTKTYTCNVNHKPSNTKVDKKVERKSCDKTHTCPRCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHED
PEVKFKWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTK
NQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK/GG
GGSGGGGS/ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGGSGGGGS
GGGGSGGGGS/NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVENLIILANNSLSSNGN
VTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS

Chain3–1C11[PD-1]_L3 SEQ ID NO: 389
DVLMTQSPDSLAVSLGERATINC**KSSQSIVHSNGNTYLE**WYQQKPGQSPKLLIY**KVSNRFS**GVPDRFSGSGSGTDFTLTISSLQAEDVAV
YYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYS
LSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 73A

XENP022642 Nivolumab_H0L0_IgG1_pI(-)_Isosteric_A_PVA_/S267K/L368D/K370S_(GGGGS)2_IL15Ra(Sushi)_IL15(non-covalent)_IgG1_pI_ISO(+RR)_/PVA_/S267K/S364K/E357Q

Chain 1 – IL-15 SEQ ID NO: 390
NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVENLIILANNSLSSNGNVTESGCKECEE
LEEKNIKEFLQSFVHIVQMFINTS

Chain2–Nivolumab_H0_IgG1_pI(-)_Isosteric_A_PVA_/S267K/L368D/K370S__(GGGGS)2_IL15Ra(Sushi) SEQ ID NO: 391
QVQLVESGGGVVQPGRSLRLDCKASGITFS**NSGMH**WVRQAPGKGLEWVA**VIWYDGSKRYYADSVKG**RFTISRDNSKNTLFLQMNSLRAED
TAVYYCAT**NDDY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLS
SVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVK
FNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVS
LTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK/GGGGSG
GGGS/ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR

Chain3-Nivolumab_H0_IgG1_pI_ISO(+RR)_/PVA_/S267K/S364K/E357Q SEQ ID NO: 392
QVQLVESGGGVVQPGRSLRLDCKASGITFS**NSGMH**WVRQAPGKGLEWVA**VIWYDGSKRYYADSVKG**RFTISRDNSKNTLFLQMNSLRAED
TAVYYCAT**NDDY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLS
SVVTVPSSSLGTKTYTCNVNHKPSNTKVDKKVERKSCDKTHTCPRCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVK
FKWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVK
LTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Chain4–Nivolumab_L0 SEQ ID NO: 393
EIVLTQSPATLSLSPGERATLSC**RASQSVSSYLA**WYQQKPGQAPRLLIY**DASNRAT**GIPARFSGSGSGTDFTLTISSLEPEDFAVYYC**QQ**
SSNWPRTFGQGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTL
TLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 73B

XENP022643Nivolumab_H0L0_IgG1_pI(-)_Isosteric_A_PVA_/S267K/L368D/K370S_IgG1_pI_ISO(+RR)_/PVA_/S267K/S364K/E357Q_(GGGGS)2_IL15Ra(Sushi)_IL15(non-covalent)

Chain1–IL-15 SEQ ID NO: 394
NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVENLIILANNSLSSNGNVTESGCKECEE
LEEKNIKEFLQSFVHIVQMFINTS

Chain2–Nivolumab_H0_IgG1_pI(-)_Isosteric_A_PVA_/S267K/L368D/K370S SEQ ID NO: 395
QVQLVESGGGVVQPGRSLRLDCKASGITFS**NSGMH**WVRQAPGKGLEWVA**VIWYDGSKRYYADSVKG**RFTISRDNSKNTLFLQMNSLRAED
TAVYYCAT**NDDY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLS
SVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVK
FNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVS
LTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain3–Nivolumab_H0_IgG1_pI_ISO(+RR)_/PVA_/S267K/S364K/E357Q_(GGGGS)2_IL15Ra(Sushi) SEQ ID NO: 396
QVQLVESGGGVVQPGRSLRLDCKASGITFS**NSGMH**WVRQAPGKGLEWVA**VIWYDGSKRYYADSVKG**RFTISRDNSKNTLFLQMNSLRAED
TAVYYCAT**NDDY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLS
SVVTVPSSSLGTKTYTCNVNHKPSNTKVDKKVERKSCDKTHTCPRCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVK
FKWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVK
LTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK/GGGGSG
GGGS/ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR

Chain4–Nivolumab_L0 SEQ ID NO: 397
EIVLTQSPATLSLSPGERATLSC**RASQSVSSYLA**WYQQKPGQAPRLLIY**DASNRAT**GIPARFSGSGSGTDFTLTISSLEPEDFAVYYC**QQ**
SSNWPRTFGQGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTL
TLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 74A

XENP022644Nivolumab_H0L0_IgG1_pI(-)_Isosteric_A_PVA_/S267K/L368D/K370S_(GGGGS)2_IL15Ra(Sushi-D96/C97)_IL15(E87C)_IgG1_pI_ISO(+RR)_/PVA_/S267K/S364K/E357Q

Chain 1 – IL-15(E87C) SEQ ID NO: 398

NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVENLIILANNSLSSNGNVTESGCKCCEELEEKNIKEFLQSFVHIVQMFINTS

Chain2-Nivolumab_H0_IgG1_pI(-)_Isosteric_A_PVA_/S267K/L368D/K370S_(GGGGS)2_IL15Ra(Sushi-D96/C97)
SEQ ID NO: 399

QVQLVESGGGVVQPGRSLRLDCKASGITFS**NSGMH**WVRQAPGKGLEWVA**VIWYDGSKRYYADSVKG**RFTISRDNSKNTLFLQMNSLRAEDTAVYYCAT**NDDY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK/GGGGSGGGGS/ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIRDC

Chain3-Nivolumab_H0_ IgG1_pI_ISO(+RR)_/PVA_/S267K/S364K/E357Q SEQ ID NO:400

QVQLVESGGGVVQPGRSLRLDCKASGITFS**NSGMH**WVRQAPGKGLEWVA**VIWYDGSKRYYADSVKG**RFTISRDNSKNTLFLQMNSLRAEDTAVYYCAT**NDDY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVNHKPSNTKVDKKVERKSCDKTHTCPRCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFKWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Chain4–Nivolumab_L0 SEQ ID NO: 401

EIVLTQSPATLSLSPGERATLSC**RASQSVSSYLA**WYQQKPGQAPRLLIY**DASNRAT**GIPARFSGSGSGTDFTLTISSLEPEDFAVYYC**QQSSNWPRT**FGQGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 74B

XENP022645 Nivolumab_H0L0_IgG1_pI(-)_Isosteric_A_PVA_/S267K/L368D/K370S_IgG1_pI_ISO(+RR)_/PVA_/S267K/S364K/E357Q_(GGGGS)2_IL15Ra(Sushi-D96/C97)_IL15(E87C)

Chain 1 – IL-15(E87C) SEQ ID NO: 402
NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVENLIILANNSLSSNGNVTESGCKCCEE
LEEKNIKEFLQSFVHIVQMFINTS

Chain2-Nivolumab_H0_ IgG1_pI(-)_Isosteric_A_PVA_/S267K/L368D/K370S SEQ ID NO: 403
QVQLVESGGGVVQPGRSLRLDCKASGITFS**NSGMH**WVRQAPGKGLEWVA**VIWYDGSKRYYADSVKG**RFTISRDNSKNTLFLQMNSLRAED
TAVYYCAT**NDDY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLS
SVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVK
FNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVS
LTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain3-Nivolumab_H0_ IgG1_pI_ISO(+RR)_/PVA_/S267K/S364K/E357Q_(GGGGS)2_IL15Ra(Sushi-D96/C97)
SEQ ID NO: 404
QVQLVESGGGVVQPGRSLRLDCKASGITFS**NSGMH**WVRQAPGKGLEWVA**VIWYDGSKRYYADSVKG**RFTISRDNSKNTLFLQMNSLRAED
TAVYYCAT**NDDY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLS
SVVTVPSSSLGTKTYTCNVNHKPSNTKVDKKVERKSCDKTHTCPRCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVK
FKWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVK
LTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK/GGGGSG
GGGS/ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIRDC

Chain4–Nivolumab_L0 SEQ ID NO: 405
EIVLTQSPATLSLSPGERATLSC**RASQSVSSYLA**WYQQKPGQAPRLLIY**DASNRAT**GIPARFSGSGSGTDFTLTISSLEPEDFAVYYC**QQ**
SSNWPRTFGQGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTL
TLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 75

1C11[PD-1]_H3L3_bivalent_IL15_N4D/N65D_IL15Ra(sushi)_(GGGGS)1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

Chain 1 - 1C11[PD-1]_H3_IL15_N4D/N65D_(GGGGS)1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S SEQ ID NO: 406

QIQLVQSGSELKKPGASVKVSCKASGYTFT**HYGMN**WVRQAPGQGLEWMG**WINTYTGEPTYADGFTG**RFVFSLDTSVSTAYLQISSLKAEDTAVYFCAR**DYYGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSC/GGGGSGGGGS/NWVDVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVEDLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/GGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 - 1C11[PD-1]_H3_IL15Ra(sushi)_(GGGGS)1_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q SEQ ID NO: 407

QIQLVQSGSELKKPGASVKVSCKASGYTFT**HYGMN**WVRQAPGQGLEWMG**WINTYTGEPTYADGFTG**RFVFSLDTSVSTAYLQISSLKAEDTAVYFCAR**DYYGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSC/GGGGSGGGGS/ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 3 - 1C11[PD-1]_L3 SEQ ID NO: 408

DVLMTQSPDSLAVSLGERATINC**KSSQSIVHSNGNTYLE**WYQQKPGQSPKLLIY**KVSNRFS**GVPDRFSGSGSGTDFTLTISSLQAEDVAVYYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 76

1C11[PD-1]_H3L3_Fab-IL15Ra(sushi)_(GGGGS)5-IL15(N4D/N65D)-1C11[PD-1]_H3L3_Fab_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S_IgG1_C220S/PVA_/S267K/S364K/E357Q

Chain 1 - 1C11[PD-1]_H3_IL15Ra(sushi)_(GGGGS)5-IL15(N4D/N65D)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S SEQ ID NO: 409
QIQLVQSGSELKKPGASVKVSCKASGYTFT**HYGMN**WVRQAPGQGLEWMG**WINTYTGEPTYADGFTG**RFVFSLDTSVSTAYLQISSLKAED
TAVYFCAR**DYYGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVH
TFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSC/GGGGSGGGGS/ITCPPPMSVEH
ADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGGSGGGGSGGGGS
GGGGS/NWVDVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVEDLIILANNSLSSNGNVTES
GCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVV
DVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKA
KGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDK
SRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 - 1C11[PD-1]_H3_IgG1_C220S/PVA_/S267K/S364K/E357Q SEQ ID NO: 410
QIQLVQSGSELKKPGASVKVSCKASGYTFT**HYGMN**WVRQAPGQGLEWMG**WINTYTGEPTYADGFTG**RFVFSLDTSVSTAYLQISSLKAED
TAVYFCAR**DYYGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVH
TFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFP
PKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEY
KCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTT
PPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 3 – 1C11[PD-1]_L3 SEQ ID NO: 411
DVLMTQSPDSLAVSLGERATINC**KSSQSIVHSNGNTYLE**WYQQKPGQSPKLLIY**KVSNRFS**GVPDRFSGSGSGTDFTLTISSLQAEDVAV
YYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYS
LSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 77A

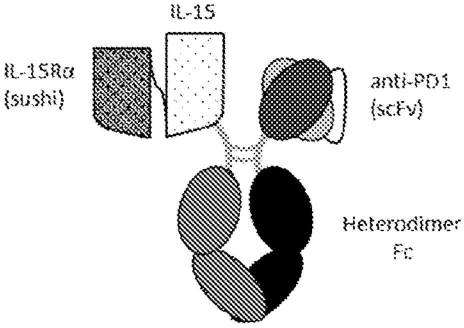
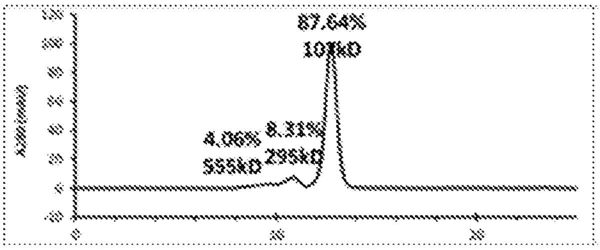
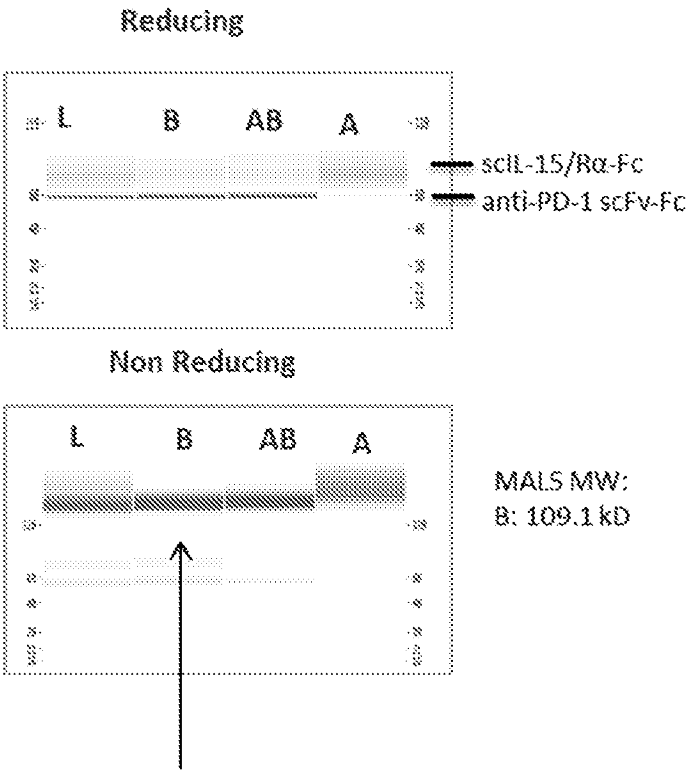


Figure 77B



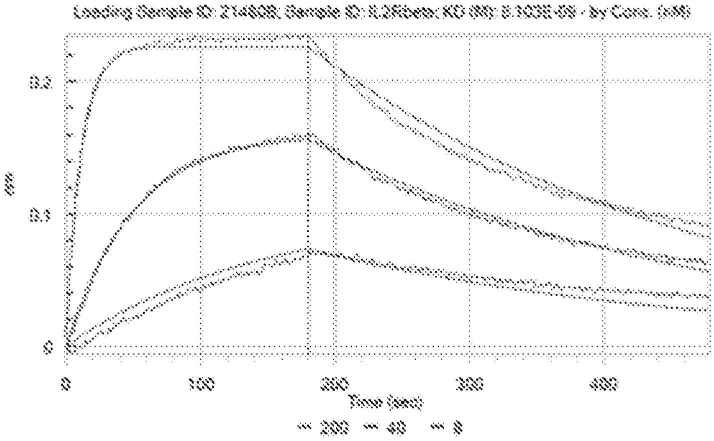
pI(MW) = 7.32 (101.0 kDa)
Protein A yield = 33.6 mg/L

Figure 77C



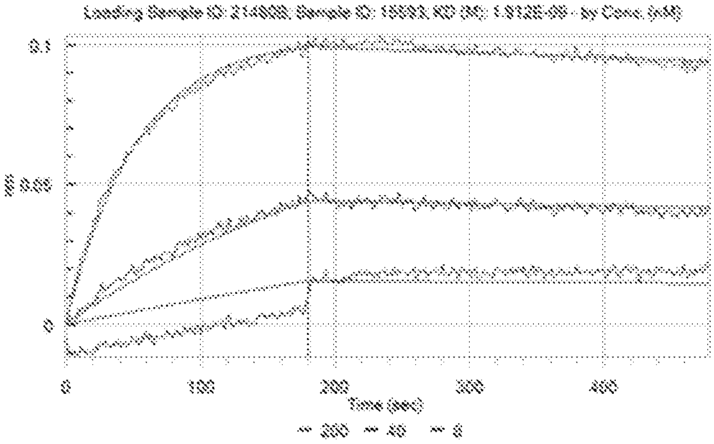
Purified
XENP21480

Figure 77D



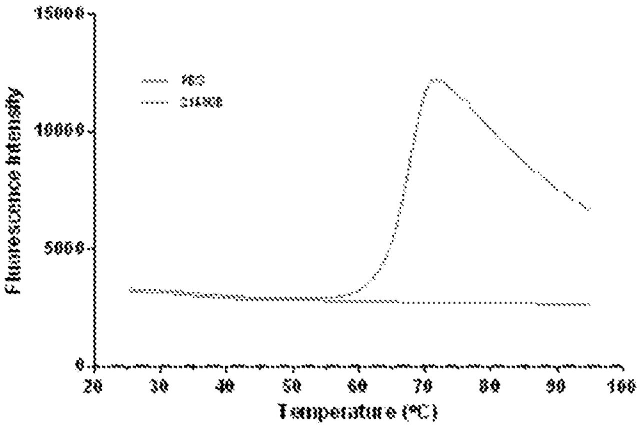
Binding to IL2Rbeta KD = 8.1 nM

Figure 77E



Binding to PD-1 KD = 1.9 nM

Figure 77F



DSF TM = 68.0 °C

Figure 78A

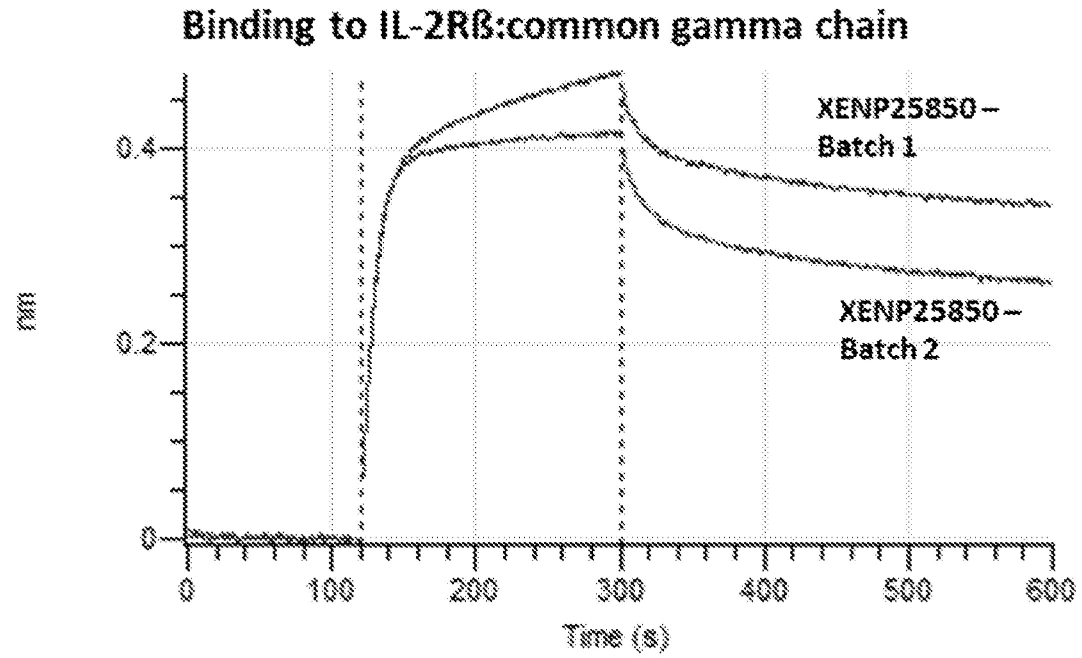


Figure 78B

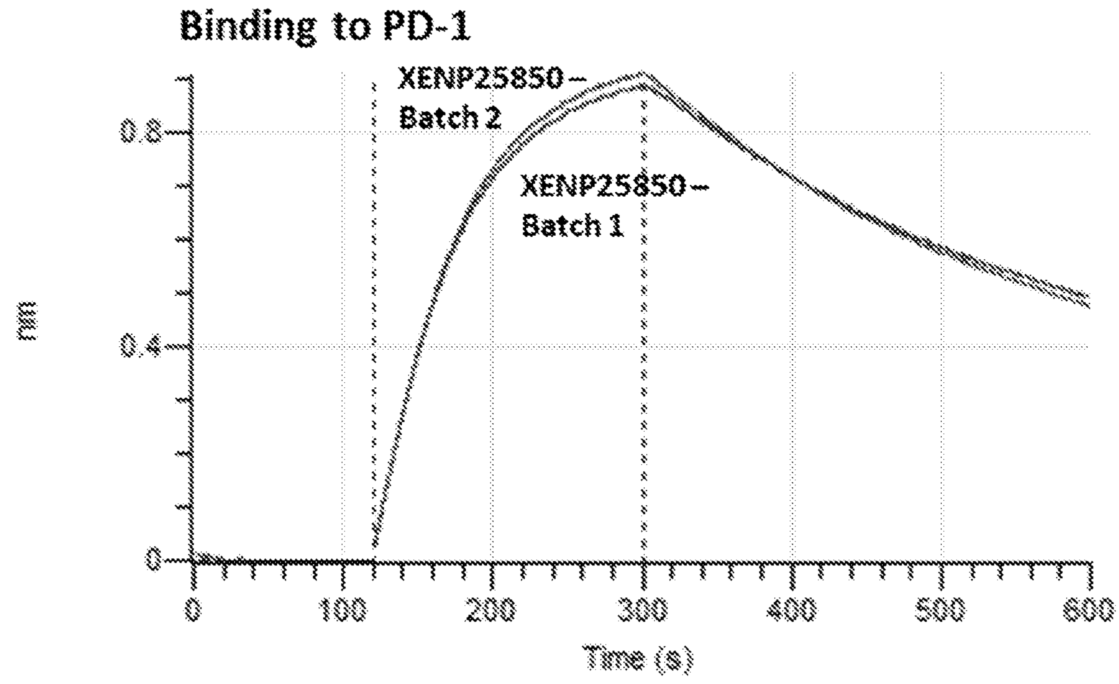


Figure 79A

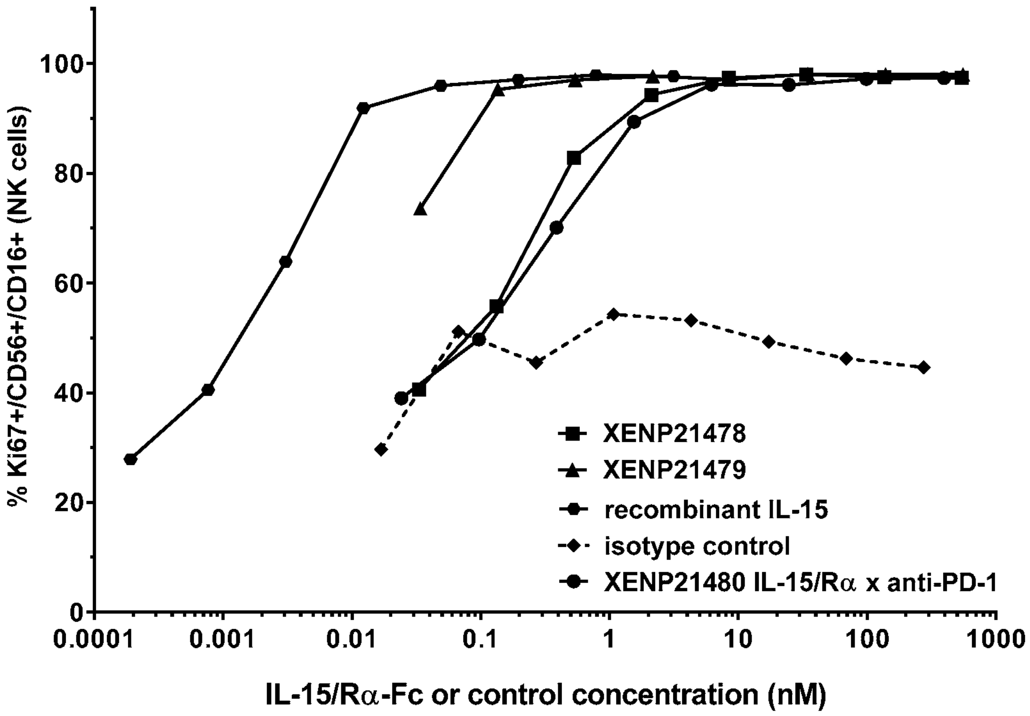


Figure 79B

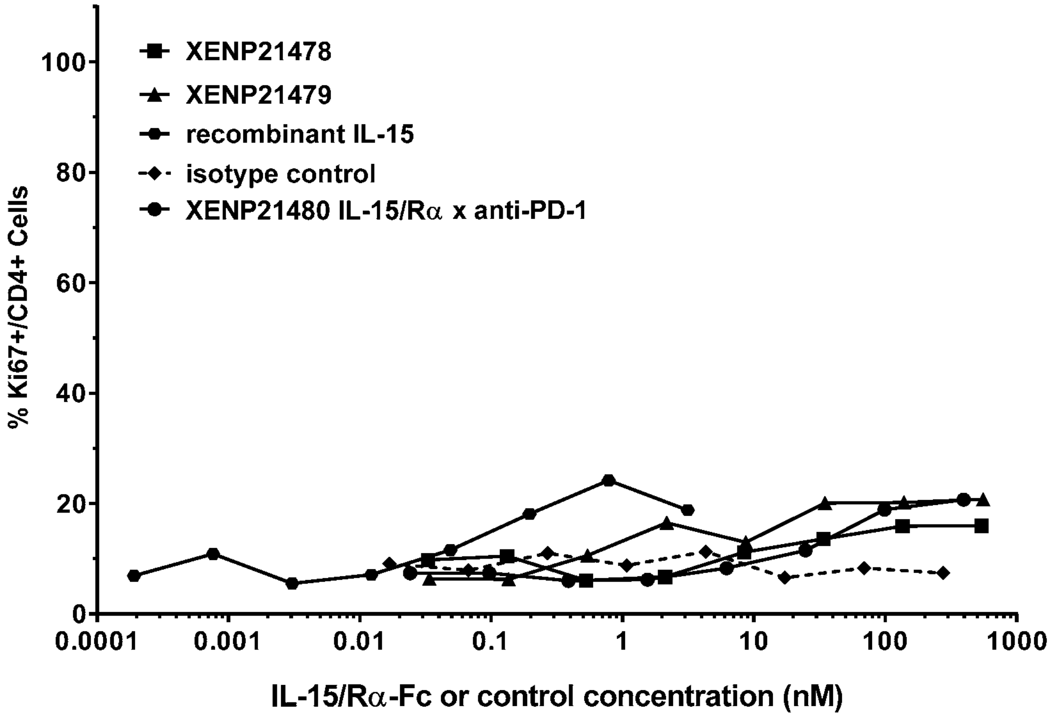


Figure 79C

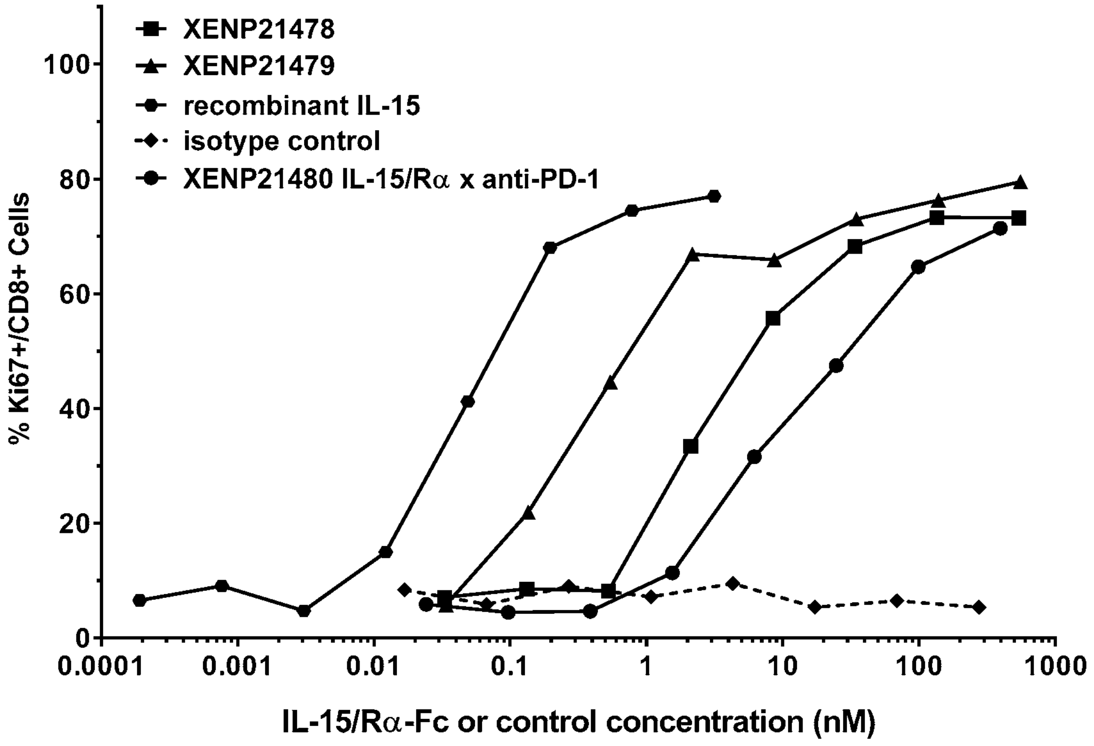

XENP21478
XENP21479
recombinant IL-15
isotype control
XENP21480 IL-15/Rα x anti-PD-1
% Ki67+/CD8+ Cells
0
20
40
60
80
100
0.0001
0.001
0.01
0.1
1
10
100
1000
IL-15/Rα-Fc or control concentration (nM)

Figure 80

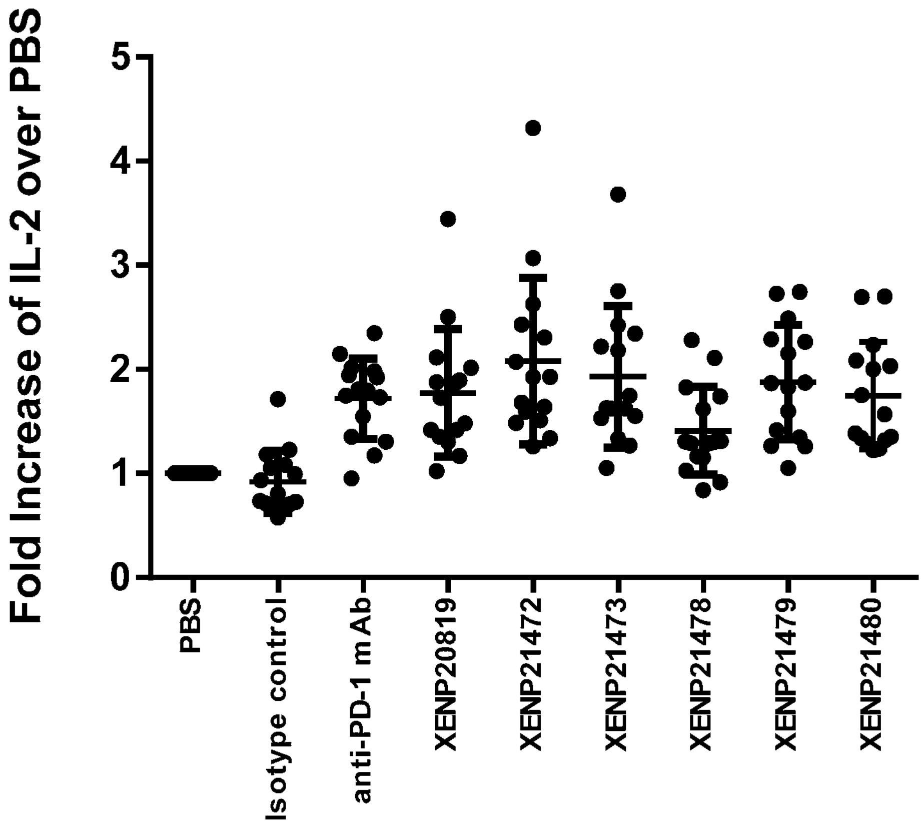

Fold Increase of IL-2 over PBS
0
1
2
3
4
5
PBS
Isotype control
anti-PD-1 mAb
XENP20819
XENP21472
XENP21473
XENP21478
XENP21479
XENP21480

Figure 81

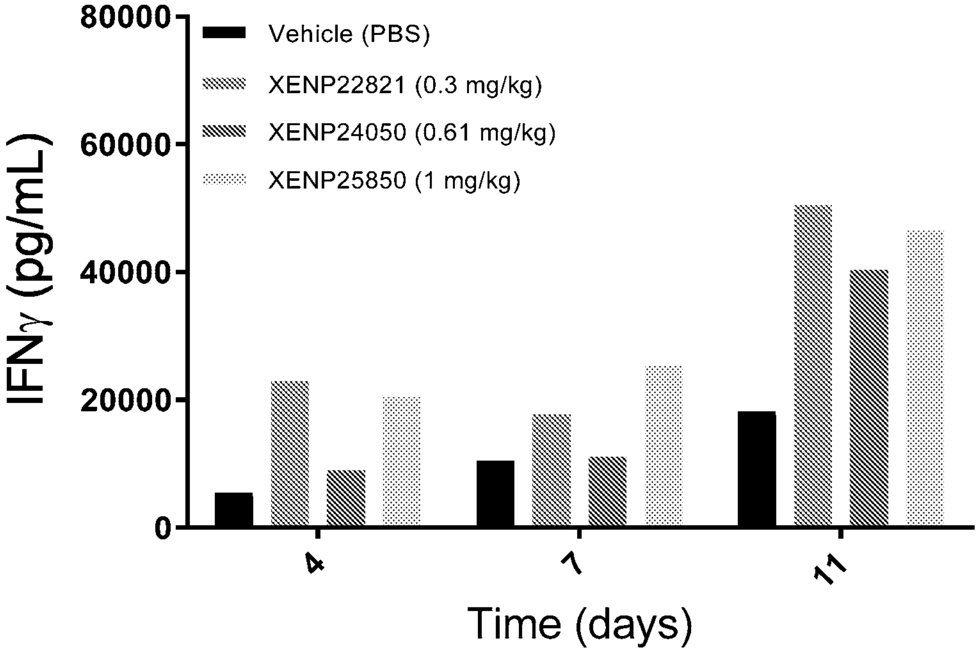

80000
60000
40000
20000
0
IFNγ (pg/mL)
Vehicle (PBS)
XENP22821 (0.3 mg/kg)
XENP24050 (0.61 mg/kg)
XENP25850 (1 mg/kg)
4
7
11
Time (days)

