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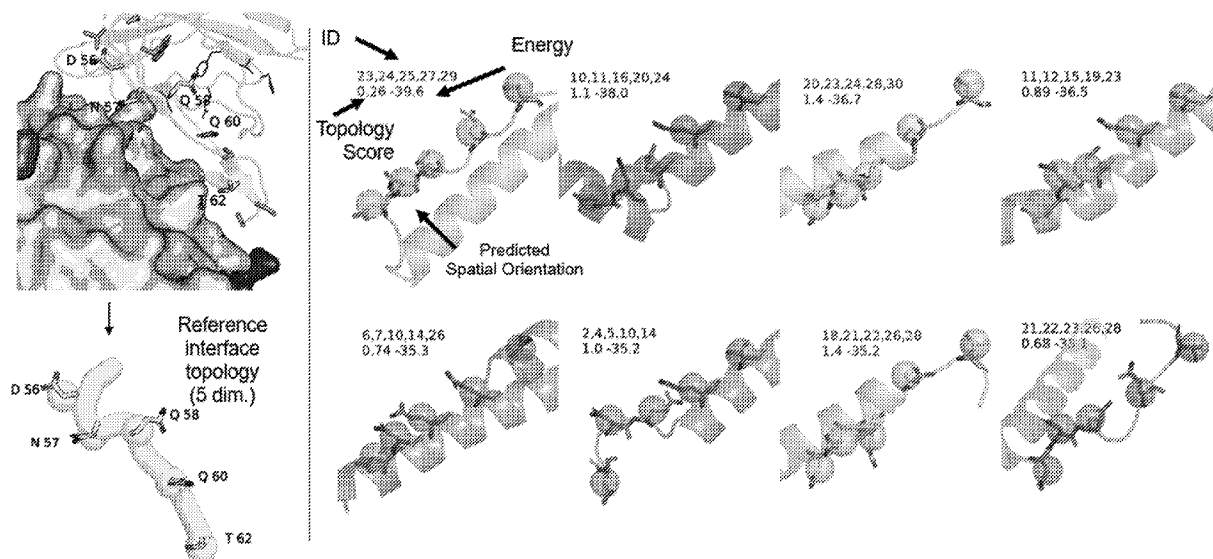


FIG. 4B

(57) Abrégé/Abstract:

Provided herein engineered polypeptides that comprise a combination of spatially-associated topological constraints, wherein at least one constraint is derived from a CD25 reference target, and methods of selecting said engineered polypeptides. Further provided are methods of using the engineered polypeptides, including as positive and/or negative selection molecules in methods of screening a library of binding molecules such as antibodies. Further provided herein are CD25 antibodies selected using these engineered polypeptides.

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(54) Title: ENGINEERED CD25 POLYPEPTIDES AND USES THEREOF

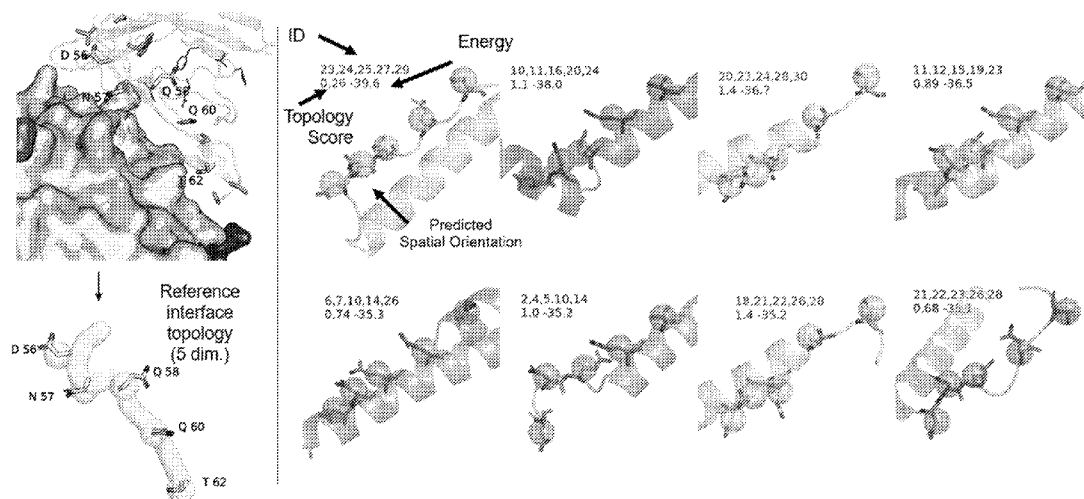


FIG. 4B

(57) **Abstract:** Provided herein engineered polypeptides that comprise a combination of spatially-associated topological constraints, wherein at least one constraint is derived from a CD25 reference target, and methods of selecting said engineered polypeptides. Further provided are methods of using the engineered polypeptides, including as positive and/or negative selection molecules in methods of screening a library of binding molecules such as antibodies. Further provided herein are CD25 antibodies selected using these engineered polypeptides.

[Continued on next page]



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ENGINEERED CD25 POLYPEPTIDES AND USES THEREOF

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of U.S. Provisional Application No. 62/902,334, filed September 18, 2019; and U.S. Provisional Application No. 62/767,431, filed November 14, 2018, the disclosures of which are incorporated by reference herein in their entireties.