Figure 82A

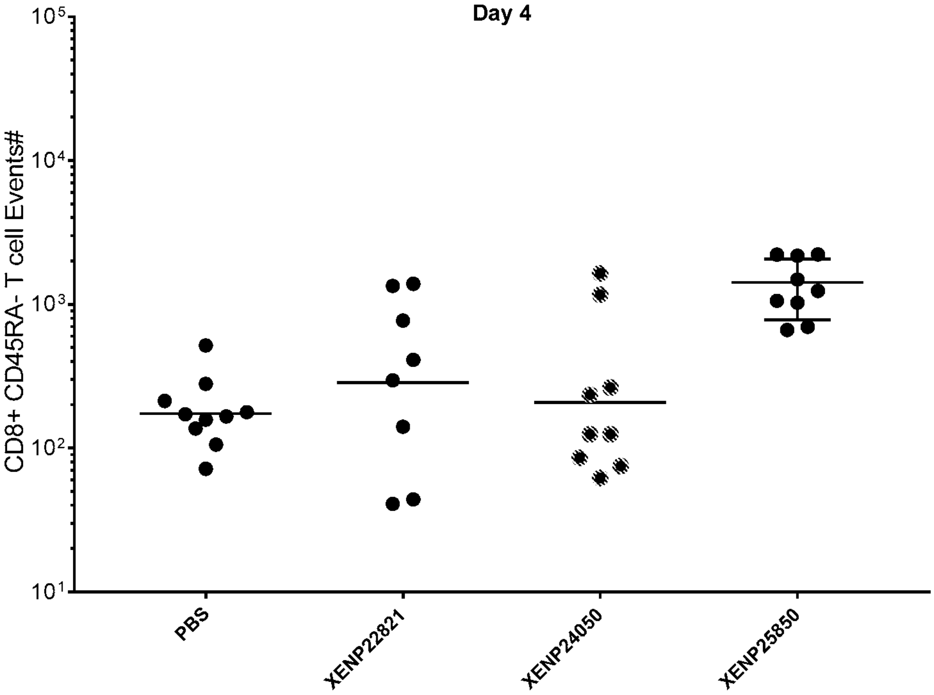


Figure 82B

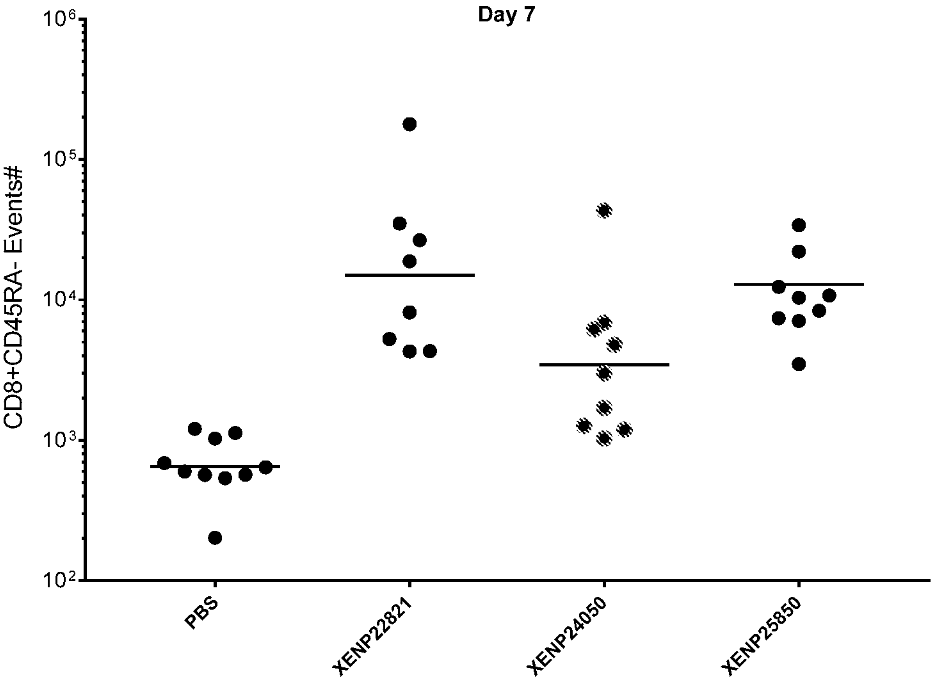


Figure 82C

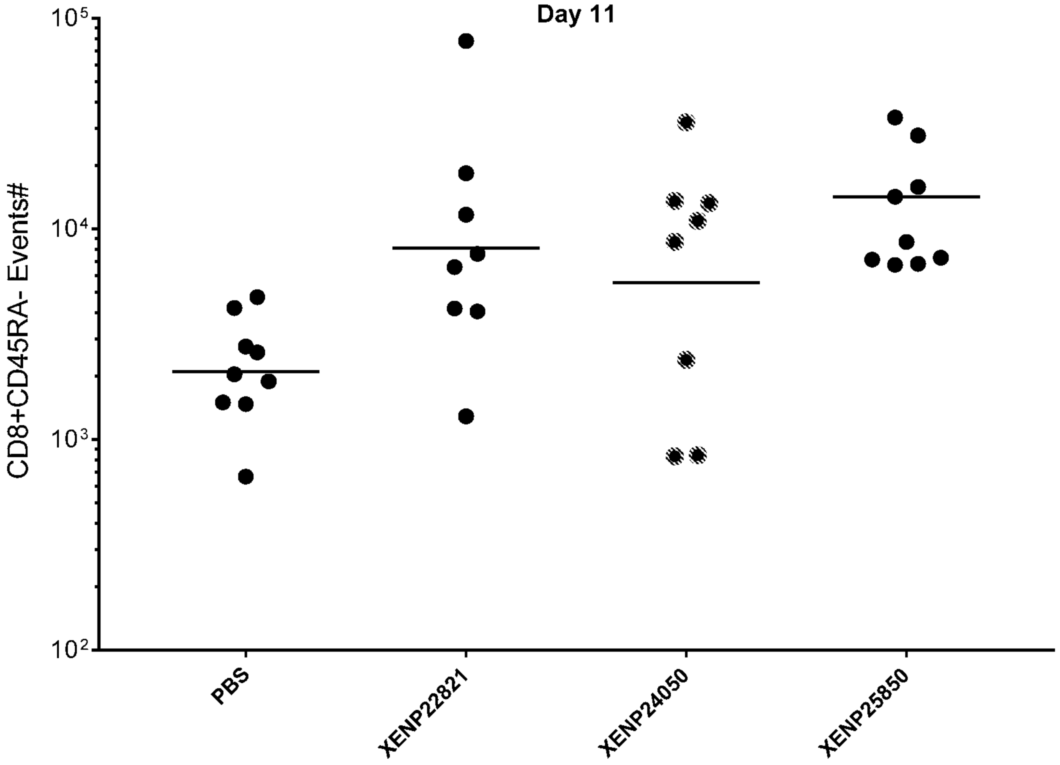

Day 11
CD8+CD45RA- Events#
10^5
10^4
10^3
10^2
PBS
XENP22821
XENP24050
XENP25850

Figure 83A

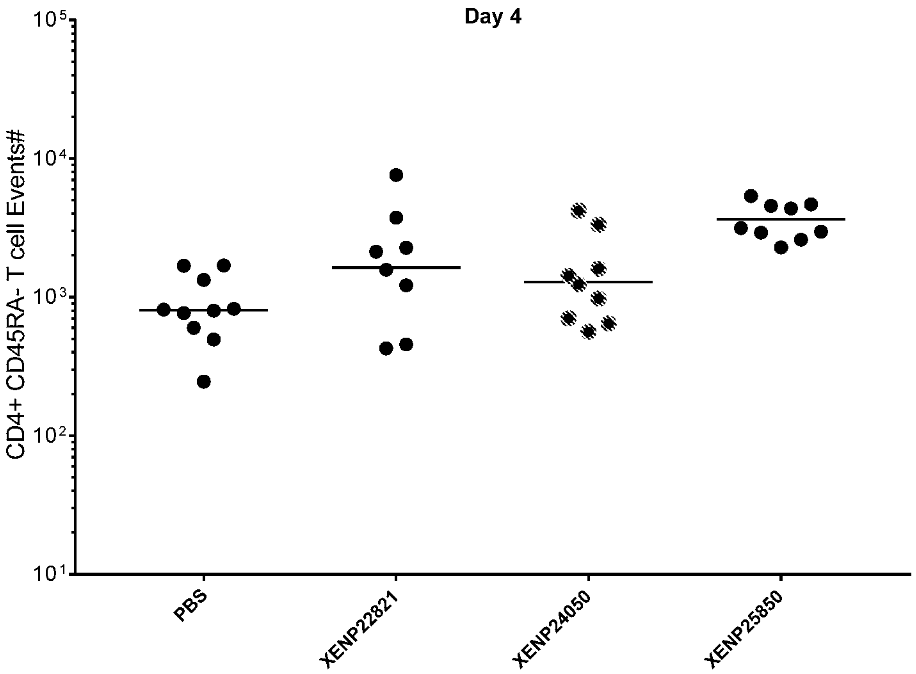


Figure 83B

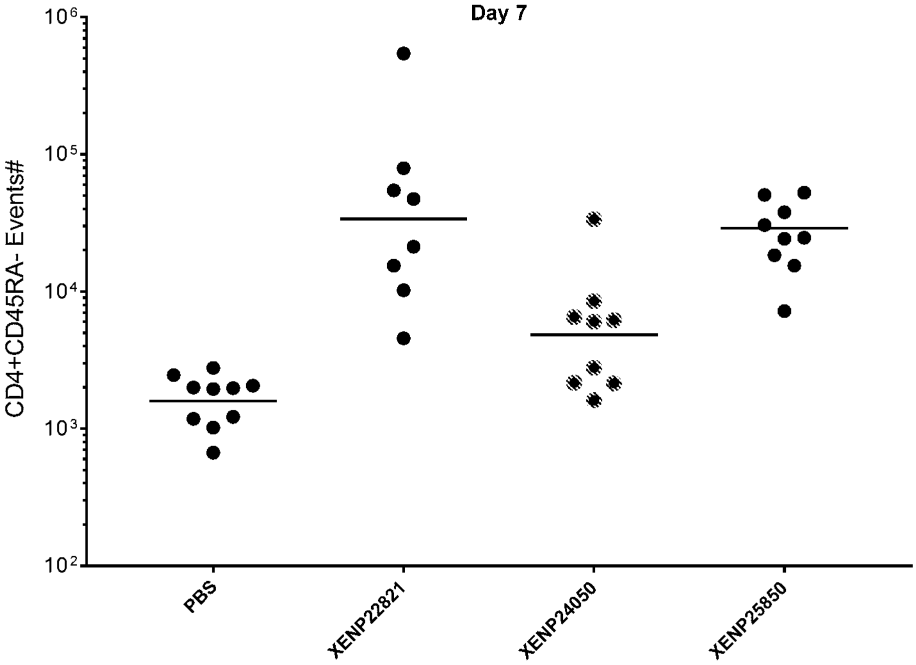


Figure 83C

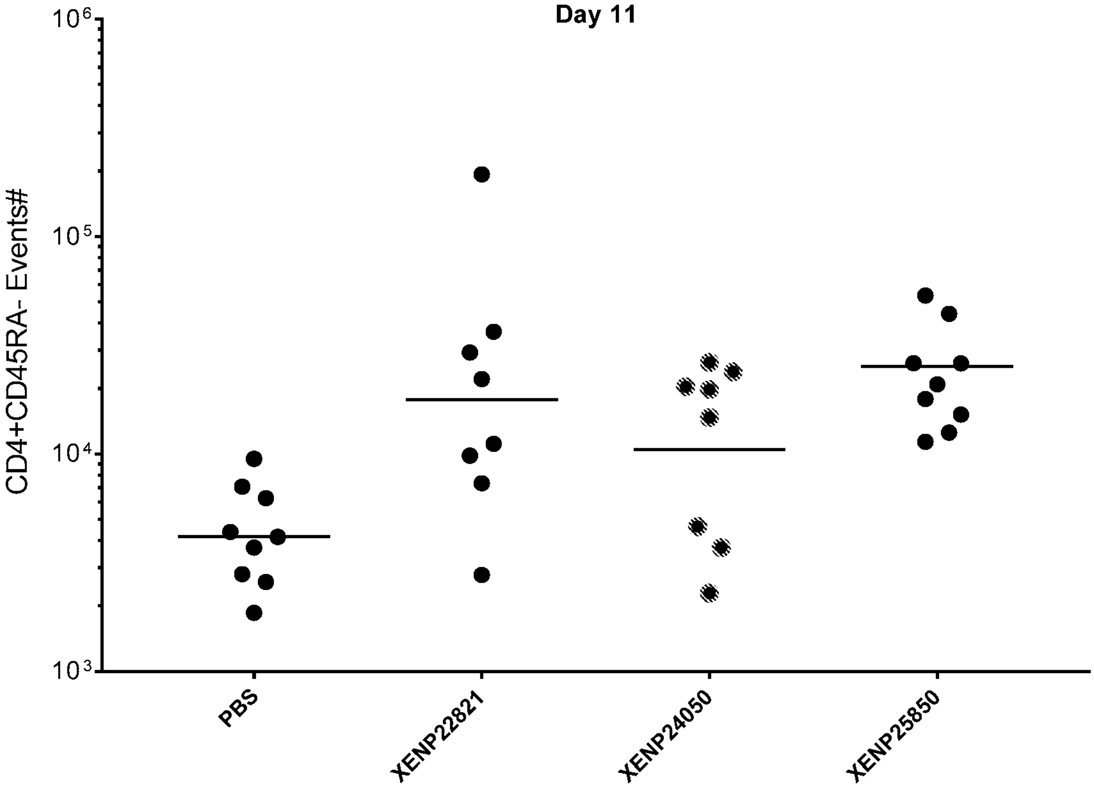

Day 11
CD4+CD45RA- Events#
10^6
10^5
10^4
10^3
PBS
XENP22821
XENP24050
XENP25850

Figure 84A

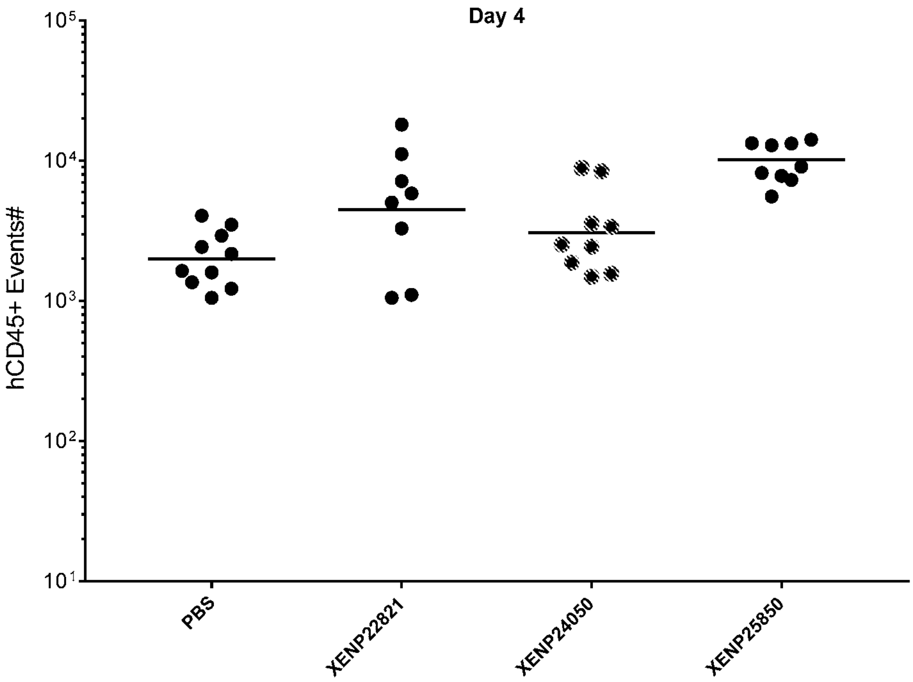


Figure 84B

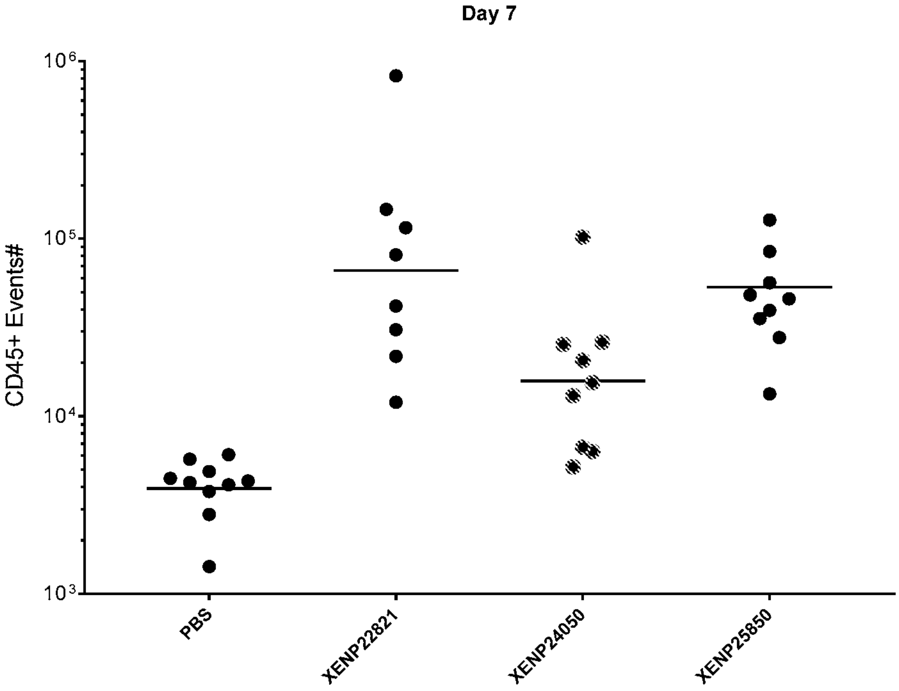


Figure 84C

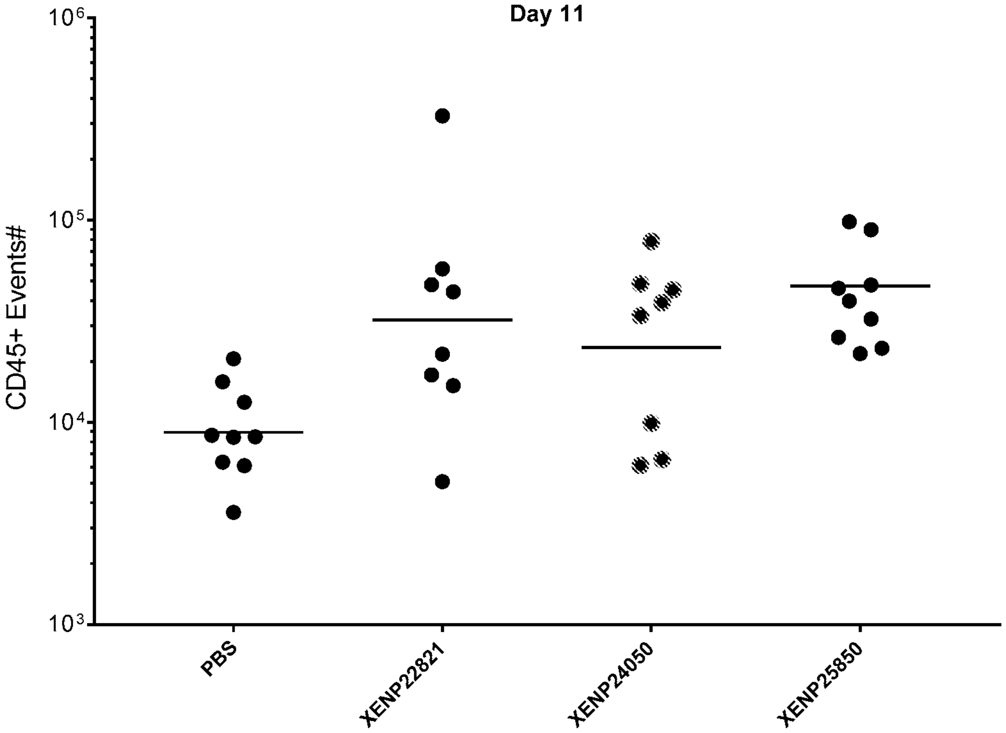

Day 11
CD45+ Events#
10^6
10^5
10^4
10^3
PBS
XENP22821
XENP24050
XENP25850

Figure 85A

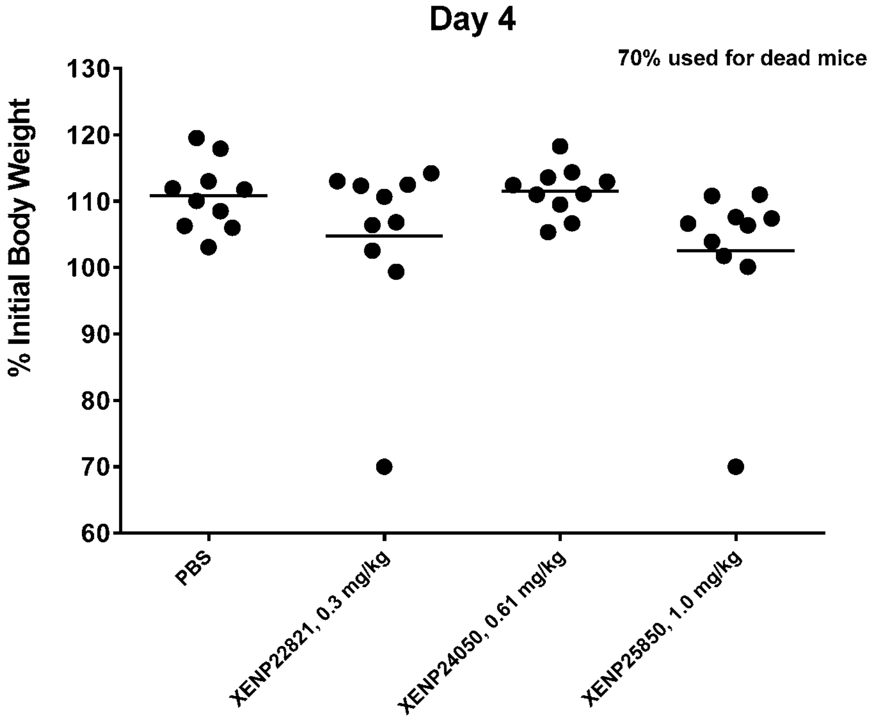


Figure 85B

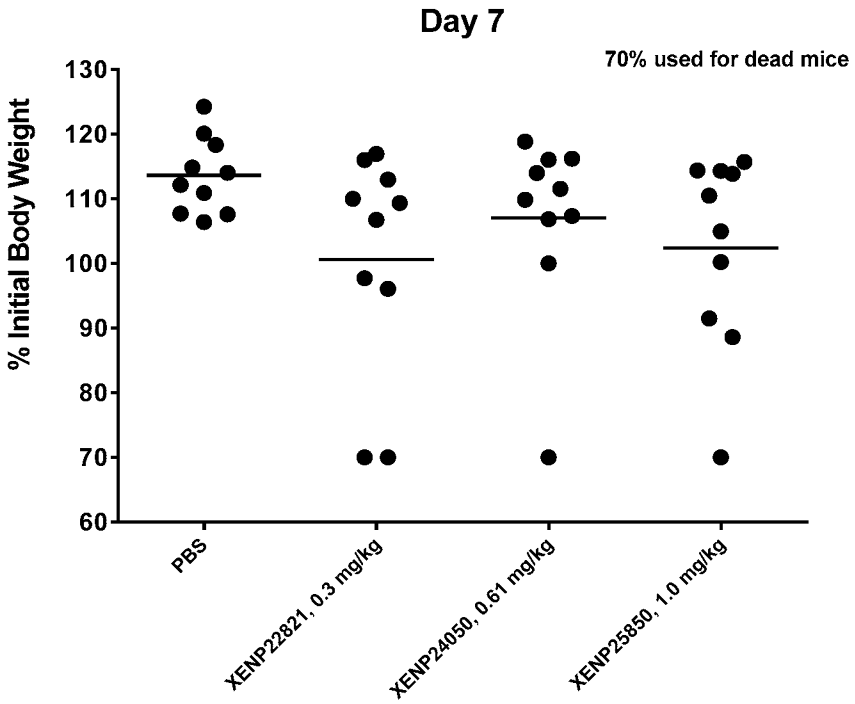


Figure 85C

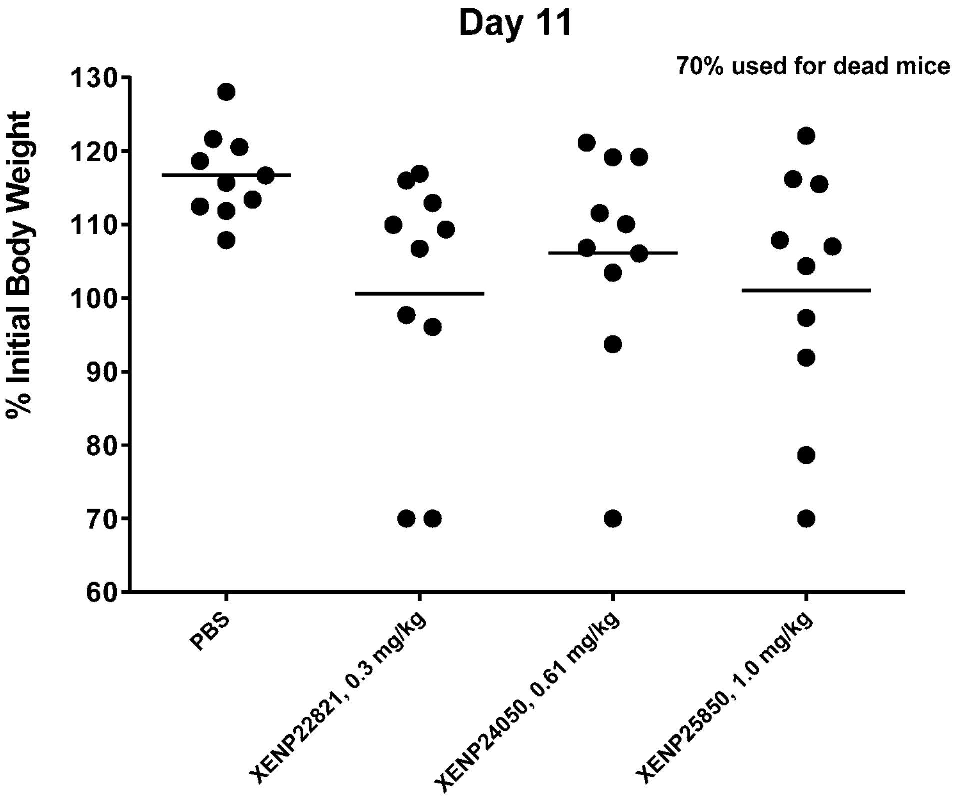

Day 11
70% used for dead mice
% Initial Body Weight
130
120
110
100
90
80
70
60
PBS
XENP22821, 0.3 mg/kg
XENP24050, 0.61 mg/kg
XENP25850, 1.0 mg/kg

Figure 86

XENP016432 Nivolumab_H0L0_IgG1_PVA_/S267K Heavy Chain SEQ ID NO: 412

QVQLVESGGGVVQPGRSLRLDCKASGITFSNSGMHWVRQAPGKGLEWVAVIWYDGSKRYYADSVKGRFTISRDNS
KNTLFLQMNSLRAEDTAVYYCATNDDYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEP
VTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPP
CPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVS
VLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAV
EWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

XENP016432 Nivolumab_H0L0_IgG1_PVA_/S267K Light Chain SEQ ID NO:413

EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASNRATGIPARFSGSGSGTDFTLTI
SSLEPEDFAVYYCQQSSNWPRTFGQGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWK
VDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 87

>XENP025951 empty-Fc-1C11[PD-1]_H3L3_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-IgG1_PVA_/S267K/S364K/E357Q

>XENP025951 empty_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S SEQ ID NO: 414
EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKP
REEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLT
CDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSL
SLSPGK

>XENP025951 1C11[PD-1]_H3L3_IgG1_PVA_/S267K/S364K/E357Q Fab-Fc Heavy Chain SEQ ID NO: 415
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP025951 1C11[PD-1]_H3L3 Light Chain SEQ ID NO: 416
DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 88A

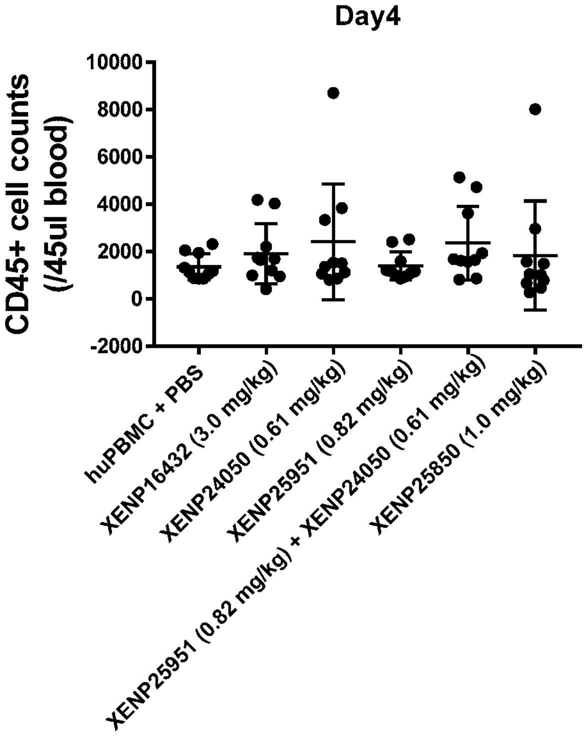


Figure 88B

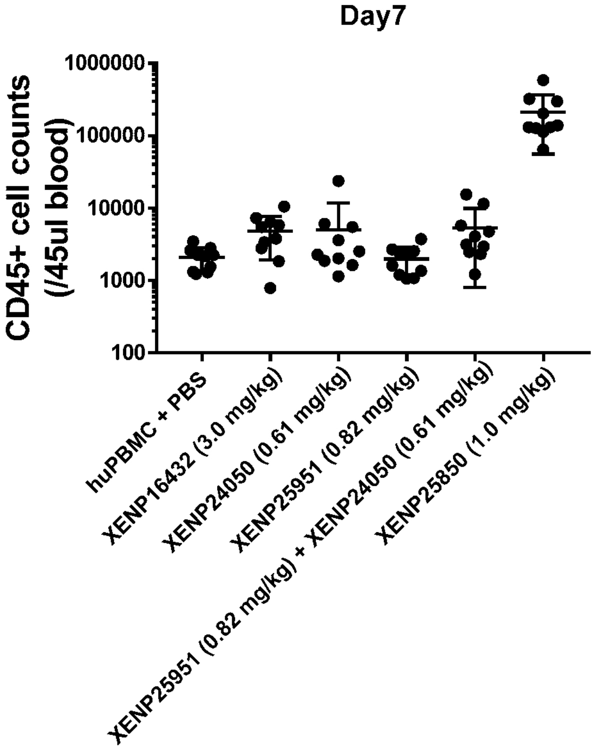


Figure 88C

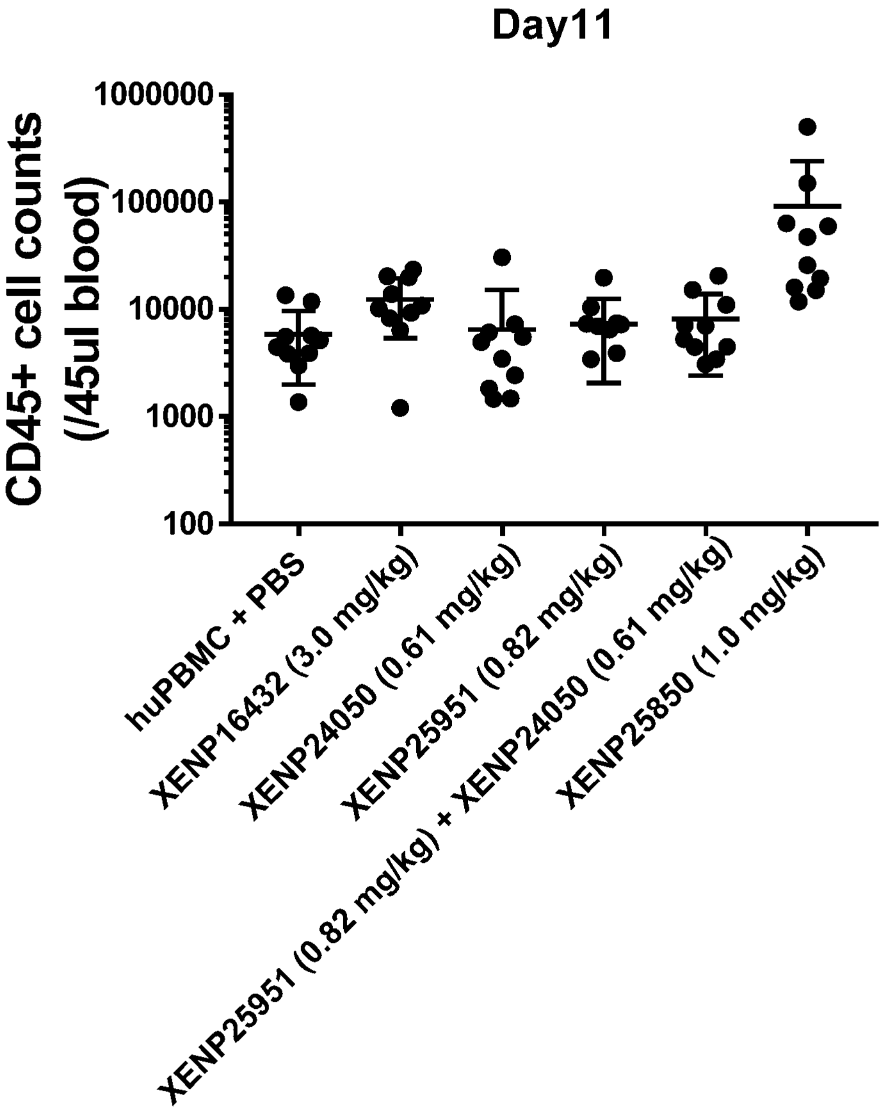

Day11
CD45+ cell counts (/45ul blood)
1000000
100000
10000
1000
100
huPBMC + PBS
XENP16432 (3.0 mg/kg)
XENP24050 (0.61 mg/kg)
XENP25951 (0.82 mg/kg)
XENP25951 (0.82 mg/kg) + XENP24050 (0.61 mg/kg)
XENP25850 (1.0 mg/kg)

Figure 89A

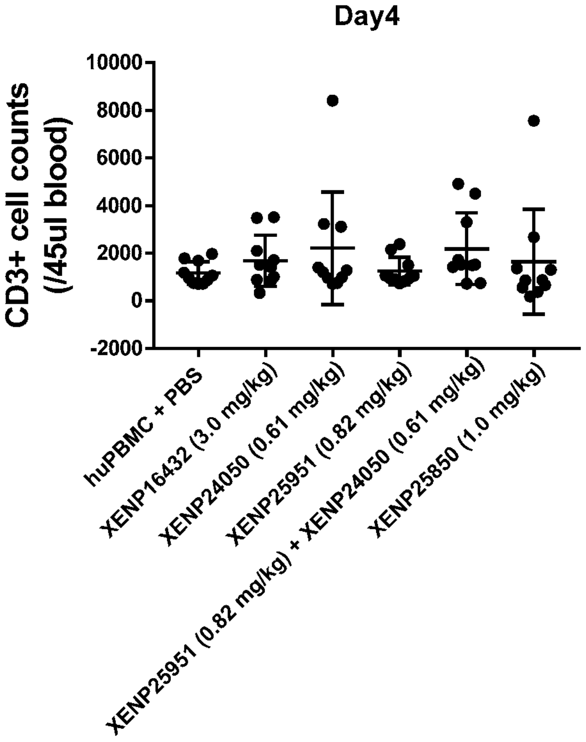


Figure 89B

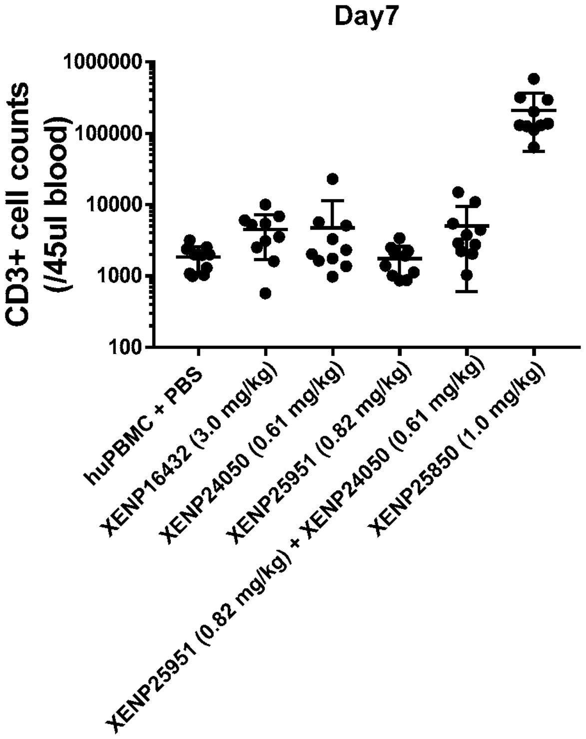


Figure 89C

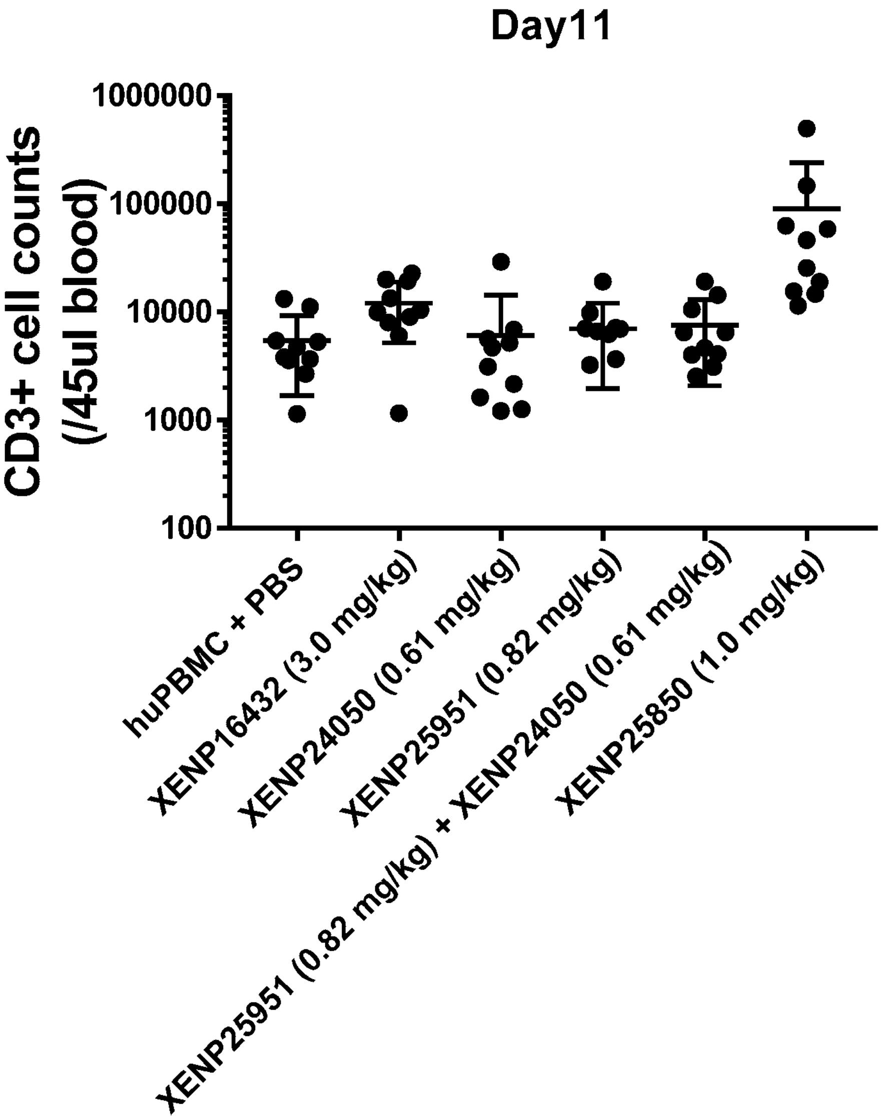

Day11
CD3+ cell counts (/45ul blood)
1000000
100000
10000
1000
100
huPBMC + PBS
XENP16432 (3.0 mg/kg)
XENP24050 (0.61 mg/kg)
XENP25951 (0.82 mg/kg)
XENP25951 (0.82 mg/kg) + XENP24050 (0.61 mg/kg)
XENP25850 (1.0 mg/kg)

Figure 90A

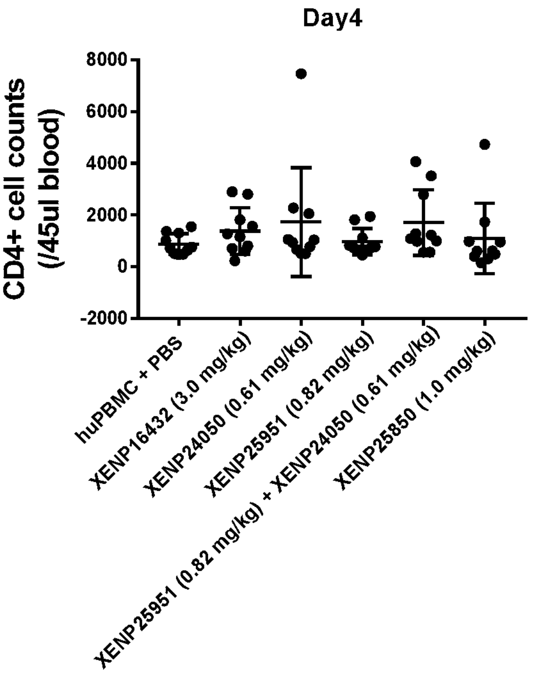


Figure 90B

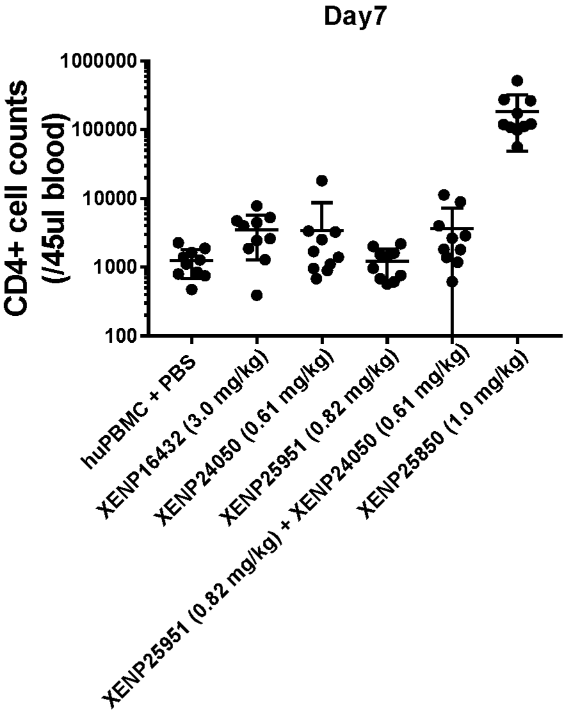


Figure 90C

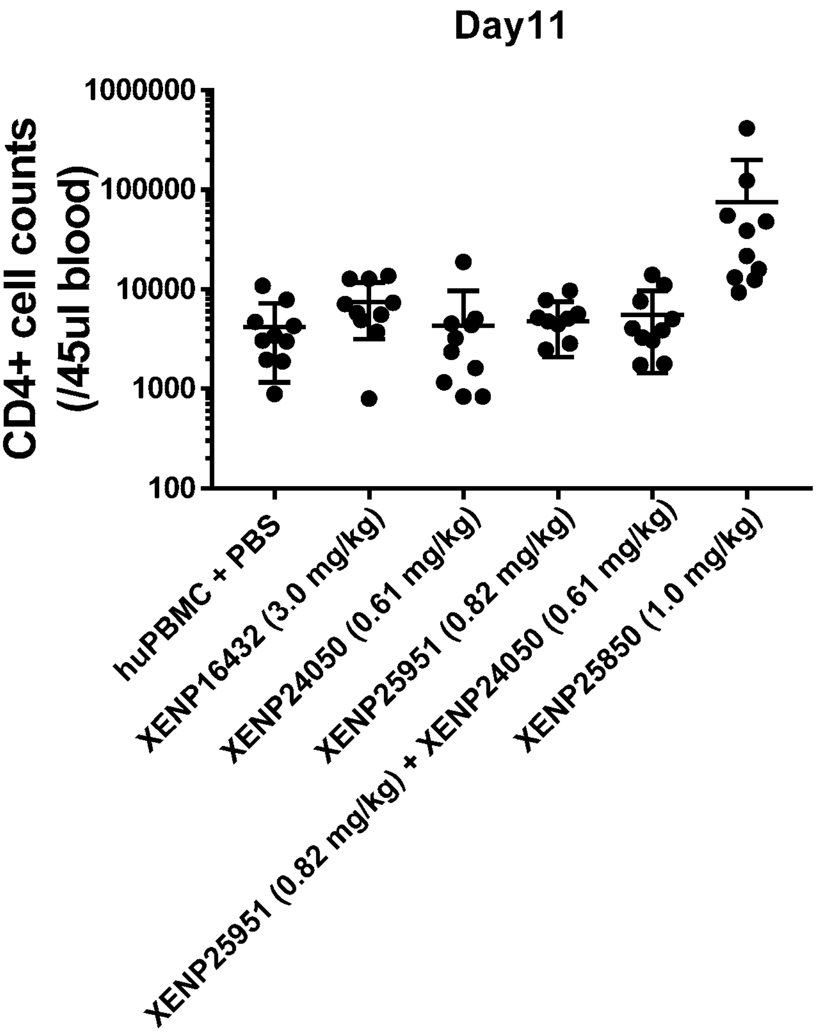

Day11
CD4+ cell counts (/45ul blood)
1000000
100000
10000
1000
100
huPBMC + PBS
XENP16432 (3.0 mg/kg)
XENP24050 (0.61 mg/kg)
XENP25951 (0.82 mg/kg)
XENP25951 (0.82 mg/kg) + XENP24050 (0.61 mg/kg)
XENP25850 (1.0 mg/kg)

Figure 91A

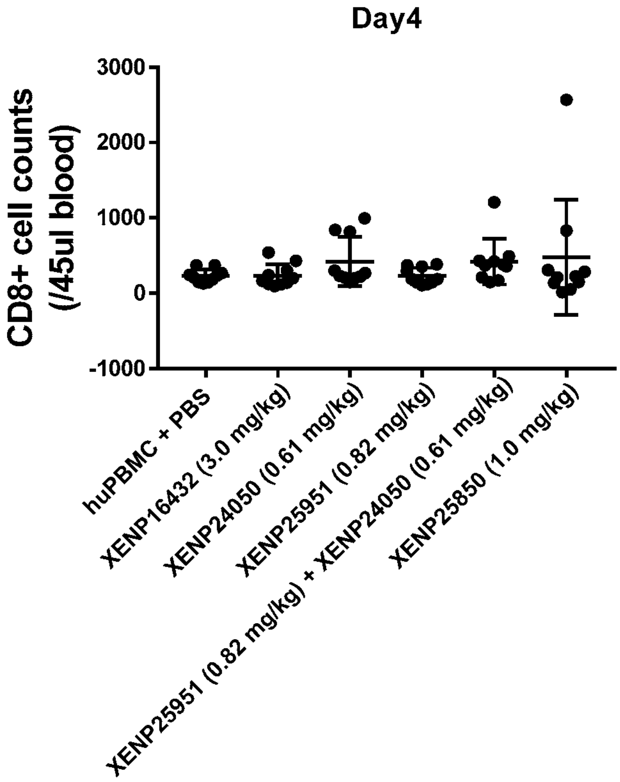


Figure 91B

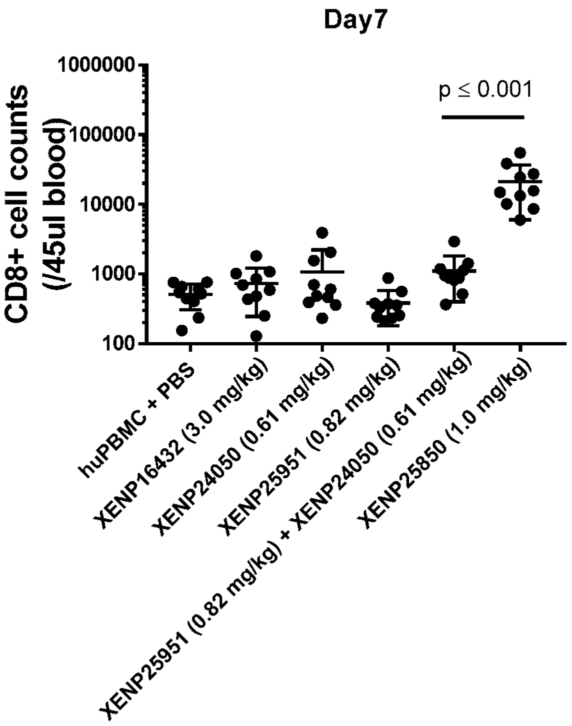


Figure 91C

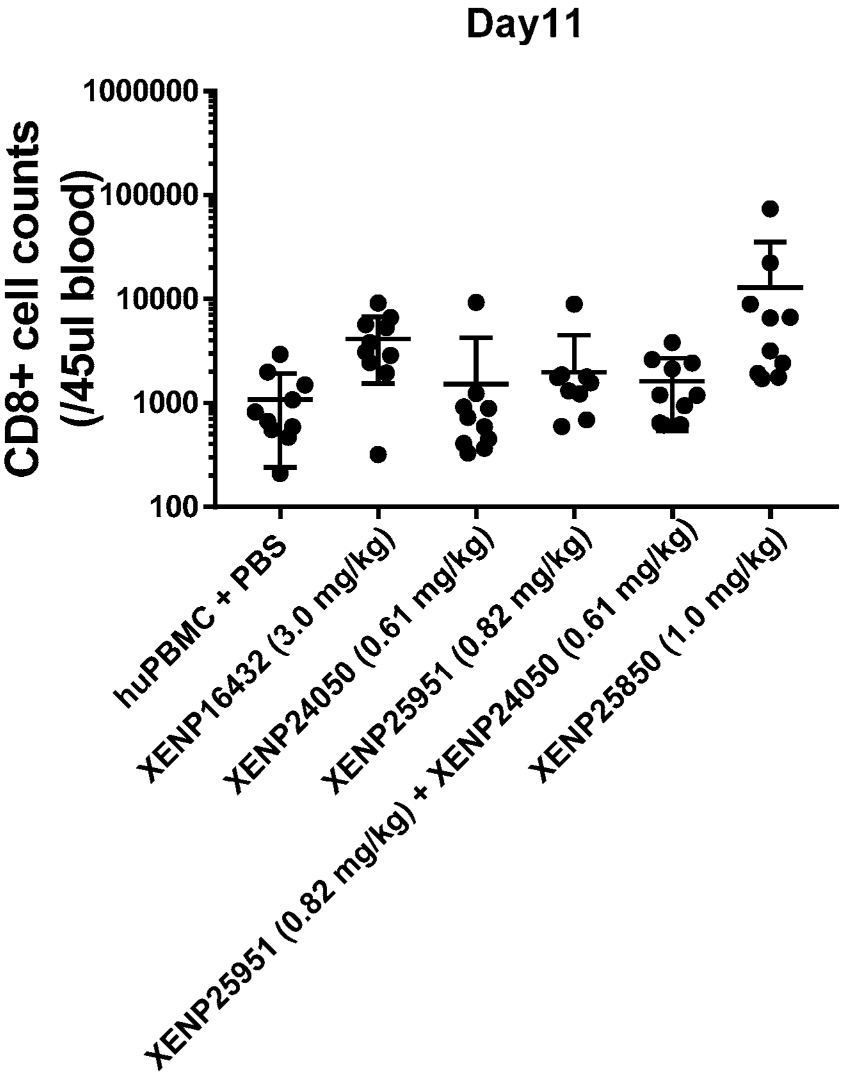

Day11
CD8+ cell counts (/45ul blood)
1000000
100000
10000
1000
100
huPBMC + PBS
XENP16432 (3.0 mg/kg)
XENP24050 (0.61 mg/kg)
XENP25951 (0.82 mg/kg)
XENP25951 (0.82 mg/kg) + XENP24050 (0.61 mg/kg)
XENP25850 (1.0 mg/kg)

Figure 92A

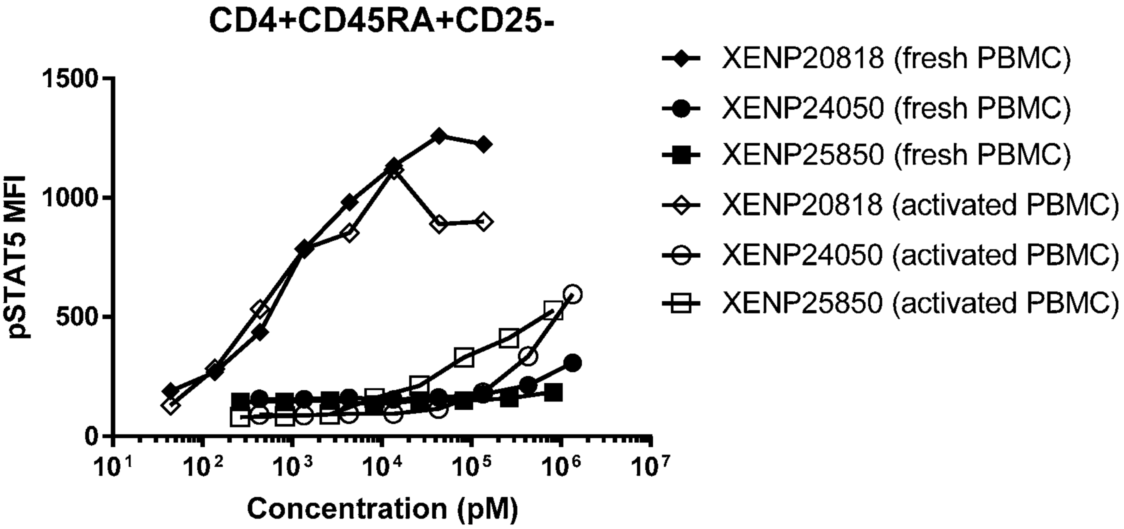


Figure 92B

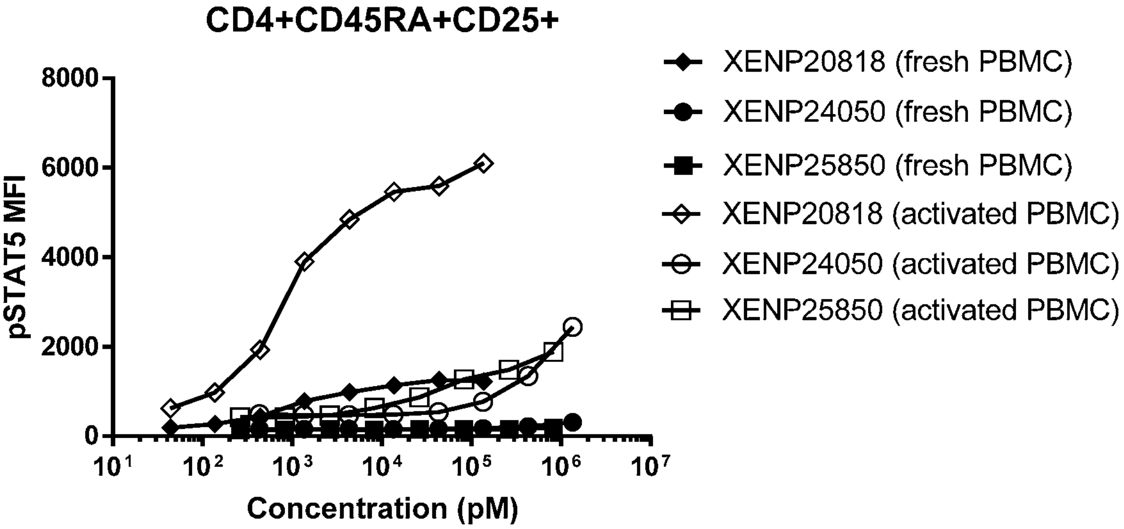


Figure 92C

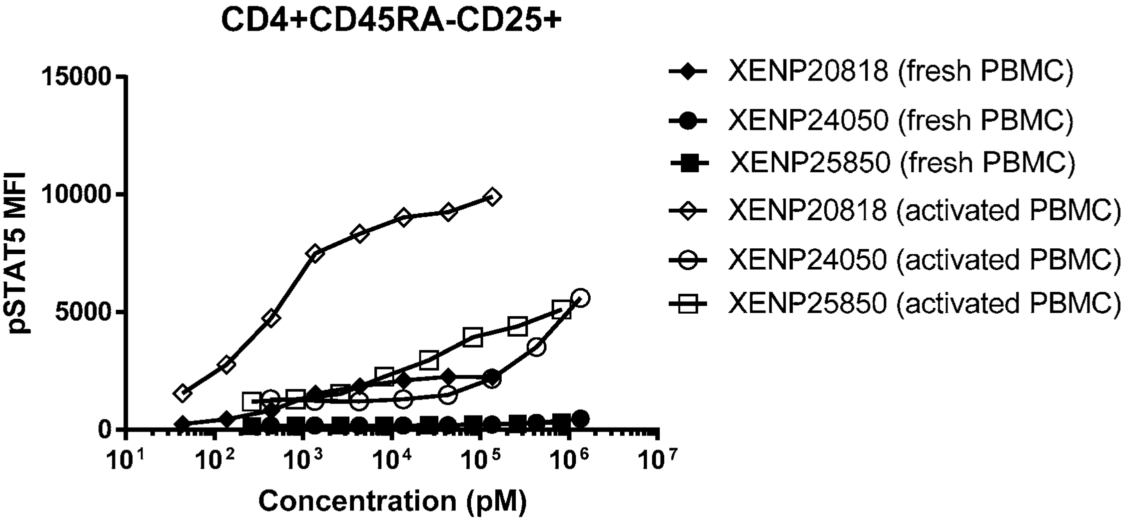


Figure 92D

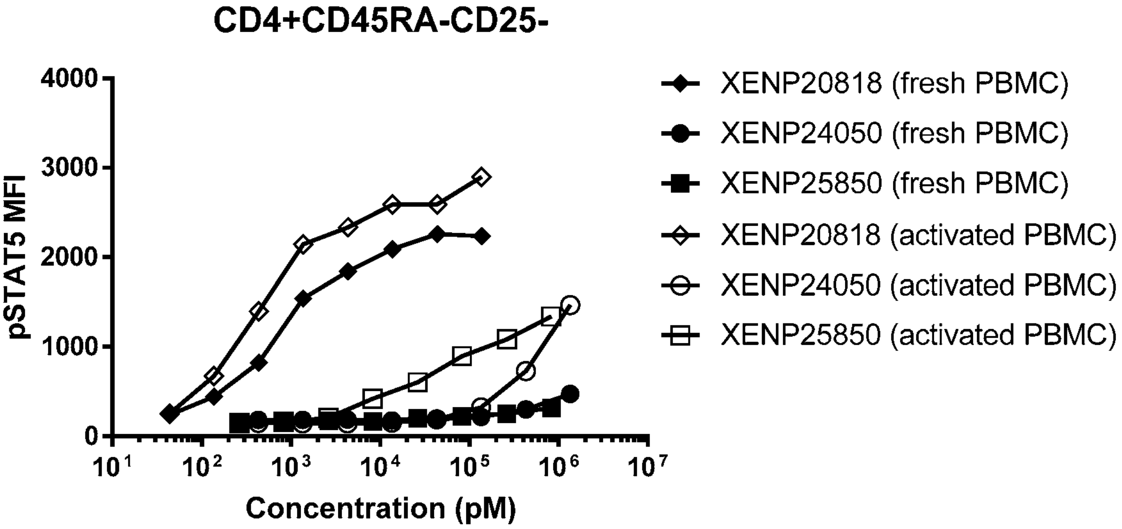


Figure 92E

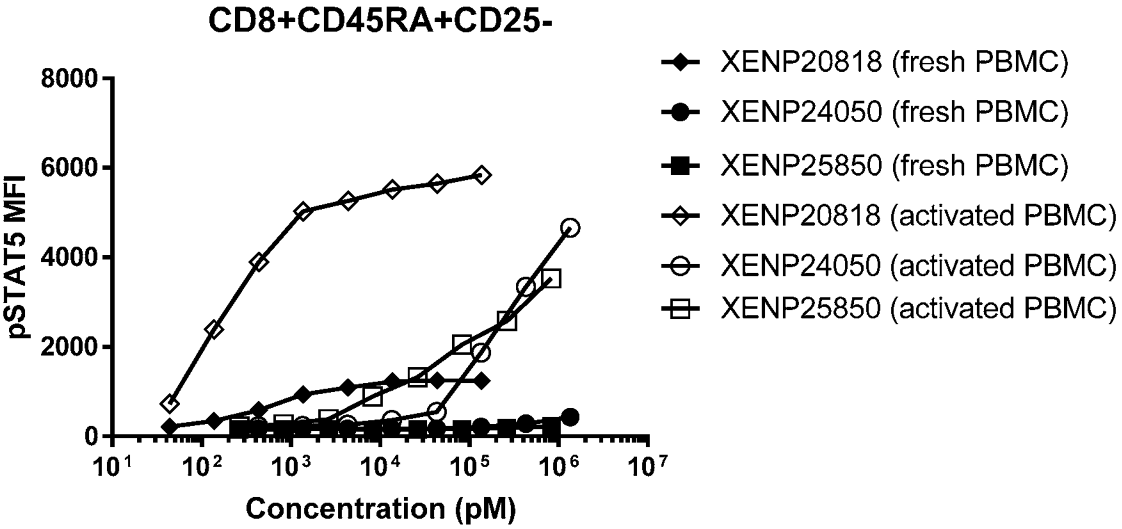


Figure 92F

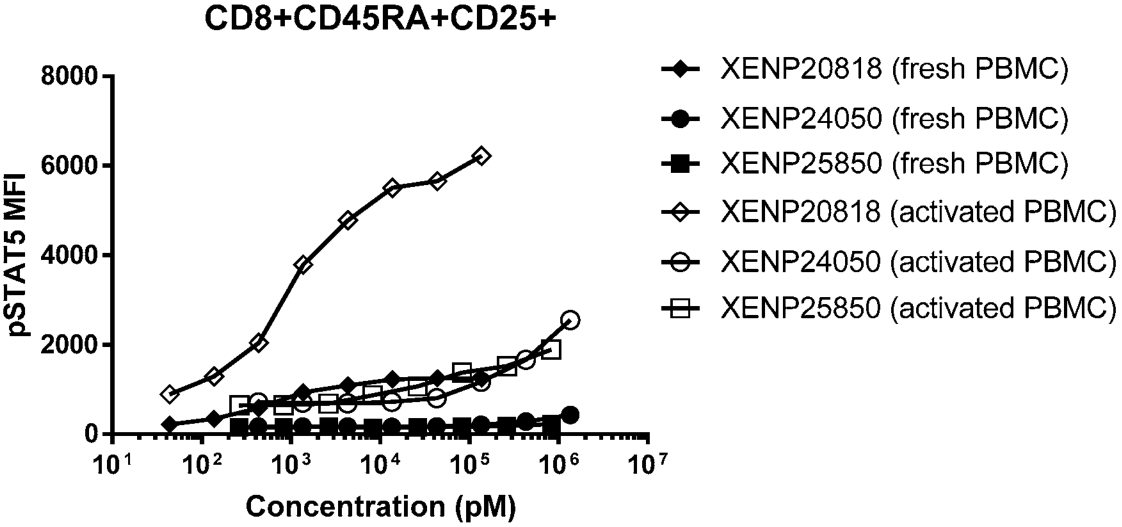


Figure 92G

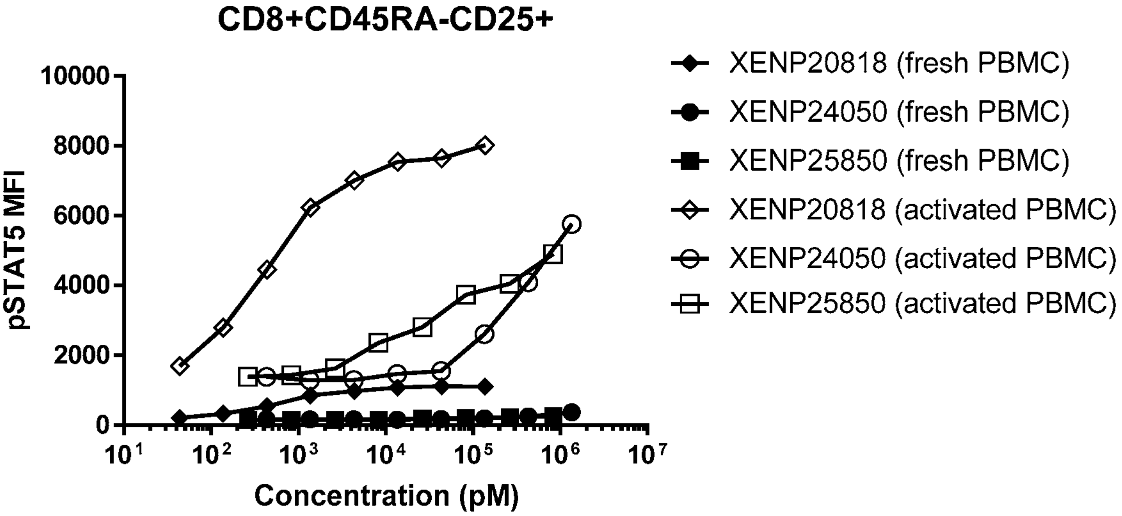


Figure 92H

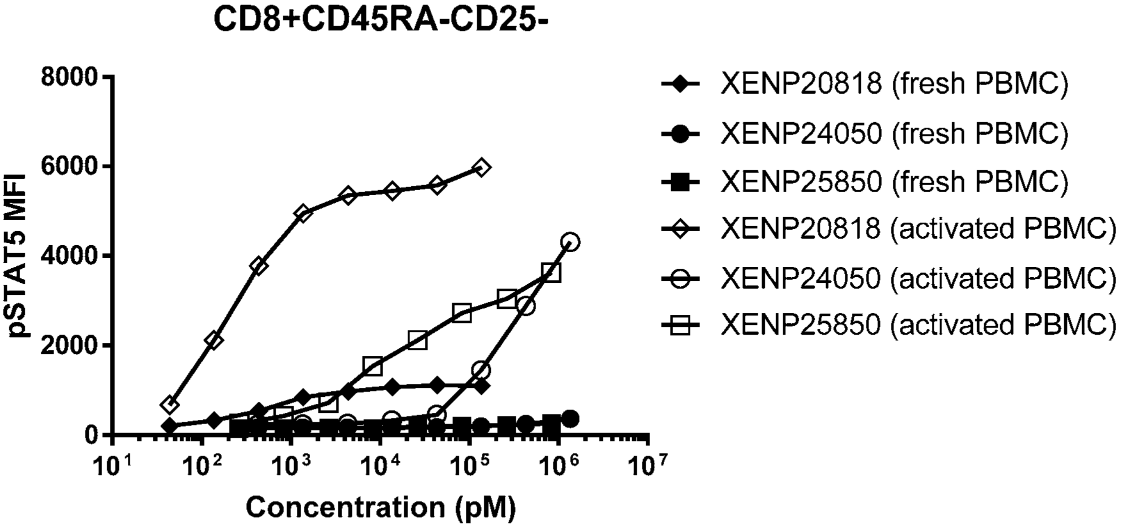


Figure 93A

>XENP022538 1C11[PD-1]_H3L3_scFv(GKPGS)4 (SEQ ID NO: 417)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRfFSGVPDRFSGSGSGTDFTLTISSLQA
EDVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP023577 1C11_H3_L3.1_scFv(GKPGS)4 (SEQ ID NO: 418)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DILMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP023579 1C11_H3_L3.3_scFv(GKPGS)4 (SEQ ID NO: 419)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVVMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP023589 1C11_H3_L3.15_scFv(GKPGS)4 (SEQ ID NO: 420)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
SVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP023601 1C11_H3_L3.23_scFv(GKPGS)4 (SEQ ID NO: 421)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERVTINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP023605 1C11_H3_L3.28_scFv(GKPGS)4 (SEQ ID NO: 422)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCRSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP023609 1C11_H3_L3.32_scFv(GKPGS)4 (SEQ ID NO: 423)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKASQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP023615 1C11_H3_L3.46_scFv(GKPGS)4 (SEQ ID NO: 424)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQPPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP023616 1C11_H3_L3.47_scFv(GKPGS)4 (SEQ ID NO: 425)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQAPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP023624 1C11_H3_L3.57_scFv(GKPGS)4 (SEQ ID NO: 426)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFTGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

Figure 93B

>XENP023626 1C11_H3_L3.59_scFv(GKPGS)4 (SEQ ID NO: 427)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISRLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP023628 1C11_H3_L3.62_scFv(GKPGS)4 (SEQ ID NO: 428)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSMQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP023629 1C11_H3_L3.63_scFv(GKPGS)4 (SEQ ID NO: 429)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSVQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP023633 1C11_H3_L3.69_scFv(GKPGS)4 (SEQ ID NO: 430)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DAAVYYCFQGSHVPNTFGGGTKVEIK

>XENP023636 1C11_H3_L3.73_scFv(GKPGS)4 (SEQ ID NO: 431)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVATYYCFQGSHVPNTFGGGTKVEIK

>XENP023640 1C11_H3_L3.81_scFv(GKPGS)4 (SEQ ID NO: 432)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGQGTKVEIK

>XENP023755 1C11_H3.1_L3_scFv(GKPGS)4 (SEQ ID NO: 433)
QVQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP023758 1C11_H3.5_L3_scFv(GKPGS)4 (SEQ ID NO: 434)
QIQLVQSGAELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP023760 1C11_H3.7_L3_scFv(GKPGS)4 (SEQ ID NO: 435)
QIQLVQSGPELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP023765 1C11_H3.18_L3_scFv(GKPGS)4 (SEQ ID NO: 436)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVKQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

Figure 93C

>XENP023770 1C11_H3.25_L3_scFv(GKPGS)4 (SEQ ID NO: 437)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTNTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP023776 1C11_H3.35_L3_scFv(GKPGS)4 (SEQ ID NO: 438)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADKFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP023779 1C11_H3.41_L3_scFv(GKPGS)4 (SEQ ID NO: 439)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFKGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP023780 1C11_H3.42_L3_scFv(GKPGS)4 (SEQ ID NO: 440)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFQGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP023781 1C11_H3.43_L3_scFv(GKPGS)4 (SEQ ID NO: 441)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRVVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP023786 1C11_H3.50_L3_scFv(GKPGS)4 (SEQ ID NO: 442)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSADTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP023793 1C11_H3.59_L3_scFv(GKPGS)4 (SEQ ID NO: 443)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
QSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP023796 1C11_H3.62_L3_scFv(GKPGS)4 (SEQ ID NO: 444)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTIYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP023811 1C11_H3.74_L3_scFv(GKPGS)4 (SEQ ID NO: 445)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

Figure 93D

>XENP024201 1C11_H3_L3.113_scFv(GKPGS)4 (SEQ ID NO: 446)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGKSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024207 1C11_H3_L3.122_scFv(GKPGS)4 (SEQ ID NO: 447)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGIPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024208 1C11_H3_L3.124_scFv(GKPGS)4 (SEQ ID NO: 448)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPARFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024209 1C11_H3_L3.125_scFv(GKPGS)4 (SEQ ID NO: 449)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSVEAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024210 1C11_H3_L3.132_scFv(GKPGS)4 (SEQ ID NO: 450)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGPGTKVEIK

>XENP024211 1C11_H3.78_L3_scFv(GKPGS)4 (SEQ ID NO: 451)
QIQLVQSGPELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTNTGEPTYADGFTGRFVFSVDTS
QSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024212 1C11_H3.80_L3_scFv(GKPGS)4 (SEQ ID NO: 452)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTNTGEPTYADGFTGRFVFSVDTS
QSTAYLQISSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024213 1C11_H3.81_L3_scFv(GKPGS)4 (SEQ ID NO: 453)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADKFKGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024214 1C11_H3.82_L3_scFv(GKPGS)4 (SEQ ID NO: 454)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADKFQGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024215 1C11_H3.83_L3_scFv(GKPGS)4 (SEQ ID NO: 455)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTNTGEPTYADGFTGRFVFSVDTS
QSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

Figure 93E

>XENP024216 1C11_H3.84_L3_scFv(GKPGS)4 (SEQ ID NO: 456)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADKFKGRFVFSLDTS
QSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024217 1C11_H3.85_L3_scFv(GKPGS)4 (SEQ ID NO: 457)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADKFQGRFVFSLDTS
QSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024218 1C11_H3.86_L3_scFv(GKPGS)4 (SEQ ID NO: 458)
EIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024221 1C11_H3.90_L3_scFv(GKPGS)4 (SEQ ID NO: 459)
QIQLVQSGSVLKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024222 1C11_H3.91_L3_scFv(GKPGS)4 (SEQ ID NO: 460)
QIQLVQSGSELVKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024226 1C11_H3.95_L3_scFv(GKPGS)4 (SEQ ID NO: 461)
QIQLVQSGSELKKPGGSVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024227 1C11_H3.96_L3_scFv(GKPGS)4 (SEQ ID NO: 462)
QIQLVQSGSELKKPGQSVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024228 1C11_H3.97_L3_scFv(GKPGS)4 (SEQ ID NO: 463)
QIQLVQSGSELKKPGESVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024247 1C11_H3.120_L3_scFv(GKPGS)4 (SEQ ID NO: 464)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGINWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024250 1C11_H3.125_L3_scFv(GKPGS)4 (SEQ ID NO: 465)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQPPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

Figure 93F

>XENP024254 1C11_H3.129_L3_scFv(GKPGS)4 (SEQ ID NO: 466)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWIGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024256 1C11_H3.134_L3_scFv(GKPGS)4 (SEQ ID NO: 467)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTKTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024263 1C11_H3.143_L3_scFv(GKPGS)4 (SEQ ID NO: 468)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPYYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024266 1C11_H3.146_L3_scFv(GKPGS)4 (SEQ ID NO: 469)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYAPGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024267 1C11_H3.147_L3_scFv(GKPGS)4 (SEQ ID NO: 470)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYATGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024268 1C11_H3.148_L3_scFv(GKPGS)4 (SEQ ID NO: 471)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYAQKFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024270 1C11_H3.150_L3_scFv(GKPGS)4 (SEQ ID NO: 472)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTERFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024274 1C11_H3.154_L3_scFv(GKPGS)4 (SEQ ID NO: 473)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSIDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024278 1C11_H3.158_L3_scFv(GKPGS)4 (SEQ ID NO: 474)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VNTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024279 1C11_H3.159_L3_scFv(GKPGS)4 (SEQ ID NO: 475)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VDTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

Figure 93G

>XENP024287 1C11_H3.168_L3_scFv(GKPGS)4 (SEQ ID NO: 476)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQINSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024291 1C11_H3.172_L3_scFv(GKPGS)4 (SEQ ID NO: 477)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKPEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024372 1C11_H3_L3.86_scFv(GKPGS)4 (SEQ ID NO: 478)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFTGVPDRFSGSGSGTDFTLTISSVQAE
DVATYYCFQGSHVPNTFGQGTKVEIK

>XENP024373 1C11_H3_L3.87_scFv(GKPGS)4 (SEQ ID NO: 479)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVVMTQSPDSL
AVSLGERVTINCKASQSIVHSNGNTYLEWYQQKPGQPPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024374 1C11_H3_L3.90_scFv(GKPGS)4 (SEQ ID NO: 480)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVVMTQSPDSL
AVSLGERATINCKASQSIVHSNGNTYLEWYQQKPGQPPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSVQAE
DAATYYCFQGSHVPNTFGQGTKVEIK

>XENP024375 1C11_H3_L3.92_scFv(GKPGS)4 (SEQ ID NO: 481)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DIVMTQSPDSL
AVSLGERVTINCKASQSIVHSNGNTYLEWYQQKPGQPPKLLIYKVSNRFTGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024376 1C11_H3_L3.94_scFv(GKPGS)4 (SEQ ID NO: 482)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DILMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFTGVPDRFSGSGSGTDFTLTISSVQAE
DAATYYCFQGSHVPNTFGQGTKVEIK

>XENP024377 1C11_H3_L3.96_scFv(GKPGS)4 (SEQ ID NO: 483)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DIVMTQSPDSL
AVSLGERATINCKASQSIVHSNGNTYLEWYQQKPGQPPKLLIYKVSNRFTGVPDRFSGSGSGTDFTLTISSVQAE
DAATYYCFQGSHVPNTFGQGTKVEIK

>XENP024378 1C11_H3_L3.105_scFv(GKPGS)4 (SEQ ID NO: 484)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
PVTPGEPATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024379 1C11_H3_L3.129_scFv(GKPGS)4 (SEQ ID NO: 485)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTINSLQAE
DAATYYCHQGSHVPNTFGGGTKVEIK

Figure 93H

>XENP024380 1C11_H3.176_L3.92_scFv(GKPGS)4 (SEQ ID NO: 486)
QIQLVQSGPELKKPGASVKVSCKASGYTFTHYGMNWVKQAPGQGLEWMGWINTNTGEPTYADKFTGRVVFSLDTS
QSTIYLQISSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DIVMTQSPDSL
AVSLGERVTINCKASQSIVHSNGNTYLEWYQQKPGQPPKLLIYKVSNRFTGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024381 1C11_H3.176_L3.94_scFv(GKPGS)4 (SEQ ID NO: 487)
QIQLVQSGPELKKPGASVKVSCKASGYTFTHYGMNWVKQAPGQGLEWMGWINTNTGEPTYADKFTGRVVFSLDTS
QSTIYLQISSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DILMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFTGVPDRFSGSGSGTDFTLTISSVQAE
DAATYYCFQGSHVPNTFGQGTKVEIK

>XENP024382 1C11_H3.176_L3.96_scFv(GKPGS)4 (SEQ ID NO: 488)
QIQLVQSGPELKKPGASVKVSCKASGYTFTHYGMNWVKQAPGQGLEWMGWINTNTGEPTYADKFTGRVVFSLDTS
QSTIYLQISSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DIVMTQSPDSL
AVSLGERATINCKASQSIVHSNGNTYLEWYQQKPGQPPKLLIYKVSNRFTGVPDRFSGSGSGTDFTLTISSVQAE
DAATYYCFQGSHVPNTFGQGTKVEIK

>XENP024414 1C11[PD-1]_H3_L3.133_scFv(GKPGS)4 (SEQ ID NO: 489)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVVMTQSPDSL
AVSLGERVTINCKASQSIVHSNGNTYLEWYQQKPGQPPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSVQAE
DAATYYCFQGSHVPNTFGQGTKVEIK

>XENP024415 1C11[PD-1]_H3_L3.134_scFv(GKPGS)4 (SEQ ID NO: 490)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVVMTQSPDSL
AVSLGERVTINCKASQSIVHSNGNTYLEWYQQKPGQPPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSVEAE
DAATYYCFQGSHVPNTFGQGTKVEIK

>XENP024416 1C11[PD-1]_H3_L3.135_scFv(GKPGS)4 (SEQ ID NO: 491)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVVMTQSPDSL
AVSLGERVTINCKASQSIVHSNGNTYLEWYQQKPGQPPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSMQAE
DAATYYCFQGSHVPNTFGQGTKVEIK

>XENP024417 1C11[PD-1]_H3_L3.136_scFv(GKPGS)4 (SEQ ID NO: 492)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVVMTQSPDSL
AVSLGERITINCKASQSIVHSNGNTYLEWYQQKPGQPPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSMQAE
DAATYYCFQGSHVPNTFGQGTKVEIK

>XENP024418 1C11[PD-1]_H3_L3.137_scFv(GKPGS)4 (SEQ ID NO: 493)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVVMTQSPDSL
AVSLGERITINCKASQSIVHSNGNTYLEWYQQKPGQPPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSVQAE
DAATYYCFQGSHVPNTFGQGTKVEIK

>XENP024419 1C11[PD-1]_H3_L3.138_scFv(GKPGS)4 (SEQ ID NO: 494)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVVMTQSPDSL
AVSLGERITINCKASQSIVHSNGNTYLEWYQQKPGQPPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSVEAE
DAATYYCFQGSHVPNTFGQGTKVEIK

Figure 93I

>XENP024420 1C11[PD-1]_H3_L3.139_scFv(GKPGS)4 (SEQ ID NO: 495)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVVMTQSPDSL
AVSLGERATINCKASQSIVHSNGNTYLEWYQQKPGQPPKLLIYKVSNRFSGIPDRFSGSGSGTDFTLTISSVQAE
DAATYYCFQGSHVPNTFGQGTKVEIK

>XENP024421 1C11[PD-1]_H3_L3.140_scFv(GKPGS)4 (SEQ ID NO: 496)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DIVMTQSPDSL
AVSLGERATINCKASQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSVEAE
DVATYYCFQGSHVPNTFGQGTKVEIK

>XENP024422 1C11[PD-1]_H3_L3.141_scFv(GKPGS)4 (SEQ ID NO: 497)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DIVMTQSPDSL
AVSLGERATINCKASQSIVHSNGNTYLEWYQQKPGQPPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSVEAE
DVATYYCFQGSHVPNTFGQGTKVEIK

>XENP024423 1C11[PD-1]_H3_L3.142_scFv(GKPGS)4 (SEQ ID NO: 498)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DIVMTQSPDSL
AVSLGERATINCKASQSIVHSNGNTYLEWYQQKPGQAPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSVEAE
DVATYYCFQGSHVPNTFGQGTKVEIK

>XENP024424 1C11[PD-1]_H3.176_L3_scFv(GKPGS)4 (SEQ ID NO: 499)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYAPGFKGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024425 1C11[PD-1]_H3.177_L3_scFv(GKPGS)4 (SEQ ID NO: 500)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYAPKFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024426 1C11[PD-1]_H3.178_L3_scFv(GKPGS)4 (SEQ ID NO: 501)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYAPGFKERFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024427 1C11[PD-1]_H3.179_L3_scFv(GKPGS)4 (SEQ ID NO: 502)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYAPKFTERFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024428 1C11[PD-1]_H3.180_L3_scFv(GKPGS)4 (SEQ ID NO: 503)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGINWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSVDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

Figure 93J

>XENP024429 1C11[PD-1]_H3.181_L3_scFv(GKPGS)4 (SEQ ID NO: 504)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGINWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSIDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024430 1C11[PD-1]_H3.182_L3_scFv(GKPGS)4 (SEQ ID NO: 505)
QIQLVQSGSELVKPGESVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024431 1C11[PD-1]_H3.183_L3_scFv(GKPGS)4 (SEQ ID NO: 506)
QIQLVQSGSVLKKPGESVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024432 1C11[PD-1]_H3.184_L3_scFv(GKPGS)4 (SEQ ID NO: 507)
QIQLVQSGSVLVKPGESVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024433 1C11[PD-1]_H3.185_L3_scFv(GKPGS)4 (SEQ ID NO: 508)
EVQLVQSGSELVKPGESVKVSCKASGYTFTHYGINWVRQPPGQGLEWIGWINTYTGEPYYAPKFTERFVFSLDTS
QDTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024434 1C11[PD-1]_H3.186_L3_scFv(GKPGS)4 (SEQ ID NO: 509)
EVQLVQSGSELVKPGESVKVSCKASGYTFTHYGINWVRQPPGQGLEWMGWINTYTGEPYYAPGFTERFVFSLDTS
VDTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024435 1C11[PD-1]_H3.187_L3_scFv(GKPGS)4 (SEQ ID NO: 510)
QVQLVQSGSELVKPGESVKVSCKASGYTFTHYGINWVRQPPGQGLEWMGWINTYTGEPYYAPGFTERFVFSLDTS
QSTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024436 1C11[PD-1]_H3.188_L3_scFv(GKPGS)4 (SEQ ID NO: 511)
QVQLVQSGSELKKPGESVKVSCKASGYTFTHYGINWVRQPPGQGLEWIGWINTYTGEPYYAPGFTGRFVFSLDTS
QSTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024437 1C11[PD-1]_H3.189_L3_scFv(GKPGS)4 (SEQ ID NO: 512)
QVQLVQSGSELKKPGASVKVSCKASGYTFTHYGINWVRQPPGQGLEWIGWINTYTGEPYYAPKFTGRFVFSLDTS
VSTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

Figure 93K

>XENP024438 1C11[PD-1]_H3.190_L3_scFv(GKPGS)4 (SEQ ID NO: 513)
QVQLVQSGSVLKKPGGSVKVSCKASGYTFTHYGINWVRQPPGQGLEWIGWINTYTGEPYYAPGFTGRFVFSLDTS
QSTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024439 1C11[PD-1]_H3.191_L3_scFv(GKPGS)4 (SEQ ID NO: 514)
QVQLVQSGSELVKPGESVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYAPGFTGRFVFSLDTS
QSTAYLQINSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024440 1C11[PD-1]_H3.192_L3_scFv(GKPGS)4 (SEQ ID NO: 515)
EVQLVQSGSVLKKPGESVKVSCKASGYTFTHYGINWVRQAPGQGLEWMGWINTYTGEPTYADGFTERFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024441 1C11[PD-1]_H3.193_L3_scFv(GKPGS)4 (SEQ ID NO: 516)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQPPGQGLEWIGWINTYTGEPTYAPGFTERFVFSLDTS
QSTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024442 1C11[PD-1]_H3.194_L3_scFv(GKPGS)4 (SEQ ID NO: 517)
EIQLVQSGSVLKKPGASVKVSCKASGYTFTHYGINWVRQAPGQGLEWIGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024443 1C11[PD-1]_H3.195_L3_scFv(GKPGS)4 (SEQ ID NO: 518)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQPPGQGLEWMGWINTYTGEPYYADGFTGRFVFSLDTS
VDTAYLQINSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024827 1C11_H3.196_L3_scFv(GKPGS)4 (SEQ ID NO: 519)
EVQLVQSGSELKKPGESVKVSCKASGYTFTHYGINWVRQPPGQGLEWIGWINTYTGEPYYAPGFTGRFVFSLDTS
QSTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024828 1C11_H3.197_L3_scFv(GKPGS)4 (SEQ ID NO: 520)
QVQLVQSGSELKKPGASVKVSCKASGYTFTHYGINWVRQPPGQGLEWIGWINTYTGEPYYAPGFTGRFVFSLDTS
QSTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024829 1C11_H3.198_L3_scFv(GKPGS)4 (SEQ ID NO: 521)
QVQLVQSGSELKKPGESVKVSCKASGYTFTHYGINWVRQPPGQGLEWIGWINTYTGEPYYADGFTGRFVFSLDTS
QSTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

Figure 93L

>XENP024830 1C11_H3.199_L3_scFv(GKPGS)4 (SEQ ID NO: 522)
QVQLVQSGSELKKPGESVKVSCKASGYTFTHYGMNWVRQPPGQGLEWIGWINTYTGEPYYAPGFTGRFVFSLDTS
QSTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024831 1C11_H3.200_L3_scFv(GKPGS)4 (SEQ ID NO: 523)
QVQLVQSGSELKKPGESVKVSCKASGYTFTHYGINWVRQPPGQGLEWIGWINTYTGEPYYAPGFTGRFVFSLDTS
QSTAYLQINSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024832 1C11_H3.201_L3_scFv(GKPGS)4 (SEQ ID NO: 524)
QVQLVQSGSELKKPGESVKVSCKASGYTFTHYGINWVRQPPGQGLEWIGWINTYTGEPYYAPGFTGRFVFSIDTS
QSTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024833 1C11_H3.202_L3_scFv(GKPGS)4 (SEQ ID NO: 525)
QVQLVQSGSELKKPGESVKVSCKASGYTFTHYGINWVRQAPGQGLEWIGWINTYTGEPYYAPGFTGRFVFSLDTS
QSTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024834 1C11_H3.203_L3_scFv(GKPGS)4 (SEQ ID NO: 526)
QVQLVQSGSELKKPGESVKVSCKASGYTFTHYGINWVRQPPGQGLEWIGWINTYTGEPYYAPGFTERFVFSLDTS
QSTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024835 1C11_H3.204_L3_scFv(GKPGS)4 (SEQ ID NO: 527)
QVQLVQSGSELKKPGESVKVSCKASGYTFTHYGINWVRQPPGQGLEWIGWINTYTGEPYYAPGFQGRFVFSLDTS
QSTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024836 1C11_H3.205_L3_scFv(GKPGS)4 (SEQ ID NO: 528)
QVQLVQSGSELKKPGESVKVSCKASGYTFTHYGINWVRQPPGQGLEWIGWINTYTGEPYYAPGFKGRFVFSLDTS
QSTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024837 1C11_H3.206_L3_scFv(GKPGS)4 (SEQ ID NO: 529)
QVQLVQSGSELKKPGESVKVSCKASGYTFTHYGINWVRQPPGQGLEWIGWINTYTGEPTYAPGFTGRFVFSLDTS
QSTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024838 1C11_H3.207_L3_scFv(GKPGS)4 (SEQ ID NO: 530)
QVQLVQSGSELKKPGESVKVSCKASGYTFTHYGINWVRQPPGQGLEWIGWINTYTGEPYYAPGFTGRFVFSLDTS
QSTAYLQISSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

Figure 93M

>XENP024839 1C11_H3.208_L3_scFv(GKPGS)4 (SEQ ID NO: 531)
QVQLVQSGSELKKPGESVKVSCKASGYTFTHYGINWVRQPPGQGLEWIGWINTYTGEPYYAPGFTGRFVFSLDTS
QDTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024840 1C11_H3.209_L3_scFv(GKPGS)4 (SEQ ID NO: 532)
QVQLVQSGSELKKPGESVKVSCKASGYTFTHYGINWVRQPPGQGLEWMGWINTYTGEPYYAPGFTGRFVFSLDTS
QSTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024841 1C11_H3.210_L3_scFv(GKPGS)4 (SEQ ID NO: 533)
QVQLVQSGSELKKPGESVKVSCKASGYTFTHYGINWVRQPPGQGLEWIGWINTYTGEPYYAPGFTGRFVFSLDTS
VSTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024842 1C11_H3.211_L3_scFv(GKPGS)4 (SEQ ID NO: 534)
QVQLVQSGPELKKPGESVKVSCKASGYTFTHYGINWVRQPPGQGLEWIGWINTYTGEPYYAPGFTGRFVFSLDTS
QSTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024843 1C11_H3.212_L3_scFv(GKPGS)4 (SEQ ID NO: 535)
QVQLVQSGSELKKPGESVKVSCKASGYTFTHYGINWVRQPPGQGLEWIGWINTYTGEPYYAPGFTGRFVFSLDTS
VDTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024844 1C11_H3.213_L3_scFv(GKPGS)4 (SEQ ID NO: 536)
QVQLVQSGPELKKPGESVKVSCKASGYTFTHYGINWVRQAPGQGLEWIGWINTYTGEPYYAPGFTGRFVFSLDTS
QDTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024845 1C11_H3.214_L3_scFv(GKPGS)4 (SEQ ID NO: 537)
QVQLVQSGPELKKPGESVKVSCKASGYTFTHYGINWVRQAPGQGLEWIGWINTYTGEPYYAPGFTGRFVFSIDTS
QSTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024846 1C11_H3.215_L3_scFv(GKPGS)4 (SEQ ID NO: 538)
QVQLVQSGPELKKPGESVKVSCKASGYTFTHYGINWVRQAPGQGLEWIGWINTYTGEPYYAPGFTGRFVFSLDTS
VSTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024847 1C11_H3.216_L3_scFv(GKPGS)4 (SEQ ID NO: 539)
QVQLVQSGPELKKPGESVKVSCKASGYTFTHYGINWVRQPPGQGLEWMGWINTYTGEPYYAPGFTGRFVFSIDTS
QSTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

Figure 93N

>XENP024848 1C11_H3.217_L3_scFv(GKPGS)4 (SEQ ID NO: 540)
QVQLVQSGPELKKPGESVKVSCKASGYTFTHYGINWVRQPPGQGLEWMGWINTYTGEPYYAPGFTGRFVFSLDTS
VSTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024849 1C11_H3.218_L3_scFv(GKPGS)4 (SEQ ID NO: 541)
QVQLVQSGPELKKPGESVKVSCKASGYTFTHYGINWVRQPPGQGLEWMGWINTYTGEPYYAPGFTGRFVFSLDTS
QDTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024850 1C11_H3.219_L3_scFv(GKPGS)4 (SEQ ID NO: 542)
QVQLVQSGSELKKPGESVKVSCKASGYTFTHYGINWVRQPPGQGLEWIGWINTYTGEPYYAPGFQERFVFSLDTS
QSTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024851 1C11_H3.220_L3_scFv(GKPGS)4 (SEQ ID NO: 543)
QVQLVQSGSELKKPGESVKVSCKASGYTFTHYGINWVRQPPGQGLEWIGWINTYTGEPYYAPGFKERFVFSLDTS
QSTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024852 1C11_H3.221_L3_scFv(GKPGS)4 (SEQ ID NO: 544)
EIQLVQSGSELKKPGESVKVSCKASGYTFTHYGINWVRQPPGQGLEWIGWINTYTGEPYYAPGFTGRFVFSLDTS
QSTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP024853 1C11[PD-1]_H3_L3.143_scFv(GKPGS)4 (SEQ ID NO: 545)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DIVMTQSPDSL
AVSLGERVTINCKASQSIVHSNGNTYLEWYQQKPGQPPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSVEAE
DVATYYCFQGSHVPNTFGQGTKVEIK

>XENP024854 1C11[PD-1]_H3_L3.144_scFv(GKPGS)4 (SEQ ID NO: 546)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DIVMTQSPDSL
AVSLGERVTINCKASQSIVHSNGNTYLEWYQQKPGQPPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSVEAE
DAATYYCFQGSHVPNTFGQGTKVEIK

>XENP024855 1C11[PD-1]_H3_L3.145_scFv(GKPGS)4 (SEQ ID NO: 547)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DIVMTQSPDSL
AVSLGERVTINCKASQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSVEAE
DVATYYCFQGSHVPNTFGQGTKVEIK

>XENP024856 1C11[PD-1]_H3_L3.146_scFv(GKPGS)4 (SEQ ID NO: 548)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DIVMTQSPDSL
AVSLGERVTINCKASQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSVEAE
DAATYYCFQGSHVPNTFGQGTKVEIK

>XENP024857 1C11[PD-1]_H3_L3.147_scFv(GKPGS)4 (SEQ ID NO: 549)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DIVMTQSPDSL
AVSLGERVTINCKASQSIVHSNGNTYLEWYQQKPGQAPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSVEAE
DVATYYCFQGSHVPNTFGQGTKVEIK

Figure 93O

>XENP024858 1C11[PD-1]_H3_L3.148_scFv(GKPGS)4 (SEQ ID NO: 550)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DIVMTQSPDSL
AVSLGERVTINCKASQSIVHSNGNTYLEWYQQKPGQAPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSVEAE
DAATYYCFQGSHVPNTFGQGTKVEIK

>XENP025295 1C11_H3.222_L3_scFv(GKPGS)4 (SEQ ID NO: 551)
QVQLVQSGPELKKPGESVKVSCKASGYTFTHYGINWVRQPPGQGLEWMGWINTYTGEPTYAPGFTGRFVFSIDTS
QSTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP025296 1C11_H3.223_L3_scFv(GKPGS)4 (SEQ ID NO: 552)
QVQLVQSGPELKKPGESVKVSCKASGYTFTHYGINWVRQPPGQGLEWMGWINTYTGEPYYAPGFTERFVFSIDTS
QSTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP025301 1C11_H3.224_L3_scFv(GKPGS)4 (SEQ ID NO: 553)
QVQLVQSGPELKKPGESVKVSCKASGYTFTHYGINWVRQPPGQGLEWMGWINTYTGEPYYAPGFQERFVFSIDTS
QSTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP025302 1C11_H3.225_L3_scFv(GKPGS)4 (SEQ ID NO: 554)
QVQLVQSGPELKKPGESVKVSCKASGYTFTHYGINWVRQAPGQGLEWMGWINTYTGEPYYAPGFTERFVFSLDTS
QDTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP025303 1C11_H3.226_L3_scFv(GKPGS)4 (SEQ ID NO: 555)
QVQLVQSGPELKKPGESVKVSCKASGYTFTHYGINWVRQAPGQGLEWMGWINTYTGEPYYAPGFQERFVFSLDTS
QDTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP025304 1C11_H3.227_L3_scFv(GKPGS)4 (SEQ ID NO: 556)
EVQLVQSGPELKKPGESVKVSCKASGYTFTHYGINWVRQAPGQGLEWMGWINTYTGEPYYAPGFTERFVFSLDTS
QDTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP025305 1C11_H3.228_L3_scFv(GKPGS)4 (SEQ ID NO: 557)
EVQLVQSGPELKKPGESVKVSCKASGYTFTHYGINWVRQAPGQGLEWMGWINTYTGEPYYAPGFQERFVFSLDTS
QDTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP025306 1C11_H3.229_L3_scFv(GKPGS)4 (SEQ ID NO: 558)
QVQLVQSGSELKKPGESVKVSCKASGYTFTHYGINWVRQPPGQGLEWMGWINTYTGEPYYAPGFQERFVFSLDTS
QSTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

Figure 93P

>XENP025307 1C11_H3.230_L3_scFv(GKPGS)4 (SEQ ID NO: 559)
QVQLVQSGSELKKPGESVKVSCKASGYTFTHYGINWVRQPPGQGLEWMGWINTYTGEPYYAPGFQERFVFSLDTS
QDTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP025308 1C11_H3.231_L3_scFv(GKPGS)4 (SEQ ID NO: 560)
QVQLVQSGSELKKPGESVKVSCKASGYTFTHYGINWVRQPPGQGLEWMGWINTYTGEPTYAPGFTGRFVFSLDTS
QSTAYLQISSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP025309 1C11_H3.232_L3_scFv(GKPGS)4 (SEQ ID NO: 561)
QVQLVQSGSELKKPGESVKVSCKASGYTFTHYGINWVRQPPGQGLEWMGWINTYTGEPTYAPGFTGRFVFSLDTS
QDTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP025310 1C11_H3.233_L3_scFv(GKPGS)4 (SEQ ID NO: 562)
EVQLVQSGSELKKPGESVKVSCKASGYTFTHYGINWVRQPPGQGLEWMGWINTYTGEPYYAPGFQERFVFSLDTS
QSTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP025311 1C11_H3.234_L3_scFv(GKPGS)4 (SEQ ID NO: 563)
EVQLVQSGSELKKPGESVKVSCKASGYTFTHYGINWVRQPPGQGLEWMGWINTYTGEPYYAPGFQERFVFSLDTS
QDTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP025312 1C11_H3.235_L3_scFv(GKPGS)4 (SEQ ID NO: 564)
EVQLVQSGSELKKPGESVKVSCKASGYTFTHYGINWVRQPPGQGLEWMGWINTYTGEPTYAPGFTGRFVFSLDTS
QSTAYLQISSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP025313 1C11_H3.236_L3_scFv(GKPGS)4 (SEQ ID NO: 565)
EVQLVQSGSELKKPGESVKVSCKASGYTFTHYGINWVRQPPGQGLEWMGWINTYTGEPTYAPGFTGRFVFSLDTS
QDTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP025314 1C11_H3.237_L3_scFv(GKPGS)4 (SEQ ID NO: 566)
QVQLVQSGSELKKPGESVKVSCKASGYTFTHYGINWVRQAPGQGLEWMGWINTYTGEPYYAPGFTERFVFSLDTS
QDTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP025315 1C11_H3.238_L3_scFv(GKPGS)4 (SEQ ID NO: 567)
QVQLVQSGSELKKPGESVKVSCKASGYTFTHYGINWVRQAPGQGLEWMGWINTYTGEPYYAPGFQERFVFSLDTS
QDTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

Figure 93Q

>XENP025316 1C11_H3.213_L3.144_scFv(GKPGS)4 (SEQ ID NO: 568)
QVQLVQSGPELKKPGESVKVSCKASGYTFTHYGINWVRQAPGQGLEWIGWINTYTGEPYYAPGFTGRFVFSLDTS
QDTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DIVMTQSPDSL
AVSLGERVTINCKASQSIVHSNGNTYLEWYQQKPGQPPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSVEAE
DAATYYCFQGSHVPNTFGQGTKVEIK

>XENP025317 1C11_H3.213_L3.148_scFv(GKPGS)4 (SEQ ID NO: 569)
QVQLVQSGPELKKPGESVKVSCKASGYTFTHYGINWVRQAPGQGLEWIGWINTYTGEPYYAPGFTGRFVFSLDTS
QDTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DIVMTQSPDSL
AVSLGERVTINCKASQSIVHSNGNTYLEWYQQKPGQAPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSVEAE
DAATYYCFQGSHVPNTFGQGTKVEIK

>XENP025318 1C11_H3.216_L3.144_scFv(GKPGS)4 (SEQ ID NO: 570)
QVQLVQSGPELKKPGESVKVSCKASGYTFTHYGINWVRQPPGQGLEWMGWINTYTGEPYYAPGFTGRFVFSIDTS
QSTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DIVMTQSPDSL
AVSLGERVTINCKASQSIVHSNGNTYLEWYQQKPGQPPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSVEAE
DAATYYCFQGSHVPNTFGQGTKVEIK

>XENP025319 1C11_H3.216_L3.148_scFv(GKPGS)4 (SEQ ID NO: 571)
QVQLVQSGPELKKPGESVKVSCKASGYTFTHYGINWVRQPPGQGLEWMGWINTYTGEPYYAPGFTGRFVFSIDTS
QSTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DIVMTQSPDSL
AVSLGERVTINCKASQSIVHSNGNTYLEWYQQKPGQAPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSVEAE
DAATYYCFQGSHVPNTFGQGTKVEIK

>XENP025320 1C11_H3.188_L3.144_scFv(GKPGS)4 (SEQ ID NO: 572)
QVQLVQSGSELKKPGESVKVSCKASGYTFTHYGINWVRQPPGQGLEWIGWINTYTGEPYYAPGFTGRFVFSLDTS
QSTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DIVMTQSPDSL
AVSLGERVTINCKASQSIVHSNGNTYLEWYQQKPGQPPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSVEAE
DAATYYCFQGSHVPNTFGQGTKVEIK

>XENP025321 1C11_H3.188_L3.148_scFv(GKPGS)4 (SEQ ID NO: 573)
QVQLVQSGSELKKPGESVKVSCKASGYTFTHYGINWVRQPPGQGLEWIGWINTYTGEPYYAPGFTGRFVFSLDTS
QSTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DIVMTQSPDSL
AVSLGERVTINCKASQSIVHSNGNTYLEWYQQKPGQAPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSVEAE
DAATYYCFQGSHVPNTFGQGTKVEIK

>XENP025802 1C11[PD-1]_H3.224_L3.144_scFv(GKPGS)4 (SEQ ID NO: 574)
QVQLVQSGPELKKPGESVKVSCKASGYTFTHYGINWVRQPPGQGLEWMGWINTYTGEPYYAPGFQERFVFSIDTS
QSTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DIVMTQSPDSL
AVSLGERVTINCKASQSIVHSNGNTYLEWYQQKPGQPPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSVEAE
DAATYYCFQGSHVPNTFGQGTKVEIK

>XENP025803 1C11[PD-1]_H3.224_L3.148_scFv(GKPGS)4 (SEQ ID NO: 575)
QVQLVQSGPELKKPGESVKVSCKASGYTFTHYGINWVRQPPGQGLEWMGWINTYTGEPYYAPGFQERFVFSIDTS
QSTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DIVMTQSPDSL
AVSLGERVTINCKASQSIVHSNGNTYLEWYQQKPGQAPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSVEAE
DAATYYCFQGSHVPNTFGQGTKVEIK

>XENP025804 1C11[PD-1]_H3.228_L3.144_scFv(GKPGS)4 (SEQ ID NO: 576)
EVQLVQSGPELKKPGESVKVSCKASGYTFTHYGINWVRQAPGQGLEWMGWINTYTGEPYYAPGFQERFVFSLDTS
QDTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DIVMTQSPDSL
AVSLGERVTINCKASQSIVHSNGNTYLEWYQQKPGQPPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSVEAE
DAATYYCFQGSHVPNTFGQGTKVEIK

>XENP025805 1C11[PD-1]_H3.228_L3.148_scFv(GKPGS)4 (SEQ ID NO: 577)
EVQLVQSGPELKKPGESVKVSCKASGYTFTHYGINWVRQAPGQGLEWMGWINTYTGEPYYAPGFQERFVFSLDTS
QDTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DIVMTQSPDSL
AVSLGERVTINCKASQSIVHSNGNTYLEWYQQKPGQAPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSVEAE
DAATYYCFQGSHVPNTFGQGTKVEIK

Figure 93R

>XENP025806 1C11[PD-1]_H3.234_L3.144_scFv(GKPGS)4 (SEQ ID NO: 578)
EVQLVQSGSELKKPGESVKVSCKASGYTFTHYGINWVRQPPGQGLEWMGWINTYTGEPYYAPGFQERFVFSLDTS
QDTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DIVMTQSPDSL
AVSLGERVTINCKASQSIVHSNGNTYLEWYQQKPGQPPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSVEAE
DAATYYCFQGSHVPNTFGQGTKVEIK

>XENP025807 1C11[PD-1]_H3.234_L3.148_scFv(GKPGS)4 (SEQ ID NO: 579)
EVQLVQSGSELKKPGESVKVSCKASGYTFTHYGINWVRQPPGQGLEWMGWINTYTGEPYYAPGFQERFVFSLDTS
QDTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DIVMTQSPDSL
AVSLGERVTINCKASQSIVHSNGNTYLEWYQQKPGQAPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSVEAE
DAATYYCFQGSHVPNTFGQGTKVEIK

>XENP025808 1C11[PD-1]_H3.239_L3.144_scFv(GKPGS)4 (SEQ ID NO: 580)
EVQLVQSGPELKKPGESVKVSCKASGYTFTHYGINWVRQPPGQGLEWMGWINTYTGEPYYAPGFQERFVFSIDTS
QSTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP025809 1C11[PD-1]_H3.240_L3.144_scFv(GKPGS)4 (SEQ ID NO: 581)
QVQLVQSGPELKKPGESVKVSCKASGYTFTHYGINWVRQPPGQGLEWMGWINTYTGEPYYAPGFQERFVFSIDTS
QDTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP025810 1C11[PD-1]_H3.241_L3.144_scFv(GKPGS)4 (SEQ ID NO: 582)
EVQLVQSGPELKKPGESVKVSCKASGYTFTHYGINWVRQPPGQGLEWMGWINTYTGEPYYAPGFQERFVFSIDTS
QDTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP025811 1C11[PD-1]_H3.239_L3.148_scFv(GKPGS)4 (SEQ ID NO: 583)
EVQLVQSGPELKKPGESVKVSCKASGYTFTHYGINWVRQPPGQGLEWMGWINTYTGEPYYAPGFQERFVFSIDTS
QSTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP025812 1C11[PD-1]_H3.240_L3.148_scFv(GKPGS)4 (SEQ ID NO: 584)
QVQLVQSGPELKKPGESVKVSCKASGYTFTHYGINWVRQPPGQGLEWMGWINTYTGEPYYAPGFQERFVFSIDTS
QDTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP025813 1C11[PD-1]_H3.241_L3.148_scFv(GKPGS)4 (SEQ ID NO: 585)
EVQLVQSGPELKKPGESVKVSCKASGYTFTHYGINWVRQPPGQGLEWMGWINTYTGEPYYAPGFQERFVFSIDTS
QDTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP025814 1C11[PD-1]_H3.239_L3.125_scFv(GKPGS)4 (SEQ ID NO: 586)
EVQLVQSGPELKKPGESVKVSCKASGYTFTHYGINWVRQPPGQGLEWMGWINTYTGEPYYAPGFQERFVFSIDTS
QSTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSVEAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

Figure 93S

>XENP025815 1C11[PD-1]_H3.240_L3.125_scFv(GKPGS)4 (SEQ ID NO: 587)
QVQLVQSGPELKKPGESVKVSCKASGYTFTHYGINWVRQPPGQGLEWMGWINTYTGEPYYAPGFQERFVFSIDTS
QDTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSVEAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP025816 1C11[PD-1]_H3.241_L3.125_scFv(GKPGS)4 (SEQ ID NO: 588)
EVQLVQSGPELKKPGESVKVSCKASGYTFTHYGINWVRQPPGQGLEWMGWINTYTGEPYYAPGFQERFVFSIDTS
QDTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DVLMTQSPDSL
AVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLTISSVEAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP025817 1C11[PD-1]_H3.239_L3.92_scFv(GKPGS)4 (SEQ ID NO: 589)
EVQLVQSGPELKKPGESVKVSCKASGYTFTHYGINWVRQPPGQGLEWMGWINTYTGEPYYAPGFQERFVFSIDTS
QSTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DIVMTQSPDSL
AVSLGERVTINCKASQSIVHSNGNTYLEWYQQKPGQPPKLLIYKVSNRFTGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP025818 1C11[PD-1]_H3.240_L3.92_scFv(GKPGS)4 (SEQ ID NO: 590)
QVQLVQSGPELKKPGESVKVSCKASGYTFTHYGINWVRQPPGQGLEWMGWINTYTGEPYYAPGFQERFVFSIDTS
QDTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DIVMTQSPDSL
AVSLGERVTINCKASQSIVHSNGNTYLEWYQQKPGQPPKLLIYKVSNRFTGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

>XENP025819 1C11[PD-1]_H3.241_L3.92_scFv(GKPGS)4 (SEQ ID NO: 591)
EVQLVQSGPELKKPGESVKVSCKASGYTFTHYGINWVRQPPGQGLEWMGWINTYTGEPYYAPGFQERFVFSIDTS
QDTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/DIVMTQSPDSL
AVSLGERVTINCKASQSIVHSNGNTYLEWYQQKPGQPPKLLIYKVSNRFTGVPDRFSGSGSGTDFTLTISSLQAE
DVAVYYCFQGSHVPNTFGGGTKVEIK

Figure 94A

>XENP022553 1C11[PD-1]_H3L3_IgG1_PVA_/S267K (SEQ ID NO: 592)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1053)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP025338 1C11[PD-1]_H3.226_L3.144_IgG1_PVA_/S267K (SEQ ID NO: 593)

Heavy Chain

QVQLVQSGPELKKPGESVKVSCKASGYTFTHYGINWVRQAPGQGLEWMGWINTYTGEPYYAPGFQERFVFSLDTS
QDTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1054)