BACKGROUND

[0001] The CD25 protein is the alpha chain of the interleukin-2 (IL-2) receptor and is a transmembrane protein present on regulatory T cells, and activated T cells. In a normal state, regulatory T cells constitutively express CD25 and act to suppress the expansion of effector T cells. Regulatory T cells maintain the healthy state and inhibit effector T cells from reacting against self antigens or over-reacting to foreign antigens. In a normal, protective immune response, effector T cells multiply after contact with foreign antigen and overcome inhibition by regulatory T cells. In case of proliferative diseases, however, cancer cells may disable the healthy immune response by increasing the amount of regulatory T cells and thereby limiting the generation of effector T cells against them. Thus, there is interest in therapeutics for to alter the proliferation of CD25-expressing regulatory T cells, for example to dampen the immune system for use in cancer therapies. These therapeutics may include CD25-targeting antibodies.

[0002] CD25-targeting antibodies can be produced by immunization of animals using CD25 immunogens, however, current methods of developing CD25 immunogens often lead to unpredictable, undesirable characteristics, such as antibody promiscuity or low cross-reactivity across species.

[0003] Thus, what is needed in the art are new engineered polypeptides having structural and/or dynamic similarity to CD25 or portions thereof, for example engineered polypeptides designed to mimic epitopes outside the IL-2 binding site.

SUMMARY

[0004] In one aspect, the disclosure provides an engineered polypeptide, wherein the engineered polypeptide shares at least 46% structural and/or dynamic identity to a CD25 reference target, wherein the CD25 reference target is a portion of a CD25 selected from CD25 residues 55-63, 13-20:127-132, 5-17, 5-11:156-163, 77-89, 147-157, 11-14, or 44-56.

[0005] In embodiments, the engineered polypeptide shares at least 60% structural and/or dynamic identity to the CD25 reference target. In embodiments, the engineered polypeptide shares at least 80% structural and/or dynamic identity to the CD25 reference target. In embodiments, the engineered polypeptide shares at least 80% sequence identity to an amino-acid sequence selected from SEQ ID NOS: 1-16. In embodiments, the engineered polypeptide shares at least 46% structural and/or dynamic identity to a CD25 reference target, wherein the CD25 reference target is a portion of CD25 selected from CD25 residues 55-63, 13-20:127-132, 5-17, 5-11:156-163, 77-89, 147-157, 11-14, or 44-56. In embodiments, the engineered polypeptide shares at least 80% structural and/or dynamic identity to the CD25 reference target. In embodiments, the structural and/or dynamic identity to the CD25 reference target is determined using the structure of CD25 deposited at PDB ID NO: 2ERJ, chain A. In embodiments, the engineered polypeptide comprises an N-terminal modification or a C-terminal modification, optionally an N-terminal Biotin-PEG₂– or a C-terminal –GSGSGK-Biotin.

[0006] In embodiments, between 10% to 98% of the amino acids of the engineered polypeptide meet one or more CD25 reference target-derived constraints. In embodiments, the amino acids that meet the one or more CD25 reference target-derived constraints have less than 8.0 Å backbone root-mean-square deviation (RMSD) structural homology with the CD25 reference target. In embodiments, the amino acids that meet the one or more CD25 reference target-derived constraints have a van der Waals surface area overlap with the reference of between 30 Å² to 3000 Å². In embodiments, the CD25 reference target-derived constraints are independently selected from the group consisting of: atomic distances; atomic fluctuations; atomic energies; chemical descriptors; solvent exposures; amino acid sequence similarity; bioinformatic descriptors; non-covalent bonding propensity; phi angles; psi angles; van der Waals radii; secondary structure propensity; amino acid adjacency; and amino acid contact.

In embodiments, the engineered polypeptide shares 46%-96% RMSIP or more structural similarity to the reference target across the amino acids of the polypeptide that meet the one or more reference target-derived constraints.

[0007] In another aspect, the disclosure provides a CD25-specific antibody comprising an antigen-binding domain that specifically binds a CD25 epitope selected from CD25 residues 55-63, 13-20:127-132, 5-17, 5-11:156-163, 77-89, 147-157, 11-14, or 44-56. In embodiments, the antibody competes for binding of CD25 with an epitope-specific reference binding agent, wherein the epitope-specific binding agent is IL-2, daclizumab, basioliximab, and/or 7G7B6. In embodiments, the antibody does not compete with an off-target reference binding agent, wherein the off-target binding agent is IL-2, daclizumab, basioliximab, and/or 7G7B6. In embodiments, the antibody has a k_{off} of less than $10^{-2}/\text{s}$, less than $10^{-3}/\text{s}$, or less than $10^{-4}/\text{s}$, wherein the k_{off} is measured using biolayer interferometry with soluble human CD25. In embodiments, the antibody has a k_{off} of between $10^{-2}/\text{s}$ $10^{-5}/\text{s}$, wherein the k_{off} is measured using biolayer interferometry with soluble human CD25. In embodiments, the antibody has a K_D less than 100 nM, less than 25 nM, or less than 5 nM, wherein the K_D is measured using biolayer interferometry with soluble human CD25. In embodiments, the antibody has a K_D between 100 nM and 1 nM, wherein the K_D is measured using biolayer interferometry with soluble human CD25.

[0008] In embodiments, the antibody specifically binds cells expressing CD25. In embodiments, the antibody binds cells expressing CD25 with a mean fluorescence intensity (MFI) of at least 10^4 or at least 10^5 . In embodiments, the antibody binds cells expressing CD25 with a mean fluorescence intensity (MFI) of between 10^4 and 10^6 . In embodiments, the antibody does not bind CD25(-) cells. In embodiments, the antibody binds CD25(-) cells with a mean fluorescence intensity (MFI) of less than 10^3 . In embodiments, the antibody comprises the six CDRs of any one of Combinations 1-126 of Table 7D.