DIVMTQSPDSLAVSLGERVTINCKASQSIVHSNGNTYLEWYQQKPGQPPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSVEAEDAATYYCFQGSHVPNTFGQGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP025339 1C11[PD-1]_H3.226_L3.148_IgG1_PVA_/S267K (SEQ ID NO: 594)

Heavy Chain

QVQLVQSGPELKKPGESVKVSCKASGYTFTHYGINWVRQAPGQGLEWMGWINTYTGEPYYAPGFQERFVFSLDTS
QDTAYLQINSLKAEDTAVYYCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1055)

DIVMTQSPDSLAVSLGERVTINCKASQSIVHSNGNTYLEWYQQKPGQAPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSVEAEDAATYYCFQGSHVPNTFGQGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP026321 1C11[PD-1]_H3.59_L3.1_IgG1_PVA_/S267K (SEQ ID NO: 595)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
QSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1056)

DILMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 94B

>XENP026322 1C11[PD-1]_H3.59_L3.38_IgG1_PVA_/S267K (SEQ ID NO: 596)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
QSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1057)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNNYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP026323 1C11[PD-1]_H3.59_L3.51_IgG1_PVA_/S267K (SEQ ID NO: 597)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
QSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1058)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYSVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP026324 1C11[PD-1]_H3.59_L3.59_IgG1_PVA_/S267K (SEQ ID NO: 598)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
QSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1059)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISRLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP026325 1C11[PD-1]_H3.59_L3.73_IgG1_PVA_/S267K (SEQ ID NO: 599)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
QSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1060)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVATYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 94C

>XENP026326 1C11[PD-1]_H3.59_L3.125_IgG1_PVA_/S267K (SEQ ID NO: 600)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
QSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1061)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSVEAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP026327 1C11[PD-1]_H3.135_L3.1_IgG1_PVA_/S267K (SEQ ID NO: 601)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTSEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1062)

DILMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP026328 1C11[PD-1]_H3.135_L3.38_IgG1_PVA_/S267K (SEQ ID NO: 602)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTSEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1063)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNNYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP026329 1C11[PD-1]_H3.135_L3.51_IgG1_PVA_/S267K (SEQ ID NO: 603)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTSEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1064)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYSVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 94D

>XENP026330 1C11[PD-1]_H3.135_L3.59_IgG1_PVA_/S267K (SEQ ID NO: 604)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTSEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1065)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISRLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP026331 1C11[PD-1]_H3.135_L3.73_IgG1_PVA_/S267K (SEQ ID NO: 605)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTSEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1066)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVATYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP026332 1C11[PD-1]_H3.135_L3.125_IgG1_PVA_/S267K (SEQ ID NO: 606)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTSEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1067)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSVEAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP026333 1C11[PD-1]_H3.138_L3.1_IgG1_PVA_/S267K (SEQ ID NO: 607)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGDPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1068)

DILMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 94E

>XENP026334 1C11[PD-1]_H3.138_L3.38_IgG1_PVA_/S267K (SEQ ID NO: 608)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGDPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1069)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNNYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP026335 1C11[PD-1]_H3.138_L3.51_IgG1_PVA_/S267K (SEQ ID NO: 609)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGDPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1070)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYSVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP026336 1C11[PD-1]_H3.138_L3.59_IgG1_PVA_/S267K (SEQ ID NO: 610)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGDPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1071)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISRLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP026337 1C11[PD-1]_H3.138_L3.73_IgG1_PVA_/S267K (SEQ ID NO: 611)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGDPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1072)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVATYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 94F

>XENP026338 1C11[PD-1]_H3.138_L3.125_IgG1_PVA_/S267K (SEQ ID NO: 612)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGDPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1073)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSVEAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP026339 1C11[PD-1]_H3.155_L3.1_IgG1_PVA_/S267K (SEQ ID NO: 613)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDNS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1074)

DILMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP026340 1C11[PD-1]_H3.155_L3.38_IgG1_PVA_/S267K (SEQ ID NO: 614)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDNS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1075)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNNYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP026341 1C11[PD-1]_H3.155_L3.51_IgG1_PVA_/S267K (SEQ ID NO: 615)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDNS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1076)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYSVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 94G

>XENP026342 1C11[PD-1]_H3.155_L3.59_IgG1_PVA_/S267K (SEQ ID NO: 616)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDNS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1077)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISRLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP026343 1C11[PD-1]_H3.155_L3.73_IgG1_PVA_/S267K (SEQ ID NO: 617)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDNS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1078)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVATYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP026344 1C11[PD-1]_H3.155_L3.125_IgG1_PVA_/S267K (SEQ ID NO: 618)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDNS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1079)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSVEAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP026917 1C11[PD-1]_H3.244_L3_IgG1_PVA_/S267K (SEQ ID NO: 619)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASTYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1080)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 94H

>XENP026918 1C11[PD-1]_H3.249_L3_IgG1_PVA_/S267K (SEQ ID NO: 620)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGDTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1081)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP026919 1C11[PD-1]_H3.250_L3_IgG1_PVA_/S267K (SEQ ID NO: 621)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGKTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1082)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP026920 1C11[PD-1]_H3.256_L3_IgG1_PVA_/S267K (SEQ ID NO: 622)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTWTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1083)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP026921 1C11[PD-1]_H3.258_L3_IgG1_PVA_/S267K (SEQ ID NO: 623)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFVHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1084)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 94I

>XENP026922 1C11[PD-1]_H3.288_L3_IgG1_PVA_/S267K (SEQ ID NO: 624)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTHTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1085)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP026923 1C11[PD-1]_H3.292_L3_IgG1_PVA_/S267K (SEQ ID NO: 625)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYSGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1086)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP026924 1C11[PD-1]_H3.303_L3_IgG1_PVA_/S267K (SEQ ID NO: 626)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYFGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1087)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP026925 1C11[PD-1]_H3_L3.149_IgG1_PVA_/S267K (SEQ ID NO: 627)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1088)

DVLMTQSPDSLAVSLGERATINCKSSQSIVYSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 94J

>XENP026926 1C11[PD-1]_H3_L3.152_IgG1_PVA_/S267K (SEQ ID NO: 628)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1089)

DVLMTQSPDSLAVSLGERATINCKSSQSIVFSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP026927 1C11[PD-1]_H3_L3.160_IgG1_PVA_/S267K (SEQ ID NO: 629)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1090)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSHGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP026928 1C11[PD-1]_H3_L3.161_IgG1_PVA_/S267K (SEQ ID NO: 630)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1091)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSEGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP026929 1C11[PD-1]_H3_L3.166_IgG1_PVA_/S267K (SEQ ID NO: 631)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1092)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNSNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 94K

>XENP026930 1C11[PD-1]_H3_L3.168_IgG1_PVA_/S267K (SEQ ID NO: 632)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1093)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNQNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP026931 1C11[PD-1]_H3_L3.180_IgG1_PVA_/S267K (SEQ ID NO: 633)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1094)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLILKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP026932 1C11[PD-1]_H3_L3.186_IgG1_PVA_/S267K (SEQ ID NO: 634)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1095)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSDRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP026933 1C11[PD-1]_H3_L3.191_IgG1_PVA_/S267K (SEQ ID NO: 635)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1096)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCEQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 94M

>XENP026934 1C11[PD-1]_H3_L3.194_IgG1_PVA_/S267K (SEQ ID NO: 636)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1097)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQDSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP026935 1C11[PD-1]_H3_L3.202_IgG1_PVA_/S267K (SEQ ID NO: 637)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1098)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGAHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP026936 1C11[PD-1]_H3_L3.204_IgG1_PVA_/S267K (SEQ ID NO: 638)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1099)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGVHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP026937 1C11[PD-1]_H3_L3.207_IgG1_PVA_/S267K (SEQ ID NO: 639)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1100)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSDVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 94N

>XENP026938 1C11[PD-1]_H3.308_L3.152_IgG1_PVA_/S267K (SEQ ID NO: 640)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTSEPTYADGFTGRFVFSLDTS
QSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1101)

DVLMTQSPDSLAVSLGERATINCKSSQSIVFSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP026939 1C11[PD-1]_H3.59_L3.152_IgG1_PVA_/S267K (SEQ ID NO: 641)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
QSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1102)

DVLMTQSPDSLAVSLGERATINCKSSQSIVFSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP026940 1C11[PD-1]_H3.303_L3.152_IgG1_PVA_/S267K (SEQ ID NO: 642)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYFGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1103)

DVLMTQSPDSLAVSLGERATINCKSSQSIVFSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP026941 1C11[PD-1]_H3.308_L3.180_IgG1_PVA_/S267K (SEQ ID NO: 643)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTSEPTYADGFTGRFVFSLDTS
QSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1104)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLILKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 94O

>XENP026942 1C11[PD-1]_H3.59_L3.180_IgG1_PVA_/S267K (SEQ ID NO: 644)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
QSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1105)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLILKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP026943 1C11[PD-1]_H3.303_L3.180_IgG1_PVA_/S267K (SEQ ID NO: 645)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYFGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1106)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLILKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP026944 1C11[PD-1]_H3.303_L3.210_IgG1_PVA_/S267K (SEQ ID NO: 646)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYFGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1107)

DILMTQSPDSLAVSLGERATINCKSSQSIVHSNGNNYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP026945 1C11[PD-1]_H3.308_L3_IgG1_PVA_/S267K (SEQ ID NO: 647)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTSEPTYADGFTGRFVFSLDTS
QSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1108)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 94P

>XENP026946 1C11[PD-1]_H3.59_L3_IgG1_PVA_/S267K (SEQ ID NO: 648)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
QSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1109)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP026947 1C11[PD-1]_H3.135_L3_IgG1_PVA_/S267K (SEQ ID NO: 649)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTSEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1110)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP026949 1C11[PD-1]_H3.308_L3.210_IgG1_PVA_/S267K (SEQ ID NO: 650)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTSEPTYADGFTGRFVFSLDTS
QSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1111)

DILMTQSPDSLAVSLGERATINCKSSQSIVHSNGNNYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP026950 1C11[PD-1]_H3_L3.210_IgG1_PVA_/S267K (SEQ ID NO: 651)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1112)

DILMTQSPDSLAVSLGERATINCKSSQSIVHSNGNNYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 94Q

>XENP026951 1C11[PD-1]_H3_L3.1_IgG1_PVA_/S267K (SEQ ID NO: 652)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1113)

DILMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP026952 1C11[PD-1]_H3_L3.38_IgG1_PVA_/S267K (SEQ ID NO: 653)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1114)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNNYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP026953 1C11[PD-1]_H3_L3.125_IgG1_PVA_/S267K (SEQ ID NO: 654)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1115)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSVEAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP026954 1C11[PD-1]_H3.308_L3.38_IgG1_PVA_/S267K (SEQ ID NO: 655)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTSEPTYADGFTGRFVFSLDTS
QSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1116)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNNYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 94R

>XENP026955 1C11[PD-1]_H3.59_L3.210_IgG1_PVA_/S267K (SEQ ID NO: 656)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
QSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1117)

DILMTQSPDSLAVSLGERATINCKSSQSIVHSNGNNYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP27643 1C11_H3_L3.211_IgG1_PVA_/S267K (SEQ ID NO: 657)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1118)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPELLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP27644 1C11_H3_L3.212_IgG1_PVA_/S267K (SEQ ID NO: 658)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1119)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPQLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP27645 1C11_H3_L3.213_IgG1_PVA_/S267K (SEQ ID NO: 659)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1120)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPTLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 94S

>XENP27646 1C11_H3_L3.214_IgG1_PVA_/S267K (SEQ ID NO: 660)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1121)

DVLMTQSPDSLAVSLGERATINCKSSQSIVISNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP27647 1C11_H3_L3.215_IgG1_PVA_/S267K (SEQ ID NO: 661)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1122)

DVLMTQSPDSLAVSLGERATINCKSSQSIVLSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP27648 1C11_H3_L3.216_IgG1_PVA_/S267K (SEQ ID NO: 662)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1123)

DVLMTQSPDSLAVSLGERATINCKSSQSIVVSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP27649 1C11_H3_L3.217_IgG1_PVA_/S267K (SEQ ID NO: 663)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1124)

DVLMTQSPDSLAVSLGERATINCKSSQSIVFSNGNNYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 94T

>XENP27650 1C11_H3_L3.218_IgG1_PVA_/S267K (SEQ ID NO: 664)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1125)

DVLMTQSPDSLAVSLGERATINCKSSQSIVYSNGNNYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP27651 1C11_H3_L3.219_IgG1_PVA_/S267K (SEQ ID NO: 665)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1126)

DILMTQSPDSLAVSLGERATINCKSSQSIVFSNGNNYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP27652 1C11_H3_L3.220_IgG1_PVA_/S267K (SEQ ID NO: 666)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1127)

DILMTQSPDSLAVSLGERATINCKSSQSIVYSNGNNYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP27839 1C11_H3.309_L3_IgG1_PVA_/S267K (SEQ ID NO: 667)

Heavy Chain

QIQLVQSESELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1128)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 94U

>XENP27840 1C11_H3.310_L3_IgG1_PVA_/S267K (SEQ ID NO: 668)

Heavy Chain

QIQLVQSSSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1129)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP27841 1C11_H3.311_L3_IgG1_PVA_/S267K (SEQ ID NO: 669)

Heavy Chain

QIQLVQSVSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1130)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP27842 1C11_H3.312_L3_IgG1_PVA_/S267K (SEQ ID NO: 670)

Heavy Chain

QIQLVQSGSELTKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1131)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP27843 1C11_H3.313_L3_IgG1_PVA_/S267K (SEQ ID NO: 671)

Heavy Chain

QIQLVQSGSELQKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1132)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 94V

>XENP27844 1C11_H3.314_L3_IgG1_PVA_/S267K (SEQ ID NO: 672)

Heavy Chain

QIQLVQSGSELYKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1133)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP27845 1C11_H3.315_L3_IgG1_PVA_/S267K (SEQ ID NO: 673)

Heavy Chain

QIQLVQSGSELLKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1134)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP27846 1C11_H3.316_L3_IgG1_PVA_/S267K (SEQ ID NO: 674)

Heavy Chain

QIQLVQSGSELKKPGASVSVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1135)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP27847 1C11_H3.317_L3_IgG1_PVA_/S267K (SEQ ID NO: 675)

Heavy Chain

QIQLVQSGSELKKPGASVTVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1136)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 94W

>XENP27848 1C11_H3.318_L3_IgG1_PVA_/S267K (SEQ ID NO: 676)

Heavy Chain

QIQLVQSGSELVKPGASVTVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1137)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP27849 1C11_H3.319_L3_IgG1_PVA_/S267K (SEQ ID NO: 677)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
QSTAYLQISSLKAEDTAVYFCARDYFGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1138)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP27850 1C11_H3.320_L3_IgG1_PVA_/S267K (SEQ ID NO: 678)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTHTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYFGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1139)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP27851 1C11_H3.321_L3_IgG1_PVA_/S267K (SEQ ID NO: 679)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYSGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYFGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1140)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 94X

>XENP27852 1C11_H3.322_L3_IgG1_PVA_/S267K (SEQ ID NO: 680)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTSEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYFGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1141)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP27853 1C11_H3.323_L3_IgG1_PVA_/S267K (SEQ ID NO: 681)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTHSGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1142)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP27854 1C11_H3.324_L3_IgG1_PVA_/S267K (SEQ ID NO: 682)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTHSGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYFGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1143)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP27855 1C11_H3.325_L3_IgG1_PVA_/S267K (SEQ ID NO: 683)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTHSGEPTYADGFTGRFVFSLDTS
QSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1144)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 94Y

>XENP27856 1C11_H3.326_L3_IgG1_PVA_/S267K (SEQ ID NO: 684)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTHSGEPTYADGFTGRFVFSLDTS
QSTAYLQISSLKAEDTAVYFCARDYFGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1145)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP27857 1C11_H3.319_L3.152_IgG1_PVA_/S267K (SEQ ID NO: 685)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
QSTAYLQISSLKAEDTAVYFCARDYFGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1146)

DVLMTQSPDSLAVSLGERATINCKSSQSIVFSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP27858 1C11_H3.320_L3.152_IgG1_PVA_/S267K (SEQ ID NO: 686)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTHTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYFGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1147)

DVLMTQSPDSLAVSLGERATINCKSSQSIVFSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP27859 1C11_H3.321_L3.152_IgG1_PVA_/S267K (SEQ ID NO: 687)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYSGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYFGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1148)

DVLMTQSPDSLAVSLGERATINCKSSQSIVFSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 94Z

>XENP27860 1C11_H3.322_L3.152_IgG1_PVA_/S267K (SEQ ID NO: 688)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTSEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYFGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1149)

DVLMTQSPDSLAVSLGERATINCKSSQSIVFSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP27861 1C11_H3.323_L3.152_IgG1_PVA_/S267K (SEQ ID NO: 689)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTHSGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1150)

DVLMTQSPDSLAVSLGERATINCKSSQSIVFSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP27862 1C11_H3.324_L3.152_IgG1_PVA_/S267K (SEQ ID NO: 690)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTHSGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYFGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1151)

DVLMTQSPDSLAVSLGERATINCKSSQSIVFSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP27863 1C11_H3.325_L3.152_IgG1_PVA_/S267K (SEQ ID NO: 691)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTHSGEPTYADGFTGRFVFSLDTS
QSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1152)

DVLMTQSPDSLAVSLGERATINCKSSQSIVFSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 94AA

>XENP27864 1C11_H3.326_L3.152_IgG1_PVA_/S267K (SEQ ID NO: 692)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTHSGEPTYADGFTGRFVFSLDTS
QSTAYLQISSLKAEDTAVYFCARDYFGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1153)

DVLMTQSPDSLAVSLGERATINCKSSQSIVFSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP27865 1C11_H3.319_L3.220_IgG1_PVA_/S267K (SEQ ID NO: 693)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
QSTAYLQISSLKAEDTAVYFCARDYFGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1154)

DILMTQSPDSLAVSLGERATINCKSSQSIVYSNGNNYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP27866 1C11_H3.320_L3.220_IgG1_PVA_/S267K (SEQ ID NO: 694)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTHTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYFGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1155)

DILMTQSPDSLAVSLGERATINCKSSQSIVYSNGNNYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP27867 1C11_H3.321_L3.220_IgG1_PVA_/S267K (SEQ ID NO: 695)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYSGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYFGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1156)

DILMTQSPDSLAVSLGERATINCKSSQSIVYSNGNNYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 94AB

>XENP27868 1C11_H3.322_L3.220_IgG1_PVA_/S267K (SEQ ID NO: 696)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTSEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYFGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1157)

DILMTQSPDSLAVSLGERATINCKSSQSIVYSNGNNYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP27869 1C11_H3.323_L3.220_IgG1_PVA_/S267K (SEQ ID NO: 697)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTHSGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1158)

DILMTQSPDSLAVSLGERATINCKSSQSIVYSNGNNYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP27870 1C11_H3.324_L3.220_IgG1_PVA_/S267K (SEQ ID NO: 698)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTHSGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYFGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1159)

DILMTQSPDSLAVSLGERATINCKSSQSIVYSNGNNYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP27871 1C11_H3.325_L3.220_IgG1_PVA_/S267K (SEQ ID NO: 699)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTHSGEPTYADGFTGRFVFSLDTS
QSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1160)

DILMTQSPDSLAVSLGERATINCKSSQSIVYSNGNNYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 94AC

>XENP27872 1C11_H3.326_L3.220_IgG1_PVA_/S267K (SEQ ID NO: 700)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTHSGEPTYADGFTGRFVFSLDTS
QSTAYLQISSLKAEDTAVYFCARDYFGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1161)

DILMTQSPDSLAVSLGERATINCKSSQSIVYSNGNNYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP27959 1C11_H3.303_L3.219_IgG1_PVA_/S267K (SEQ ID NO: 701)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYFGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1162)

DILMTQSPDSLAVSLGERATINCKSSQSIVFSNGNNYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP27960 1C11_H3.303_L3.220_IgG1_PVA_/S267K (SEQ ID NO: 702)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYFGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1163)

DILMTQSPDSLAVSLGERATINCKSSQSIVYSNGNNYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP27961 1C11_H3.320_L3.219_IgG1_PVA_/S267K (SEQ ID NO: 703)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTHTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYFGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1164)

DILMTQSPDSLAVSLGERATINCKSSQSIVFSNGNNYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 94AD

>XENP27962 1C11_H3.323_L3.219_IgG1_PVA_/S267K (SEQ ID NO: 704)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTHSGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1165)

DILMTQSPDSLAVSLGERATINCKSSQSIVFSNGNNYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP27963 1C11_H3.324_L3.219_IgG1_PVA_/S267K (SEQ ID NO: 705)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTHSGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYFGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1166)

DILMTQSPDSLAVSLGERATINCKSSQSIVFSNGNNYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP28024 1C11_H3.327_L3.220_IgG1_PVA_/S267K (SEQ ID NO: 706)

Heavy Chain

QIQLVQSGSELLKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTHTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYFGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1167)

DILMTQSPDSLAVSLGERATINCKSSQSIVYSNGNNYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP28025 1C11_H3.328_L3.220_IgG1_PVA_/S267K (SEQ ID NO: 707)

Heavy Chain

QIQLVQSGSELKKPGASVSVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTHTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYFGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1168)

DILMTQSPDSLAVSLGERATINCKSSQSIVYSNGNNYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 94AE

>XENP28026 1C11_H3.329_L3.220_IgG1_PVA_/S267K (SEQ ID NO: 708)

Heavy Chain

QIQLVQSGSELLKPGASVSVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTHTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYFGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1169)

DILMTQSPDSLAVSLGERATINCKSSQSIVYSNGNNYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP28027 1C11_H3.330_L3.220_IgG1_PVA_/S267K (SEQ ID NO: 709)

Heavy Chain

QIQLVQSGSELLKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTHSGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1170)

DILMTQSPDSLAVSLGERATINCKSSQSIVYSNGNNYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP28028 1C11_H3.331_L3.220_IgG1_PVA_/S267K (SEQ ID NO: 710)

Heavy Chain

QIQLVQSGSELKKPGASVSVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTHSGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1171)

DILMTQSPDSLAVSLGERATINCKSSQSIVYSNGNNYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP28029 1C11_H3.332_L3.220_IgG1_PVA_/S267K (SEQ ID NO: 711)

Heavy Chain

QIQLVQSGSELLKPGASVSVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTHSGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1172)

DILMTQSPDSLAVSLGERATINCKSSQSIVYSNGNNYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 94AF

>XENP28030 1C11_H3.333_L3.220_IgG1_PVA_/S267K (SEQ ID NO: 712)

Heavy Chain

QIQLVQSGSELLKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTHSGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYFGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1173)

DILMTQSPDSLAVSLGERATINCKSSQSIVYSNGNNYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP28031 1C11_H3.334_L3.220_IgG1_PVA_/S267K (SEQ ID NO: 713)

Heavy Chain

QIQLVQSGSELKKPGASVSVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTHSGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYFGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1174)

DILMTQSPDSLAVSLGERATINCKSSQSIVYSNGNNYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP28032 1C11_H3.335_L3.220_IgG1_PVA_/S267K (SEQ ID NO: 714)

Heavy Chain

QIQLVQSGSELLKPGASVSVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTHSGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYFGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1175)

DILMTQSPDSLAVSLGERATINCKSSQSIVYSNGNNYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP28033 1C11_H3.336_L3.220_IgG1_PVA_/S267K (SEQ ID NO: 715)

Heavy Chain

QIQLVQSGSELLKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYFGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1176)

DILMTQSPDSLAVSLGERATINCKSSQSIVYSNGNNYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 94AG

>XENP28034 1C11_H3.337_L3.220_IgG1_PVA_/S267K (SEQ ID NO: 716)

Heavy Chain

QIQLVQSGSELKKPGASVSVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYFGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1177)

DILMTQSPDSLAVSLGERATINCKSSQSIVYSNGNNYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP28035 1C11_H3.338_L3.220_IgG1_PVA_/S267K (SEQ ID NO: 717)

Heavy Chain

QIQLVQSGSELLKPGASVSVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYFGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1178)

DILMTQSPDSLAVSLGERATINCKSSQSIVYSNGNNYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP28651 1C11_H3.327_L3.152_IgG1_PVA_/S267K (SEQ ID NO: 718)

Heavy Chain

QIQLVQSGSELLKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTHTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYFGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1179)

DVLMTQSPDSLAVSLGERATINCKSSQSIVFSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP28652 1C11_H3.328_L3.152_IgG1_PVA_/S267K (SEQ ID NO: 719)

Heavy Chain

QIQLVQSGSELKKPGASVSVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTHTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYFGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1180)

DVLMTQSPDSLAVSLGERATINCKSSQSIVFSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 94AH

>XENP28653 1C11_H3.329_L3.152_IgG1_PVA_/S267K (SEQ ID NO: 720)

Heavy Chain

QIQLVQSGSELLKPGASVSVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTHTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYFGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1181)

DVLMTQSPDSLAVSLGERATINCKSSQSIVFSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP28654 1C11_H3.23_L3_IgG1_PVA_/S267K (SEQ ID NO: 721)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGYINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1182)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP28655 1C11_H3.28_L3_IgG1_PVA_/S267K (SEQ ID NO: 722)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGETTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1183)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP28656 1C11_H3.35_L3_IgG1_PVA_/S267K (SEQ ID NO: 723)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADKFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1184)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 94AI

>XENP28657 1C11_H3_L3.71_IgG1_PVA_/S267K (SEQ ID NO: 724)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1185)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDIAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP28658 1C11_H3_L3.74_IgG1_PVA_/S267K (SEQ ID NO: 725)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1186)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCQQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP28659 1C11_H3_L3.77_IgG1_PVA_/S267K (SEQ ID NO: 726)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1187)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQYSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP29029 1C11_H3.246_L3_IgG1_PVA_/S267K (SEQ ID NO: 727)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGLTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1188)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 94AJ

>XENP29030 1C11_H3.247_L3_IgG1_PVA_/S267K (SEQ ID NO: 728)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGHTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1189)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP29031 1C11_H3.248_L3_IgG1_PVA_/S267K (SEQ ID NO: 729)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGQTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1190)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP29032 1C11_H3.254_L3_IgG1_PVA_/S267K (SEQ ID NO: 730)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYQFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1191)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP29033 1C11_H3.263_L3_IgG1_PVA_/S267K (SEQ ID NO: 731)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTQYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1192)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 94AK

>XENP29034 1C11_H3.264_L3_IgG1_PVA_/S267K (SEQ ID NO: 732)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTDYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1193)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP29035 1C11_H3.265_L3_IgG1_PVA_/S267K (SEQ ID NO: 733)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTRYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1194)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP29036 1C11_H3.269_L3_IgG1_PVA_/S267K (SEQ ID NO: 734)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHLGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1195)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP29037 1C11_H3.276_L3_IgG1_PVA_/S267K (SEQ ID NO: 735)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWFRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1196)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 94AL

>XENP29038 1C11_H3.283_L3_IgG1_PVA_/S267K (SEQ ID NO: 736)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWIQTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1197)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP29039 1C11_H3.284_L3_IgG1_PVA_/S267K (SEQ ID NO: 737)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWIETYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1198)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP29040 1C11_H3.285_L3_IgG1_PVA_/S267K (SEQ ID NO: 738)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWIHTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1199)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP29041 1C11_H3.286_L3_IgG1_PVA_/S267K (SEQ ID NO: 739)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWISTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1200)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 94AM

>XENP29042 1C11_H3.289_L3_IgG1_PVA_/S267K (SEQ ID NO: 740)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTLTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1201)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP29043 1C11_H3.290_L3_IgG1_PVA_/S267K (SEQ ID NO: 741)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTWTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1202)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP29044 1C11_H3.294_L3_IgG1_PVA_/S267K (SEQ ID NO: 742)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYIGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1203)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP29045 1C11_H3.296_L3_IgG1_PVA_/S267K (SEQ ID NO: 743)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGKPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1204)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 94AN

>XENP29046 1C11_H3_L3.155_IgG1_PVA_/S267K (SEQ ID NO: 744)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1205)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHTNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP29047 1C11_H3_L3.157_IgG1_PVA_/S267K (SEQ ID NO: 745)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1206)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHQNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP29048 1C11_H3_L3.163_IgG1_PVA_/S267K (SEQ ID NO: 746)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1207)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSRGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP29049 1C11_H3_L3.173_IgG1_PVA_/S267K (SEQ ID NO: 747)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1208)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTFLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 94AO

>XENP29050 1C11_H3_L3.181_IgG1_PVA_/S267K (SEQ ID NO: 748)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1209)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIWKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP29051 1C11_H3_L3.182_IgG1_PVA_/S267K (SEQ ID NO: 749)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1210)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIQKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP29052 1C11_H3_L3.189_IgG1_PVA_/S267K (SEQ ID NO: 750)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1211)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSRRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP29053 1C11_H3_L3.192_IgG1_PVA_/S267K (SEQ ID NO: 751)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1212)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQASHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 94AP

>XENP29054 1C11_H3_L3.193_IgG1_PVA_/S267K (SEQ ID NO: 752)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1213)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQSSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP29055 1C11_H3_L3.196_IgG1_PVA_/S267K (SEQ ID NO: 753)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1214)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQQSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP29056 1C11_H3_L3.198_IgG1_PVA_/S267K (SEQ ID NO: 754)

Heavy Chain

QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain (SEQ ID NO:1215)

DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQLSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 95A

>XenD17478 1C11[PD-1]_H3_IgG1_PVA_/S267K (SEQ ID NO: 755)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XenD18576 1C11_H3.59_IgG1_PVA_/S267K (SEQ ID NO: 756)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
QSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XenD22097 1C11_H3.242_IgG1_PVA_/S267K (SEQ ID NO: 757)
QIQLVQSGSELKKPGASVKVSCKASAYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XenD22098 1C11_H3.243_IgG1_PVA_/S267K (SEQ ID NO: 758)
QIQLVQSGSELKKPGASVKVSCKASSYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XenD22099 1C11_H3.244_IgG1_PVA_/S267K (SEQ ID NO: 759)
QIQLVQSGSELKKPGASVKVSCKASTYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XenD22100 1C11_H3.245_IgG1_PVA_/S267K (SEQ ID NO: 760)
QIQLVQSGSELKKPGASVKVSCKASGWTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XenD22101 1C11_H3.246_IgG1_PVA_/S267K (SEQ ID NO: 761)
QIQLVQSGSELKKPGASVKVSCKASGLTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Figure 95B

>XenD22102 1C11_H3.247_IgG1_PVA_/S267K (SEQ ID NO: 762)
QIQLVQSGSELKKPGASVKVSCKASGHTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XenD22103 1C11_H3.248_IgG1_PVA_/S267K (SEQ ID NO: 763)
QIQLVQSGSELKKPGASVKVSCKASGQTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XenD22104 1C11_H3.249_IgG1_PVA_/S267K (SEQ ID NO: 764)
QIQLVQSGSELKKPGASVKVSCKASGDTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XenD22105 1C11_H3.250_IgG1_PVA_/S267K (SEQ ID NO: 765)
QIQLVQSGSELKKPGASVKVSCKASGKTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XenD22106 1C11_H3.251_IgG1_PVA_/S267K (SEQ ID NO: 766)
QIQLVQSGSELKKPGASVKVSCKASGYVFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XenD22107 1C11_H3.252_IgG1_PVA_/S267K (SEQ ID NO: 767)
QIQLVQSGSELKKPGASVKVSCKASGYAFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XenD22108 1C11_H3.253_IgG1_PVA_/S267K (SEQ ID NO: 768)
QIQLVQSGSELKKPGASVKVSCKASGYIFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Figure 95C

>XenD22109 1C11_H3.254_IgG1_PVA_/S267K (SEQ ID NO: 769)
QIQLVQSGSELKKPGASVKVSCKASGYQFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XenD22110 1C11_H3.255_IgG1_PVA_/S267K (SEQ ID NO: 770)
QIQLVQSGSELKKPGASVKVSCKASGYTYTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XenD22111 1C11_H3.256_IgG1_PVA_/S267K (SEQ ID NO: 771)
QIQLVQSGSELKKPGASVKVSCKASGYTWTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XenD22112 1C11_H3.257_IgG1_PVA_/S267K (SEQ ID NO: 772)
QIQLVQSGSELKKPGASVKVSCKASGYTHTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XenD22113 1C11_H3.258_IgG1_PVA_/S267K (SEQ ID NO: 773)
QIQLVQSGSELKKPGASVKVSCKASGYTFVHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XenD22114 1C11_H3.259_IgG1_PVA_/S267K (SEQ ID NO: 774)
QIQLVQSGSELKKPGASVKVSCKASGYTFAHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XenD22115 1C11_H3.260_IgG1_PVA_/S267K (SEQ ID NO: 775)
QIQLVQSGSELKKPGASVKVSCKASGYTFIHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Figure 95D

>XenD22116 1C11_H3.261_IgG1_PVA_/S267K (SEQ ID NO: 776)
QIQLVQSGSELKKPGASVKVSCKASGYTFQHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XenD22117 1C11_H3.262_IgG1_PVA_/S267K (SEQ ID NO: 777)
QIQLVQSGSELKKPGASVKVSCKASGYTFTYYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XenD22118 1C11_H3.263_IgG1_PVA_/S267K (SEQ ID NO: 778)
QIQLVQSGSELKKPGASVKVSCKASGYTFTQYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XenD22119 1C11_H3.264_IgG1_PVA_/S267K (SEQ ID NO: 779)
QIQLVQSGSELKKPGASVKVSCKASGYTFTDYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XenD22120 1C11_H3.265_IgG1_PVA_/S267K (SEQ ID NO: 780)
QIQLVQSGSELKKPGASVKVSCKASGYTFTRYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XenD22121 1C11_H3.266_IgG1_PVA_/S267K (SEQ ID NO: 781)
QIQLVQSGSELKKPGASVKVSCKASGYTFTFYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XenD22122 1C11_H3.267_IgG1_PVA_/S267K (SEQ ID NO: 782)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHFGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Figure 95E

>XenD22123 1C11_H3.268_IgG1_PVA_/S267K (SEQ ID NO: 783)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHHGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XenD22124 1C11_H3.269_IgG1_PVA_/S267K (SEQ ID NO: 784)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHLGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XenD22125 1C11_H3.270_IgG1_PVA_/S267K (SEQ ID NO: 785)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHWGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XenD22126 1C11_H3.271_IgG1_PVA_/S267K (SEQ ID NO: 786)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYTMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XenD22127 1C11_H3.272_IgG1_PVA_/S267K (SEQ ID NO: 787)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYQMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XenD22128 1C11_H3.273_IgG1_PVA_/S267K (SEQ ID NO: 788)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGLNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XenD22129 1C11_H3.274_IgG1_PVA_/S267K (SEQ ID NO: 789)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWLRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Figure 95F

>XenD22130 1C11_H3.275_IgG1_PVA_/S267K (SEQ ID NO: 790)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWTRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XenD22131 1C11_H3.276_IgG1_PVA_/S267K (SEQ ID NO: 791)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWFRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XenD22132 1C11_H3.277_IgG1_PVA_/S267K (SEQ ID NO: 792)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMTWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XenD22133 1C11_H3.278_IgG1_PVA_/S267K (SEQ ID NO: 793)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMDWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XenD22134 1C11_H3.279_IgG1_PVA_/S267K (SEQ ID NO: 794)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMQWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XenD22135 1C11_H3.280_IgG1_PVA_/S267K (SEQ ID NO: 795)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMEWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XenD22136 1C11_H3.281_IgG1_PVA_/S267K (SEQ ID NO: 796)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGFINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Figure 95G

>XenD22137 1C11_H3.282_IgG1_PVA_/S267K (SEQ ID NO: 797)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGHINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XenD22138 1C11_H3.283_IgG1_PVA_/S267K (SEQ ID NO: 798)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWIQTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XenD22139 1C11_H3.284_IgG1_PVA_/S267K (SEQ ID NO: 799)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWIETYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XenD22140 1C11_H3.285_IgG1_PVA_/S267K (SEQ ID NO: 800)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWIHTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XenD22141 1C11_H3.286_IgG1_PVA_/S267K (SEQ ID NO: 801)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWISTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XenD22142 1C11_H3.287_IgG1_PVA_/S267K (SEQ ID NO: 802)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTFTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XenD22143 1C11_H3.288_IgG1_PVA_/S267K (SEQ ID NO: 803)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTHTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Figure 95H

>XenD22144 1C11_H3.289_IgG1_PVA_/S267K (SEQ ID NO: 804)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTLTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XenD22145 1C11_H3.290_IgG1_PVA_/S267K (SEQ ID NO: 805)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTWTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XenD22146 1C11_H3.291_IgG1_PVA_/S267K (SEQ ID NO: 806)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYVGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XenD22147 1C11_H3.292_IgG1_PVA_/S267K (SEQ ID NO: 807)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYSGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XenD22148 1C11_H3.293_IgG1_PVA_/S267K (SEQ ID NO: 808)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYAGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XenD22149 1C11_H3.294_IgG1_PVA_/S267K (SEQ ID NO: 809)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYIGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XenD22150 1C11_H3.295_IgG1_PVA_/S267K (SEQ ID NO: 810)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGQPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Figure 95I

>XenD22151 1C11_H3.296_IgG1_PVA_/S267K (SEQ ID NO: 811)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGKPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XenD22152 1C11_H3.297_IgG1_PVA_/S267K (SEQ ID NO: 812)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDFYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XenD22153 1C11_H3.298_IgG1_PVA_/S267K (SEQ ID NO: 813)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDQYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XenD22154 1C11_H3.299_IgG1_PVA_/S267K (SEQ ID NO: 814)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDHYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XenD22155 1C11_H3.300_IgG1_PVA_/S267K (SEQ ID NO: 815)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDRYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XenD22156 1C11_H3.301_IgG1_PVA_/S267K (SEQ ID NO: 816)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDKYGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XenD22157 1C11_H3.302_IgG1_PVA_/S267K (SEQ ID NO: 817)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYWGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Figure 95J

>XenD22158 1C11_H3.303_IgG1_PVA_/S267K (SEQ ID NO: 818)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYFGSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XenD22159 1C11_H3.304_IgG1_PVA_/S267K (SEQ ID NO: 819)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYASSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XenD22160 1C11_H3.305_IgG1_PVA_/S267K (SEQ ID NO: 820)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYSSSPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XenD22161 1C11_H3.306_IgG1_PVA_/S267K (SEQ ID NO: 821)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPFWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XenD22162 1C11_H3.307_IgG1_PVA_/S267K (SEQ ID NO: 822)
QIQLVQSGSELKKPGASVKVSCKASGYTFTHYGMNWVRQAPGQGLEWMGWINTYTGEPTYADGFTGRFVFSLDTS
VSTAYLQISSLKAEDTAVYFCARDYYGSSPWWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Figure 96A

>XenD17482 1C11[PD-1]_L3 (SEQ ID NO: 823)
DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XenD18472 1C11_L3.38 (SEQ ID NO: 824)
DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNNYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XenD22163 1C11[PD-1]_L3.149 (SEQ ID NO: 825)
DVLMTQSPDSLAVSLGERATINCKSSQSIVYSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XenD22164 1C11[PD-1]_L3.150 (SEQ ID NO: 826)
DVLMTQSPDSLAVSLGERATINCKSSQSIVQSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XenD22165 1C11[PD-1]_L3.151 (SEQ ID NO: 827)
DVLMTQSPDSLAVSLGERATINCKSSQSIVDSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XenD22166 1C11[PD-1]_L3.152 (SEQ ID NO: 828)
DVLMTQSPDSLAVSLGERATINCKSSQSIVFSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XenD22167 1C11[PD-1]_L3.153 (SEQ ID NO: 829)
DVLMTQSPDSLAVSLGERATINCKSSQSIVTSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XenD22168 1C11[PD-1]_L3.154 (SEQ ID NO: 830)
DVLMTQSPDSLAVSLGERATINCKSSQSIVKSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XenD22169 1C11[PD-1]_L3.155 (SEQ ID NO: 831)
DVLMTQSPDSLAVSLGERATINCKSSQSIVHTNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XenD22170 1C11[PD-1]_L3.156 (SEQ ID NO: 832)
DVLMTQSPDSLAVSLGERATINCKSSQSIVHANGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XenD22171 1C11[PD-1]_L3.157 (SEQ ID NO: 833)
DVLMTQSPDSLAVSLGERATINCKSSQSIVHQNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 96B

>XenD22172 1C11[PD-1]_L3.158 (SEQ ID NO: 834)
DVLMTQSPDSLAVSLGERATINCKSSQSIVHGNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XenD22173 1C11[PD-1]_L3.159 (SEQ ID NO: 835)
DVLMTQSPDSLAVSLGERATINCKSSQSIVHVNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XenD22174 1C11[PD-1]_L3.160 (SEQ ID NO: 836)
DVLMTQSPDSLAVSLGERATINCKSSQSIVHSHGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XenD22175 1C11[PD-1]_L3.161 (SEQ ID NO: 837)
DVLMTQSPDSLAVSLGERATINCKSSQSIVHSEGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XenD22176 1C11[PD-1]_L3.162 (SEQ ID NO: 838)
DVLMTQSPDSLAVSLGERATINCKSSQSIVHSSGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XenD22177 1C11[PD-1]_L3.163 (SEQ ID NO: 839)
DVLMTQSPDSLAVSLGERATINCKSSQSIVHSRGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XenD22178 1C11[PD-1]_L3.164 (SEQ ID NO: 840)
DVLMTQSPDSLAVSLGERATINCKSSQSIVHSLGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XenD22179 1C11[PD-1]_L3.165 (SEQ ID NO: 841)
DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNANTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XenD22180 1C11[PD-1]_L3.166 (SEQ ID NO: 842)
DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNSNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XenD22181 1C11[PD-1]_L3.167 (SEQ ID NO: 843)
DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNTNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XenD22182 1C11[PD-1]_L3.168 (SEQ ID NO: 844)
DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNQNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 96C

>XenD22183 1C11[PD-1]_L3.169 (SEQ ID NO: 845)
DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGDTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XenD22184 1C11[PD-1]_L3.170 (SEQ ID NO: 846)
DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGHTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XenD22185 1C11[PD-1]_L3.171 (SEQ ID NO: 847)
DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGETYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XenD22186 1C11[PD-1]_L3.172 (SEQ ID NO: 848)
DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGRTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XenD22187 1C11[PD-1]_L3.173 (SEQ ID NO: 849)
DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTFLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XenD22188 1C11[PD-1]_L3.174 (SEQ ID NO: 850)
DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTHLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XenD22189 1C11[PD-1]_L3.175 (SEQ ID NO: 851)
DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTLLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XenD22190 1C11[PD-1]_L3.176 (SEQ ID NO: 852)
DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTWLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XenD22191 1C11[PD-1]_L3.177 (SEQ ID NO: 853)
DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTQLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XenD22192 1C11[PD-1]_L3.178 (SEQ ID NO: 854)
DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIFKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XenD22193 1C11[PD-1]_L3.179 (SEQ ID NO: 855)
DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIHKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 96D

>XenD22194 1C11[PD-1]_L3.180 (SEQ ID NO: 856)
DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLILKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XenD22195 1C11[PD-1]_L3.181 (SEQ ID NO: 857)
DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIWKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XenD22196 1C11[PD-1]_L3.182 (SEQ ID NO: 858)
DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIQKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XenD22197 1C11[PD-1]_L3.183 (SEQ ID NO: 859)
DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKISNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XenD22198 1C11[PD-1]_L3.184 (SEQ ID NO: 860)
DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKLSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XenD22199 1C11[PD-1]_L3.185 (SEQ ID NO: 861)
DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKSSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XenD22200 1C11[PD-1]_L3.186 (SEQ ID NO: 862)
DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSDRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XenD22201 1C11[PD-1]_L3.187 (SEQ ID NO: 863)
DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSHRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XenD22202 1C11[PD-1]_L3.188 (SEQ ID NO: 864)
DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSERFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XenD22203 1C11[PD-1]_L3.189 (SEQ ID NO: 865)
DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSRRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XenD22204 1C11[PD-1]_L3.190 (SEQ ID NO: 866)
DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCMQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 96E

>XenD22205 1C11[PD-1]_L3.191 (SEQ ID NO: 867)
DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCEQGSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XenD22206 1C11[PD-1]_L3.192 (SEQ ID NO: 868)
DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQASHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XenD22207 1C11[PD-1]_L3.193 (SEQ ID NO: 869)
DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQSSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XenD22208 1C11[PD-1]_L3.194 (SEQ ID NO: 870)
DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQDSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XenD22209 1C11[PD-1]_L3.195 (SEQ ID NO: 871)
DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQTSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XenD22210 1C11[PD-1]_L3.196 (SEQ ID NO: 872)
DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQQSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XenD22211 1C11[PD-1]_L3.197 (SEQ ID NO: 873)
DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQHSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XenD22212 1C11[PD-1]_L3.198 (SEQ ID NO: 874)
DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQLSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XenD22213 1C11[PD-1]_L3.199 (SEQ ID NO: 875)
DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQRSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XenD22214 1C11[PD-1]_L3.200 (SEQ ID NO: 876)
DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQFSHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XenD22215 1C11[PD-1]_L3.201 (SEQ ID NO: 877)
DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGTHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 96F

>XenD22216 1C11[PD-1]_L3.202 (SEQ ID NO: 878)
DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGAHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XenD22217 1C11[PD-1]_L3.203 (SEQ ID NO: 879)
DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGQHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XenD22218 1C11[PD-1]_L3.204 (SEQ ID NO: 880)
DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGVHVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XenD22219 1C11[PD-1]_L3.205 (SEQ ID NO: 881)
DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSYVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XenD22220 1C11[PD-1]_L3.206 (SEQ ID NO: 882)
DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSQVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XenD22221 1C11[PD-1]_L3.207 (SEQ ID NO: 883)
DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSDVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XenD22222 1C11[PD-1]_L3.208 (SEQ ID NO: 884)
DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSFVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XenD22223 1C11[PD-1]_L3.209 (SEQ ID NO: 885)
DVLMTQSPDSLAVSLGERATINCKSSQSIVHSNGNTYLEWYQQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYCFQGSTVPNTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 97A

XENP	Variant Name	K_D (M)	k_a (1/Ms)	k_d (1/s)	VH Variants	VL Variants	T_m (°C)
22538	1C11_H3_L3	1.84E-08	2.14E+05	3.93E-03			53.5
23577	1C11_H3_L3.1	9.95E-09	2.40E+05	2.38E-03		V2I	53.5
23579	1C11_H3_L3.3	1.54E-08	1.74E+05	2.68E-03		L3V	54.5
23589	1C11_H3_L3.15	1.50E-08	2.45E+05	3.67E-03		A12S	53.5
23601	1C11_H3_L3.23	3.87E-08	1.26E+05	4.90E-03		A19V	54
23605	1C11_H3_L3.28	1.57E-08	2.16E+05	3.39E-03		K24R	53.5
23609	1C11_H3_L3.32	2.20E-08	2.90E+05	6.37E-03		S25A	54
24201	1C11_H3_L3.113	1.98E-08	1.98E+05	3.92E-03		Q48K	54
23615	1C11_H3_L3.46	1.88E-08	2.51E+05	4.73E-03		S49P	54
23616	1C11_H3_L3.47	1.21E-08	4.26E+05	5.14E-03		S49A	54
23624	1C11_H3_L3.57	1.45E-08	2.55E+05	3.68E-03		S62T	53.5
24207	1C11_H3_L3.122	1.16E-09	5.68E+05	6.61E-04		V64I	53.5
24208	1C11_H3_L3.124	1.62E-08	1.80E+05	2.92E-03		D66A	53.5
23626	1C11_H3_L3.59	1.03E-08	3.41E+05	3.52E-03		S83R	53
23628	1C11_H3_L3.62	1.55E-08	1.68E+05	2.60E-03		L84M	54
23629	1C11_H3_L3.63	4.51E-08	9.98E+04	4.50E-03		L84V	55
24209	1C11_H3_L3.125	6.81E-09	3.50E+05	2.38E-03		L84V Q85E	54.5
23633	1C11_H3_L3.69	3.38E-08	2.04E+05	6.91E-03		V89A	54
23636	1C11_H3_L3.73	1.19E-08	2.22E+05	2.65E-03		V91T	54
23640	1C11_H3_L3.81	2.33E-08	1.51E+05	3.52E-03		G108Q	54
24210	1C11_H3_L3.132	1.63E-08	1.81E+05	2.95E-03		G108P	53.5
24372	1C11_H3_L3.86	1.94E-08	2.06E+05	3.98E-03		S62T L84V V91T G108Q	55.5
24373	1C11_H3_L3.87	2.17E-08	1.60E+05	3.48E-03		L3V A19V S25A S49P	56
24374	1C11_H3_L3.90	2.50E-08	1.70E+05	4.26E-03		L3V S25A S49P L84V V89A V91T G108Q	57
24375	1C11_H3_L3.92	1.89E-08	1.70E+05	3.22E-03		V2I L3V A19V S25A S49P S62T	56

Figure 97B

XENP	Variant Name	K_D (M)	k_a (1/Ms)	k_d (1/s)	VH Variants	VL Variants	T_m (°C)
24376	1C11_H3_L3.94	1.85E-08	1.77E+05	3.27E-03		V2I S62T L84V V89A V91T G108Q	56
24377	1C11_H3_L3.96	2.65E-08	1.63E+05	4.33E-03		V2I L3V S25A S49P S62T L84V V89A V91T G108Q	57.5
24378	1C11_H3_L3.105	2.04E-08	1.88E+05	3.85E-03		A12P S14T L15P R18P	71.5
24379	1C11_H3_L3.129					S82N V89A V91T F95H	49.5
24380	1C11_H3.176_L3.92				D66P T69K	V2I L3V A19V S25A S49P S62T	59
24381	1C11_H3.176_L3.94				D66P T69K	V2I S62T L84V V89A V91T G108Q	60
24382	1C11_H3.176_L3.96				D66P T69K	V2I L3V S25A S49P S62T L84V V89A V91T G108Q	62
24414	1C11_H3_L3.133					L3V A19V S25A S49P L84V V89A V91T G108Q	58.5
24415	1C11_H3_L3.134					L3V A19V S25A S49P L84V Q85E V89A V91T G108Q	58
24416	1C11_H3_L3.135					L3V A19V S25A S49P L84M V89A V91T G108Q	57.5
24417	1C11_H3_L3.136					L3V A19I S25A S49P L84M V89A V91T G108Q	57

Figure 97C

XENP	Variant Name	K_D (M)	k_a (1/Ms)	k_d (1/s)	VH Variants	VL Variants	Tm (°C)
24418	1C11_H3_L3.137					L3V A19I S25A S49P L84V V89A V91T G108Q	58
24419	1C11_H3_L3.138					L3V A19I S25A S49P L84V Q85E V89A V91T G108Q	58
24420	1C11_H3_L3.139					L3V S25A S49P V64I L84V V89A V91T G108Q	57.5
24421	1C11_H3_L3.140					V2I L3V S25A L84V Q85E V91T G108Q	56
24422	1C11_H3_L3.141	3.37E-08	2.63E+05	8.87E-03		V2I L3V S25A S49P L84V Q85E V91T G108Q	57
24423	1C11_H3_L3.142	3.55E-08	2.50E+05	8.86E-03		V2I L3V S25A S49A L84V Q85E V91T G108Q	57
24422	1C11_H3_L3.141					V2I L3V S25A S49P L84V Q85E V91T G108Q	56.5
24853	1C11_H3_L3.143					V2I L3V A19V S25A S49P L84V Q85E V91T G108Q	57.5
24854	1C11_H3_L3.144					V2I L3V A19V S25A S49P L84V Q85E V89A V91T G108Q	58.5

Figure 97D

XENP	Variant Name	K_D (M)	k_a (1/Ms)	k_d (1/s)	VH Variants	VL Variants	T_m (°C)
24855	1C11_H3_L3.145					V2I L3V A19V S25A L84V Q85E V91T G108Q	56.5
24856	1C11_H3_L3.146					V2I L3V A19V S25A L84V Q85E V89A V91T G108Q	57.5
24857	1C11_H3_L3.147					V2I L3V A19V S25A S49A L84V Q85E V91T G108Q	57
24858	1C11_H3_L3.148					V2I L3V A19V S25A S49A L84V Q85E V89A V91T G108Q	58
24218	1C11_H3.86_L3	1.90E-08	1.64E+05	3.12E-03	Q1E		
23755	1C11_H3.1_L3	2.42E-08	1.57E+05	3.80E-03	I2V		
23758	1C11_H3.5_L3	1.91E-08	2.48E+05	4.73E-03	S9A		
23760	1C11_H3.7_L3	4.19E-08	1.76E+05	7.37E-03	S9P		
24221	1C11_H3.90_L3	2.53E-08	1.68E+05	4.24E-03	E10V		
24222	1C11_H3.91_L3	2.47E-08	1.72E+05	4.26E-03	K12V		
24226	1C11_H3.95_L3	2.00E-08	1.92E+05	3.84E-03	A16G		
24227	1C11_H3.96_L3	2.30E-08	1.74E+05	4.00E-03	A16Q		
24228	1C11_H3.97_L3	2.42E-08	1.87E+05	4.52E-03	A16E		
24247	1C11_H3.120_L3	2.14E-08	2.02E+05	4.32E-03	M36I		
23765	1C11_H3.18_L3	1.56E-08	1.51E+05	2.35E-03	R40K		
24250	1C11_H3.125_L3	1.80E-08	2.04E+05	3.66E-03	A42P		
24254	1C11_H3.129_L3	2.37E-08	3.03E+05	7.19E-03	M50I		
24256	1C11_H3.134_L3	2.17E-08	2.48E+05	5.38E-03	Y56K		
23770	1C11_H3.25_L3	3.40E-08	1.84E+05	6.25E-03	Y56N		
24263	1C11_H3.143_L3	3.19E-08	2.02E+05	6.46E-03	T63Y		
24266	1C11_H3.146_L3	2.30E-08	2.20E+05	5.06E-03	D66P		
24267	1C11_H3.147_L3	2.04E-08	2.22E+05	4.52E-03	D66T		
24268	1C11_H3.148_L3	2.26E-08	1.89E+05	4.26E-03	D66Q G67K		
23776	1C11_H3.35_L3	6.92E-08	6.25E+04	4.32E-03	G67K		
23779	1C11_H3.41_L3	3.44E-08	1.04E+05	3.57E-03	T69K		
23780	1C11_H3.42_L3	2.78E-08	1.09E+05	3.04E-03	T69Q		

Figure 97E

XENP	Variant Name	K_D (M)	k_a (1/Ms)	k_d (1/s)	VH Variants	VL Variants	T_m (°C)
24270	1C11_H3.150_L3	1.89E-08	2.02E+05	3.81E-03	G70E		
23781	1C11_H3.43_L3	1.60E-08	2.42E+05	3.89E-03	F72V		
23786	1C11_H3.50_L3	1.80E-08	1.40E+05	2.52E-03	L76V		
24274	1C11_H3.154_L3	2.24E-08	1.99E+05	4.46E-03	L76I		
23793	1C11_H3.59_L3	9.74E-09	4.40E+05	4.28E-03	V80Q		
24279	1C11_H3.159_L3	2.29E-08	2.39E+05	5.45E-03	S81D		
24278	1C11_H3.158_L3	1.59E-08	2.19E+05	3.48E-03	S81N		
23796	1C11_H3.62_L3	1.62E-08	3.90E+05	6.32E-03	A83I		
24287	1C11_H3.168_L3	2.25E-08	1.96E+05	4.40E-03	S88N		
24291	1C11_H3.172_L3	2.41E-08	2.10E+05	5.06E-03	A92P		
23811	1C11_H3.74_L3	3.90E-08	2.00E+05	7.82E-03	F99Y		
24211	1C11_H3.78_L3	4.75E-08	2.37E+05	1.13E-02	S9P Y56N L76V V80Q		
24212	1C11_H3.80_L3	3.88E-08	2.64E+05	1.02E-02	Y56N L76V V80Q F99Y		
24213	1C11_H3.81_L3	2.22E-08	1.94E+05	4.30E-03	G67K T69K		
24214	1C11_H3.82_L3	1.60E-08	1.98E+05	3.16E-03	G67K T69Q		
24215	1C11_H3.83_L3	3.57E-08	2.71E+05	9.67E-03	Y56N L76V V80Q		
24216	1C11_H3.84_L3	2.01E-08	1.78E+05	3.59E-03	G67K T69K V80Q		
24217	1C11_H3.85_L3	1.78E-08	1.92E+05	3.41E-03	G67K T69Q V80Q		
24424	1C11_H3.176_L3				D66P T69K		58
24425	1C11_H3.177_L3				D66P G67K		58.5
24426	1C11_H3.178_L3				D66P T69K G70E		59
24427	1C11_H3.179_L3				D66P G67K G70E		58.5
24428	1C11_H3.180_L3				M36I L76V		55.5
24429	1C11_H3.181_L3				M36I L76I		55.5
24430	1C11_H3.182_L3				K12V A16E		54
24431	1C11_H3.183_L3				E10V A16E		56
24432	1C11_H3.184_L3				E10V K12V A16E		55.5
24433	1C11_H3.185_L3				Q1E I2V K12V A16E M36I A42P M50I T63Y D66P G67K G70E V80Q S81D S88N F99Y		61

Figure 97F

XENP	Variant Name	K_D (M)	k_a (1/Ms)	k_d (1/s)	VH Variants	VL Variants	T_m (°C)
24434	1C11_H3.186_L3				Q1E I2V K12V A16E M36I A42P T63Y D66P G70E S81D S88N F99Y		61.5
24435	1C11_H3.187_L3				I2V K12V A16E M36I A42P T63Y D66P G70E V80Q S88N F99Y		62
24436	1C11_H3.188_L3	5.32E-08	3.20E+05	1.71E-02	I2V A16E M36I A42P M50I T63Y D66P V80Q S88N F99Y		62.5
24437	1C11_H3.189_L3				I2V M36I A42P M50I T63Y D66P G67K S88N F99Y		61
24438	1C11_H3.190_L3				I2V E10V A16G M36I A42P M50I T63Y D66P V80Q S88N F99Y		60.5
24439	1C11_H3.191_L3				I2V K12V A16E D66P V80Q S88N		58.5
24440	1C11_H3.192_L3				Q1E I2V E10V A16E M36I G70E		58
24441	1C11_H3.193_L3				A42P M50I D66P G70E V80Q S88N F99Y		59.5
24442	1C11_H3.194_L3				Q1E E10V M36I M50I		56

Figure 97G

XENP	Variant Name	K_D (M)	k_a (1/Ms)	k_d (1/s)	VH Variants	VL Variants	T_m (°C)
24443	1C11_H3.195_L3				A42P T63Y S81D S88N		55
24436	1C11_H3.188_L3				I2V A16E M36I A42P M50I T63Y D66P V80Q S88N F99Y		61.5
24827	1C11_H3.196_L3				Q1E I2V A16E M36I A42P M50I T63Y D66P V80Q S88N F99Y		61
24828	1C11_H3.197_L3				I2V M36I A42P M50I T63Y D66P V80Q S88N F99Y		60
24829	1C11_H3.198_L3				I2V A16E M36I A42P M50I T63Y V80Q S88N F99Y		59
24830	1C11_H3.199_L3				I2V A16E A42P M50I T63Y D66P V80Q S88N F99Y		60.5
24831	1C11_H3.200_L3				I2V A16E M36I A42P M50I T63Y D66P V80Q S88N		61
24832	1C11_H3.201_L3				I2V A16E M36I A42P M50I T63Y D66P L76I V80Q S88N F99Y		62
24833	1C11_H3.202_L3				I2V A16E M36I M50I T63Y D66P V80Q S88N F99Y		61.5

Figure 97H

XENP	Variant Name	K_D (M)	k_a (1/Ms)	k_d (1/s)	VH Variants	VL Variants	T_m (°C)
24834	1C11_H3.203_L3				I2V A16E M36I A42P M50I T63Y D66P G70E V80Q S88N F99Y		62.5
24835	1C11_H3.204_L3				I2V A16E M36I A42P M50I T63Y D66P T69Q V80Q S88N F99Y		62.5
24836	1C11_H3.205_L3				I2V A16E M36I A42P M50I T63Y D66P T69K V80Q S88N F99Y		62.5
24837	1C11_H3.206_L3				I2V A16E M36I A42P M50I D66P V80Q S88N F99Y		62
24838	1C11_H3.207_L3				I2V A16E M36I A42P M50I T63Y D66P V80Q F99Y		61.5
24839	1C11_H3.208_L3				I2V A16E M36I A42P M50I T63Y D66P V80Q S81D S88N F99Y		61.5
24840	1C11_H3.209_L3				I2V A16E M36I A42P T63Y D66P V80Q S88N F99Y		63
24841	1C11_H3.210_L3				I2V A16E M36I A42P M50I T63Y D66P S88N F99Y		61.5

Figure 97I

XENP	Variant Name	K^D (M)	k_a (1/Ms)	k_d (1/s)	VH Variants	VL Variants	T_m (°C)
24842	1C11_H3.211_L3				I2V S9P A16E M36I A42P M50I T63Y D66P V80Q S88N F99Y		63.5
24843	1C11_H3.212_L3				I2V A16E M36I A42P M50I T63Y D66P S81D S88N F99Y		61
24844	1C11_H3.213_L3				I2V S9P A16E M36I M50I T63Y D66P V80Q S81D S88N F99Y		62.5
24845	1C11_H3.214_L3				I2V S9P A16E M36I M50I T63Y D66P L76I V80Q S88N F99Y		62.5
24846	1C11_H3.215_L3				I2V S9P A16E M36I M50I T63Y D66P S88N F99Y		62.5
24847	1C11_H3.216_L3				I2V S9P A16E M36I A42P T63Y D66P L76I V80Q S88N F99Y		65.5
24848	1C11_H3.217_L3				I2V S9P A16E M36I A42P T63Y D66P S88N F99Y		64
24849	1C11_H3.218_L3				I2V S9P A16E M36I A42P T63Y D66P V80Q S81D S88N F99Y		63.5

Figure 97J

XENP	Variant Name	K_D (M)	k_a (1/Ms)	k_d (1/s)	VH Variants	VL Variants	T_m (°C)
24850	1C11_H3.219_L3				I2V A16E M36I A42P M50I T63Y D66P T69Q G70E V80Q S88N F99Y		63
24851	1C11_H3.220_L3				I2V A16E M36I A42P M50I T63Y D66P T69K G70E V80Q S88N F99Y		62.5
24852	1C11_H3.221_L3				Q1E A16E M36I A42P M50I T63Y D66P V80Q S88N F99Y		
25295	1C11_H3.222_L3				I2V S9P A16E M36I A42P D66P L76I V80Q S88N F99Y		64
25296	1C11_H3.223_L3	3.21E-08			I2V S9P A16E M36I A42P T63Y D66P G70E L76I V80Q S88N F99Y		67
25301	1C11_H3.224_L3	3.06E-08			I2V S9P A16E M36I A42P T63Y D66P T69Q G70E L76I V80Q S88N F99Y		67
25302	1C11_H3.225_L3	3.22E-08			I2V S9P A16E M36I T63Y D66P G70E V80Q S81D S88N F99Y		64.5
25303	1C11_H3.226_L3	3.35E-08			I2V S9P A16E M36I T63Y D66P T69Q G70E V80Q S81D S88N F99Y		64.5

Figure 97K

XENP	Variant Name	K_D (M)	k_a (1/Ms)	k_d (1/s)	VH Variants	VL Variants	T_m (°C)
25304	1C11_H3.227_L3				Q1E I2V S9P A16E M36I T63Y D66P G70E V80Q S81D S88N F99Y		64.5
25305	1C11_H3.228_L3				Q1E I2V S9P A16E M36I T63Y D66P T69Q G70E V80Q S81D S88N F99Y		65
25306	1C11_H3.229_L3	3.79E-08			I2V A16E M36I A42P T63Y D66P T69Q G70E V80Q S88N F99Y		64.5
25307	1C11_H3.230_L3	4.19E-08			I2V A16E M36I A42P T63Y D66P T69Q G70E V80Q S81D S88N F99Y		64
25308	1C11_H3.231_L3	3.01E-08			I2V A16E M36I A42P D66P V80Q F99Y		61.5
25309	1C11_H3.232_L3	3.32E-08			I2V A16E M36I A42P D66P V80Q S81D S88N F99Y		61.5
25310	1C11_H3.233_L3				Q1E I2V A16E M36I A42P T63Y D66P T69Q G70E V80Q S88N F99Y		64.5
25311	1C11_H3.234_L3				Q1E I2V A16E M36I A42P T63Y D66P T69Q G70E V80Q S81D S88N F99Y		63.5

Figure 97L

XENP	Variant Name	K_D (M)	k_a (1/Ms)	k_d (1/s)	VH Variants	VL Variants	T_m (°C)
25312	1C11_H3.235_L3	3.14E-08			Q1E I2V A16E M36I A42P D66P V80Q F99Y		61.5
25313	1C11_H3.236_L3	3.94E-08			Q1E I2V A16E M36I A42P D66P V80Q S81D S88N F99Y		61.5
25314	1C11_H3.237_L3	3.44E-08			I2V A16E M36I T63Y D66P G70E V80Q S81D S88N F99Y		63
25315	1C11_H3.238_L3	3.84E-08			I2V A16E M36I T63Y D66P T69Q G70E V80Q S81D S88N F99Y		63.5
25316	1C11_H3.213_L3.144				I2V S9P A16E M36I M50I T63Y D66P V80Q S81D S88N F99Y		60, 71.5
25317	1C11_H3.213_L3.148				I2V S9P A16E M36I M50I T63Y D66P V80Q S81D S88N F99Y		59.5, 70.5
25318	1C11_H3.216_L3.144				I2V S9P A16E M36I A42P T63Y D66P L76I V80Q S88N F99Y		73
25319	1C11_H3.216_L3.148				I2V S9P A16E M36I A42P T63Y D66P L76I V80Q S88N F99Y		72.5

Figure 97M

XENP	Variant Name	K_D (M)	k_a (1/Ms)	k_d (1/s)	VH Variants	VL Variants	T_m (°C)
25320	1C11_H3.188_L3.144	5.04E-08			I2V A16E M36I A42P M50I T63Y D66P V80Q S88N F99Y	V2I L3V A19V S25A S49P L84V Q85E V89A V91T G108Q	60, 71
25321	1C11_H3.188_L3.148	4.13E-08			I2V A16E M36I A42P M50I T63Y D66P V80Q S88N F99Y	V2I L3V A19V S25A S49A L84V Q85E V89A V91T G108Q	59.5, 70.5
25802	1C11_H3.224_L3.144	3.31E-08			I2V S9P A16E M36I A42P T63Y D66P T69Q G70E L76I V80Q S88N F99Y	V2I L3V A19V S25A S49P L84V Q85E V89A V91T G108Q	
25803	1C11_H3.224_L3.148	3.12E-08			I2V S9P A16E M36I A42P T63Y D66P T69Q G70E L76I V80Q S88N F99Y	V2I L3V A19V S25A S49A L84V Q85E V89A V91T G108Q	
(25338)	1C11_H3.226_L3.144	4.37E-08			I2V S9P A16E M36I T63Y D66P T69Q G70E V80Q S81D S88N F99Y	V2I L3V A19V S25A S49P L84V Q85E V89A V91T G108Q	
(25339)	1C11_H3.226_L3.148	4.18E-08			I2V S9P A16E M36I T63Y D66P T69Q G70E V80Q S81D S88N F99Y	V2I L3V A19V S25A S49A L84V Q85E V89A V91T G108Q	
24436	1C11_H3.188_L3	5.32E-08			I2V A16E M36I A42P M50I T63Y D66P V80Q S88N F99Y		
24422	1C11_H3_L3.141	3.37E-08				V2I L3V S25A S49P L84V Q85E V91T G108Q	

Figure 97N

XENP	Variant Name	K_D (M)	k_a (1/Ms)	k_d (1/s)	VH Variants	VL Variants	T_m (°C)
24423	1C11_H3_L3.142	3.55E-08				V2I L3V S25A S49A L84V Q85E V91T G108Q	
25802	1C11_H3.224_L3.144	3.31E-08			I2V S9P A16E M36I A42P T63Y D66P T69Q G70E L76I V80Q S88N F99Y	V2I L3V A19V S25A S49P L84V Q85E V89A V91T G108Q	74
25803	1C11_H3.224_L3.148	3.12E-08			I2V S9P A16E M36I A42P T63Y D66P T69Q G70E L76I V80Q S88N F99Y	V2I L3V A19V S25A S49A L84V Q85E V89A V91T G108Q	73.5
25804	1C11_H3.228_L3.144	3.88E-08	2.59E+05	1.00E-02	Q1E I2V S9P A16E M36I T63Y D66P T69Q G70E V80Q S81D S88N F99Y	V2I L3V A19V S25A S49P L84V Q85E V89A V91T G108Q	62, 72.5
25805	1C11_H3.228_L3.148	4.19E-08	2.37E+05	9.94E-03	Q1E I2V S9P A16E M36I T63Y D66P T69Q G70E V80Q S81D S88N F99Y	V2I L3V A19V S25A S49A L84V Q85E V89A V91T G108Q	62, 72
25806	1C11_H3.234_L3.144	2.74E-08	2.83E+05	7.75E-03	Q1E I2V A16E M36I A42P T63Y D66P T69Q G70E V80Q S81D S88N F99Y	V2I L3V A19V S25A S49P L84V Q85E V89A V91T G108Q	60.5, 71.5
25807	1C11_H3.234_L3.148	3.75E-08	2.32E+05	8.69E-03	Q1E I2V A16E M36I A42P T63Y D66P T69Q G70E V80Q S81D S88N F99Y	V2I L3V A19V S25A S49A L84V Q85E V89A V91T G108Q	60.5, 71

Figure 97O

XENP	Variant Name	K_D (M)	k_a (1/Ms)	k_d (1/s)	VH Variants	VL Variants	T_m (^{O}C)
25808	1C11_H3.239_L3.144	4.26E-08	2.19E+05	9.34E-03	Q1E I2V S9P A16E M36I A42P T63Y D66P T69Q G70E L76I V80Q S88N F99Y	V2I L3V A19V S25A S49P L84V Q85E V89A V91T G108Q	74
25809	1C11_H3.240_L3.144	4.31E-08	2.43E+05	1.05E-02	I2V S9P A16E M36I A42P T63Y D66P T69Q G70E L76I V80Q S81D S88N F99Y	V2I L3V A19V S25A S49P L84V Q85E V89A V91T G108Q	73.5
25810	1C11_H3.241_L3.144	4.05E-08	2.18E+05	8.84E-03	Q1E I2V S9P A16E M36I A42P T63Y D66P T69Q G70E L76I V80Q S81D S88N F99Y	V2I L3V A19V S25A S49P L84V Q85E V89A V91T G108Q	73.5
25811	1C11_H3.239_L3.148	4.47E-08	2.27E+05	1.02E-02	Q1E I2V S9P A16E M36I A42P T63Y D66P T69Q G70E L76I V80Q S88N F99Y	V2I L3V A19V S25A S49A L84V Q85E V89A V91T G108Q	73.5
25812	1C11_H3.240_L3.148	2.75E-08	3.22E+05	8.85E-03	I2V S9P A16E M36I A42P T63Y D66P T69Q G70E L76I V80Q S81D S88N F99Y	V2I L3V A19V S25A S49A L84V Q85E V89A V91T G108Q	72.5
25813	1C11_H3.241_L3.148	3.33E-08	2.86E+05	9.53E-03	Q1E I2V S9P A16E M36I A42P T63Y D66P T69Q G70E L76I V80Q S81D S88N F99Y	V2I L3V A19V S25A S49A L84V Q85E V89A V91T G108Q	72.5

Figure 97P

XENP	Variant Name	K_D (M)	k_a (1/Ms)	k_d (1/s)	VH Variants	VL Variants	T_m (°C)
25814	1C11_H3.239_L3.125	4.16E-08	3.15E+05	1.31E-02	Q1E I2V S9P A16E M36I A42P T63Y D66P T69Q G70E L76I V80Q S88N F99Y	L84V Q85E	68
25815	1C11_H3.240_L3.125	5.08E-08	2.80E+05	1.42E-02	I2V S9P A16E M36I A42P T63Y D66P T69Q G70E L76I V80Q S81D S88N F99Y	L84V Q85E	67
25816	1C11_H3.241_L3.125	4.34E-08	3.34E+05	1.45E-02	Q1E I2V S9P A16E M36I A42P T63Y D66P T69Q G70E L76I V80Q S81D S88N F99Y	L84V Q85E	67
25817	1C11_H3.239_L3.92	3.46E-08	2.66E+05	9.22E-03	Q1E I2V S9P A16E M36I A42P T63Y D66P T69Q G70E L76I V80Q S88N F99Y	V2I L3V A19V S25A S49P S62T	71
25818	1C11_H3.240_L3.92	3.15E-08	3.01E+05	9.49E-03	I2V S9P A16E M36I A42P T63Y D66P T69Q G70E L76I V80Q S81D S88N F99Y	V2I L3V A19V S25A S49P S62T	70
25819	1C11_H3.241_L3.92	3.31E-08	3.05E+05	1.01E-02	Q1E I2V S9P A16E M36I A42P T63Y D66P T69Q G70E L76I V80Q S81D S88N F99Y	V2I L3V A19V S25A S49P S62T	70

Figure 97Q

XENP	Variant Name	K_D (M)	k_a (1/Ms)	k_d (1/s)	VH Variants	VL Variants	T_m (°C)
24854	1C11_H3_L3.144	3.01E-08	2.20E+05	6.61E-03		V2I L3V A19V S25A S49P L84V Q85E V89A V91T G108Q	58.5
24858	1C11_H3_L3.148	2.65E-08	2.53E+05	6.69E-03		V2I L3V A19V S25A S49A L84V Q85E V89A V91T G108Q	58
24847	1C11_H3.216_L3	3.79E-08	2.66E+05	1.01E-02	I2V S9P A16E M36I A42P T63Y D66P L76I V80Q S88N F99Y		65.5
25305	1C11_H3.228_L3	3.70E-08	3.13E+05	1.16E-02	Q1E I2V S9P A16E M36I T63Y D66P T69Q G70E V80Q S81D S88N F99Y		65
25311	1C11_H3.234_L3	3.29E-08	3.06E+05	1.01E-02	Q1E I2V A16E M36I A42P T63Y D66P T69Q G70E V80Q S81D S88N F99Y		63.5
25318	1C11_H3.216_L3.144	3.87E-08	2.57E+05	9.93E-03	I2V S9P A16E M36I A42P T63Y D66P L76I V80Q S88N F99Y	V2I L3V A19V S25A S49P L84V Q85E V89A V91T G108Q	73
25319	1C11_H3.216_L3.148	4.36E-08	2.45E+05	1.07E-02	I2V S9P A16E M36I A42P T63Y D66P L76I V80Q S88N F99Y	V2I L3V A19V S25A S49A L84V Q85E V89A V91T G108Q	72.5

Figure 98

XENP	Variant	K_D (M)	k_a (1/Ms)	k_d (1/s)
26321	1C11[PD-1]_H3.59_L3.1	1.28E-08	1.90E+05	2.43E-03
26322	1C11[PD-1]_H3.59_L3.38	7.15E-09	2.13E+05	1.52E-03
26323	1C11[PD-1]_H3.59_L3.51	1.54E-08	2.23E+05	3.44E-03
26324	1C11[PD-1]_H3.59_L3.59	1.74E-08	1.98E+05	3.43E-03
26325	1C11[PD-1]_H3.59_L3.73	1.86E-08	1.92E+05	3.56E-03
26326	1C11[PD-1]_H3.59_L3.125	1.78E-08	2.05E+05	3.64E-03
26327	1C11[PD-1]_H3.135_L3.1	1.45E-08	2.04E+05	2.96E-03
26328	1C11[PD-1]_H3.135_L3.38	8.90E-09	2.19E+05	1.94E-03
26329	1C11[PD-1]_H3.135_L3.51	1.86E-08	2.10E+05	3.90E-03
26330	1C11[PD-1]_H3.135_L3.59	1.66E-08	2.30E+05	3.82E-03
26331	1C11[PD-1]_H3.135_L3.73	1.81E-08	2.10E+05	3.81E-03
26332	1C11[PD-1]_H3.135_L3.125	1.92E-08	2.05E+05	3.93E-03
26333	1C11[PD-1]_H3.138_L3.1	1.81E-08	1.92E+05	3.49E-03
26334	1C11[PD-1]_H3.138_L3.38	1.33E-08	1.99E+05	2.64E-03
26335	1C11[PD-1]_H3.138_L3.51	2.61E-08	2.01E+05	5.25E-03
26336	1C11[PD-1]_H3.138_L3.59	1.92E-08	2.31E+05	4.44E-03
26337	1C11[PD-1]_H3.138_L3.73	1.94E-08	3.26E+05	6.32E-03
26338	1C11[PD-1]_H3.138_L3.125	2.20E-08	3.19E+05	7.01E-03
26339	1C11[PD-1]_H3.155_L3.1	1.78E-08	3.05E+05	5.41E-03
26340	1C11[PD-1]_H3.155_L3.38	1.42E-08	3.20E+05	4.55E-03
26341	1C11[PD-1]_H3.155_L3.51	2.86E-08	2.80E+05	8.01E-03
26342	1C11[PD-1]_H3.155_L3.59	2.27E-08	3.10E+05	7.03E-03
26343	1C11[PD-1]_H3.155_L3.73	2.55E-08	2.91E+05	7.41E-03
26344	1C11[PD-1]_H3.155_L3.125	2.03E-08	3.66E+05	7.41E-03
22553	1C11[PD-1]_H3L3	1.94E-08	3.24E+05	6.29E-03

Figure 99

XENP	Variant Name	K_D (M)	k_a (1/Ms)	k_d (1/s)
22553	1C11_H3L3	2.98E-08	3.70E+05	1.10E-02
26322	1C11_H3.59_L3.38	1.27E-08	3.13E+05	3.99E-03
26917	1C11_H3.244_L3	6.48E-08	4.54E+05	2.94E-02
26918	1C11_H3.249_L3	6.00E-08	4.91E+05	2.95E-02
26919	1C11_H3.250_L3	3.16E-07	3.65E+05	1.15E-01
26920	1C11_H3.256_L3	2.95E-08	3.07E+05	9.05E-03
26921	1C11_H3.258_L3	2.53E-08	4.16E+05	1.05E-02
26922	1C11_H3.288_L3	1.95E-08	4.18E+05	8.16E-03
26923	1C11_H3.292_L3	2.02E-08	3.34E+05	6.75E-03
26924	1C11_H3.303_L3	1.48E-08	3.60E+05	5.34E-03
26925	1C11_H3_L3.149	7.35E-09	6.55E+05	4.82E-03
26926	1C11_H3_L3.152	6.27E-09	4.55E+05	2.85E-03
26927	1C11_H3_L3.160	4.29E-07	1.95E+05	8.37E-02
26928	1C11_H3_L3.161	3.33E-07	3.51E+05	1.17E-01
26929	1C11_H3_L3.166	3.14E-08	4.25E+05	1.34E-02
26930	1C11_H3_L3.168	3.18E-08	4.57E+05	1.45E-02
26931	1C11_H3_L3.180	1.14E-07	3.64E+05	4.13E-02
26932	1C11_H3_L3.186	6.14E-08	4.25E+05	2.61E-02
26933	1C11_H3_L3.191	5.89E-08	4.40E+05	2.59E-02
26934	1C11_H3_L3.194	1.04E-07	2.44E+05	2.54E-02
26935	1C11_H3_L3.202	2.64E-08	3.69E+05	9.74E-03
26936	1C11_H3_L3.204	2.97E-08	3.86E+05	1.15E-02
26937	1C11_H3_L3.207	3.14E-08	2.94E+05	9.23E-03
26938	1C11_H3.308_L3.152	1.42E-08	1.79E+05	2.53E-03
26939	1C11_H3.59_L3.152	1.56E-08	4.02E+05	6.25E-03
26940	1C11_H3.303_L3.152	3.41E-09	5.18E+05	1.77E-03
26941	1C11_H3.308_L3.180	4.34E-08	4.97E+05	2.16E-02
26942	1C11_H3.59_L3.180	5.74E-08	4.45E+05	2.55E-02
26943	1C11_H3.303_L3.180	4.20E-08	3.53E+05	1.48E-02
26944	1C11_H3.303_L3.210	1.04E-08	4.14E+05	4.28E-03
26945	1C11_H3.308_L3	3.22E-08	4.00E+05	1.29E-02
26946	1C11_H3.59_L3	3.71E-08	4.90E+05	1.81E-02
26947	1C11_H3.135_L3	4.76E-08	3.75E+05	1.79E-02
26949	1C11_H3.308_L3.210	2.37E-08	2.84E+05	6.71E-03
26950	1C11_H3_L3.210	1.98E-08	2.25E+05	4.45E-03
26951	1C11_H3_L3.1	4.71E-08	2.38E+05	1.12E-02
26952	1C11_H3_L3.38	2.85E-08	3.44E+05	9.79E-03
26953	1C11_H3_L3.125	5.60E-08	4.16E+05	2.33E-02
26954	1C11_H3.308_L3.38	2.29E-08	3.31E+05	7.58E-03
26955	1C11_H3.59_L3.210	1.98E-08	2.89E+05	5.72E-03

Figure 100

		Human PD-1		
TA	Variant	K_D (M)	k_a (1/Ms)	k_d (1/s)
XENP27643	1C11_H3_L3.211	2.95E-08	3.57E+05	1.05E-02
XENP27644	1C11_H3_L3.212	2.57E-08	3.75E+05	9.63E-03
XENP27645	1C11_H3_L3.213	3.32E-08	3.16E+05	1.05E-02
XENP27646	1C11_H3_L3.214	7.26E-08	4.75E+05	3.45E-02
XENP27647	1C11_H3_L3.215	7.90E-08	7.89E+05	6.23E-02
XENP27648	1C11_H3_L3.216	1.25E-07	7.64E+05	9.52E-02
XENP27649	1C11_H3_L3.217	7.18E-09	3.81E+05	2.73E-03
XENP27650	1C11_H3_L3.218	5.80E-09	3.53E+05	2.05E-03
XENP27651	1C11_H3_L3.219	6.72E-09	3.40E+05	2.29E-03
XENP27652	1C11_H3_L3.220	5.02E-09	3.43E+05	1.72E-03
XENP16432	Nivolumab_H0L0	1.02E-08	3.38E+05	3.43E-03

Figure 101

		Human PD-1		
TA	**Variant**	**K_D (M)**	**k_a (1/Ms)**	**k_d (1/s)**
XENP27839	1C11_H3.309_L3	4.63E-08	3.02E+05	1.40E-02
XENP27840	1C11_H3.310_L3	6.02E-08	2.84E+05	1.71E-02
XENP27841	1C11_H3.311_L3	5.30E-08	3.06E+05	1.62E-02
XENP27842	1C11_H3.312_L3	5.07E-08	3.31E+05	1.68E-02
XENP27843	1C11_H3.313_L3	4.92E-08	3.14E+05	1.54E-02
XENP27844	1C11_H3.314_L3	4.93E-08	3.85E+05	1.90E-02
XENP27845	1C11_H3.315_L3	3.15E-08	3.40E+05	1.07E-02
XENP27846	1C11_H3.316_L3	3.77E-08	3.51E+05	1.32E-02
XENP27847	1C11_H3.317_L3	5.04E-08	3.41E+05	1.72E-02
XENP27848	1C11_H3.318_L3	7.16E-08	2.84E+05	2.03E-02
XENP27849	1C11_H3.319_L3	2.44E-08	3.31E+05	8.07E-03
XENP27850	1C11_H3.320_L3	1.60E-08	2.96E+05	4.73E-03
XENP27851	1C11_H3.321_L3	1.19E-08	3.95E+05	4.70E-03
XENP27852	1C11_H3.322_L3	1.91E-08	3.17E+05	6.06E-03
XENP27853	1C11_H3.323_L3	1.25E-08	3.87E+05	4.81E-03
XENP27854	1C11_H3.324_L3	7.17E-09	4.18E+05	3.00E-03
XENP27855	1C11_H3.325_L3	1.67E-08	4.03E+05	6.74E-03
XENP27856	1C11_H3.326_L3	1.16E-08	3.67E+05	4.25E-03
XENP27857	1C11_H3.319_L3.152	8.51E-09	3.15E+05	2.68E-03
XENP27858	1C11_H3.320_L3.152	5.66E-09	3.75E+05	2.12E-03
XENP27859	1C11_H3.321_L3.152	5.60E-09	3.40E+05	1.90E-03
XENP27860	1C11_H3.322_L3.152	8.41E-09	3.09E+05	2.60E-03
XENP27861	1C11_H3.323_L3.152	4.39E-09	3.82E+05	1.68E-03
XENP27862	1C11_H3.324_L3.152	3.46E-09	4.06E+05	1.41E-03
XENP27863	1C11_H3.325_L3.152	6.61E-09	4.88E+05	3.23E-03
XENP27864	1C11_H3.326_L3.152	6.12E-09	5.02E+05	3.07E-03
XENP27865	1C11_H3.319_L3.220	5.46E-09	3.37E+05	1.84E-03
XENP27866	1C11_H3.320_L3.220	4.13E-09	3.44E+05	1.42E-03
XENP27867	1C11_H3.321_L3.220	5.89E-09	4.50E+05	2.65E-03
XENP27868	1C11_H3.322_L3.220	7.13E-09	4.00E+05	2.85E-03
XENP27869	1C11_H3.323_L3.220	4.70E-09	3.86E+05	1.82E-03
XENP27870	1C11_H3.324_L3.220	4.48E-09	4.26E+05	1.91E-03
XENP27871	1C11_H3.325_L3.220	5.34E-09	5.44E+05	2.90E-03
XENP27872	1C11_H3.326_L3.220	3.91E-09	3.78E+05	1.48E-03
XENP22553	1C11_H3L3	6.19E-08	3.04E+05	1.88E-02
XENP26940	1C11_H3.303_L3.152	7.36E-09	3.67E+05	2.70E-03

Figure 102

			Human PD-1	
TA	**Variant**	**K_D (M)**	**k_a (1/Ms)**	**k_d (1/s)**
XENP22553	1C11_H3L3	1.54E-08	3.17E+05	4.87E-03
XENP26940	1C11_H3.303_L3.152	6.74E-09	2.57E+05	1.73E-03
XENP27858	1C11_H3.320_L3.152	3.07E-09	3.23E+05	9.91E-04
XENP27861	1C11_H3.323_L3.152	4.14E-09	4.74E+05	1.97E-03
XENP27862	1C11_H3.324_L3.152	4.48E-09	3.25E+05	1.46E-03
XENP27959	1C11_H3.303_L3.219	3.58E-09	2.56E+05	9.14E-04
XENP27960	1C11_H3.303_L3.220	2.30E-09	2.47E+05	5.68E-04
XENP27961	1C11_H3.320_L3.219	2.75E-09	3.28E+05	9.01E-04
XENP27962	1C11_H3.323_L3.219	2.32E-09	3.60E+05	8.34E-04
XENP27963	1C11_H3.324_L3.219	2.96E-09	3.71E+05	1.10E-03

Figure 103

			Human PD-1	
TA	**Variant**	**K_D (M)**	**k_a (1/Ms)**	**k_d (1/s)**
XENP28024	1C11_H3.327_L3.220	1.39E-09	2.35E+05	3.25E-04
XENP28025	1C11_H3.328_L3.220	1.85E-09	2.17E+05	4.02E-04
XENP28026	1C11_H3.329_L3.220	1.78E-09	2.50E+05	4.45E-04
XENP28027	1C11_H3.330_L3.220	2.18E-09	3.03E+05	6.61E-04
XENP28028	1C11_H3.331_L3.220	2.15E-09	3.42E+05	7.35E-04
XENP28029	1C11_H3.332_L3.220	2.57E-09	2.94E+05	7.56E-04
XENP28030	1C11_H3.333_L3.220	2.37E-09	2.71E+05	6.44E-04
XENP28031	1C11_H3.334_L3.220	2.43E-09	2.56E+05	6.21E-04
XENP28032	1C11_H3.335_L3.220	2.11E-09	2.45E+05	5.18E-04
XENP28033	1C11_H3.336_L3.220	5.29E-09	1.79E+05	9.50E-04
XENP28034	1C11_H3.337_L3.220	2.92E-09	2.82E+05	8.23E-04
XENP28035	1C11_H3.338_L3.220	5.54E-09	2.55E+05	1.41E-03
XENP22553	1C11_H3L3	1.80E-08	2.13E+05	3.82E-03
XENP26940	1C11_H3.303_L3.152	5.18E-09	1.41E+05	7.28E-04
XENP27960	1C11_H3.303_L3.220	3.35E-09	2.45E+05	8.19E-04
XENP27866	1C11_H3.320_L3.220	3.26E-09	3.67E+05	1.20E-03
XENP27869	1C11_H3.323_L3.220	4.13E-09	2.55E+05	1.05E-03
XENP27870	1C11_H3.324_L3.220	7.56E-09	2.41E+05	1.82E-03
XENP27959	1C11_H3.303_L3.219	6.47E-09	1.82E+05	1.17E-03
XENP27961	1C11_H3.320_L3.219	4.22E-09	2.60E+05	1.10E-03
XENP27962	1C11_H3.323_L3.219	4.58E-09	3.95E+05	1.81E-03
XENP27963	1C11_H3.324_L3.219	4.63E-09	2.73E+05	1.27E-03

Figure 104

		Human PD-1			Cynomolgus PD-1		
TA	Variant	KD (M)	ka (1/Ms)	kd (1/s)	KD (M)	ka (1/Ms)	kd (1/s)
XENP28651	1C11_H3.327_L3.152	4.14E-09	2.03E+05	8.41E-04	5.23E-09	3.38E+05	1.77E-03
XENP28652	1C11_H3.328_L3.152	7.74E-09	1.77E+05	1.37E-03	1.10E-08	2.63E+05	2.89E-03
XENP28653	1C11_H3.329_L3.152	4.95E-09	1.93E+05	9.55E-04	7.78E-09	3.59E+05	2.79E-03

Figure 105A

Variant Name	HC XenD	LC XenD	VH Variants	VL Variants	K_D (M)	k_a (1/Ms)	k_d (1/s)
1C11_H3L3	XenD17478	XenD17482	-	-	5.35E-08	2.27E+05	1.22E-02
1C11_H3.59_L3.38	XenD18576	XenD18472	V80Q	T37N	1.57E-08	3.08E+05	4.83E-03
1C11_H3.242_L3	XenD22097	XenD17482	G26A	-	3.65E-08	2.92E+05	1.07E-02
1C11_H3.243_L3	XenD22098	XenD17482	G26S	-	3.08E-08	3.96E+05	1.22E-02
1C11_H3.244_L3	XenD22099	XenD17482	G26T	-	1.46E-08	3.82E+05	5.56E-03
1C11_H3.245_L3	XenD22100	XenD17482	Y27W	-	2.94E-08	5.02E+05	1.48E-02
1C11_H3.246_L3	XenD22101	XenD17482	Y27L	-	8.55E-08	5.15E+05	4.41E-02
1C11_H3.247_L3	XenD22102	XenD17482	Y27H	-	1.38E-07	2.73E+05	3.76E-02
1C11_H3.248_L3	XenD22103	XenD17482	Y27Q	-	1.06E-07	3.44E+05	3.66E-02
1C11_H3.249_L3	XenD22104	XenD17482	Y27D	-	4.70E-08	4.63E+05	2.18E-02
1C11_H3.250_L3	XenD22105	XenD17482	Y27K	-	1.50E-08	6.61E+05	9.88E-03
1C11_H3.251_L3	XenD22106	XenD17482	T28V	-	3.37E-08	2.48E+05	8.35E-03
1C11_H3.252_L3	XenD22107	XenD17482	T28A	-	7.63E-08	2.57E+05	1.96E-02
1C11_H3.253_L3	XenD22108	XenD17482	T28I	-	7.03E-08	2.86E+05	2.01E-02
1C11_H3.254_L3	XenD22109	XenD17482	T28Q	-	8.07E-08	2.15E+05	1.73E-02
1C11_H3.255_L3	XenD22110	XenD17482	F29Y	-	2.81E-08	3.45E+05	9.70E-03
1C11_H3.256_L3	XenD22111	XenD17482	F29W	-	1.86E-08	4.70E+05	8.73E-03
1C11_H3.257_L3	XenD22112	XenD17482	F29H	-	7.52E-08	6.83E+05	5.14E-02
1C11_H3.258_L3	XenD22113	XenD17482	T30V	-	1.56E-08	2.99E+05	4.68E-03
1C11_H3.259_L3	XenD22114	XenD17482	T30A	-	3.48E-08	3.72E+05	1.29E-02
1C11_H3.260_L3	XenD22115	XenD17482	T30I	-	4.18E-08	2.64E+05	1.11E-02
1C11_H3.261_L3	XenD22116	XenD17482	T30Q	-	3.05E-08	1.98E+05	6.04E-03
1C11_H3.262_L3	XenD22117	XenD17482	H31Y	-	5.45E-08	3.56E+05	1.94E-02
1C11_H3.263_L3	XenD22118	XenD17482	H31Q	-	1.15E-07	4.80E+05	5.49E-02
1C11_H3.264_L3	XenD22119	XenD17482	H31D	-	8.37E-08	4.58E+05	3.83E-02
1C11_H3.265_L3	XenD22120	XenD17482	H31R	-	1.60E-07	4.80E+05	7.66E-02
1C11_H3.266_L3	XenD22121	XenD17482	H31F	-	7.75E-08	5.45E+05	4.22E-02
1C11_H3.267_L3	XenD22122	XenD17482	Y34F	-	4.88E-08	4.38E+05	2.14E-02
1C11_H3.268_L3	XenD22123	XenD17482	Y34H	-	6.76E-08	2.63E+05	1.78E-02

Figure 105B

Variant Name	HC XenD	LC XenD	VH Variants	VL Variants	K_D (M)	k_a (1/Ms)	k_d (1/s)
1C11_H3.269_L3	XenD22124	XenD17482	Y34L	-	1.03E-07	4.99E+05	5.14E-02
1C11_H3.270_L3	XenD22125	XenD17482	Y34W	-	6.17E-08	4.47E+05	2.76E-02
1C11_H3.271_L3	XenD22126	XenD17482	G35T	-			
1C11_H3.272_L3	XenD22127	XenD17482	G35Q	-			
1C11_H3.273_L3	XenD22128	XenD17482	M36L	-	4.82E-08	4.15E+05	2.00E-02
1C11_H3.274_L3	XenD22129	XenD17482	V39L	-	4.14E-08	3.21E+05	1.33E-02
1C11_H3.275_L3	XenD22130	XenD17482	V39T	-			
1C11_H3.276_L3	XenD22131	XenD17482	V39F	-	1.42E-07	4.07E+05	5.76E-02
1C11_H3.277_L3	XenD22132	XenD17482	G51T	-			
1C11_H3.278_L3	XenD22133	XenD17482	G51D	-			
1C11_H3.279_L3	XenD22134	XenD17482	G51Q	-			
1C11_H3.280_L3	XenD22135	XenD17482	G51E	-			
1C11_H3.281_L3	XenD22136	XenD17482	W52F	-	2.64E-07	9.36E+05	2.47E-01
1C11_H3.282_L3	XenD22137	XenD17482	W52H	-			
1C11_H3.283_L3	XenD22138	XenD17482	N54Q	-	2.10E-07	6.90E+05	1.45E-01
1C11_H3.284_L3	XenD22139	XenD17482	N54E	-	1.06E-07	1.66E+06	1.75E-01
1C11_H3.285_L3	XenD22140	XenD17482	N54H	-	2.10E-07	1.17E+06	2.45E-01
1C11_H3.286_L3	XenD22141	XenD17482	N54S	-	1.66E-07	7.93E+05	1.32E-01
1C11_H3.287_L3	XenD22142	XenD17482	Y56F	-	5.24E-08	4.32E+05	2.26E-02
1C11_H3.288_L3	XenD22143	XenD17482	Y56H	-	2.05E-08	3.45E+05	7.08E-03
1C11_H3.289_L3	XenD22144	XenD17482	Y56L	-	9.79E-08	3.36E+05	3.29E-02
1C11_H3.290_L3	XenD22145	XenD17482	Y56W	-	8.91E-08	3.37E+05	3.00E-02
1C11_H3.291_L3	XenD22146	XenD17482	T59V	-	5.44E-08	4.71E+05	2.56E-02
1C11_H3.292_L3	XenD22147	XenD17482	T59S	-	3.16E-08	3.08E+05	9.72E-03
1C11_H3.293_L3	XenD22148	XenD17482	T59A	-	4.33E-08	3.67E+05	1.59E-02
1C11_H3.294_L3	XenD22149	XenD17482	T59I	-	1.53E-07	3.40E+05	5.22E-02
1C11_H3.295_L3	XenD22150	XenD17482	E61Q	-	6.46E-08	3.06E+05	1.98E-02
1C11_H3.296_L3	XenD22151	XenD17482	E61K	-	1.20E-07	2.01E+05	2.42E-02
1C11_H3.297_L3	XenD22152	XenD17482	Y110F	-	3.99E-08	3.68E+05	1.47E-02