[0009] In embodiments, the antibody comprising six complementarity determining regions (CDRs) for any one of YU390-B12, YU397-F01, YU397-D01, YU398-A11, YU404-H01, YU400-B07, YU400-D09, YU401-B01, YU401-G07, YU404-C02, YU403-G07, YU403-G05, YU391-B12, YU400-A03, YU400-D02, YU392-A09, YU392-B11, YU392-B12, YU392-E05,

YU392-E06, YU392-G08, YU389-A03, YU392-G09, YU392-G12, YU392-H02, YU392-H04, YU402-F01, YU389-B11, YU394-D08, or YU390-A11, as provided in Table 3A and Table 3B.

[0010] In embodiments, the antibody comprises a heavy chain variable region and a light chain variable region that each share at least 90%, 95%, 99%, or 100% sequence identity with the heavy chain variable region and the light chain variable region of YU390-B12, YU397-F01, YU397-D01, YU398-A11, YU404-H01, YU400-B07, YU400-D09, YU401-B01, YU401-G07, YU404-C02, YU403-G07, YU403-G05, YU391-B12, YU400-A03, YU400-D02, YU392-A09, YU392-B11, YU392-B12, YU392-E05, YU392-E06, YU392-G08, YU389-A03, YU392-G09, YU392-G12, YU392-H02, YU392-H04, YU402-F01, YU389-B11, YU394-D08, or YU390-A11, as provided in Table 5. In embodiments, the antibody is a full-length immunoglobulin G monoclonal antibody. In embodiments, the antibody comprises single chain variable fragment (scFv) that share at least 90%, 95%, 99%, or 100% sequence identity with the scFv sequence of YU390-B12, YU397-F01, YU397-D01, YU398-A11, YU404-H01, YU400-B07, YU400-D09, YU401-B01, YU401-G07, YU404-C02, YU403-G07, YU403-G05, YU391-B12, YU400-A03, YU400-D02, YU392-A09, YU392-B11, YU392-B12, YU392-E05, YU392-E06, YU392-G08, YU389-A03, YU392-G09, YU392-G12, YU392-H02, YU392-H04, YU402-F01, YU389-B11, YU394-D08, or YU390-A11, as provided in Table 5.

[0011] In embodiments, the antibody is a human antibody. In embodiments, the antibody is a humanized antibody. In embodiments, the antibody is a chimeric antibody. In embodiments, the antibody comprises a mouse variable domain and a human constant domain. In embodiments, the antibody also binds cynomolgous monkey CD25.

[0012] In another aspect, the disclosure provides a pharmaceutical composition comprising any antibody of disclosure and optionally a pharmaceutically acceptable excipient. In another aspect, the disclosure provides a method of treating a subject in need of treatment comprising administering to the subject a therapeutically effective amount of any antibody or pharmaceutical composition of the disclosure. In embodiments, the subject suffers from a cancer. In embodiments, the subject suffers from an autoimmune disease or disorder.

In another aspect, the disclosure provides a method of depleting the number of regulatory T cells in a subject comprising administering to the subject a therapeutically effective amount of any antibody or pharmaceutical composition of the disclosure. In embodiments, the subject suffers from a cancer. In embodiments, the subject suffers from an autoimmune disease or disorder.

[0013] In another aspect, the disclosure provides a kit comprising the antibodies of any antibody or pharmaceutical composition of the disclosure.

[0014] In some aspects, provided herein is an engineered immunogen having at least 60% sequence similarity to a sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, and SEQ ID NO: 11. In some embodiments, the engineered immunogen has at least 80% similarity to the sequence. In other embodiments, the engineered immunogen has at least 90% similarity to the sequence. In certain embodiments, the engineered immunogen shares at least one characteristic with CD25. In still further embodiments, the engineered immunogen binds to an antibody of CD25. In some embodiments, the engineered immunogen has higher binding affinity to an antibody of CD25 at pH below 7.0, compared to binding affinity at pH between about 7.3 and about 7.5. In some embodiments, the engineered immunogen has higher binding affinity to an antibody of CD25 at pH between about 6.4 and about 6.6, compared to binding affinity at pH between about 7.3 and about 7.5.

[0015] In yet other embodiments, provided herein is a method of producing an antibody, comprising immunizing an animal with an engineered immunogen having at least 60% sequence similarity to a sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, and SEQ ID NO: 11; and producing an antibody. In some embodiments of the method, the antibody is an antibody to CD25. In certain embodiments, the antibody exhibits higher binding affinity for CD25 at pH below 7.0, compared to binding affinity at pH between about 7.3 and about 7.5. In still further embodiments, the antibody exhibits higher binding affinity for CD25 at pH between about 6.4 and about 6.6, compared to binding affinity at pH between about 7.3 and about 7.5. In some embodiments, the antibody does not block binding of CD25 to IL-2. In other embodiments, the antibody does block binding of

CD25 to IL-2. The method of any one of claims 8 to 11, wherein the antibody does not block binding of CD25 to IL-2. In some embodiments, the antibody prevents heterotrimerization of IL-2R-alpha, IL-2R-beta, and IL-2R-gamma. In certain embodiments, the antibody is capable of binding to both the cis orientation and the trans orientation of CD25.