Figure 105C

Variant Name	HC XenD	LC XenD	VH Variants	VL Variants	K_D (M)	k_a (1/Ms)	k_d (1/s)
1C11_H3.298_L3	XenD22153	XenD17482	Y110Q	-	4.00E-08	3.93E+05	1.57E-02
1C11_H3.299_L3	XenD22154	XenD17482	Y110H	-	4.16E-08	4.67E+05	1.94E-02
1C11_H3.300_L3	XenD22155	XenD17482	Y110R	-	2.99E-08	3.00E+05	8.98E-03
1C11_H3.301_L3	XenD22156	XenD17482	Y110K	-	7.04E-08	4.22E+05	2.97E-02
1C11_H3.302_L3	XenD22157	XenD17482	Y111W	-	4.23E-07	2.37E+05	1.00E-01
1C11_H3.303_L3	XenD22158	XenD17482	Y111F	-	1.37E-08	2.67E+05	3.66E-03
1C11_H3.304_L3	XenD22159	XenD17482	G112A	-	2.98E-07	3.29E+05	9.81E-02
1C11_H3.305_L3	XenD22160	XenD17482	G112S	-	7.23E-07	1.29E+05	9.35E-02
1C11_H3.306_L3	XenD22161	XenD17482	Y116F	-	3.62E-08	3.34E+05	1.21E-02
1C11_H3.307_L3	XenD22162	XenD17482	Y116W	-	6.87E-08	2.99E+05	2.05E-02
1C11_H3_L3.149	XenD17478	XenD22163	-	H31Y	5.36E-09	3.71E+05	1.99E-03
1C11_H3_L3.150	XenD17478	XenD22164	-	H31Q	1.64E-06	1.89E+05	3.11E-01
1C11_H3_L3.151	XenD17478	XenD22165	-	H31D	1.94E-06	1.39E+05	2.69E-01
1C11_H3_L3.152	XenD17478	XenD22166	-	H31F	2.88E-09	4.05E+05	1.17E-03
1C11_H3_L3.153	XenD17478	XenD22167	-	H31T	2.71E-07	1.22E+06	3.30E-01
1C11_H3_L3.154	XenD17478	XenD22168	-	H31K	8.36E-08	3.83E+06	3.20E-01
1C11_H3_L3.155	XenD17478	XenD22169	-	S32T	7.09E-08	2.95E+05	2.09E-02
1C11_H3_L3.156	XenD17478	XenD22170	-	S32A	4.05E-08	3.78E+05	1.53E-02
1C11_H3_L3.157	XenD17478	XenD22171	-	S32Q	7.70E-08	2.89E+05	2.22E-02
1C11_H3_L3.158	XenD17478	XenD22172	-	S32G	4.47E-08	2.52E+05	1.13E-02
1C11_H3_L3.159	XenD17478	XenD22173	-	S32V	4.54E-08	3.28E+05	1.49E-02
1C11_H3_L3.160	XenD17478	XenD22174	-	N33H	2.46E-08	7.40E+05	1.82E-02
1C11_H3_L3.161	XenD17478	XenD22175	-	N33E	2.51E-08	8.32E+05	2.09E-02
1C11_H3_L3.162	XenD17478	XenD22176	-	N33S	5.26E-08	4.53E+05	2.38E-02
1C11_H3_L3.163	XenD17478	XenD22177	-	N33R	9.95E-08	5.83E+05	5.80E-02
1C11_H3_L3.164	XenD17478	XenD22178	-	N33L	3.48E-08	7.39E+05	2.57E-02
1C11_H3_L3.165	XenD17478	XenD22179	-	G34A	3.22E-08	3.04E+05	9.76E-03
1C11_H3_L3.166	XenD17478	XenD22180	-	G34S	1.88E-08	4.56E+05	8.57E-03
1C11_H3_L3.167	XenD17478	XenD22181	-	G34T	2.52E-08	4.26E+05	1.07E-02

Figure 105D

Variant Name	HC XenD	LC XenD	VH Variants	VL Variants	K_D (M)	k_a (1/Ms)	k_d (1/s)
1C11_H3_L3.168	XenD17478	XenD22182	-	G34Q	1.22E-08	4.73E+05	5.75E-03
1C11_H3_L3.169	XenD17478	XenD22183	-	N35D	4.98E-08	3.34E+05	1.66E-02
1C11_H3_L3.170	XenD17478	XenD22184	-	N35H	3.64E-08	3.67E+05	1.34E-02
1C11_H3_L3.171	XenD17478	XenD22185	-	N35E	5.63E-08	3.60E+05	2.03E-02
1C11_H3_L3.172	XenD17478	XenD22186	-	N35R	3.66E-08	2.60E+05	9.49E-03
1C11_H3_L3.173	XenD17478	XenD22187	-	Y38F	2.69E-07	4.99E+05	1.34E-01
1C11_H3_L3.174	XenD17478	XenD22188	-	Y38H	1.22E-07	3.68E+06	4.49E-01
1C11_H3_L3.175	XenD17478	XenD22189	-	Y38L			
1C11_H3_L3.176	XenD17478	XenD22190	-	Y38W	1.90E-06	2.95E+05	5.61E-01
1C11_H3_L3.177	XenD17478	XenD22191	-	Y38Q			
1C11_H3_L3.178	XenD17478	XenD22192	-	Y55F	5.59E-08	3.80E+05	2.13E-02
1C11_H3_L3.179	XenD17478	XenD22193	-	Y55H	7.74E-08	3.17E+05	2.46E-02
1C11_H3_L3.180	XenD17478	XenD22194	-	Y55L	5.86E-09	8.21E+05	4.81E-03
1C11_H3_L3.181	XenD17478	XenD22195	-	Y55W	1.12E-07	5.20E+05	5.83E-02
1C11_H3_L3.182	XenD17478	XenD22196	-	Y55Q	1.07E-07	3.95E+05	4.23E-02
1C11_H3_L3.183	XenD17478	XenD22197	-	V57I	4.03E-08	3.76E+05	1.51E-02
1C11_H3_L3.184	XenD17478	XenD22198	-	V57L	4.31E-08	4.10E+05	1.77E-02
1C11_H3_L3.185	XenD17478	XenD22199	-	V57S	4.78E-08	3.69E+05	1.76E-02
1C11_H3_L3.186	XenD17478	XenD22200	-	N59D	3.45E-08	4.04E+05	1.40E-02
1C11_H3_L3.187	XenD17478	XenD22201	-	N59H	6.37E-08	3.30E+05	2.10E-02
1C11_H3_L3.188	XenD17478	XenD22202	-	N59E	6.21E-08	4.35E+05	2.70E-02
1C11_H3_L3.189	XenD17478	XenD22203	-	N59R	1.27E-07	3.52E+05	4.46E-02
1C11_H3_L3.190	XenD17478	XenD22204	-	F95M	6.64E-08	3.37E+05	2.24E-02
1C11_H3_L3.191	XenD17478	XenD22205	-	F95E	4.91E-08	5.92E+05	2.91E-02
1C11_H3_L3.192	XenD17478	XenD22206	-	G97A	1.48E-07	3.79E+05	5.60E-02
1C11_H3_L3.193	XenD17478	XenD22207	-	G97S	2.63E-07	3.60E+05	9.47E-02
1C11_H3_L3.194	XenD17478	XenD22208	-	G97D	4.62E-08	4.49E+05	2.07E-02
1C11_H3_L3.195	XenD17478	XenD22209	-	G97T	3.45E-06	6.12E+04	2.11E-01
1C11_H3_L3.196	XenD17478	XenD22210	-	G97Q	1.27E-07	3.19E+05	4.05E-02

Figure 105E

Variant Name	HC XenD	LC XenD	VH Variants	VL Variants	K_D (M)	k_a (1/Ms)	k_d (1/s)
1C11_H3_L3.197	XenD17478	XenD22211	-	G97H			
1C11_H3_L3.198	XenD17478	XenD22212	-	G97L	9.47E-08	8.29E+05	7.85E-02
1C11_H3_L3.199	XenD17478	XenD22213	-	G97R			
1C11_H3_L3.200	XenD17478	XenD22214	-	G97F			
1C11_H3_L3.201	XenD17478	XenD22215	-	S98T	5.22E-08	3.05E+05	1.59E-02
1C11_H3_L3.202	XenD17478	XenD22216	-	S98A	1.99E-08	3.89E+05	7.76E-03
1C11_H3_L3.203	XenD17478	XenD22217	-	S98Q	3.14E-08	6.06E+05	1.91E-02
1C11_H3_L3.204	XenD17478	XenD22218	-	S98V	1.28E-08	4.92E+05	6.30E-03
1C11_H3_L3.205	XenD17478	XenD22219	-	H99Y	5.46E-08	3.89E+05	2.13E-02
1C11_H3_L3.206	XenD17478	XenD22220	-	H99Q	4.57E-08	2.75E+05	1.26E-02
1C11_H3_L3.207	XenD17478	XenD22221	-	H99D	3.48E-08	3.48E+05	1.21E-02
1C11_H3_L3.208	XenD17478	XenD22222	-	H99F	5.16E-08	3.91E+05	2.02E-02
1C11_H3_L3.209	XenD17478	XenD22223	-	H99T	2.93E-08	4.26E+05	1.25E-02

Figure 106

Variant Name	HC XenD	LC XenD	VH Variants	VL Variants	K_D (M)	k_a (1/Ms)	k_d (1/s)
1C11_H3.244_L3	XenD22099	XenD17482	G26T	-	6.48E-08	4.54E+05	2.94E-02
1C11_H3.249_L3	XenD22104	XenD17482	Y27D	-	6.00E-08	4.91E+05	2.95E-02
1C11_H3.250_L3	XenD22105	XenD17482	Y27K	-	3.16E-07	3.65E+05	1.15E-01
1C11_H3.256_L3	XenD22111	XenD17482	F29W	-	2.95E-08	3.07E+05	9.05E-03
1C11_H3.258_L3	XenD22113	XenD17482	T30V	-	2.53E-08	4.16E+05	1.05E-02
1C11_H3.288_L3	XenD22143	XenD17482	Y56H	-	1.95E-08	4.18E+05	8.16E-03
1C11_H3.292_L3	XenD22147	XenD17482	T59S	-	2.02E-08	3.34E+05	6.75E-03
1C11_H3.303_L3	XenD22158	XenD17482	Y111F	-	1.48E-08	3.60E+05	5.34E-03
1C11_H3_L3.149	XenD17478	XenD22163	-	H31Y	7.35E-09	6.55E+05	4.82E-03
1C11_H3_L3.152	XenD17478	XenD22166	-	H31F	6.27E-09	4.55E+05	2.85E-03
1C11_H3_L3.160	XenD17478	XenD22174	-	N33H	4.29E-07	1.95E+05	8.37E-02
1C11_H3_L3.161	XenD17478	XenD22175	-	N33E	3.33E-07	3.51E+05	1.17E-01
1C11_H3_L3.166	XenD17478	XenD22180	-	G34S	3.14E-08	4.25E+05	1.34E-02
1C11_H3_L3.168	XenD17478	XenD22182	-	G34Q	3.18E-08	4.57E+05	1.45E-02
1C11_H3_L3.180	XenD17478	XenD22194	-	Y55L	1.14E-07	3.64E+05	4.13E-02
1C11_H3_L3.186	XenD17478	XenD22200	-	N59D	6.14E-08	4.25E+05	2.61E-02
1C11_H3_L3.191	XenD17478	XenD22205	-	F95E	5.89E-08	4.40E+05	2.59E-02
1C11_H3_L3.194	XenD17478	XenD22208	-	G97D	1.04E-07	2.44E+05	2.54E-02
1C11_H3_L3.202	XenD17478	XenD22216	-	S98A	2.64E-08	3.69E+05	9.74E-03
1C11_H3_L3.204	XenD17478	XenD22218	-	S98V	2.97E-08	3.86E+05	1.15E-02
1C11_H3_L3.207	XenD17478	XenD22221	-	H99D	3.14E-08	2.94E+05	9.23E-03

Figure 107

XENP	Variant	human PD-1 K_D (M)	cyno PD-1 K_D (M)
21461	Pembrolizumab_H0L0	4.48E-09	1.17E-09
16432	Nivolumab_H0L0	4.46E-09	4.09E-09
21575	1C11[PD-1]_H0L0	8.65E-09	1.39E-08
22553	1C11[PD-1]_H3L3	8.35E-09	1.23E-08
25842	1C11[PD-1]_H3.241_L3.92	7.74E-09	1.30E-08
26917	1C11[PD-1]_H3.244_L3	1.19E-08	1.94E-08
26322	1C11[PD-1]_H3.59_L3.38	3.77E-09	7.73E-09
26926	1C11[PD-1]_H3_L3.152	1.69E-09	2.33E-09
26940	1C11[PD-1]_H3.303_L3.152	1.31E-09	3.00E-09

Figure 108

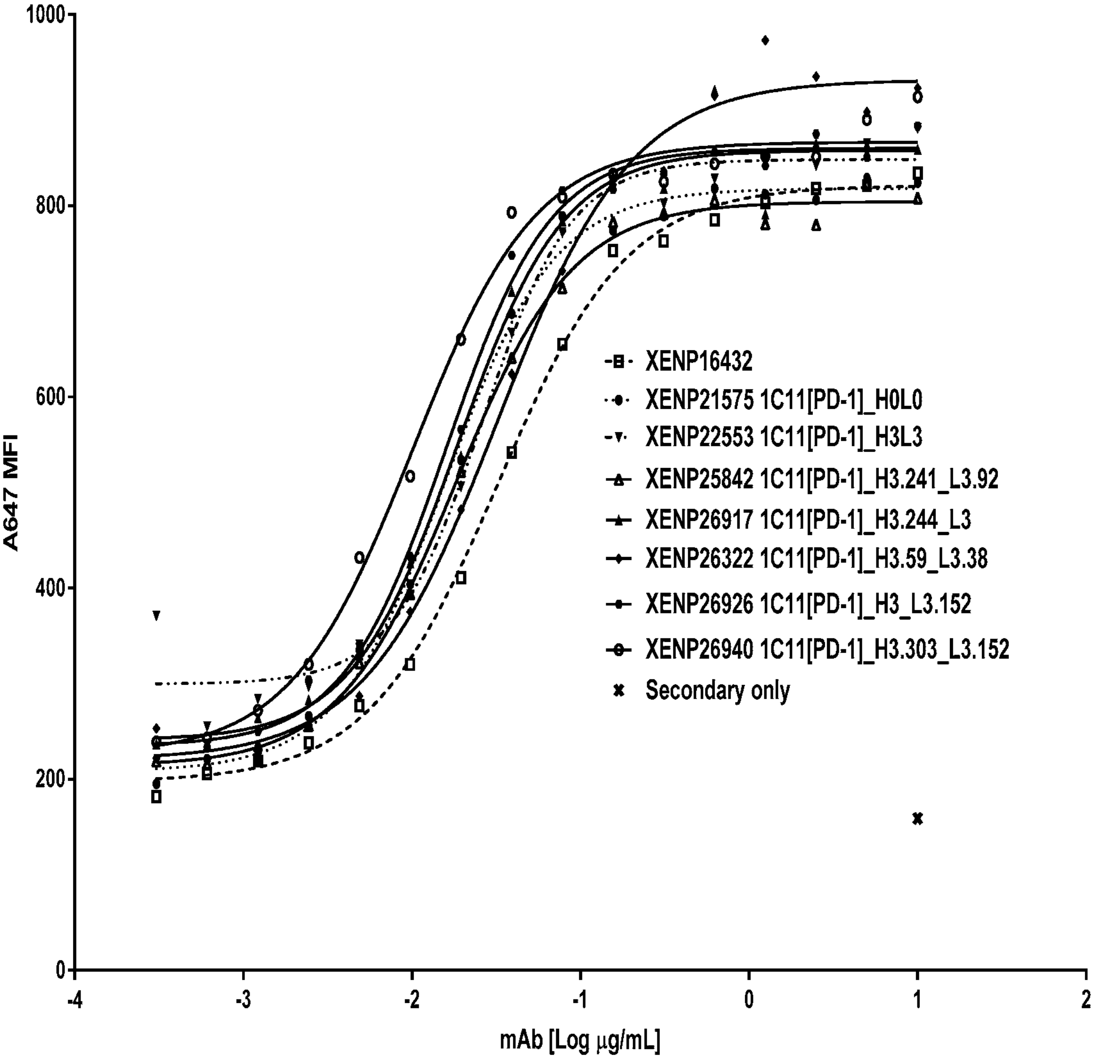

1000
800
600
400
200
0
A647 MFI
-4
-3
-2
-1
0
1
2
mAb [Log µg/mL]
XENP16432
XENP21575 1C11[PD-1]_H0L0
XENP22553 1C11[PD-1]_H3L3
XENP25842 1C11[PD-1]_H3.241_L3.92
XENP26917 1C11[PD-1]_H3.244_L3
XENP26322 1C11[PD-1]_H3.59_L3.38
XENP26926 1C11[PD-1]_H3_L3.152
XENP26940 1C11[PD-1]_H3.303_L3.152
Secondary only

Figure 109A

>XENP29159 human_IL15Ra(sushi)_(GGGGS)5-human_IL15(N4D/N65D;single-chain)-1C11[PD-1]_H3.329_L3.220_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-IgG1_PVA_/S267K/S364K/E357Q

Chain 1 - human_IL15Ra(sushi)_(GGGGS)5-human_IL15(N4D/N65D;single-chain)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-(SEQ ID NO: 886)

ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGG
SGGGGSGGGGSGGGGS/NWVDVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDAS
IHDTVEDLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPP
VAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESD
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 - 1C11[PD-1]_H3.329_IgG1_PVA_/S267K/S364K/E357Q-(SEQ ID NO: 887)

QIQLVQSGSELLKPGASVSVSCKASGYTFT**HYGMN**WVRQAPGQGLEWMG**WINTHTGEPTYADGFTG**RFVFSLDTS
VSTAYLQISSLKAEDTAVYFCAR**DYFGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 3 - 1C11[PD-1]_L3.220 (SEQ ID NO: 888)

DILMTQSPDSLAVSLGERATINC**KSSQSIVYSNGNNYLE**WYQQKPGQSPKLLIY**KVSNRFS**GVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP29160 human_IL15Ra(sushi)_(GGGGS)5-human_IL15(N4D/N65D;single-chain)-1C11[PD-1]_H3.303_L3.152_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-IgG1_PVA_/S267K/S364K/E357Q

Chain 1 - human_IL15Ra(sushi)_(GGGGS)5-human_IL15(N4D/N65D;single-chain)_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-(SEQ ID NO: 889)

ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGG
SGGGGSGGGGSGGGGS/NWVDVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDAS
IHDTVEDLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPP
VAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESD
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 - 1C11[PD-1]_H3.303_IgG1_PVA_/S267K/S364K/E357Q-(SEQ ID NO: 890)

QIQLVQSGSELKKPGASVKVSCKASGYTFT**HYGMN**WVRQAPGQGLEWMG**WINTYTGEPTYADGFTG**RFVFSLDTS
VSTAYLQISSLKAEDTAVYFCAR**DYFGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 3 - 1C11[PD-1]_L3.152-(SEQ ID NO: 891)

DVLMTQSPDSLAVSLGERATINC**KSSQSIVFSNGNTYLE**WYQQKPGQSPKLLIY**KVSNRFS**GVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 109B

> human_IL15Ra(sushi)_(GGGGS)5-human_IL15(N4D/N65D;single-chain)-1C11[PD-1]_ H3.234_L3.144_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-IgG1_PVA_/S267K/S364K/E357Q

Chain 1 - human_IL15Ra(sushi)_(GGGGS)5-human_IL15(N4D/N65D;single-chain)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-(SEQ ID NO: 892)

ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGG
SGGGGSGGGGSGGGGS/NWVDVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDAS
IHDTVEDLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPP
VAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESD
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 - 1C11[PD-1]_ H3.234_IgG1_PVA_/S267K/S364K/E357Q-(SEQ ID NO: 893)

EVQLVQSGSELKKPGESVKVSCKASGYTFT**HYGIN**WVRQPPGQGLEWMG**WINTYTGEPYYAPGFQE**RFVFSLDTS
QDTAYLQINSLKAEDTAVYYCAR**DYYGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 3 - 1C11[PD-1]_ L3.144 (SEQ ID NO: 894)

DIVMTQSPDSLAVSLGERVTINC**KASQSIVHSNGNTYLE**WYQQKPGQPPKLLIY**KVSNRFS**GVPDRFSGSGSGTD
FTLTISSVEAEDAATYYC**FQGSHVPNT**FGQGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

> human_IL15Ra(sushi)_(GGGGS)5-human_IL15(N4D/N65D;single-chain)-1C11[PD-1]_ H3.240_L3.148_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-IgG1_PVA_/S267K/S364K/E357Q

Chain 1 - human_IL15Ra(sushi)_(GGGGS)5-human_IL15(N4D/N65D;single-chain)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-(SEQ ID NO: 895)

ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGG
SGGGGSGGGGSGGGGS/NWVDVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDAS
IHDTVEDLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPP
VAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESD
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 - 1C11[PD-1]_ H3.240_IgG1_PVA_/S267K/S364K/E357Q-(SEQ ID NO: 896)

QVQLVQSGPELKKPGESVKVSCKASGYTFT**HYGIN**WVRQPPGQGLEWMG**WINTYTGEPYYAPGFQE**RFVFSIDTS
QDTAYLQINSLKAEDTAVYYCAR**DYYGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 3 - 1C11[PD-1]_ L3.148-(SEQ ID NO: 897)

DVLMTQSPDSLAVSLGERATINC**KSSQSIVHSNGNTYLE**WYQQKPGQSPKLLIY**KVSNRFS**GVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 109C

> human_IL15Ra(sushi)_(GGGGS)5-human_IL15(N4D/N65D;single-chain)-1C11[PD-1]_H3.241_L3.148_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-IgG1_PVA_/S267K/S364K/E357Q

Chain 1 - human_IL15Ra(sushi)_(GGGGS)5-human_IL15(N4D/N65D;single-chain)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 898)

ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGG
SGGGGSGGGGSGGGGS/NWVDVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDAS
IHDTVEDLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPP
VAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESD
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 - 1C11[PD-1]_ H3.241_IgG1_PVA_/S267K/S364K/E357Q-(SEQ ID NO: 899)

EVQLVQSGPELKKPGESVKVSCKASGYTFT**HYGIN**WVRQPPGQGLEWMG**WINTYTGEPYYAPGFQE**RFVFSIDTS
QDTAYLQINSLKAEDTAVYYCAR**DYYGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 3 - 1C11[PD-1]_ L3.148-(SEQ ID NO: 900)

DVLMTQSPDSLAVSLGERATINC**KSSQSIVHSNGNTYLE**WYQQKPGQSPKLLIY**KVSNRFS**GVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

> human_IL15Ra(sushi)_(GGGGS)5-human_IL15(N4D/N65D;single-chain)-1C11[PD-1]_H3.241_L3.92_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-IgG1_PVA_/S267K/S364K/E357Q

Chain 1 - human_IL15Ra(sushi)_(GGGGS)5-human_IL15(N4D/N65D;single-chain)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-(SEQ ID NO: 901)

ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGG
SGGGGSGGGGSGGGGS/NWVDVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDAS
IHDTVEDLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPP
VAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESD
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 - 1C11[PD-1]_ H3.241_IgG1_PVA_/S267K/S364K/E357Q-(SEQ ID NO: 902)

EVQLVQSGPELKKPGESVKVSCKASGYTFT**HYGIN**WVRQPPGQGLEWMG**WINTYTGEPYYAPGFQE**RFVFSIDTS
QDTAYLQINSLKAEDTAVYYCAR**DYYGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 3 - 1C11[PD-1]_ L3.92-(SEQ ID NO: 903)

DIVMTQSPDSLAVSLGERVTINC**KASQSIVHSNGNTYLE**WYQQKPGQPPKLLIY**KVSNRFT**GVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 109D

> human_IL15Ra(sushi)_(GGGGS)5-human_IL15(N4D/N65D;single-chain)-1C11[PD-1]_ H3.328_L3.152_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-IgG1_PVA_/S267K/S364K/E357Q

Chain 1 - human_IL15Ra(sushi)_(GGGGS)5-human_IL15(N4D/N65D;single-chain)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-(SEQ ID NO: 904)

ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGG
SGGGGSGGGGSGGGGS/NWVDVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDAS
IHDTVEDLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPP
VAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESD
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 - 1C11[PD-1]_ H3.328_IgG1_PVA_/S267K/S364K/E357Q-(SEQ ID NO: 905)

QIQLVQSGSELKKPGASVSVSCKASGYTFT**HYGMN**WVRQAPGQGLEWMG**WINTHTGEPTYADGFTG**RFVFSLDTS
VSTAYLQISSLKAEDTAVYFCAR**DYFGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 3 - 1C11[PD-1]_ L3.152-(SEQ ID NO: 906)

DVLMTQSPDSLAVSLGERATINC**KSSQSIVFSNGNTYLE**WYQQKPGQSPKLLIY**KVSNRFS**GVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 110A-Figure 110B

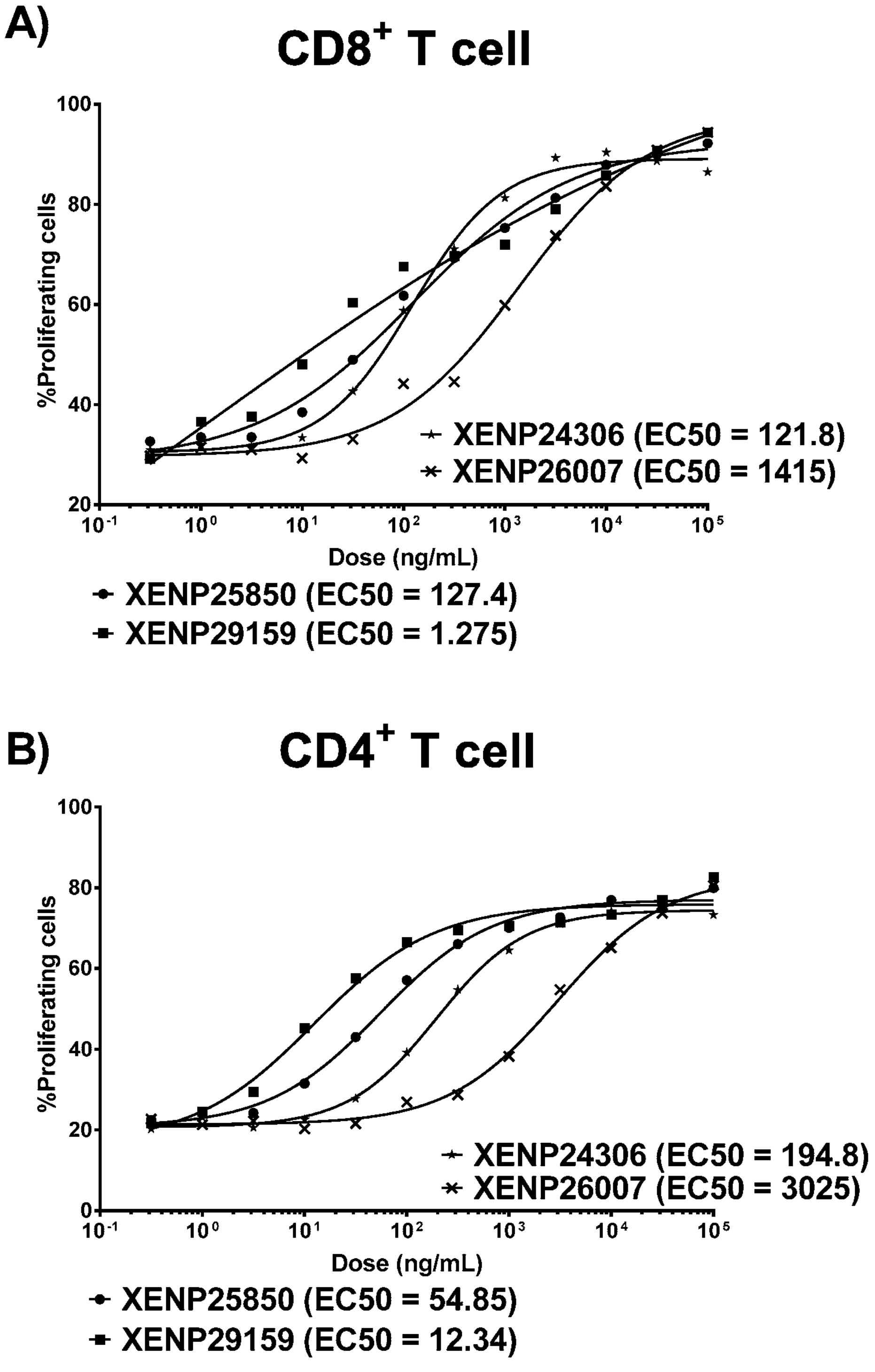
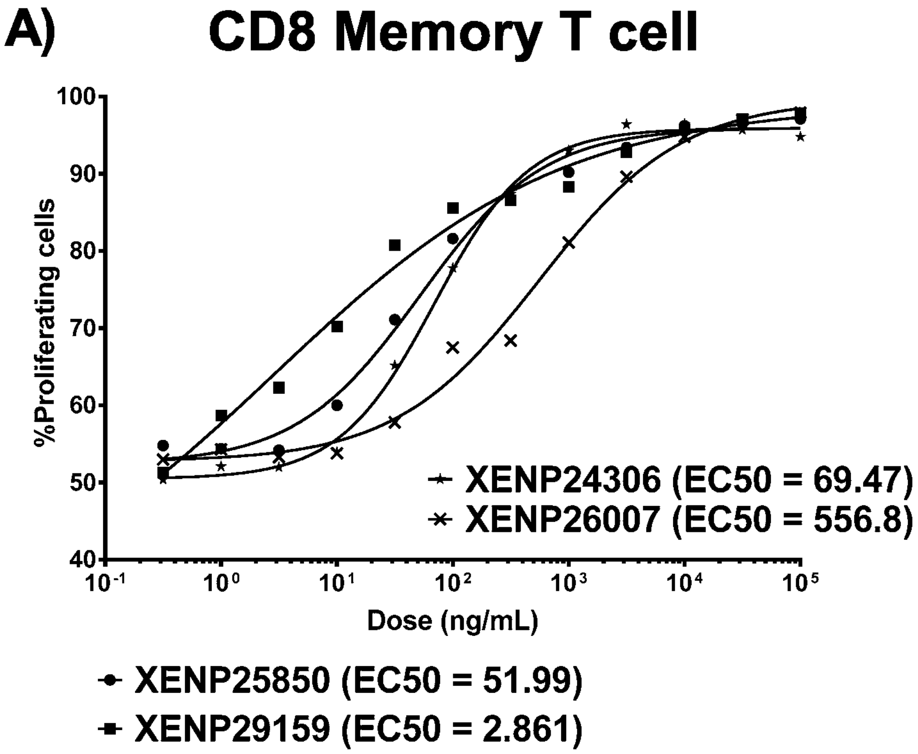


Figure 111A-Figure 111B



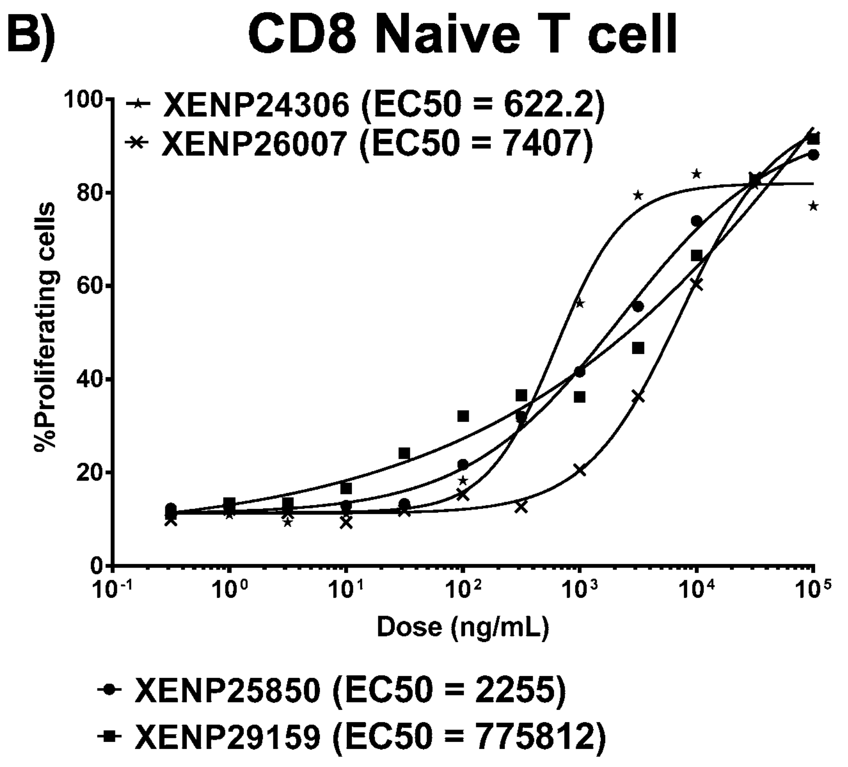
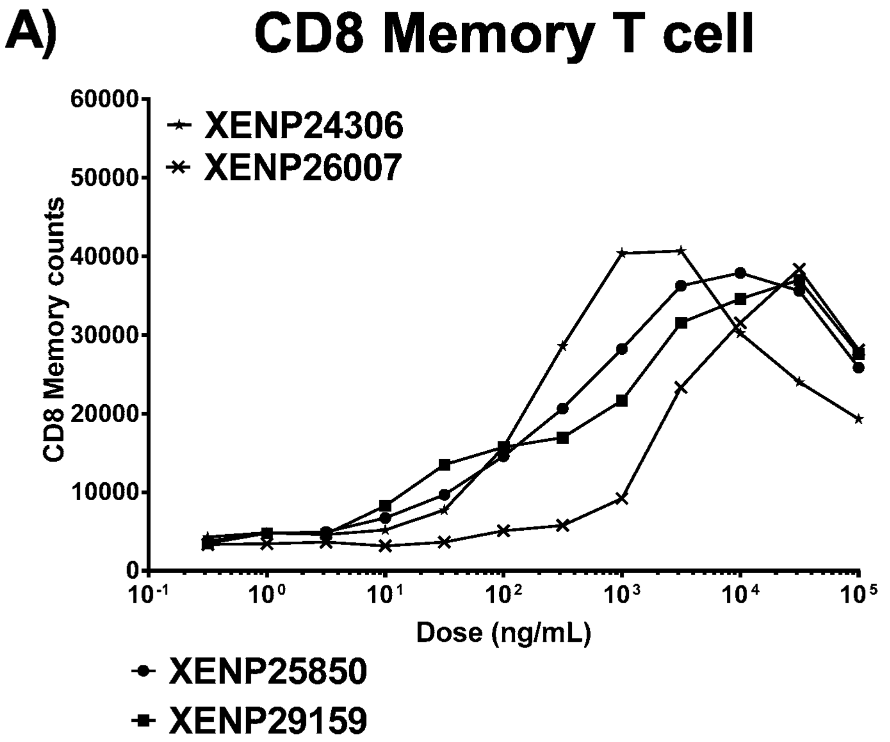


Figure 112A-Figure 112B



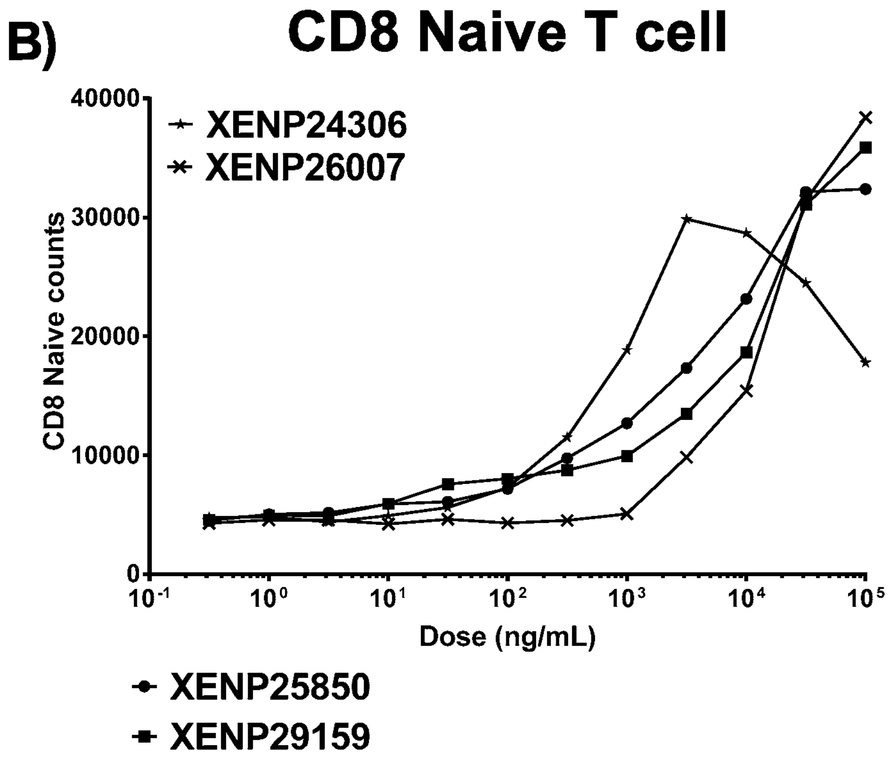
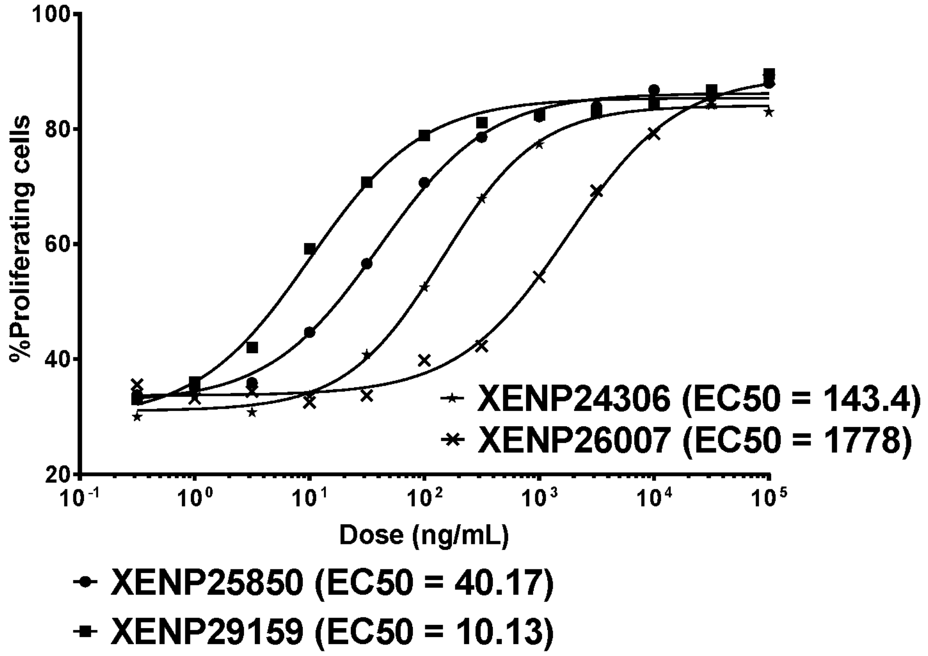


Figure 113A-Figure 113B

A) CD4 Memory T cell



B) CD4 Naive T cell

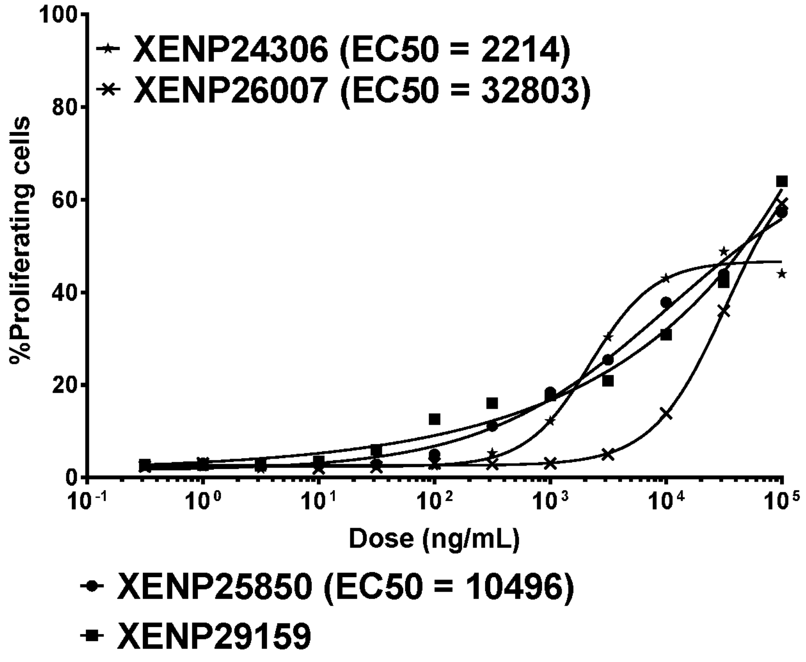
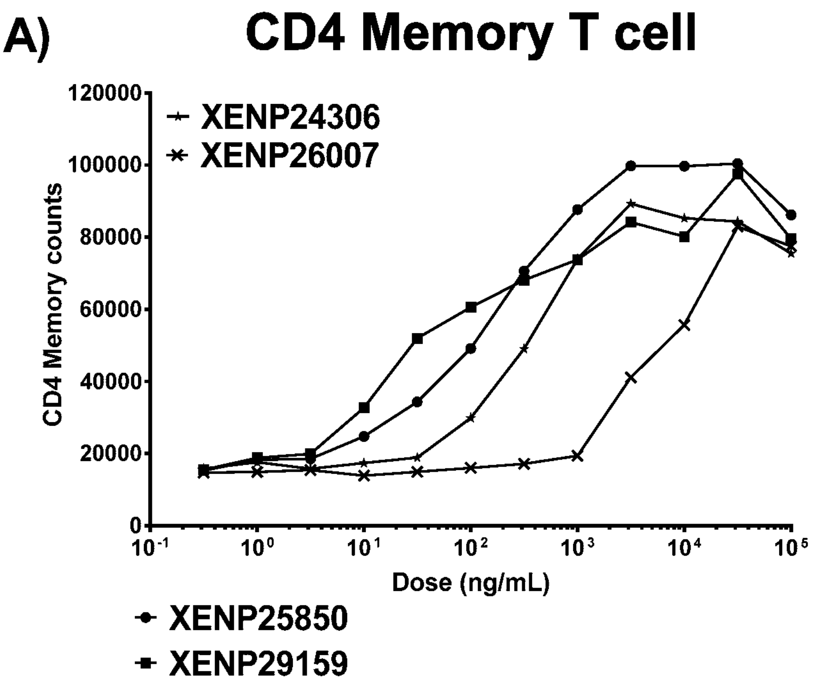


Figure 114A-Figure 114B



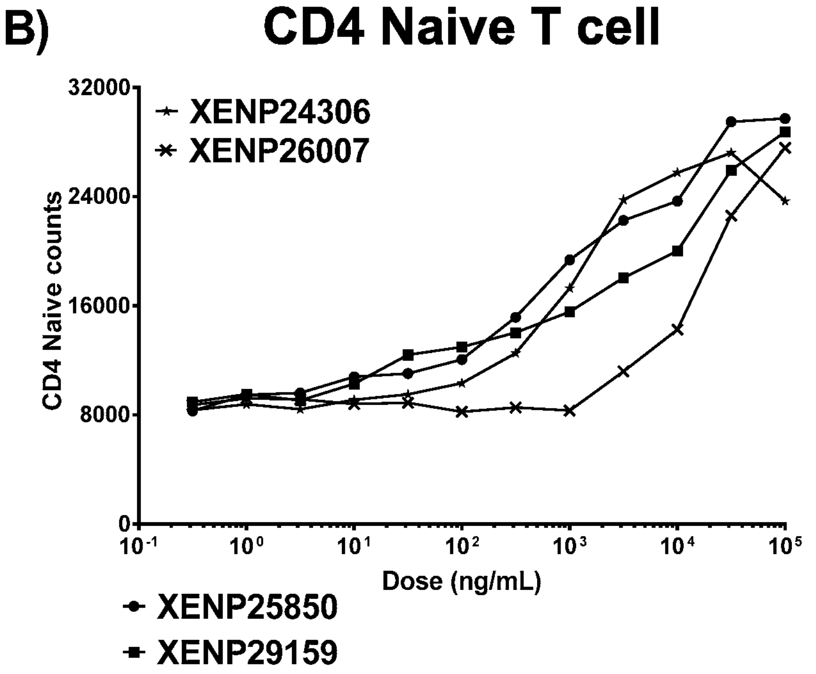
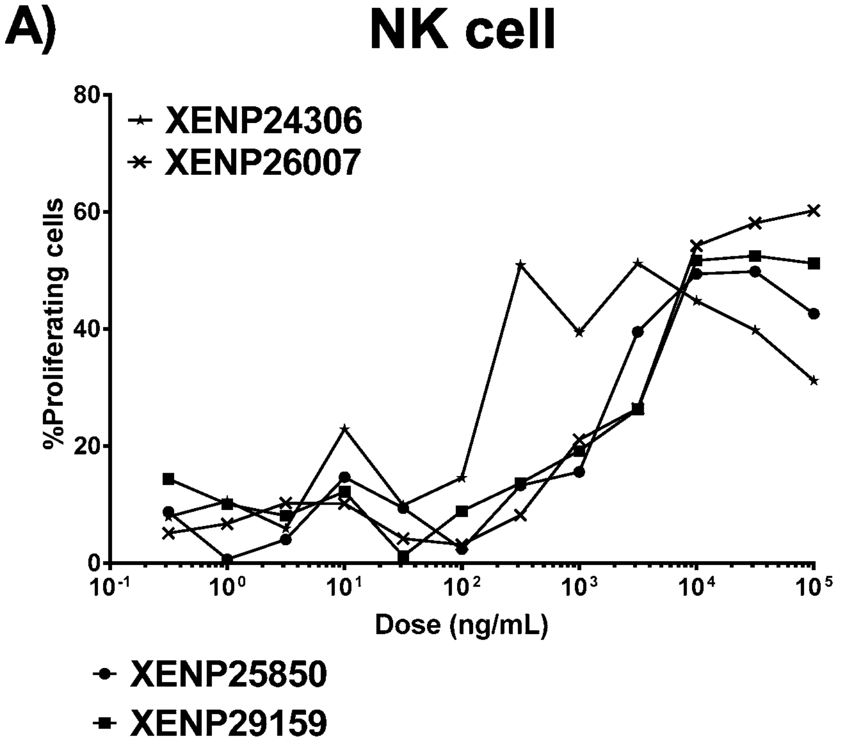


Figure 115A-Figure 115B



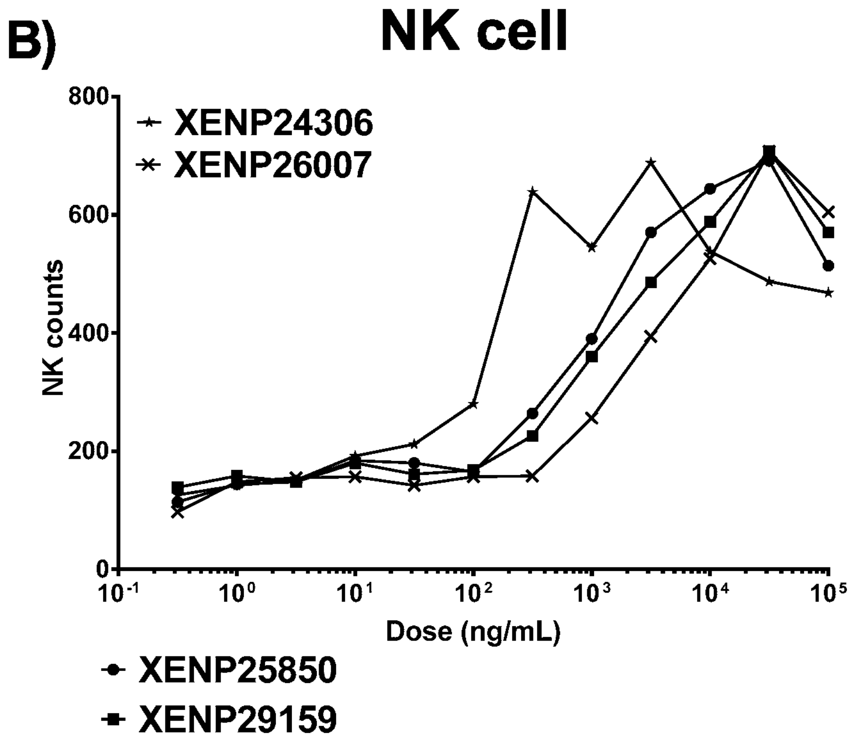


Figure 116A-Figure 116D

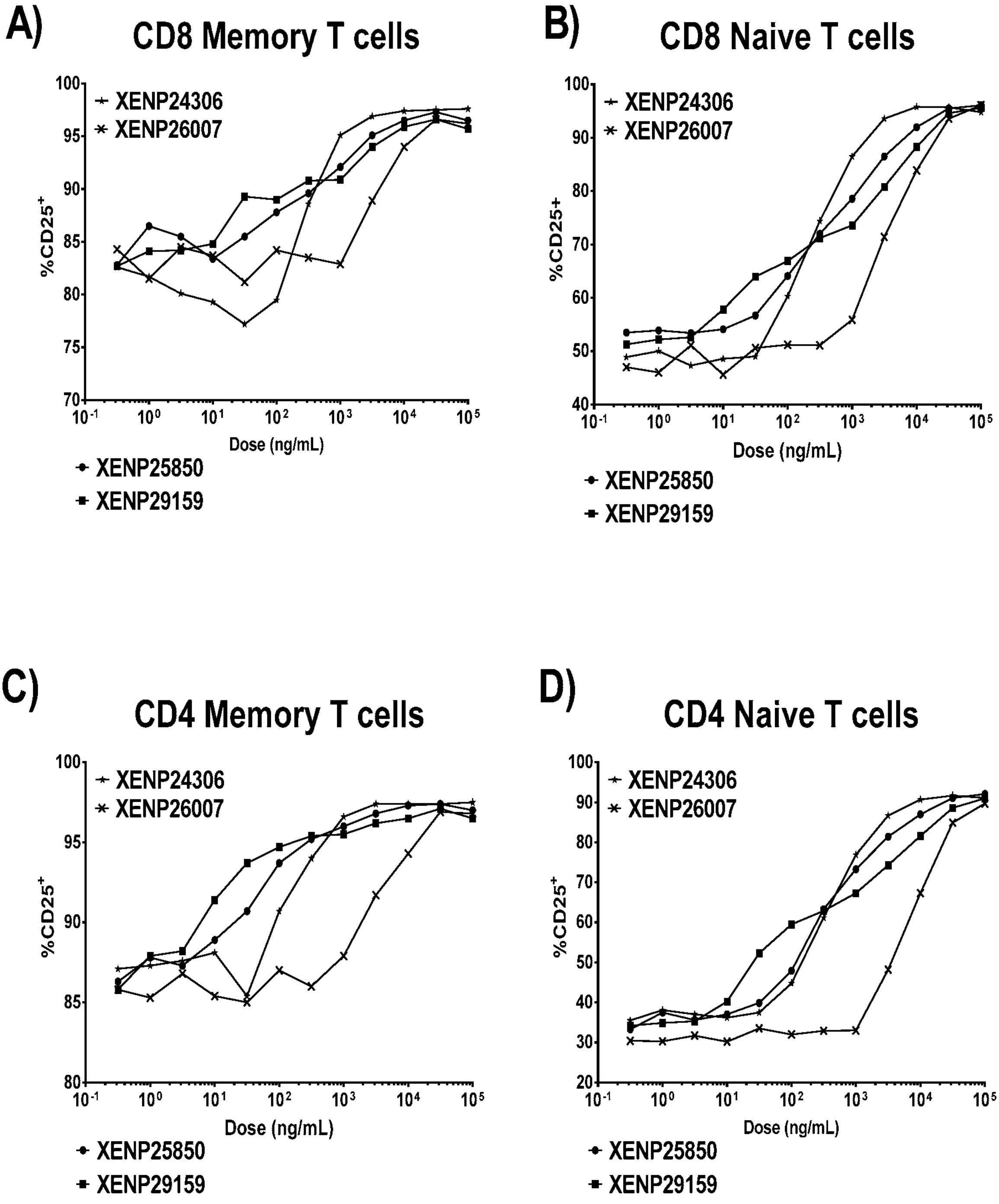


Figure 117A-Figure 117D

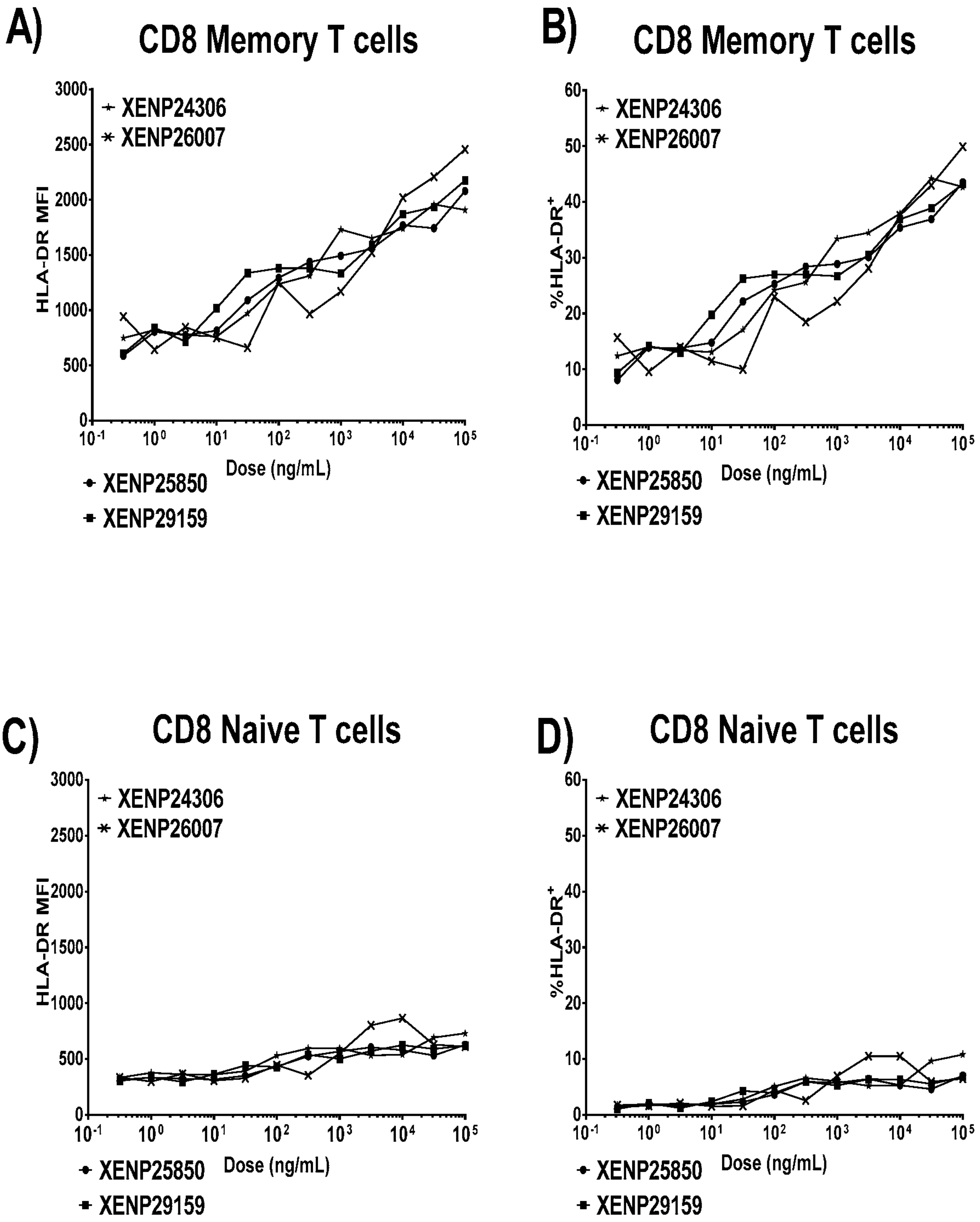


Figure 118A-Figure 118D

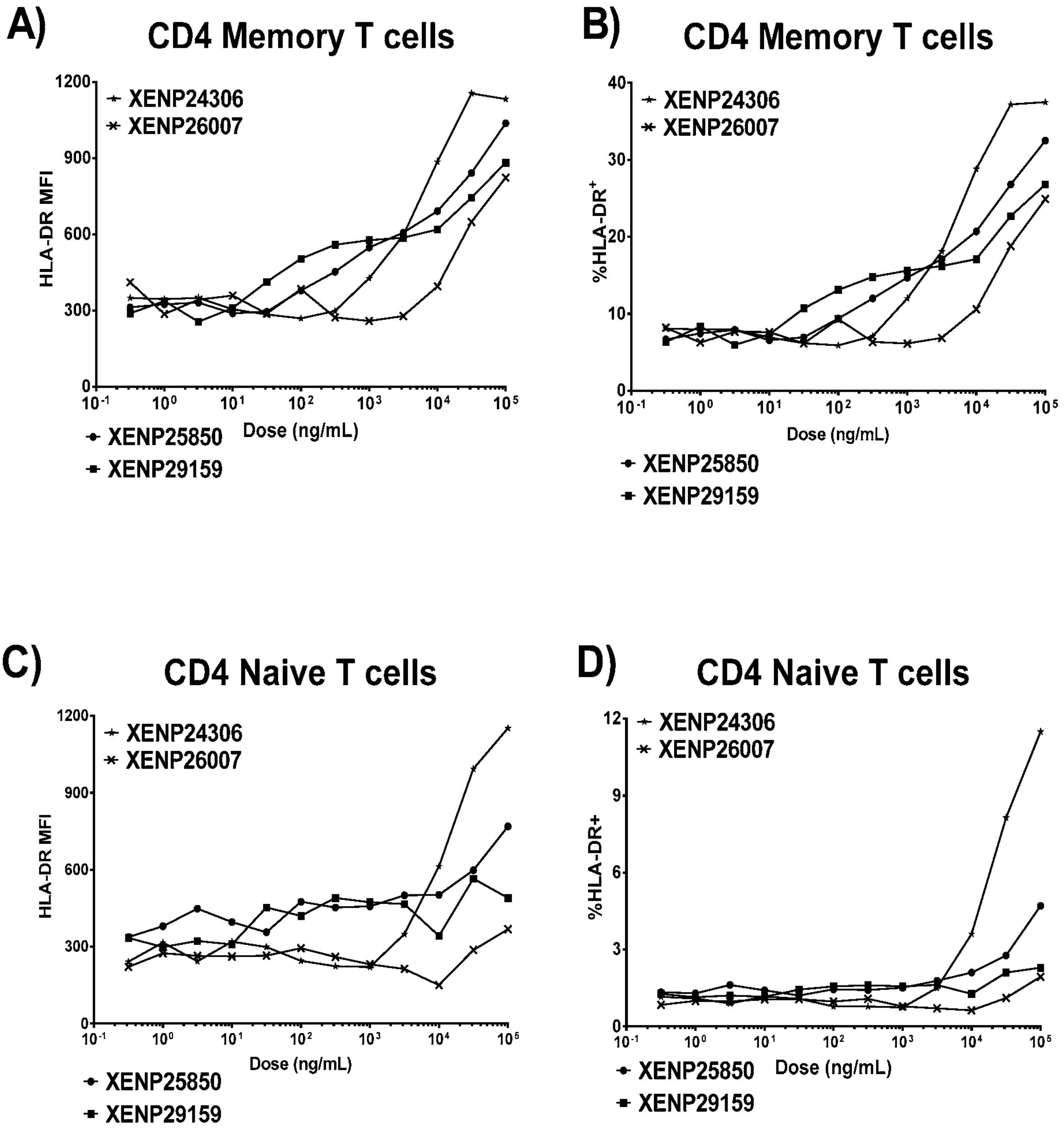


Figure 119

>XENP22853 human_IL15_(GGGGS)1-human_IL15Ra(Sushi)_(GGGGS)1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S-Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q/M428L/N434S

XENP22853 Chain 1 - human_IL15_(GGGGS)1-Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S (SEQ ID NO: 907)

NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVENLII
LANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/GGGGS/EPKSSDKTHTCPPCP
APPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNST
YRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTC
DVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVLHEALHSH
YTQKSLSLSPGK

XENP22853 Chain 2 - human_IL15Ra(Sushi)_(GGGGS)1-
Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q/M428L/N434S-**(SEQ ID NO: 908)**

ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GG
GGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVD
GVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQV
YTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSR
WQQGNVFSCSVLHEALHSHYTQKSLSLSPGK

Figure 120

>XENP24113 human_IL15_N4D/N65D_(GGGGS)1-human_IL15Ra(Sushi)_(GGGGS)1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S-Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q/M428L/N434S

XENP24113 Chain 1 - human_IL15_N4D/N65D_(GGGGS)1-Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S-(SEQ ID NO: 909)

NWVDVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVEDLII
LANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/GGGGS/EPKSSDKTHTCPPCP
APPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNST
YRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTC
DVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVLHEALHSH
YTQKSLSLSPGK

XENP24113 Chain 2 - human_IL15Ra(Sushi)_(GGGGS)1-Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q/M428L/N434S-(SEQ ID NO: 910)

ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GG
GGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVD
GVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQV
YTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSR
WQQGNVFSCSVLHEALHSHYTQKSLSLSPGK

Figure 121

>XENP24294 human IL15Ra(sushi) (GGGGS)5-human IL15 N4D/N65D (single-Chain)-empty-Fc Fc(216) IgG1 pI(-) Isosteric A C220S/PVA /S267K/L368D/K370S/M428L/N434S-Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q/M428L/N434S

XENP24294 Chain 1 - human_IL15Ra(sushi)_(GGGGS)5-human_IL15_N4D/N65D_(single-Chain)-Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S-(SEQ ID NO: 911)

ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGGSGGGGSGGGGSGGGGS/NWVDVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVEDLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVLHEALHSHYTQKSLSLSPGK

XENP24294 Chain 2 - empty-Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q/M428L/N434S-(SEQ ID NO: 912)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKSLSLSPGK

Figure 122

>XENP24306 human IL15 D30N/E64Q/N65D (GGGGS)1-human_IL15Ra(Sushi) (GGGGS)1 Fc(216) IgG1 pI(-) Isosteric A C220S/PVA /S267K/L368D/K370S/M428L/N434S-Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q/M428L/N434S

XENP24306 Chain 1 - human_IL15_D30N/E64Q/N65D_(GGGGS)1-Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S-(SEQ ID NO: 913)

NWVNVISDLKKIEDLIQSMHIDATLYTESNVHPSCKVTAMKCFLLELQVISLESGDASIHDTVQDLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/GGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVLHEALHSHYTQKSLSLSPGK

XENP24306 Chain 2 - human_IL15Ra(Sushi)_(GGGGS)1-
Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q/M428L/N434S-**(SEQ ID NO: 914)**

ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKSLSLSPGK

Figure 123

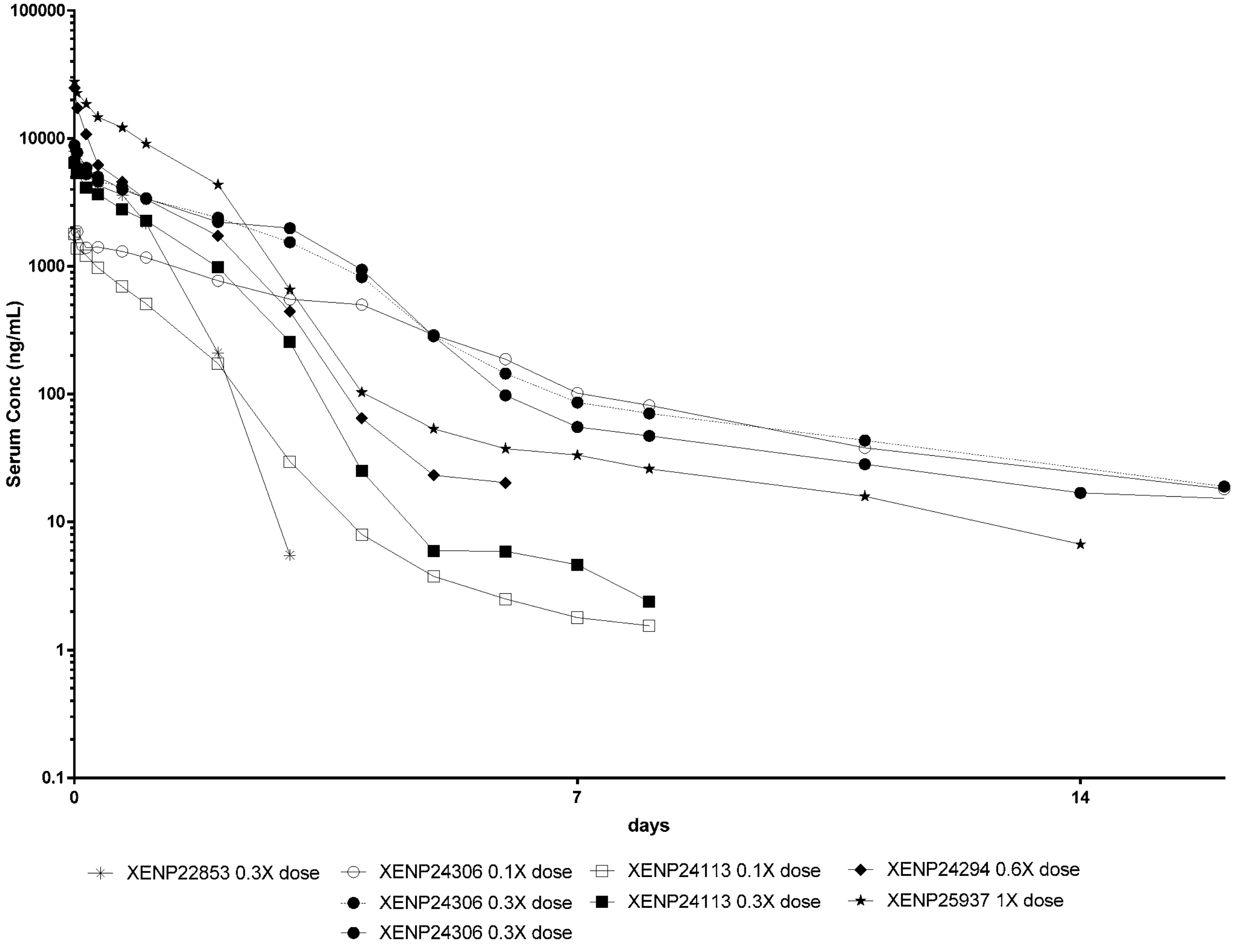

Serum Conc (ng/mL)
100000
10000
1000
100
10
1
0.1
0
7
14
days
XENP22853 0.3X dose
XENP24306 0.1X dose
XENP24306 0.3X dose
XENP24306 0.3X dose
XENP24113 0.1X dose
XENP24113 0.3X dose
XENP24294 0.6X dose
XENP25937 1X dose

Figure 124A

>XENP21993 human_IL15Ra(sushi)_(GGGGS)5-human_IL15(single-chain)-empty-Fc_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

Chain 1 - human_IL15Ra(sushi)_(GGGGS)5-human_IL15(single-chain)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 915)

ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GG
GGSGGGGSGGGGSGGGGSGGGGS/NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFL
LELQVISLESGDASIHDTVENLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFIN
TS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDG
VEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVY
TLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW
EQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 - empty_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q (SEQ ID NO: 916)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEV
HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLP
PSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQG
NVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP24050 human_IL15Ra(sushi)_(GGGGS)5-human_IL15_N4D/N65D_(single-chain)-empty-Fc_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

Chain 1 - human_IL15Ra(sushi)_(GGGGS)5-human_IL15_N4D/N65D_(single-chain)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 917)

ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GG
GGSGGGGSGGGGSGGGGSGGGGS/NWVDVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFL
LELQVISLESGDASIHDTVEDLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFIN
TS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDG
VEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVY
TLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW
EQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 - empty_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q (SEQ ID NO: 918)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEV
HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLP
PSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQG
NVFSCSVMHEALHNHYTQKSLSLSPGK

Figure 124B

>XENP29281 human IL15Ra(sushi) (GGGGS)5-human IL15 D30N (single-chain)-empty-Fc Fc(216) IgG1 pI(-) Isosteric A C220S/PVA /S267K/L368D/K370S-Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q

Chain 1 - human_IL15Ra(sushi)_(GGGGS)5-human_IL15_D30N_(single-chain)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 919)

ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GG
GGSGGGGSGGGGSGGGGSGGGGS/NWVNVISDLKKIEDLIQSMHIDATLYTESNVHPSCKVTAMKCFL
LELQVISLESGDASIHDTVENLIIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFIN
TS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDG
VEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVY
TLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW
EQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 - empty_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q (SEQ ID NO: 920)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEV
HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLP
PSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQG
NVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP29285 human IL15Ra(sushi) (GGGGS)5-human IL15 D30N/N65D (single-chain)-empty-Fc Fc(216) IgG1 pI(-) Isosteric A C220S/PVA /S267K/L368D/K370S-Fc(216) IgG1 C220S/PVA /S267K/S364K/E357Q

Chain 1 - human_IL15Ra(sushi)_(GGGGS)5-human_IL15_D30N/N65D_(single-chain)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 921)

ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GG
GGSGGGGSGGGGSGGGGSGGGGS/NWVNVISDLKKIEDLIQSMHIDATLYTESNVHPSCKVTAMKCFL
LELQVISLESGDASIHDTVEDLIIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFIN
TS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDG
VEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVY
TLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW
EQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 - empty_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q (SEQ ID NO: 922)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEV
HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLP
PSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQG
NVFSCSVMHEALHNHYTQKSLSLSPGK

Figure 124C

>XENP29286 human_IL15Ra(sushi)_(GGGGS)5-human_IL15_D30N/E64Q/N65D_(single-chain)-empty-Fc_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q

Chain 1 - human_IL15Ra(sushi)_(GGGGS)5-human_IL15_D30N/E64Q/N65D_(single-chain)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 923)

ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGGSGGGGSGGGGSGGGGS/NWVNVISDLKKIEDLIQSMHIDATLYTESNVHPSCKVTAMKCFLLELQVISLESGDASIHDTVQDLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 - empty_Fc(216)_IgG1_C220S/PVA_/S267K/S364K/E357Q (SEQ ID NO: 924)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Figure 125A

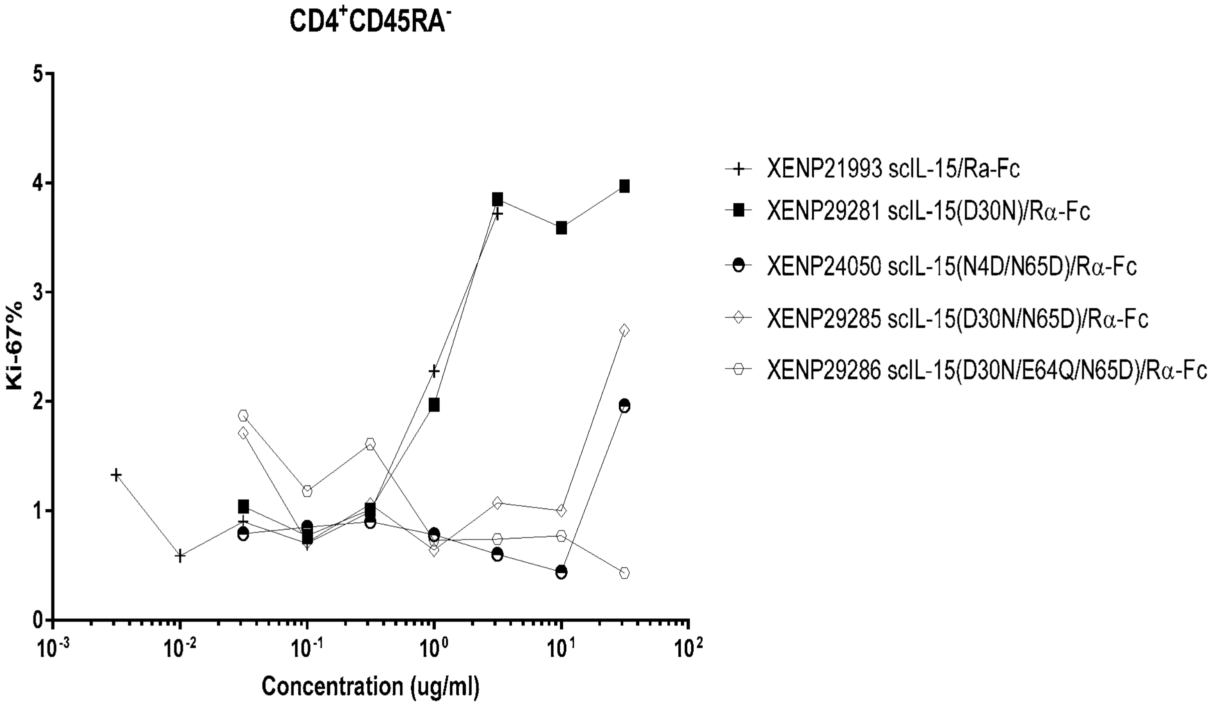


Figure 125B

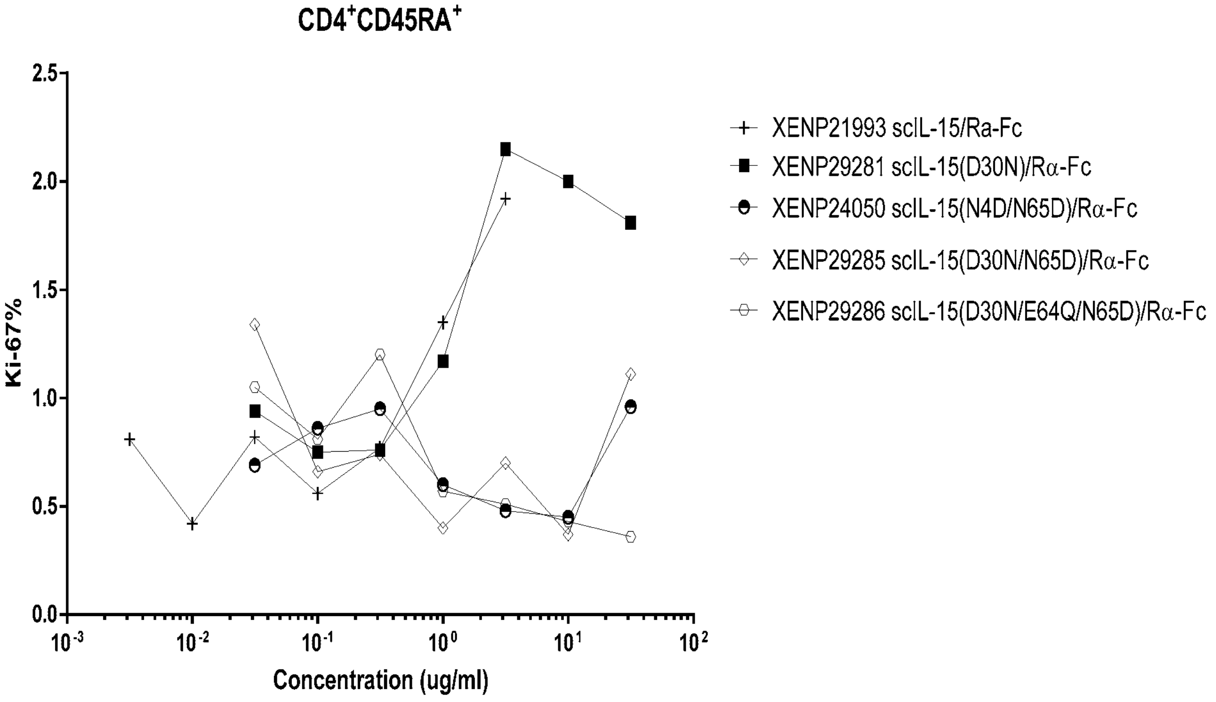


Figure 125C

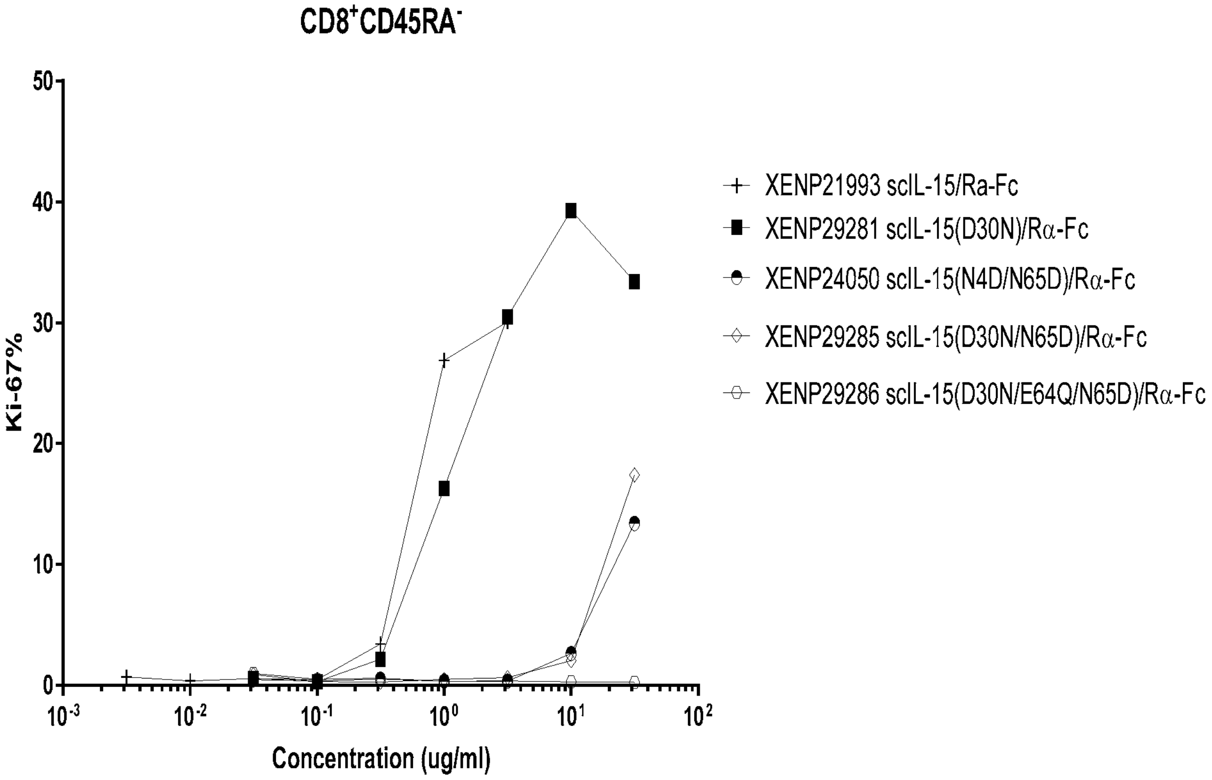


Figure 125D

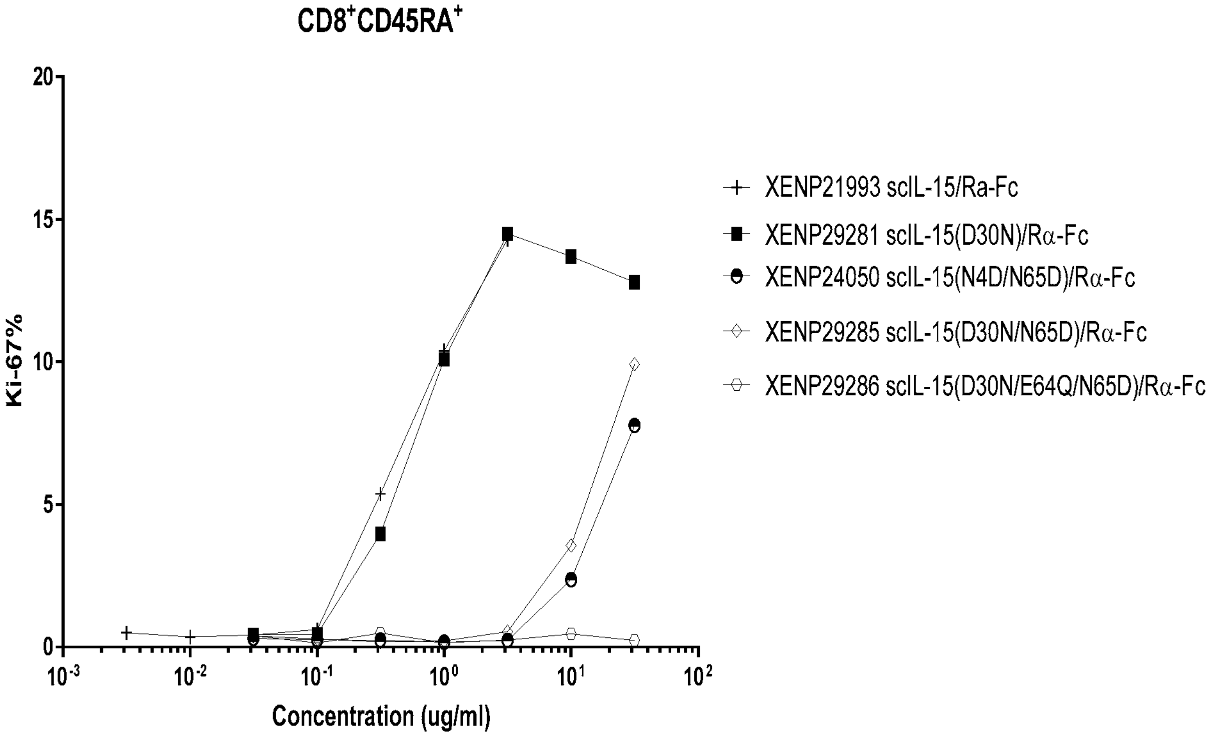


Figure 125E

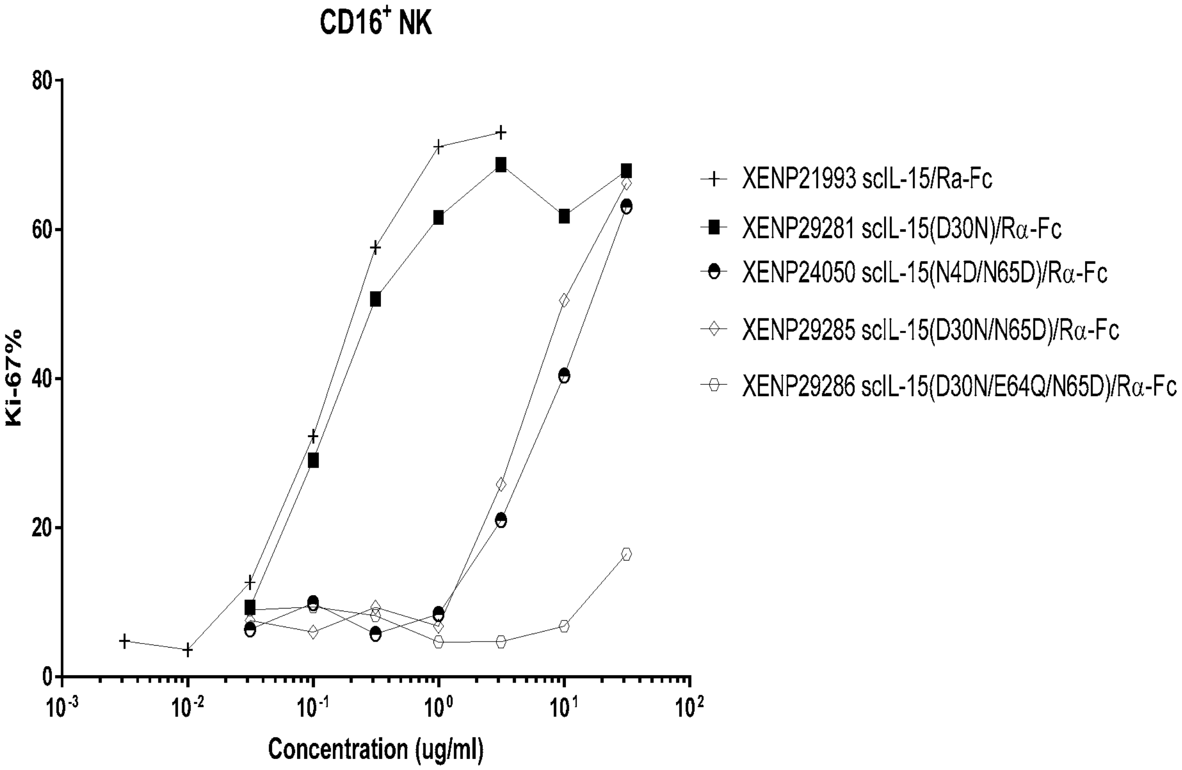


Figure 125F

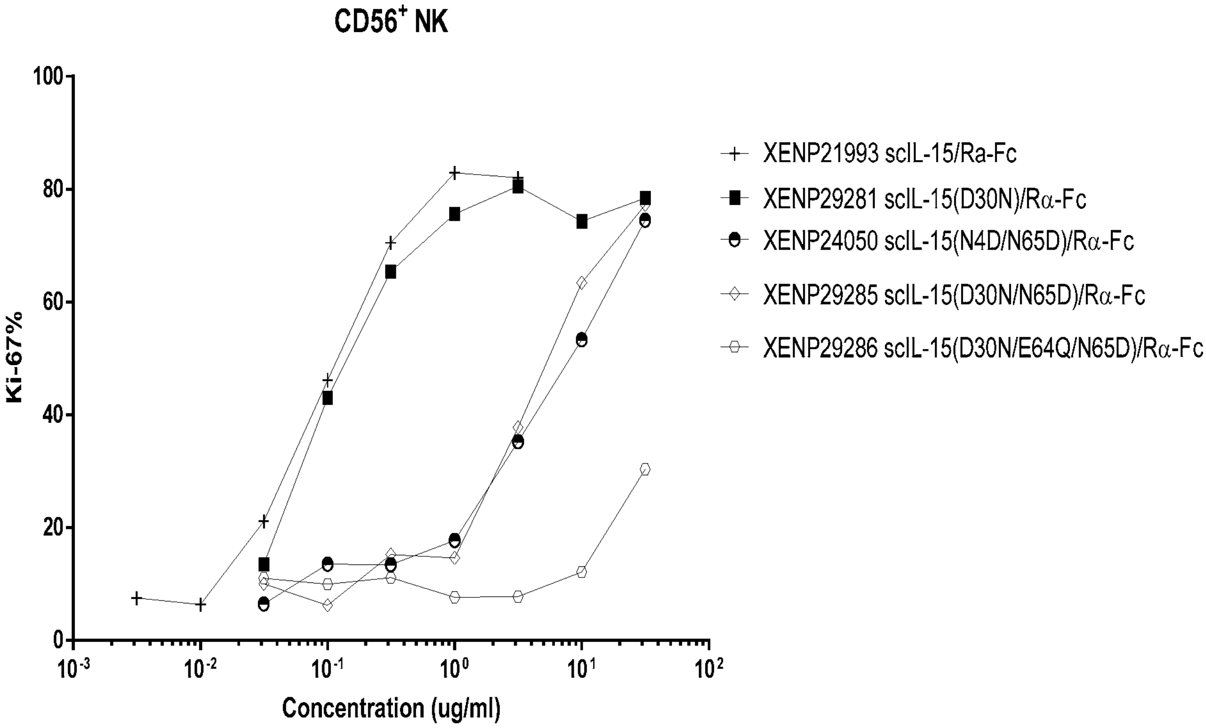


Figure 125G

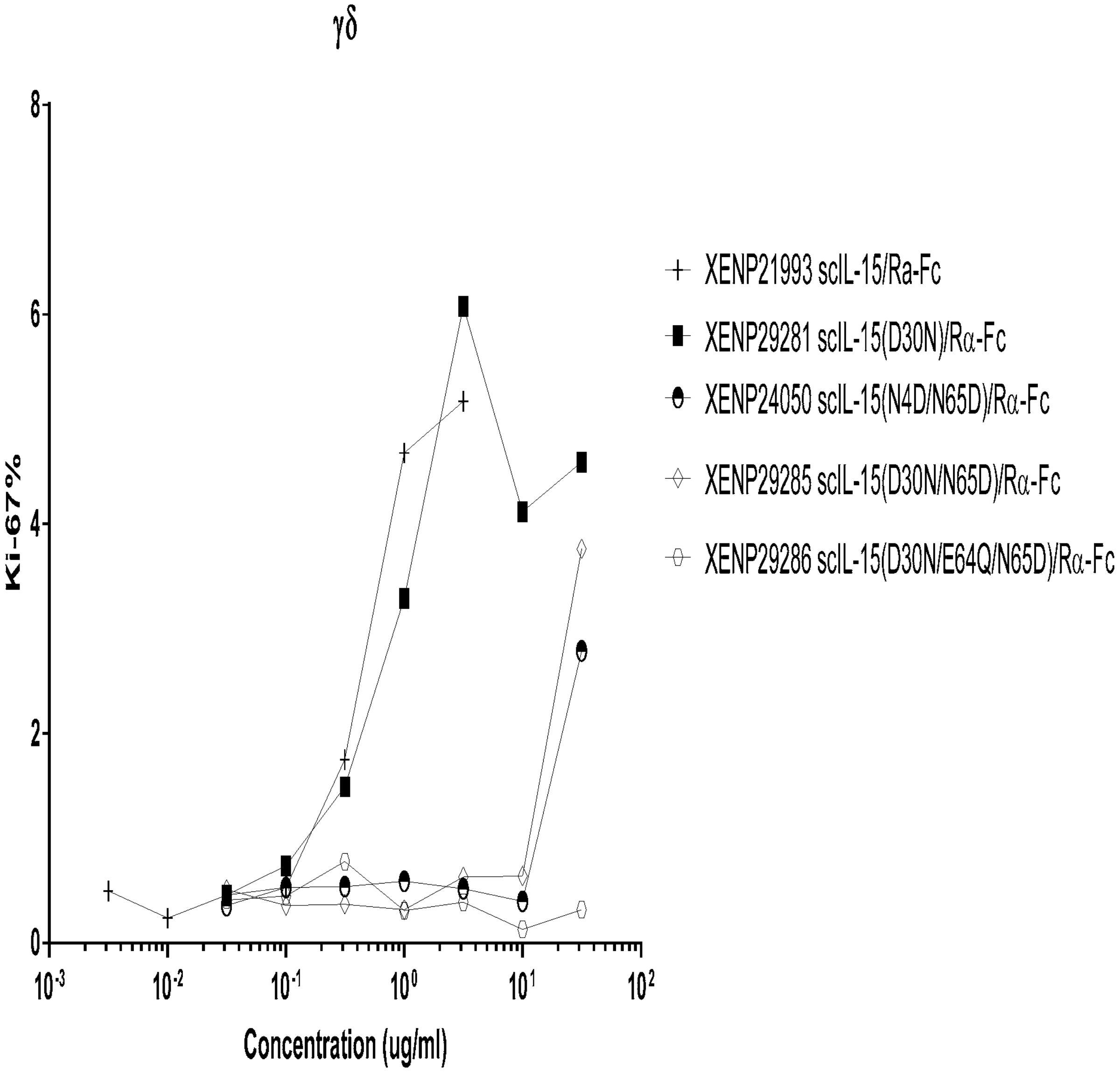

γδ
Ki-67%
0
2
4
6
8
10^{-3}
10^{-2}
10^{-1}
10^{0}
10^{1}
10^{2}
Concentration (ug/ml)
XENP21993 scIL-15/Ra-Fc
XENP29281 scIL-15(D30N)/Rα-Fc
XENP24050 scIL-15(N4D/N65D)/Rα-Fc
XENP29285 scIL-15(D30N/N65D)/Rα-Fc
XENP29286 scIL-15(D30N/E64Q/N65D)/Rα-Fc

Figure 126A

>XENP29482 human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/N65D;single-chain)-1C11[PD-1]_H3L3_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-IgG1_PVA_/S267K/S364K/E357Q

Chain 1 - human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/N65D;single-chain)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 925)

ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGGSGGGGSGGGGSGGGGS/NWVNVISDLKKIEDLIQSMHIDATLYTESNVHPSCKVTAMKCFLLELQVISLESGDASIHDTVEDLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 - 1C11[PD-1]_H3_IgG1_PVA_/S267K/S364K/E357Q (SEQ ID NO: 926)

QIQLVQSGSELKKPGASVKVSCKASGYTFT**HYGMN**WVRQAPGQGLEWMG**WINTYTGEPTYADGFTG**RFVFSLDTSVSTAYLQISSLKAEDTAVYFCAR**DYYGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 3 - 1C11[PD-1]_L3 (SEQ ID NO: 1216)

DVLMTQSPDSLAVSLGERATINC**KSSQSIVHSNGNTYLE**WYQQKPGQSPKLLIY**KVSNRFS**GVPDRFSGSGSGTDFTLTISSLQAEDVAVYYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

> human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/N65D;single-chain)-1C11[PD-1]_H3.329_L3.220_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-IgG1_PVA_/S267K/S364K/E357Q

Chain 1 - human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/N65D;single-chain)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 927)

ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGGSGGGGSGGGGSGGGGS/NWVNVISDLKKIEDLIQSMHIDATLYTESNVHPSCKVTAMKCFLLELQVISLESGDASIHDTVEDLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 - 1C11[PD-1]_H3.329_IgG1_PVA_/S267K/S364K/E357Q (SEQ ID NO: 928)

QIQLVQSGSELLKPGASVSVSCKASGYTFT**HYGMN**WVRQAPGQGLEWMG**WINTHTGEPTYADGFTG**RFVFSLDTSVSTAYLQISSLKAEDTAVYFCAR**DYFGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 3 - 1C11[PD-1]_L3.220 (SEQ ID NO: 929)

DILMTQSPDSLAVSLGERATINC**KSSQSIVYSNGNNYLE**WYQQKPGQSPKLLIY**KVSNRFS**GVPDRFSGSGSGTDFTLTISSLQAEDVAVYYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 126B

> human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/N65D;single-chain)-1C11[PD-1]_H3.303_L3.152_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-IgG1_PVA_/S267K/S364K/E357Q

Chain 1 - human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/N65D;single-chain)_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 930)

ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGG
SGGGGSGGGGSGGGGS/NWVNVISDLKKIEDLIQSMHIDATLYTESNVHPSCKVTAMKCFLLELQVISLESGDAS
IHDTVEDLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPP
VAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESD
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 - 1C11[PD-1]_H3.303_IgG1_PVA_/S267K/S364K/E357Q (SEQ ID NO: 931)

QIQLVQSGSELKKPGASVKVSCKASGYTFT**HYGMN**WVRQAPGQGLEWMG**WINTYTGEPTYADGFTG**RFVFSLDTS
VSTAYLQISSLKAEDTAVYFCAR**DYFGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 3 - 1C11[PD-1]_L3.152 (SEQ ID NO: 932)

DVLMTQSPDSLAVSLGERATINC**KSSQSIVFSNGNTYLE**WYQQKPGQSPKLLIY**KVSNRFS**GVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

> human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/N65D;single-chain)-1C11[PD-1]_H3.234_L3.144_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-IgG1_PVA_/S267K/S364K/E357Q

Chain 1 - human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/N65D;single-chain)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 933)

ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGG
SGGGGSGGGGSGGGGS/NWVNVISDLKKIEDLIQSMHIDATLYTESNVHPSCKVTAMKCFLLELQVISLESGDAS
IHDTVEDLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPP
VAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESD
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 - 1C11[PD-1]_ H3.234_IgG1_PVA_/S267K/S364K/E357Q (SEQ ID NO: 934)

EVQLVQSGSELKKPGESVKVSCKASGYTFT**HYGIN**WVRQPPGQGLEWMG**WINTYTGEPYYAPGFQE**RFVFSLDTS
QDTAYLQINSLKAEDTAVYYCAR**DYYGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 3 - 1C11[PD-1]_ L3.144 (SEQ ID NO: 935)

DIVMTQSPDSLAVSLGERVTINC**KASQSIVHSNGNTYLE**WYQQKPGQPPKLLIY**KVSNRFS**GVPDRFSGSGSGTD
FTLTISSVEAEDAATYYC**FQGSHVPNT**FGQGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 126C

> human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/N65D;single-chain)-1C11[PD-1]_ H3.240_L3.148_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-IgG1_PVA_/S267K/S364K/E357Q

Chain 1 - human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/N65D;single-chain)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 936)

ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGG
SGGGGSGGGGSGGGGS/NWVNVISDLKKIEDLIQSMHIDATLYTESNVHPSCKVTAMKCFLLELQVISLESGDAS
IHDTVEDLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPP
VAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESD
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 - 1C11[PD-1]_ H3.240_IgG1_PVA_/S267K/S364K/E357Q (SEQ ID NO: 937)