DESCRIPTION OF THE FIGURES

[0016] The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the Office upon request and payment of the necessary fee. The present application can be understood by reference to the following description taking in conjunction with the accompanying figures.

[0017] **FIG. 1** provides a schematic demonstrating construction of an exemplary combination of three spatially-associated topological constraints, for use in selecting an engineered polypeptide as described herein.

[0018] **FIG. 2** provides a schematic of the steps involved in some exemplary methods of determining the reference-derived spatially-associated topological constraints and their use in selecting an engineered polypeptide. The engineered polypeptides are herein referred to as meso-scale molecules, MEMs, or meso-scale peptides.

[0019] **FIGS. 3A-3C** provide schematics demonstrating the selection of a group of engineered polypeptides using the methods described herein. **FIG. 3A** shows the extraction of spatially-associated topological information about an interface of interest in a reference, and use thereof in defining a topological constraint for use in selecting an engineered polypeptide. **FIG. 3B** provides a schematic detailing the *in silico* screen step, demonstrating how mismatched candidates are discarded while candidates that match the topology are retained. **FIG. 3C** presents the top 12 selected engineered polypeptide candidates identified.

[0020] **FIGS. 4A-4B** provide a second set of schematics demonstrating the selection of a different group of engineered polypeptides based on a different set of reference parameters, using the methods described herein. **FIG. 4A** shows extraction of spatially-associated topological

information and construction of a topology matrix. **FIG. 4B** provides a list of top 8 engineered polypeptide candidates selected by *in silico* comparing candidates to the topological constraints.

[0021] **FIG. 5** is a schematic providing an overview of the design of an exemplary programmable *in vitro* selection using engineered polypeptides as described herein, and also using native proteins as positive (T) or negative (X) selection molecules.

[0022] **FIG. 6** shows a diagram of eight epitopes on CD25 outside the IL-2 interface targeted for generation of the engineered polypeptides of the disclosure.

[0023] **FIG. 7** shows 16 engineered polypeptides designed to mimic eight epitopes outside the IL-2 interface on CD25. In each diagram the CD25 target epitope residues are shown in gold. Scaffold residues designed to support these epitope residues are shown in gray.

[0024] **FIG. 8** shows diagrams of computationally determined deviation of the engineered polypeptide from target epitope. The engineered polypeptides show similarity in structure and dynamics to the target epitope (46% to 96% RMSIP).

[0025] **FIG. 9** show ELISA analysis for 384 anti-CD25 scFv clones per *in vitro* selection strategy. Eight CD25 epitopes were targeted with 32 programmed selection strategies. The figures show the ELISA analysis of individual scFv's from each selection strategy. Each scFv was tested by ELISA against full-length CD25. Selection strategies S1-S32 are ordered by epitope number 1-8, corresponding to the epitope shown in **FIG. 6**.

[0026] **FIG. 10** shows that MEM-programmed selection schemes enrich distinct high affinity clonal subsets. Histograms for two different selection strategies (Scheme A and Scheme B) for each of three MEM polypeptides are shown. The schemes in the right panel resulted in higher numbers of high-affinity clones. Panning with full-length CD25 results in comparatively few high-affinity clones.

[0027] **FIG. 11** shows data from biolayer interferometry for 1433 anti-CD25 scFv's identified by phage display panning. The y-axis plots k_{off} (1/s) for each clone. Median observed k_{on} was 1.35×10^5 (1/Ms). K_D estimates assume k_{on} of 4.5×10^4 (1/Ms). 1433 out of 1475 tested

screening hits (97%) are confirmed to bind CD25. The plot depicts the off-rate distribution for the 1433 confirmed hits.

[0028] **FIG. 12** shows data from biolayer interferometry for anti-CD25 scFv's identified by phage display panning. Hits are identified by panning strategy used. Data is shown for only those hits with k_{off} of less than $10^{-3}/s$.

[0029] **FIG. 13** shows data from flow cytometry for anti-CD25 scFv's identified by phage display panning. The CD25 specificity the different scFv antibodies were evaluated on flow cytometer using cells that express CD25 [CD25(+)] or do not express CD25 [CD25(-)].

[0030] **FIG. 14A-14B** show data from flow cytometry for anti-CD25 scFv's identified by phage display panning. Hits are identified by panning strategy used. **FIG. 14A** shows bind to CD25(+) cells. **FIG. 14B** shows binding to control CD25(-) cells.

[0031] **FIG. 15** show amino acid residue enrichment at each CDR H3 position in a representative enrichment strategy (S12).

[0032] **FIG. 16** shows a graph of sequence diversity during each round of MEM- or CD25-steered *in vitro* selection.

[0033] **FIG. 17** shows a graph of CDR length during each round of MEM- or CD25-steered *in vitro* selection.

[0034] **FIG. 18** shows ribbon diagrams of CD25 indicated the approximate binding sites for IL-2 and three antibodies (daclizumab, Tusk 7G7B6, and basiliximab) used in epitope resolution with a four-target competitive binding assay.

[0035] **FIG. 19** shows that full-length CD25 panning clones are dominated by IL-2 interface epitope. Most clones are blocked by IL-2, daclizumab, and basiliximab, but not 7G7B6.

[0036] **FIG. 20** shows that 147-157 epitope MEM-steered clones primarily bind at the intended epitope. Most clones are blocked by daclizumab but not by IL-2, basiliximab, or 7G7B6.

[0037] **FIG. 21** shows that 6-17 epitope MEM-steered clones primarily bind at the intended epitope. Most clones are blocked by 7G7B6 but not by IL-2, daclizumab, or basiliximab.

[0038] **FIG. 22** shows that 13-20:127-132 epitope MEM-steered clones primarily bind at the intended epitope. Most clones are blocked by 7G7B6 but not by IL-2, daclizumab, or basiliximab.

[0039] **FIG. 23** shows that 44-56 epitope MEM-steered clones primarily bind at the intended epitope. The clones divided into two profiles. In profile 1, clones are blocked by 7G7B6 but not by IL-2, daclizumab, or basiliximab. In profile 2, clones are blocked by IL-2, daclizumab, and basiliximab, but not 7G7B6. These blocking profiles indicate binding to the intended epitope from different approach angles.

[0040] **FIG. 24** shows that 55-63 epitope MEM-steered clones primarily bind at the intended epitope. The clones divided into three profiles. In profile 1, clones are blocked by 7G7B6 but not by IL-2, daclizumab, or basiliximab. In profile 2, clones are blocked by IL-2, daclizumab, and basiliximab, but not 7G7B6. These blocking profiles indicate binding to the intended epitope from different approach angles. In profile 3, clones are blocked by IL-2 and 7G7B6, but not daclizumab or basiliximab. These blocking profiles indicate binding to the intended epitope from different approach angles.

[0041] **FIG. 25** shows alanine mutations designed to confirm or reject that MEM-steered clones bin the intended epitopes. The eight epitopes are indicated in color. Sites of residues mutated to alanine are shown by red sticks.

[0042] **FIG. 26** shows alanine mutations in the 147-157 CD25 epitope do not impact global or local stability. For each mutant and wild-type: RMSD from 3 independent 100 ns MD simulations in explicit solvent for each of 8 different starting apo-CD25 configurations using the crystal structure as the reference.

[0043] **FIG. 27** shows reliability of Ala-mutant epitope mapping demonstrated with basiliximab control antibody. Ala mutant binding responses corroborate crystal structure of the

basiliximab epitope. The basiliximab–CD25 epitope known from X-ray crystal structures is shown in orange.

[0044] **FIG. 28** shows reliability of Ala-mutant epitope mapping demonstrated with daclizumab control antibody. Ala mutant binding responses corroborate crystal structure of the daclizumab epitope. The daclizumab–CD25 epitope known from X-ray crystal structures is shown in orange. Inset at bottom left shows an epitope zoom, showing T175A impact on daclizumab binding.

[0045] **FIG. 29** shows reliability of Ala-mutant epitope mapping demonstrated with 7G7B6 control antibody. Ala mutant binding responses corroborate peptide mapping of the 7G7B6 epitope.

[0046] **FIG. 30** shows epitope mapping of MEM-programmed selection hits for the 147-157 epitope. Most hits show ala mutation sensitivity in the intended epitope.

[0047] **FIG. 31** shows sensitivity to alanine substitution of various MEM-steered antibodies hits. Functional epitope diversity is observed. MEM-steered hits have distinct in-epitope alanine substitution position sensitivity.

[0048] **FIG. 32** presents a model of CD25 (ribbon) binding with IL-2 ligand (space-filling), IL-2R-gamma, and IL-2R-beta. The left and right arrows indicate selected sections of CD25 that were used to develop engineered immunogens that mimic CD25.

[0049] **FIG. 33A** is an exemplary graph of molecule stability vs. root mean square deviation (RMSD) evaluation at physiological pH for an engineered immunogen developed using as an initial input the section of CD25 indicated with the left arrow in **FIG. 32**.

[0050] **FIG. 33B** is an exemplary graph of molecule stability vs. root mean square deviation (RMSD) evaluation at physiological pH for an engineered immunogen developed using as an initial input the section of CD25 indicated with the right arrow in **FIG. 32**.

[0051] **FIG. 33C** is an exemplary graph of molecule stability vs. root mean square deviation (RMSD) evaluation at tumor microenvironment pH (lower pH) for the engineered immunogen in

FIG. 2B (developed using as an initial input the section of CD25 indicated with the right arrow in FIG. 32).

[0052] FIG. 34A is a model of IL-2 binding with the IL-2R complex, showing the CD25 section (ribbon), IL-2 (1), IL-2R-gamma (2), and IL-2R-beta (3).

[0053] FIG. 34B is another view of IL-2 binding with the IL-2R complex, listing areas of CD25 that were used as inputs to develop different selected exemplary engineered immunogens.

[0054] FIG. 34C is another view of IL-2 binding with the IL-2R complex listing areas of CD25 that were used as inputs to develop different selected exemplary engineered immunogens.

DETAILED DESCRIPTION

[0055] Provided herein are engineered polypeptides that share structural and/or dynamic identity with a portion of reference CD25 target. Epitopes of interest include but are not limited to the eight epitopes shown in FIG. 6. In some embodiments, the selected epitope is non-overlapping with the binding site (epitope) for IL-2, daclizumab, and/or basiliximab. In some embodiments, the epitope overlaps the epitope for 7G7B6. In some embodiments, the selected epitope is selected from 55-63, 12-20:127-132 (a discontinuous epitope), 5-17, 5-11:156-163 (a discontinuous epitope), 77-89, 147-157, 11-14, or 44-56. In some embodiments, the engineered polypeptides are conformationally stable and represent CD25 epitopes that are involved in interactions with antibodies that bind specifically to CD25. In some embodiments, the engineered polypeptides represent a surface portion of CD25 that is not known to interact with antibodies that bind specifically to CD25. Such engineered polypeptides may be used, for example, to select and/or produce antibodies that bind specifically to CD25.