QVQLVQSGPELKKPGESVKVSCKASGYTFT**HYGIN**WVRQPPGQGLEWMG**WINTYTGEPYYAPGFQE**RFVFSIDTS
QDTAYLQINSLKAEDTAVYYCAR**DYYGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 3 - 1C11[PD-1]_ L3.148 (SEQ ID NO: 938)

DVLMTQSPDSLAVSLGERATINC**KSSQSIVHSNGNTYLE**WYQQKPGQSPKLLIY**KVSNRFS**GVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

> human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/N65D;single-chain)-1C11[PD-1]_ H3.241_L3.148_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-IgG1_PVA_/S267K/S364K/E357Q

Chain 1 - human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/N65D;single-chain)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 939)

ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGG
SGGGGSGGGGSGGGGS/NWVNVISDLKKIEDLIQSMHIDATLYTESNVHPSCKVTAMKCFLLELQVISLESGDAS
IHDTVEDLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPP
VAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESD
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 - 1C11[PD-1]_ H3.241_IgG1_PVA_/S267K/S364K/E357Q (SEQ ID NO: 940)

EVQLVQSGPELKKPGESVKVSCKASGYTFT**HYGIN**WVRQPPGQGLEWMG**WINTYTGEPYYAPGFQE**RFVFSIDTS
QDTAYLQINSLKAEDTAVYYCAR**DYYGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 3 - 1C11[PD-1]_ L3.148 (SEQ ID NO: 941)

DVLMTQSPDSLAVSLGERATINC**KSSQSIVHSNGNTYLE**WYQQKPGQSPKLLIY**KVSNRFS**GVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 126D

**> human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/N65D;single-chain)-1C11[PD-1]_
H3.241_L3.92_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-
IgG1_PVA_/S267K/S364K/E357Q**

Chain 1 - human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/N65D;single-chain)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 942)
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGG
SGGGGSGGGGSGGGGS/NWVNVISDLKKIEDLIQSMHIDATLYTESNVHPSCKVTAMKCFLLELQVISLESGDAS
IHDTVEDLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPP
VAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESD
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 - 1C11[PD-1]_ H3.241_IgG1_PVA_/S267K/S364K/E357Q (SEQ ID NO: 943)
EVQLVQSGPELKKPGESVKVSCKASGYTFT**HYGIN**WVRQPPGQGLEWMG**WINTYTGEPYYAPGFQE**RFVFSIDTS
QDTAYLQINSLKAEDTAVYYCAR**DYYGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 3 - 1C11[PD-1]_ L3.92 (SEQ ID NO: 944)
DIVMTQSPDSLAVSLGERVTINC**KASQSIVHSNGNTYLE**WYQQKPGQPPKLLIY**KVSNRFT**GVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

**> human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/N65D;single-chain)-1C11[PD-1]_
H3.328_L3.152_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-
IgG1_PVA_/S267K/S364K/E357Q**

Chain 1 - human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/N65D;single-chain)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 945)
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGG
SGGGGSGGGGSGGGGS/NWVNVISDLKKIEDLIQSMHIDATLYTESNVHPSCKVTAMKCFLLELQVISLESGDAS
IHDTVEDLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPP
VAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESD
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 - 1C11[PD-1]_ H3.328_IgG1_PVA_/S267K/S364K/E357Q (SEQ ID NO: 946)
QIQLVQSGSELKKPGASVSVSCKASGYTFT**HYGMN**WVRQAPGQGLEWMG**WINTHTGEPTYADGFTG**RFVFSLDTS
VSTAYLQISSLKAEDTAVYFCAR**DYFGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 3 - 1C11[PD-1]_ L3.152 (SEQ ID NO: 947)
DVLMTQSPDSLAVSLGERATINC**KSSQSIVFSNGNTYLE**WYQQKPGQSPKLLIY**KVSNRFS**GVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 127A

> human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/E64Q/N65D;single-chain)-1C11[PD-1]_H3L3_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-IgG1_PVA_/S267K/S364K/E357Q

Chain 1 - human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/E64Q/N65D;single-chain)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 948)
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGGSGGGGSGGGGSGGGGS/NWVNVISDLKKIEDLIQSMHIDATLYTESNVHPSCKVTAMKCFLLELQVISLESGDASIHDTVQDLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 - 1C11[PD-1]_H3_IgG1_PVA_/S267K/S364K/E357Q (SEQ ID NO: 949)
QIQLVQSGSELKKPGASVKVSCKASGYTFT**HYGMN**WVRQAPGQGLEWMG**WINTYTGEPTYADGFTG**RFVFSLDTSVSTAYLQISSLKAEDTAVYFCAR**DYYGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 3 - 1C11[PD-1]_L3 (SEQ ID NO: 950)
DVLMTQSPDSLAVSLGERATINC**KSSQSIVHSNGNTYLE**WYQQKPGQSPKLLIY**KVSNRFS**GVPDRFSGSGSGTDFTLTISSLQAEDVAVYYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

> human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/E64Q/N65D;single-chain)-1C11[PD-1]_H3.329_L3.220_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-IgG1_PVA_/S267K/S364K/E357Q

Chain 1 - human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/E64Q/N65D;single-chain)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 951)
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGGSGGGGSGGGGSGGGGS/NWVNVISDLKKIEDLIQSMHIDATLYTESNVHPSCKVTAMKCFLLELQVISLESGDASIHDTVQDLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 - 1C11[PD-1]_H3.329_IgG1_PVA_/S267K/S364K/E357Q (SEQ ID NO: 952)
QIQLVQSGSELLKPGASVSVSCKASGYTFT**HYGMN**WVRQAPGQGLEWMG**WINTHTGEPTYADGFTG**RFVFSLDTSVSTAYLQISSLKAEDTAVYFCAR**DYFGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 3 - 1C11[PD-1]_L3.220 (SEQ ID NO: 953)
DILMTQSPDSLAVSLGERATINC**KSSQSIVYSNGNNYLE**WYQQKPGQSPKLLIY**KVSNRFS**GVPDRFSGSGSGTDFTLTISSLQAEDVAVYYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 127B

> human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/E64Q/N65D;single-chain)-1C11[PD-1]_H3.303_L3.152_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-IgG1_PVA_/S267K/S364K/E357Q

Chain 1 - human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/E64Q/N65D;single-chain)_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 954)
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGG
SGGGGSGGGGSGGGGS/NWVNVISDLKKIEDLIQSMHIDATLYTESNVHPSCKVTAMKCFLLELQVISLESGDAS
IHDTVQDLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPP
VAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESD
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 - 1C11[PD-1]_H3.303_IgG1_PVA_/S267K/S364K/E357Q (SEQ ID NO: 955)
QIQLVQSGSELKKPGASVKVSCKASGYTFT**HYGMN**WVRQAPGQGLEWMG**WINTYTGEPTYADGFTG**RFVFSLDTS
VSTAYLQISSLKAEDTAVYFCAR**DYFGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 3 - 1C11[PD-1]_L3.152 (SEQ ID NO: 956)
DVLMTQSPDSLAVSLGERATINC**KSSQSIVFSNGNTYLE**WYQQKPGQSPKLLIY**KVSNRFS**GVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

> human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/E64Q/N65D;single-chain)-1C11[PD-1]_H3.234_L3.144_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-IgG1_PVA_/S267K/S364K/E357Q

Chain 1 - human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/E64Q/N65D;single-chain)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 957)
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGG
SGGGGSGGGGSGGGGS/NWVNVISDLKKIEDLIQSMHIDATLYTESNVHPSCKVTAMKCFLLELQVISLESGDAS
IHDTVQDLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPP
VAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESD
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 - 1C11[PD-1]_ H3.234_IgG1_PVA_/S267K/S364K/E357Q (SEQ ID NO: 958)
EVQLVQSGSELKKPGESVKVSCKASGYTFT**HYGIN**WVRQPPGQGLEWMG**WINTYTGEPYYAPGFQE**RFVFSLDTS
QDTAYLQINSLKAEDTAVYYCAR**DYYGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 3 - 1C11[PD-1]_ L3.144 (SEQ ID NO: 959)
DIVMTQSPDSLAVSLGERVTINC**KASQSIVHSNGNTYLE**WYQQKPGQPPKLLIY**KVSNRFS**GVPDRFSGSGSGTD
FTLTISSVEAEDAATYYC**FQGSHVPNT**FGQGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 127C

> human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/E64Q/N65D;single-chain)-1C11[PD-1]_ H3.240_L3.148_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-IgG1_PVA_/S267K/S364K/E357Q

Chain 1 - human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/E64Q/N65D;single-chain)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 960)

ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGG
SGGGGSGGGGSGGGGS/NWVNVISDLKKIEDLIQSMHIDATLYTESNVHPSCKVTAMKCFLLELQVISLESGDAS
IHDTVQDLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPP
VAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESD
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 - 1C11[PD-1]_ H3.240_IgG1_PVA_/S267K/S364K/E357Q (SEQ ID NO: 961)

QVQLVQSGPELKKPGESVKVSCKASGYTFT**HYGIN**WVRQPPGQGLEWMG**WINTYTGEPYYAPGFQE**RFVFSIDTS
QDTAYLQINSLKAEDTAVYYCAR**DYYGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 3 - 1C11[PD-1]_ L3.148 (SEQ ID NO: 962)

DVLMTQSPDSLAVSLGERATINC**KSSQSIVHSNGNTYLE**WYQQKPGQSPKLLIY**KVSNRFS**GVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

> human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/E64Q/N65D;single-chain)-1C11[PD-1]_ H3.241_L3.148_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-IgG1_PVA_/S267K/S364K/E357Q

Chain 1 - human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/E64Q/N65D;single-chain)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 963)

ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGG
SGGGGSGGGGSGGGGS/NWVNVISDLKKIEDLIQSMHIDATLYTESNVHPSCKVTAMKCFLLELQVISLESGDAS
IHDTVQDLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPP
VAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESD
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 - 1C11[PD-1]_ H3.241_IgG1_PVA_/S267K/S364K/E357Q (SEQ ID NO: 964)

EVQLVQSGPELKKPGESVKVSCKASGYTFT**HYGIN**WVRQPPGQGLEWMG**WINTYTGEPYYAPGFQE**RFVFSIDTS
QDTAYLQINSLKAEDTAVYYCAR**DYYGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 3 - 1C11[PD-1]_ L3.148 (SEQ ID NO: 965)

DVLMTQSPDSLAVSLGERATINC**KSSQSIVHSNGNTYLE**WYQQKPGQSPKLLIY**KVSNRFS**GVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 127D

> human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/E64Q/N65D;single-chain)-1C11[PD-1]_ H3.241_L3.92_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-IgG1_PVA_/S267K/S364K/E357Q

Chain 1 - human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/E64Q/N65D;single-chain)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 966)

ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGG
SGGGGSGGGGSGGGGS/NWVNVISDLKKIEDLIQSMHIDATLYTESNVHPSCKVTAMKCFLLELQVISLESGDAS
IHDTVQDLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPP
VAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESD
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 - 1C11[PD-1]_ H3.241_IgG1_PVA_/S267K/S364K/E357Q (SEQ ID NO: 967)

EVQLVQSGPELKKPGESVKVSCKASGYTFT**HYGIN**WVRQPPGQGLEWMG**WINTYTGEPYYAPGFQE**RFVFSIDTS
QDTAYLQINSLKAEDTAVYYCAR**DYYGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 3 - 1C11[PD-1]_ L3.92 (SEQ ID NO: 968)

DIVMTQSPDSLAVSLGERVTINC**KASQSIVHSNGNTYLE**WYQQKPGQPPKLLIY**KVSNRFT**GVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

> human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/E64Q/N65D;single-chain)-1C11[PD-1]_ H3.328_L3.152_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-IgG1_PVA_/S267K/S364K/E357Q

Chain 1 - human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/E64Q/N65D;single-chain)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 969)

ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGG
SGGGGSGGGGSGGGGS/NWVNVISDLKKIEDLIQSMHIDATLYTESNVHPSCKVTAMKCFLLELQVISLESGDAS
IHDTVQDLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPP
VAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESD
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 - 1C11[PD-1]_ H3.328_IgG1_PVA_/S267K/S364K/E357Q (SEQ ID NO: 970)

QIQLVQSGSELKKPGASVSVSCKASGYTFT**HYGMN**WVRQAPGQGLEWMG**WINTHTGEPTYADGFTG**RFVFSLDTS
VSTAYLQISSLKAEDTAVYFCAR**DYFGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 3 - 1C11[PD-1]_ L3.152 (SEQ ID NO: 971)

DVLMTQSPDSLAVSLGERATINC**KSSQSIVFSNGNTYLE**WYQQKPGQSPKLLIY**KVSNRFS**GVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 128A

XENP025937human_IL15Ra(sushi)_(GGGGS)5-human_IL15(N4D/N65D;single-chain)-1C11[PD-1]_H3L3_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S-IgG1_PVA_/S267K/S364K/E357Q/M428L/N434S

Chain 1 - 1C11[PD-1]_H3_ IgG1_PVA_/S267K/S364K/E357Q/M428L/N434S (SEQ ID NO: 972)
QIQLVQSGSELKKPGASVKVSCKASGYTFT**HYGMN**WVRQAPGQGLEWMG**WINTYTGEPTYADGFTG**RFVFSLDTSVSTAYLQISSLKAED
TAVYFCAR**DYYGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGL
YSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHED
PEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTK
NQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKSLSLSPGK

Chain2-human_IL15Ra(sushi)_(GGGGS)5-human_IL15(N4D/N65D;single-chain)_ Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S (SEQ ID NO: 973)
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGGSGGGGSGGGGSGGGG
S/NWVDVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVEDLIILANNSLSSNGNVTESGCKEC
EELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYV
DGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDV
SGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVLHEALHSHYTQKSLSLSPGK

Chain3-1C11[PD-1]_L3 (SEQ ID NO: 974)
DVLMTQSPDSLAVSLGERATINC**KSSQSIVHSNGNTYLE**WYQQKPGQSPKLLIY**KVSNRFS**GVPDRFSGSGSGTDFTLTISSLQAEDVAV
YYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYS
LSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

> human_IL15Ra(sushi)_(GGGGS)5-human_IL15(N4D/N65D;single-chain)-1C11[PD-1]_H3.329_L3.220_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S-IgG1_PVA_/S267K/S364K/E357Q/M428L/N434S

Chain 1 - human_IL15Ra(sushi)_(GGGGS)5-human_IL15(N4D/N65D;single-chain)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S (SEQ ID NO: 975)
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGG
SGGGGSGGGGSGGGGS/NWVDVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDAS
IHDTVEDLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPP
VAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESD
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVLHEALHSHYTQKSLSLSPGK

Chain 2 - 1C11[PD-1]_H3.329_IgG1_PVA_/S267K/S364K/E357Q/M428L/N434S (SEQ ID NO: 976)
QIQLVQSGSELLKPGASVSVSCKASGYTFT**HYGMN**WVRQAPGQGLEWMG**WINTHTGEPTYADGFTG**RFVFSLDTS
VSTAYLQISSLKAEDTAVYFCAR**DYFGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKSLSLSPGK

Chain 3 - 1C11[PD-1]_L3.220 (SEQ ID NO: 977)
DILMTQSPDSLAVSLGERATINC**KSSQSIVYSNGNNYLE**WYQQKPGQSPKLLIY**KVSNRFS**GVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 128B

> human_IL15Ra(sushi)_(GGGGS)5-human_IL15(N4D/N65D;single-chain)-1C11[PD-1]_H3.303_L3.152_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S-IgG1_PVA_/S267K/S364K/E357Q/M428L/N434S

Chain 1 - human_IL15Ra(sushi)_(GGGGS)5-human_IL15(N4D/N65D;single-chain)_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S (SEQ ID NO: 978)

ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGGSGGGGSGGGGSGGGGS/NWVDVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVEDLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVLHEALHSHYTQKSLSLSPGK

Chain 2 - 1C11[PD-1]_H3.303_IgG1_PVA_/S267K/S364K/E357Q/M428L/N434S (SEQ ID NO: 979)

QIQLVQSGSELKKPGASVKVSCKASGYTFT**HYGMN**WVRQAPGQGLEWMG**WINTYTGEPTYADGFTG**RFVFSLDTSVSTAYLQISSLKAEDTAVYFCAR**DYFGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKSLSLSPGK

Chain 3 - 1C11[PD-1]_L3.152 (SEQ ID NO: 980)

DVLMTQSPDSLAVSLGERATINC**KSSQSIVFSNGNTYLE**WYQQKPGQSPKLLIY**KVSNRFS**GVPDRFSGSGSGTDFTLTISSLQAEDVAVYYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

> human_IL15Ra(sushi)_(GGGGS)5-human_IL15(N4D/N65D;single-chain)-1C11[PD-1]_H3.234_L3.144_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S-IgG1_PVA_/S267K/S364K/E357Q/M428L/N434S

Chain 1 - human_IL15Ra(sushi)_(GGGGS)5-human_IL15(N4D/N65D;single-chain)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S (SEQ ID NO: 981)

ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGGSGGGGSGGGGSGGGGS/NWVDVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDASIHDTVEDLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVLHEALHSHYTQKSLSLSPGK

Chain 2 - 1C11[PD-1]_ H3.234_IgG1_PVA_/S267K/S364K/E357Q/M428L/N434S (SEQ ID NO: 982)

EVQLVQSGSELKKPGESVKVSCKASGYTFT**HYGIN**WVRQPPGQGLEWMG**WINTYTGEPYYAPGFQE**RFVFSLDTSQDTAYLQINSLKAEDTAVYYCAR**DYYGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKSLSLSPGK

Chain 3 - 1C11[PD-1]_ L3.144 (SEQ ID NO: 983)

DIVMTQSPDSLAVSLGERVTINC**KASQSIVHSNGNTYLE**WYQQKPGQPPKLLIY**KVSNRFS**GVPDRFSGSGSGTDFTLTISSVEAEDAATYYC**FQGSHVPNT**FGQGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 128C

**> human_IL15Ra(sushi)_(GGGGS)5-human_IL15(N4D/N65D;single-chain)-1C11[PD-1]_
H3.240_L3.148_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S-
IgG1_PVA_/S267K/S364K/E357Q/M428L/N434S**

Chain 1 - human_IL15Ra(sushi)_(GGGGS)5-human_IL15(N4D/N65D;single-chain)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S (SEQ ID NO: 984)
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGG
SGGGGSGGGGSGGGGS/NWVDVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDAS
IHDTVEDLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPP
VAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESD
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVLHEALHSHYTQKSLSLSPGK

Chain 2 - 1C11[PD-1]_ H3.240_IgG1_PVA_/S267K/S364K/E357Q/M428L/N434S (SEQ ID NO: 985)
QVQLVQSGPELKKPGESVKVSCKASGYTFT**HYGIN**WVRQPPGQGLEWMG**WINTYTGEPYYAPGFQE**RFVFSIDTS
QDTAYLQINSLKAEDTAVYYCAR**DYYGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKSLSLSPGK

Chain 3 - 1C11[PD-1]_ L3.148 (SEQ ID NO: 986)
DVLMTQSPDSLAVSLGERATINC**KSSQSIVHSNGNTYLE**WYQQKPGQSPKLLIY**KVSNRFS**GVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

**> human_IL15Ra(sushi)_(GGGGS)5-human_IL15(N4D/N65D;single-chain)-1C11[PD-1]_
H3.241_L3.148_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S-
IgG1_PVA_/S267K/S364K/E357Q/M428L/N434S**

Chain 1 - human_IL15Ra(sushi)_(GGGGS)5-human_IL15(N4D/N65D;single-chain)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S (SEQ ID NO: 987)
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGG
SGGGGSGGGGSGGGGS/NWVDVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDAS
IHDTVEDLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPP
VAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESD
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVLHEALHSHYTQKSLSLSPGK

Chain 2 - 1C11[PD-1]_ H3.241_IgG1_PVA_/S267K/S364K/E357Q/M428L/N434S (SEQ ID NO: 988)
EVQLVQSGPELKKPGESVKVSCKASGYTFT**HYGIN**WVRQPPGQGLEWMG**WINTYTGEPYYAPGFQE**RFVFSIDTS
QDTAYLQINSLKAEDTAVYYCAR**DYYGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKSLSLSPGK

Chain 3 - 1C11[PD-1]_ L3.148 (SEQ ID NO: 989)
DVLMTQSPDSLAVSLGERATINC**KSSQSIVHSNGNTYLE**WYQQKPGQSPKLLIY**KVSNRFS**GVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 128D

> human_IL15Ra(sushi)_(GGGGS)5-human_IL15(N4D/N65D;single-chain)-1C11[PD-1]_ H3.241_L3.92_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S-IgG1_PVA_/S267K/S364K/E357Q/M428L/N434S

Chain 1 - human_IL15Ra(sushi)_(GGGGS)5-human_IL15(N4D/N65D;single-chain)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S (SEQ ID NO: 990)
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGG
SGGGGSGGGGSGGGGS/NWVDVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDAS
IHDTVEDLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPP
VAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESD
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVLHEALHSHYTQKSLSLSPGK

Chain 2 - 1C11[PD-1]_ H3.241_IgG1_PVA_/S267K/S364K/E357Q/M428L/N434S (SEQ ID NO: 991)
EVQLVQSGPELKKPGESVKVSCKASGYTFT**HYGIN**WVRQPPGQGLEWMG**WINTYTGEPYYAPGFQE**RFVFSIDTS
QDTAYLQINSLKAEDTAVYYCAR**DYYGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKSLSLSPGK

Chain 3 - 1C11[PD-1]_ L3.92 (SEQ ID NO: 992)
DIVMTQSPDSLAVSLGERVTINC**KASQSIVHSNGNTYLE**WYQQKPGQPPKLLIY**KVSNRFT**GVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

> human_IL15Ra(sushi)_(GGGGS)5-human_IL15(N4D/N65D;single-chain)-1C11[PD-1]_ H3.328_L3.152_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S-IgG1_PVA_/S267K/S364K/E357Q/M428L/N434S

Chain 1 - human_IL15Ra(sushi)_(GGGGS)5-human_IL15(N4D/N65D;single-chain)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S (SEQ ID NO: 993)
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGG
SGGGGSGGGGSGGGGS/NWVDVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDAS
IHDTVEDLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPP
VAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESD
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVLHEALHSHYTQKSLSLSPGK

Chain 2 - 1C11[PD-1]_ H3.328_IgG1_PVA_/S267K/S364K/E357Q/M428L/N434S (SEQ ID NO: 994)
QIQLVQSGSELKKPGASVSVSCKASGYTFT**HYGMN**WVRQAPGQGLEWMG**WINTHTGEPTYADGFTG**RFVFSLDTS
VSTAYLQISSLKAEDTAVYFCAR**DYFGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKSLSLSPGK

Chain 3 - 1C11[PD-1]_ L3.152 (SEQ ID NO: 995)
DVLMTQSPDSLAVSLGERATINC**KSSQSIVFSNGNTYLE**WYQQKPGQSPKLLIY**KVSNRFS**GVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 128E

> human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/N65D;single-chain)-1C11[PD-1]_H3L3_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S-IgG1_PVA_/S267K/S364K/E357Q/M428L/N434S

Chain 1 - human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/N65D;single-chain)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S (SEQ ID NO: 996)
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGG
SGGGGSGGGGSGGGGS/NWVNVISDLKKIEDLIQSMHIDATLYTESNVHPSCKVTAMKCFLLELQVISLESGDAS
IHDTVEDLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPP
VAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESD
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVLHEALHSHYTQKSLSLSPGK

Chain 2 - 1C11[PD-1]_H3_IgG1_PVA_/S267K/S364K/E357Q/M428L/N434S (SEQ ID NO: 997)
QIQLVQSGSELKKPGASVKVSCKASGYTFT**HYGMN**WVRQAPGQGLEWMG**WINTYTGEPTYADGFTG**RFVFSLDTS
VSTAYLQISSLKAEDTAVYFCAR**DYYGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKSLSLSPGK

Chain 3 - 1C11[PD-1]_L3 (SEQ ID NO: 998)
DVLMTQSPDSLAVSLGERATINC**KSSQSIVHSNGNTYLE**WYQQKPGQSPKLLIY**KVSNRFS**GVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

> human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/N65D;single-chain)-1C11[PD-1]_H3.329_L3.220_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S-IgG1_PVA_/S267K/S364K/E357Q/M428L/N434S

Chain 1 - human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/N65D;single-chain)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S (SEQ ID NO: 999)
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGG
SGGGGSGGGGSGGGGS/NWVNVISDLKKIEDLIQSMHIDATLYTESNVHPSCKVTAMKCFLLELQVISLESGDAS
IHDTVEDLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPP
VAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESD
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVLHEALHSHYTQKSLSLSPGK

Chain 2 - 1C11[PD-1]_H3.329_IgG1_PVA_/S267K/S364K/E357Q/M428L/N434S (SEQ ID NO: 1000)
QIQLVQSGSELLKPGASVSVSCKASGYTFT**HYGMN**WVRQAPGQGLEWMG**WINTHTGEPTYADGFTG**RFVFSLDTS
VSTAYLQISSLKAEDTAVYFCAR**DYFGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKSLSLSPGK

Chain 3 - 1C11[PD-1]_L3.220 (SEQ ID NO: 1001)
DILMTQSPDSLAVSLGERATINC**KSSQSIVYSNGNNYLE**WYQQKPGQSPKLLIY**KVSNRFS**GVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 128F

> human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/N65D;single-chain)-1C11[PD-1]_H3.303_L3.152_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S-IgG1_PVA_/S267K/S364K/E357Q/M428L/N434S

Chain 1 - human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/N65D;single-chain)_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S (SEQ ID NO: 1002)
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGG
SGGGGSGGGGSGGGGS/NWVNVISDLKKIEDLIQSMHIDATLYTESNVHPSCKVTAMKCFLLELQVISLESGDAS
IHDTVEDLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPP
VAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESD
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVLHEALHSHYTQKSLSLSPGK

Chain 2 - 1C11[PD-1]_H3.303_IgG1_PVA_/S267K/S364K/E357Q/M428L/N434S (SEQ ID NO: 1003)
QIQLVQSGSELKKPGASVKVSCKASGYTFT**HYGMN**WVRQAPGQGLEWMG**WINTYTGEPTYADGFTG**RFVFSLDTS
VSTAYLQISSLKAEDTAVYFCAR**DYFGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKSLSLSPGK

Chain 3 - 1C11[PD-1]_L3.152 (SEQ ID NO: 1004)
DVLMTQSPDSLAVSLGERATINC**KSSQSIVFSNGNTYLE**WYQQKPGQSPKLLIY**KVSNRFS**GVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

> human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/N65D;single-chain)-1C11[PD-1]_H3.234_L3.144_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S-IgG1_PVA_/S267K/S364K/E357Q/M428L/N434S

Chain 1 - human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/N65D;single-chain)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S (SEQ ID NO: 1005)
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGG
SGGGGSGGGGSGGGGS/NWVNVISDLKKIEDLIQSMHIDATLYTESNVHPSCKVTAMKCFLLELQVISLESGDAS
IHDTVEDLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPP
VAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESD
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVLHEALHSHYTQKSLSLSPGK

Chain 2 - 1C11[PD-1]_ H3.234_IgG1_PVA_/S267K/S364K/E357Q/M428L/N434S (SEQ ID NO: 1006)
EVQLVQSGSELKKPGESVKVSCKASGYTFT**HYGIN**WVRQPPGQGLEWMG**WINTYTGEPYYAPGFQE**RFVFSLDTS
QDTAYLQINSLKAEDTAVYYCAR**DYYGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKSLSLSPGK

Chain 3 - 1C11[PD-1]_ L3.144 (SEQ ID NO: 1007)
DIVMTQSPDSLAVSLGERVTINC**KASQSIVHSNGNTYLE**WYQQKPGQPPKLLIY**KVSNRFS**GVPDRFSGSGSGTD
FTLTISSVEAEDAATYYC**FQGSHVPNT**FGQGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 128G

> human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/N65D;single-chain)-1C11[PD-1]_ H3.240_L3.148_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S-IgG1_PVA_/S267K/S364K/E357Q/M428L/N434S

Chain 1 - human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/N65D;single-chain)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S (SEQ ID NO: 1008)

ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGG
SGGGGSGGGGSGGGGS/NWVNVISDLKKIEDLIQSMHIDATLYTESNVHPSCKVTAMKCFLLELQVISLESGDAS
IHDTVEDLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPP
VAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESD
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVLHEALHSHYTQKSLSLSPGK

Chain 2 - 1C11[PD-1]_ H3.240_IgG1_PVA_/S267K/S364K/E357Q/M428L/N434S (SEQ ID NO: 1009)

QVQLVQSGPELKKPGESVKVSCKASGYTFT**HYGIN**WVRQPPGQGLEWMG**WINTYTGEPYYAPGFQE**RFVFSIDTS
QDTAYLQINSLKAEDTAVYYCAR**DYYGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKSLSLSPGK

Chain 3 - 1C11[PD-1]_ L3.148 (SEQ ID NO: 1010)

DVLMTQSPDSLAVSLGERATINC**KSSQSIVHSNGNTYLE**WYQQKPGQSPKLLIY**KVSNRFS**GVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

> human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/N65D;single-chain)-1C11[PD-1]_ H3.241_L3.148_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S-IgG1_PVA_/S267K/S364K/E357Q/M428L/N434S

Chain 1 - human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/N65D;single-chain)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S (SEQ ID NO: 1011)

ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGG
SGGGGSGGGGSGGGGS/NWVNVISDLKKIEDLIQSMHIDATLYTESNVHPSCKVTAMKCFLLELQVISLESGDAS
IHDTVEDLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPP
VAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESD
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVLHEALHSHYTQKSLSLSPGK

Chain 2 - 1C11[PD-1]_ H3.241_IgG1_PVA_/S267K/S364K/E357Q/M428L/N434S (SEQ ID NO: 1012)

EVQLVQSGPELKKPGESVKVSCKASGYTFT**HYGIN**WVRQPPGQGLEWMG**WINTYTGEPYYAPGFQE**RFVFSIDTS
QDTAYLQINSLKAEDTAVYYCAR**DYYGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKSLSLSPGK

Chain 3 - 1C11[PD-1]_ L3.148 (SEQ ID NO: 1013)

DVLMTQSPDSLAVSLGERATINC**KSSQSIVHSNGNTYLE**WYQQKPGQSPKLLIY**KVSNRFS**GVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 128H

> human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/N65D;single-chain)-1C11[PD-1]_ H3.241_L3.92_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S-IgG1_PVA_/S267K/S364K/E357Q/M428L/N434S

Chain 1 - human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/N65D;single-chain)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S (SEQ ID NO: 1014)

ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGGSGGGGSGGGGSGGGGS/NWVNVISDLKKIEDLIQSMHIDATLYTESNVHPSCKVTAMKCFLLELQVISLESGDASIHDTVEDLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVLHEALHSHYTQKSLSLSPGK

Chain 2 - 1C11[PD-1]_ H3.241_IgG1_PVA_/S267K/S364K/E357Q/M428L/N434S (SEQ ID NO: 1015)

EVQLVQSGPELKKPGESVKVSCKASGYTFT**HYGIN**WVRQPPGQGLEWMG**WINTYTGEPYYAPGFQE**RFVFSIDTSQDTAYLQINSLKAEDTAVYYCAR**DYYGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKSLSLSPGK

Chain 3 - 1C11[PD-1]_ L3.92 (SEQ ID NO: 1016)

DIVMTQSPDSLAVSLGERVTINC**KASQSIVHSNGNTYLE**WYQQKPGQPPKLLIY**KVSNRFT**GVPDRFSGSGSGTDFTLTISSLQAEDVAVYYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

> human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/N65D;single-chain)-1C11[PD-1]_ H3.328_L3.152_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S-IgG1_PVA_/S267K/S364K/E357Q/M428L/N434S

Chain 1 - human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/N65D;single-chain)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S (SEQ ID NO: 1017)

ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGGSGGGGSGGGGSGGGGS/NWVNVISDLKKIEDLIQSMHIDATLYTESNVHPSCKVTAMKCFLLELQVISLESGDASIHDTVEDLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVLHEALHSHYTQKSLSLSPGK

Chain 2 - 1C11[PD-1]_ H3.328_IgG1_PVA_/S267K/S364K/E357Q/M428L/N434S (SEQ ID NO: 1018)

QIQLVQSGSELKKPGASVSVSCKASGYTFT**HYGMN**WVRQAPGQGLEWMG**WINTHTGEPTYADGFTG**RFVFSLDTSVSTAYLQISSLKAEDTAVYFCAR**DYFGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKSLSLSPGK

Chain 3 - 1C11[PD-1]_ L3.152 (SEQ ID NO: 1019)

DVLMTQSPDSLAVSLGERATINC**KSSQSIVFSNGNTYLE**WYQQKPGQSPKLLIY**KVSNRFS**GVPDRFSGSGSGTDFTLTISSLQAEDVAVYYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 128I

> human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/E64Q/N65D;single-chain)-1C11[PD-1]_H3L3_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S-IgG1_PVA_/S267K/S364K/E357Q/M428L/N434S

Chain 1 - human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/E64Q/N65D;single-chain)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S (SEQ ID NO: 1020)
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGG
SGGGGSGGGGSGGGGS/NWVNVISDLKKIEDLIQSMHIDATLYTESNVHPSCKVTAMKCFLLELQVISLESGDAS
IHDTVQDLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPP
VAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESD
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVLHEALHSHYTQKSLSLSPGK

Chain 2 - 1C11[PD-1]_H3_IgG1_PVA_/S267K/S364K/E357Q/M428L/N434S (SEQ ID NO: 1021)
QIQLVQSGSELKKPGASVKVSCKASGYTFT**HYGMN**WVRQAPGQGLEWMG**WINTYTGEPTYADGFTG**RFVFSLDTS
VSTAYLQISSLKAEDTAVYFCAR**DYYGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKSLSLSPGK

Chain 3 - 1C11[PD-1]_L3 (SEQ ID NO: 1022)
DVLMTQSPDSLAVSLGERATINC**KSSQSIVHSNGNTYLE**WYQQKPGQSPKLLIY**KVSNRFS**GVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

> human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/E64Q/N65D;single-chain)-1C11[PD-1]_H3.329_L3.220_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S-IgG1_PVA_/S267K/S364K/E357Q/M428L/N434S

Chain 1 - human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/E64Q/N65D;single-chain)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S (SEQ ID NO: 1023)
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGG
SGGGGSGGGGSGGGGS/NWVNVISDLKKIEDLIQSMHIDATLYTESNVHPSCKVTAMKCFLLELQVISLESGDAS
IHDTVQDLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPP
VAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESD
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVLHEALHSHYTQKSLSLSPGK

Chain 2 - 1C11[PD-1]_H3.329_IgG1_PVA_/S267K/S364K/E357Q/M428L/N434S (SEQ ID NO: 1024)
QIQLVQSGSELLKPGASVSVSCKASGYTFT**HYGMN**WVRQAPGQGLEWMG**WINTHTGEPTYADGFTG**RFVFSLDTS
VSTAYLQISSLKAEDTAVYFCAR**DYFGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKSLSLSPGK

Chain 3 - 1C11[PD-1]_L3.220 (SEQ ID NO: 1025)
DILMTQSPDSLAVSLGERATINC**KSSQSIVYSNGNNYLE**WYQQKPGQSPKLLIY**KVSNRFS**GVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 128J

> human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/E64Q/N65D;single-chain)-1C11[PD-1]_H3.303_L3.152_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S-IgG1_PVA_/S267K/S364K/E357Q/M428L/N434S

Chain 1 - human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/E64Q/N65D;single-chain)_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S (SEQ ID NO: 1026)

ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGG
SGGGGSGGGGSGGGGS/NWVNVISDLKKIEDLIQSMHIDATLYTESNVHPSCKVTAMKCFLLELQVISLESGDAS
IHDTVQDLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPP
VAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESD
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVLHEALHSHYTQKSLSLSPGK

Chain 2 - 1C11[PD-1]_H3.303_IgG1_PVA_/S267K/S364K/E357Q/M428L/N434S (SEQ ID NO: 1027)

QIQLVQSGSELKKPGASVKVSCKASGYTFT**HYGMN**WVRQAPGQGLEWMG**WINTYTGEPTYADGFTG**RFVFSLDTS
VSTAYLQISSLKAEDTAVYFCAR**DYFGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKSLSLSPGK

Chain 3 - 1C11[PD-1]_L3.152 (SEQ ID NO: 1028)

DVLMTQSPDSLAVSLGERATINC**KSSQSIVFSNGNTYLE**WYQQKPGQSPKLLIY**KVSNRFS**GVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

> human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/E64Q/N65D;single-chain)-1C11[PD-1]_H3.234_L3.144_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S-IgG1_PVA_/S267K/S364K/E357Q/M428L/N434S

Chain 1 - human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/E64Q/N65D;single-chain)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S (SEQ ID NO: 1029)

ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGG
SGGGGSGGGGSGGGGS/NWVNVISDLKKIEDLIQSMHIDATLYTESNVHPSCKVTAMKCFLLELQVISLESGDAS
IHDTVQDLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPP
VAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESD
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVLHEALHSHYTQKSLSLSPGK

Chain 2 - 1C11[PD-1]_ H3.234_IgG1_PVA_/S267K/S364K/E357Q/M428L/N434S (SEQ ID NO: 1030)

EVQLVQSGSELKKPGESVKVSCKASGYTFT**HYGIN**WVRQPPGQGLEWMG**WINTYTGEPYYAPGFQE**RFVFSLDTS
QDTAYLQINSLKAEDTAVYYCAR**DYYGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKSLSLSPGK

Chain 3 - 1C11[PD-1]_ L3.144 (SEQ ID NO: 1031)

DIVMTQSPDSLAVSLGERVTINC**KASQSIVHSNGNTYLE**WYQQKPGQPPKLLIY**KVSNRFS**GVPDRFSGSGSGTD
FTLTISSVEAEDAATYYC**FQGSHVPNT**FGQGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 128K

> human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/E64Q/N65D;single-chain)-1C11[PD-1]_ H3.240_L3.148_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S-IgG1_PVA_/S267K/S364K/E357Q/M428L/N434S

Chain 1 - human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/E64Q/N65D;single-chain)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S (SEQ ID NO: 1032)
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGG
SGGGGSGGGGSGGGGS/NWVNVISDLKKIEDLIQSMHIDATLYTESNVHPSCKVTAMKCFLLELQVISLESGDAS
IHDTVQDLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPP
VAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESD
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVLHEALHSHYTQKSLSLSPGK

Chain 2 - 1C11[PD-1]_ H3.240_IgG1_PVA_/S267K/S364K/E357Q/M428L/N434S (SEQ ID NO: 1033)
QVQLVQSGPELKKPGESVKVSCKASGYTFT**HYGIN**WVRQPPGQGLEWMG**WINTYTGEPYYAPGFQE**RFVFSIDTS
QDTAYLQINSLKAEDTAVYYCAR**DYYGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKSLSLSPGK

Chain 3 - 1C11[PD-1]_ L3.148 (SEQ ID NO: 1034)
DVLMTQSPDSLAVSLGERATINC**KSSQSIVHSNGNTYLE**WYQQKPGQSPKLLIY**KVSNRFS**GVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

> human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/E64Q/N65D;single-chain)-1C11[PD-1]_ H3.241_L3.148_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S-IgG1_PVA_/S267K/S364K/E357Q/M428L/N434S

Chain 1 - human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/E64Q/N65D;single-chain)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S (SEQ ID NO: 1035)
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGG
SGGGGSGGGGSGGGGS/NWVNVISDLKKIEDLIQSMHIDATLYTESNVHPSCKVTAMKCFLLELQVISLESGDAS
IHDTVQDLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPP
VAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESD
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVLHEALHSHYTQKSLSLSPGK

Chain 2 - 1C11[PD-1]_ H3.241_IgG1_PVA_/S267K/S364K/E357Q/M428L/N434S (SEQ ID NO: 1051)
EVQLVQSGPELKKPGESVKVSCKASGYTFT**HYGIN**WVRQPPGQGLEWMG**WINTYTGEPYYAPGFQE**RFVFSIDTS
QDTAYLQINSLKAEDTAVYYCAR**DYYGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKSLSLSPGK

Chain 3 - 1C11[PD-1]_ L3.148 (SEQ ID NO: 1052)
DVLMTQSPDSLAVSLGERATINC**KSSQSIVHSNGNTYLE**WYQQKPGQSPKLLIY**KVSNRFS**GVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 128L

> human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/E64Q/N65D;single-chain)-1C11[PD-1]_ H3.241_L3.92_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S-IgG1_PVA_/S267K/S364K/E357Q/M428L/N434S

Chain 1 - human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/E64Q/N65D;single-chain)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S (SEQ ID NO: 1036)
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGG
SGGGGSGGGGSGGGGS/NWVNVISDLKKIEDLIQSMHIDATLYTESNVHPSCKVTAMKCFLLELQVISLESGDAS
IHDTVQDLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPP
VAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESD
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVLHEALHSHYTQKSLSLSPGK

Chain 2 - 1C11[PD-1]_ H3.241_IgG1_PVA_/S267K/S364K/E357Q/M428L/N434S (SEQ ID NO: 1037)
EVQLVQSGPELKKPGESVKVSCKASGYTFT**HYGIN**WVRQPPGQGLEWMG**WINTYTGEPYYAPGFQE**RFVFSIDTS
QDTAYLQINSLKAEDTAVYYCAR**DYYGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKSLSLSPGK

Chain 3 - 1C11[PD-1]_ L3.92 (SEQ ID NO: 1038)
DIVMTQSPDSLAVSLGERVTINC**KASQSIVHSNGNTYLE**WYQQKPGQPPKLLIY**KVSNRFT**GVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

> human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/E64Q/N65D;single-chain)-1C11[PD-1]_ H3.328_L3.152_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S-IgG1_PVA_/S267K/S364K/E357Q/M428L/N434S

Chain 1 - human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/E64Q/N65D;single-chain)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S/M428L/N434S (SEQ ID NO: 1039)
ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGG
SGGGGSGGGGSGGGGS/NWVNVISDLKKIEDLIQSMHIDATLYTESNVHPSCKVTAMKCFLLELQVISLESGDAS
IHDTVQDLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPP
VAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESD
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVLHEALHSHYTQKSLSLSPGK

Chain 2 - 1C11[PD-1]_ H3.328_IgG1_PVA_/S267K/S364K/E357Q/M428L/N434S (SEQ ID NO: 1040)
QIQLVQSGSELKKPGASVSVSCKASGYTFT**HYGMN**WVRQAPGQGLEWMG**WINTHTGEPTYADGFTG**RFVFSLDTS
VSTAYLQISSLKAEDTAVYFCAR**DYFGSSPY**WGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY
FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKSLSLSPGK

Chain 3 - 1C11[PD-1]_ L3.152 (SEQ ID NO: 1041)
DVLMTQSPDSLAVSLGERATINC**KSSQSIVFSNGNTYLE**WYQQKPGQSPKLLIY**KVSNRFS**GVPDRFSGSGSGTD
FTLTISSLQAEDVAVYYC**FQGSHVPNT**FGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA
KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 129A

>XENP26007 human_IL15Ra(sushi)_(GGGGS)5-human_IL15(N4D/N65D;single-Chain)-Numax_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-IgG1_PVA_/S267K/S364K/E357Q

Chain 1 - human_IL15Ra(sushi)_(GGGGS)5-human_IL15(N4D/N65D;single-Chain)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S scIL-15/Rα-Fc Chain (SEQ ID NO: 1042)

ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGG
SGGGGSGGGGSGGGGS/NWVDVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLESGDAS
IHDTVEDLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPP
VAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESD
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 - Numax_IgG1_PVA_/S267K/S364K/E357Q Heavy Chain (SEQ ID NO: 1043)

QVTLRESGPALVKPTQTLTLTCTFSGFSLSTAGMSVGWIRQPPGKALEWLADIWWDDKKHYNPSLKDRLTISKDT
SKNQVVLKVTNMDPADTATYYCARDMIFNFYFDVWGQGTTVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLV
KDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCD
KTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYN
STYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGF
YPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 3 - Numax Light Chain (SEQ ID NO: 1044)

DIQMTQSPSTLSASVGDRVTITCSASSRVGYMHWYQQKPGKAPKLLIYDTSKLASGVPSRFSGSGSGTEFTLTIS
SLQPDDFATYYCFQGSGYPFTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKV
DNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP29481 human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/N65D;single-chain)-Numax_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-IgG1_PVA_/S267K/S364K/E357Q

Chain 1 - human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/N65D;single-chain)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 1045)

ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGG
SGGGGSGGGGSGGGGS/NWVNVISDLKKIEDLIQSMHIDATLYTESNVHPSCKVTAMKCFLLELQVISLESGDAS
IHDTVEDLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPP
VAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESD
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 - Numax_IgG1_PVA_/S267K/S364K/E357Q (SEQ ID NO: 1046)

QVTLRESGPALVKPTQTLTLTCTFSGFSLSTAGMSVGWIRQPPGKALEWLADIWWDDKKHYNPSLKDRLTISKDT
SKNQVVLKVTNMDPADTATYYCARDMIFNFYFDVWGQGTTVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLV
KDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCD
KTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYN
STYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGF
YPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 3 - Numax LC (SEQ ID NO: 1047)

DIQMTQSPSTLSASVGDRVTITCSASSRVGYMHWYQQKPGKAPKLLIYDTSKLASGVPSRFSGSGSGTEFTLTIS
SLQPDDFATYYCFQGSGYPFTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKV
DNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 129B

>XENP30432 human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/E64Q/N65D;single-chain)-Numax_IgG1_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S-IgG1_PVA_/S267K/S364K/E357Q

Chain 1 - human_IL15Ra(sushi)_(GGGGS)5-human_IL15(D30N/E64Q/N65D;single-chain)_Fc(216)_IgG1_pI(-)_Isosteric_A_C220S/PVA_/S267K/L368D/K370S (SEQ ID NO: 1048)

ITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIR/GGGGSGGGG
SGGGGSGGGGSGGGGS/NWVNVISDLKKIEDLIQSMHIDATLYTESNVHPSCKVTAMKCFLLELQVISLESGDAS
IHDTVQDLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS/EPKSSDKTHTCPPCPAPP
VAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESD
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 2 - Numax_VH_IgG1_IgG1_PVA_/S267K/S364K/E357Q (SEQ ID NO: 1049)

QVTLRESGPALVKPTQTLTLTCTFSGFSLSTAGMSVGWIRQPPGKALEWLADIWWDDKKHYNPSLKDRLTISKDT
SKNQVVLKVTNMDPADTATYYCARDMIFNFYFDVWGQGTTVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLV
KDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCD
KTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYN
STYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGF
YPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Chain 3 - Numax LC (SEQ ID NO: 1050)

DIQMTQSPSTLSASVGDRVTITCSASSRVGYMHWYQQKPGKAPKLLIYDTSKLASGVPSRFSGSGSGTEFTLTIS
SLQPDDFATYYCFQGSGYPFTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKV
DNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2019/028206

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07K16/28 A61K38/17 A61K38/20 C07K14/54 C07K14/715
A61P35/00
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C07K A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPO-Internal, EMBASE, BIOSIS, Sequence Search, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 2015/018528 A1 (CYTUNE PHARMA [FR]; UNIV PARIS DESCARTES [FR] ET AL.) 12 February 2015 (2015-02-12) claims 1,3 -----	1-17
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☒ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

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"A" document defining the general state of the art which is not considered to be of particular relevance

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Date of the actual completion of the international search 19 July 2019	Date of mailing of the international search report 05/08/2019
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Authorized officer Saame, Tina

International application No
PCT/US2019/028206

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

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Y	WO 2012/146628 A1 (ROCHE GLYCART AG [CH]; AST OLIVER [CH] ET AL.) 1 November 2012 (2012-11-01) page 31, line 9 - line 11; claims 1-6,10; figure 2C -----	1-17
Y	US 2016/355608 A1 (BERNETT MATTHEW J [US] ET AL) 8 December 2016 (2016-12-08) figures 29-32 -----	1-17
X,P	WO 2018/071918 A1 (XENCOR INC [US]) 19 April 2018 (2018-04-19) figure 64D -----	1-17
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2

International application No.
PCT/US2019/028206

INTERNATIONAL SEARCH REPORT

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of a sequence listing:

   a. ☐ forming part of the international application as filed:
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   b. ☐ furnished together with the international application under PCT Rule 13*ter*.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.

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2. ☐ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2019/028206

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PCT/US2019/028206

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