I. Engineered polypeptides.

[0056] In some embodiments, the engineered polypeptide provided herein shares at least 46% structural and/or dynamic identity to a CD25 reference target, wherein the CD25 reference target is a portion of CD25 selected from those listed in the table below. As generally provided herein, the % structural/dynamic identity is the root mean square inner product (RMSIP) identity

(as provided herein above) X 100%. In some embodiments, the structural identity refers to sequence identity.

Reference Target No.	CD25 Residues	Sequence
1	55-63	SWDNQCQCT
2	13-20:127-132	ATFKAMA:MVYYQC
3	5-17	DDPPEIPHATFKA
4	5-11:156-163	DDPPEIP:RWTQPQLI
5	77-89	QP EEQKERKTTEM
6	147-157	VCKMTHGKTRW
7	11-14	IPHA
8	44-56	YMLCTGSSSHSSW

[0057] In some embodiments, the engineered polypeptide provided herein 80% sequence identity to an amino-acid sequence selected from:

CD <u>C</u> <u>Q</u> A <u>Q</u> WT PGMRAPGYDPYCLNC
MVY <u>C</u> <u>Q</u> PDCT <u>A</u> K <u>C</u> MHGCDRDTMKECCDRLK
DD <u>C</u> <u>P</u> <u>E</u> V <u>P</u> HAT <u>F</u> KGPGQKWEGPGGGDCSK
DDC <u>I</u> <u>E</u> V <u>P</u> GPAECAERACRAQEE <u>R</u> Q <u>R</u> <u>Q</u> <u>P</u> <u>Q</u> <u>C</u> <u>I</u>
AE <u>E</u> E <u>K</u> I <u>K</u> IE <u>Q</u> KER <u>K</u> TTIKLAKEAK
CHLQIM <u>THGK</u> IIYVPC
DDGDRCAKEH <u>E</u> IP <u>H</u> ATGEECQKRDKS

CKQLVIYF <u>TGNSS</u> HSSVFYIYYDC
GSGDEDCKKFQSD <u>DNW</u> <u>ENY</u> TSTR <u>HL</u> <u>TF</u> CDEKRS
GSGNEEIEKKIKDC <u>TGNSSHSSW</u> EAEALCKK
GSGDERIERLIKEC <u>TGNSSHSSW</u> EAEALCALRR
GSGSHPCAYWRWVI <u>KMTHGKTRW</u> VLELVFCYRD
GSGKCEEEAKKIAS <u>KMTHGKTR</u> EEEAEEYLKKC
GSGDDESEKRTTERDTRKCTKAKAN <u>DNQCQP</u> <u>TE</u>
GSGSSEWDKWVEEWYKKMCTEAKKN <u>DNQCQP</u> <u>TK</u>
GSGQCRVWVFRNGDKILYIYEDCDN <u>DNQHQQ</u> <u>TL</u>

[0058] In some embodiments, the polypeptide shares at least 60%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, or at least 95% structural and/or dynamic identity to the CD25 reference target. In some embodiments, polypeptide shares at least 60%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, or at least 95% sequence identity to the CD25 reference target.

[0059] In some embodiments, the engineered polypeptide is designed to mimic a selected CD25 epitope. For example, in some embodiments, the polypeptide comprises a meso-scale engineered molecule, *e.g.* a meso-scale engineered polypeptide. Provided herein are methods of selecting meso-scale engineered polypeptides, and compositions comprising and methods of using said engineered polypeptides. For example, provided herein are methods of using engineered polypeptides in *in vitro* selection of antibodies.

[0060] The engineered polypeptides of the present disclosure are between 1 kDa and 10 kDa, referred to herein as “meso-scale”. Engineered polypeptides of this size may, in some embodiments, have certain advantages, such as protein-like functionality, a large theoretical space from which to select candidates, cell permeability, and/or structural and dynamical variability. The terms meso-scale peptides and meso-scale polypeptides are used interchangeably herein, and the term meso-scale molecules (MEM) is intended to cover these.

[0061] The methods provided herein comprise identifying a plurality of spatially-associated topological constraints, some of which may be derived from a CD25 reference target, constructing a combination of said constraints, comparing candidate peptides with said combination, and selecting a candidate that has constraints which overlap with the combination. By using spatially-associated topological constraints, different aspects of an engineered polypeptide can be included in the combination depending on the intended use, or desired function, or another desired characteristic. Further, not all constraints must, in some embodiments, be derived from a CD25 reference target. Through such methods, in some embodiments the selected engineered polypeptides are not simply variations of a CD25 reference target (such as might be obtained through peptide mutagenesis or progressive modification of a single reference), but rather may have a different overall structure than the reference peptide, while still retaining desired functional characteristics and/or key substructures.

[0062] Further provided herein are methods of using said engineered polypeptides, which include methods of programmable *in vitro* selection using one or more engineered polypeptides. Such selection may be used, for example, in the identification of antibodies.

[0063] These methods and engineered polypeptides are described in greater detail below.

II. Methods of Selecting Engineered polypeptides

[0064] In some aspects, provided herein are methods of selecting an engineered polypeptide, comprising:

identifying one or more topological characteristics of a CD25 reference target;

designing spatially-associated constraints for each topological characteristic to produce a combination of CD25 reference target-derived constraints;

comparing spatially-associated topological characteristics of candidate peptides with the combination derived from the CD25 reference target; and

selecting a candidate peptide with spatially-associated topological characteristics that overlap with the combination of constraints derived from the CD25 reference target.

[0065] In some embodiments, one or more additional spatially-associated topological constraints that are not derived from the CD25 reference target are included in the combination.

a. Spatially-associated Topological Constraints

[0066] The engineered polypeptides described herein are selected based on how closely they match a combination of spatially-associated topological constraints. This combination may also be described using the mathematical concept of a “tensor”. In such a combination (or tensor), each constraint is independently described in three dimensional space (e.g., spatially-associated), and the combination of these constraints in three dimensional space provides, for example, a representational “map” of different desired characteristics and their desired level (if applicable) relative to location. This map is not, in some embodiments, based on a linear or otherwise pre-determined amino acid backbone, and therefore can allow for flexibility in the structures that could fulfill the desired combination, as described. For example, in some embodiments, the “map” includes a spatial area wherein the prescribed constraint limitations could be adequately met by two adjacent amino acids – in some embodiments, these amino acids could be directly bonded (e.g., two contiguous amino acids) while in other embodiments, the amino acids are not directly bonded to each other but could be brought together in space by the folding of the peptide (e.g., are not contiguous amino acids). The separate constraints themselves are also not necessarily based on structure, but could include, for example, chemical descriptors and/or functional descriptors. In some embodiments, constraints include structural descriptors, such as a desired secondary structure or amino acid residue. In certain embodiments, each constraint is independently selected.

[0067] For example, **FIG. 1** is a schematic demonstrating the construction of a representative combination of spatially-associated topological constraints. The three constraints in **FIG. 1** are sequence, nearest neighbor distance, and atomic motion, with nearest neighbor distance and atomic motion combined into one graphic. As shown, some constraints are mapped independent of the location of the backbone (e.g., atomic motion of certain side chains), therefore allowing for a much greater variety of structural configurations to be tried, compared to just varying one or more positions on a reference scaffold. The three different constraints and their spatial descriptions are combined into a matrix (e.g., tensor), and then a series of candidate peptides can be compared with this combination to identify new engineered polypeptides which meet the desired criteria. In some embodiments, one or more additional non-reference derived constraints is also included in the combination. Comparison of candidate peptides with a defined combination may be done, for example, using *in silico* methods to evaluate the constraints of each candidate peptide against the desired combination, and rate how well candidates match. Said candidates which have the desired level of overlap with the prescribed combination may then be synthesized using standard peptide synthetic methods known to one of skill in the art, and evaluated.

[0068] In some embodiments, the combination of constraints comprises at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, between 3 to 12, between 3 to 10, between 3 to 8, between 3 to 6, or 3, or 4, or 5, or 6 independently selected spatially-associated topological constraints. One or more of the constraints is derived from a CD25 reference target. In some embodiments, each of the constraints is derived from the CD25 reference target. In other embodiments, at least one constraint is derived from the CD25 reference target, and the remaining constraints are not derived from the reference target. For example, in some embodiments, between 1 and 9 constraints, between 1 and 7 constraints, between 1 and 5 constraints, or between 1 and 3 constraints are derived from the CD25 reference target, and between 1 and 9 constraints, between 1 and 7 constraints, between 1 and 5 constraints, or between 1 and 3 constraints are not derived from the CD25 reference target.

[0069] Once the combination of constraints has been constructed, a series of candidate peptides is compared to said combination to identify one or more new engineered polypeptides which meet the desired criteria. In some embodiments, at least 5, at least 10, at least 15, at least

20, at least 25, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80, at least 90, at least 100, at least 125, at least 150, at least 175, at least 200, or at least 250 or more candidate peptides are compared to the combination to identify one or more new engineered polypeptides which meet the desired criteria. In some embodiments, more than 250 candidate peptides, more than 300 candidate peptides, more than 400 candidate peptides, more than 500 candidate peptides, more than 600 candidate peptides, or more than 750 candidate peptides are compared, for example. In some embodiments, topological characteristic simulations are used to evaluate the topological characteristic overlap, if any, of a candidate peptide compared to the combination of constraints. In some embodiments, one or more candidate peptides are also compared to the CD25 reference target, and overlap, if any, of candidate peptide topological characteristics with CD25 reference target topological characteristics is evaluated. In some embodiments, the engineered polypeptide is identified from a computational sample of more than 5, more than 10, more than 20, more than 30, more than 40, more than 50, more than 60, more than 70, more than 80, more than 90, or more than 100 distinct peptide and topological characteristic simulations and an engineered polypeptide is selected, wherein the selected engineered polypeptide has the highest topological characteristic overlap compared the CD25 reference target, out of the total sampled population.

[0070] The spatially-associated topological constraints used to construct the desired combination (e.g., the desired tensor) may each be independently selected from a wide group of possible characteristics. These may include, for example, constraints describing structural, dynamical, chemical, or functional characteristics, or any combinations thereof.

[0071] Structural constraints may include, for example, atomic distance, amino acid sequence similarity, solvent exposure, phi angle, psi angle, secondary structure, or amino acid contact, or any combinations thereof.

[0072] Dynamical constraints may include, for example, atomic fluctuation, atomic energy, van der Waals radii, amino acid adjacency, or non-covalent bonding propensity. Atomic energy may include, for example, pairwise attractive energy between two atoms, pairwise repulsive energy between two atoms, atom-level solvation energy, pairwise charged attraction energy

between two atoms, pairwise hydrogen bonding attraction energy between two atoms, or non-covalent bonding energy, or any combinations thereof.

[0073] Chemical characteristics may include, for example, chemical descriptors. Such chemical descriptors may include, for example, hydrophobicity, polarity, atomic volume, atomic radius, net charge, logP, HPLC retention, van der Waals radii, charge patterns, or H-bonding patterns, or any combinations thereof.

[0074] Functional characteristics may include, for example, bioinformatic descriptors, biological responses, or biological functions. Bioinformatic descriptors may include, for example, BLOSUM similarity, pKa, zScale, Cruciani Properties, Kidera Factors, VHSE-scale, ProtFP, MS-WHIM scores, T-scale, ST-scale, Transmembrane tendency, protein buried area, helix propensity, sheet propensity, coil propensity, turn propensity, immunogenic propensity, antibody epitope occurrence, and/or protein interface occurrence, or any combinations thereof.

[0075] In some embodiments, designing the constraints incorporates information about per-residue energy, per-residue interaction, per-residue fluctuation, per-residue atomic distance, per-residue chemical descriptor, per-residue solvent exposure, per-residue amino acid sequence similarity, per-residue bioinformatic descriptor, per-residue non-covalent bonding propensity, per-residue phi/psi angles, per-residue van der Waals radii, per-residue secondary structure propensity, per-residue amino acid adjacency, or per-residue amino acid contact. In some embodiments, these characteristics are used for a subset of the total residues in the CD25 reference target, or a subset of the total residues of the total combination of constraints, or a combination thereof. In some embodiments, one or more different characteristics are used for one or more different residues. That is, in some embodiments, one or more characteristics are used for a subset of residues, and at least one different characteristic is used for a different subset of residues. In some embodiments, one or more of said characteristics used to design one or more constraints is determined by computer simulation. Suitable computer simulation methods may include, for example, molecular dynamics simulations, Monte Carlo simulations, coarse-grained simulations, Gaussian network models, machine learning, or any combinations thereof.

[0076] In some embodiments multiple constraints are selected from one category. For example, in some embodiments, the combination comprises two or more constraints that are independently a type of biological response. In some embodiments, two or more constraints are independently a type of secondary structure. In certain embodiments, two or more constraints are independently a type of chemical descriptor. In other embodiments, the combination comprises no overlapping categories of constraints.

[0077] In some embodiments, one or more constraints is independently associated with a biological response or biological function. In some embodiments, said constraint is a spatially defined atom(s)-level constraint, or spatially defined shape/area/volume-level constraint (such as a characteristic shape/area/volume that can be satisfied by several different atomic compositions), or a spatially defined dynamic-level constraint (such as a characteristic dynamic or set of dynamics that can be satisfied by several different atomic compositions).

[0078] In some embodiments, one or more constraints is derived from a protein structure or peptide structure associated with a biological function or biological response. For example, in some embodiments, one or more constraints is derived from an extracellular domain, such as a G protein-coupled receptor (GPCR) extracellular domain, or an ion channel extracellular domain. In some embodiments, one or more constraints is derived from a protein-protein interface junction. In some embodiments, one or more constraints is derived from a protein-peptide interface junction, such as MHC-peptide or GPCR-peptide interfaces. In certain embodiments, the atoms or amino acids constrained to such a protein or peptide structure are atoms or amino acids associated with a biological function or biological response. In some embodiments, the atoms or amino acids in the engineered polypeptide constrained to such a protein or peptide structure are atoms or amino acids derived from a CD25 reference target. In some embodiments, one or more constraints is derived from a polymorphic region of a CD25 reference target (e.g., a region subject to allelic variation between individuals).

[0079] In some embodiments, the one or more atoms associated with a biological function or biological response are selected from the group consisting of carbon, oxygen, nitrogen, hydrogen, sulfur, phosphorus, sodium, potassium, zinc, manganese, magnesium, copper, iron,

molybdenum, and nickel. In certain embodiments, the atoms are selected from the group consisting of oxygen, nitrogen, sulfur, and hydrogen.

[0080] In some embodiments, wherein one of the constraints is one or more amino acids associated with a biological function or biological response, and/or the engineered polypeptide comprises one or more amino acids associated with a biological function or biological response, the one or more amino acids are independently selected from the group consisting of the 20 proteinogenic naturally occurring amino acids, non-proteinogenic naturally occurring amino acids, and non-natural amino acids. In some embodiments, the non-natural amino acids are chemically synthesized. In certain embodiments, the one or more amino acids are selected from the 20 proteinogenic naturally occurring amino acids. In other embodiments, the one or more amino acids are selected from the non-proteinogenic naturally occurring amino acids. In still further embodiments, the one or more amino acids are selected from non-natural amino acids. In still further embodiments, the one or more amino acids are selected from a combination of 20 proteinogenic naturally occurring amino acids, non-proteinogenic naturally occurring amino acids, and non-natural amino acids.

[0081] While the combination of constraints used to select an engineered polypeptide as described herein comprises at least one constraint derived from a CD25 reference target, in some embodiments one or more constraints of the combination are not derived from a CD25 reference target. Thus, in certain embodiments, the selected engineered polypeptide comprises one or more characteristics that are not shared with the CD25 reference target.

[0082] In some embodiments, one or more constraints derived from the CD25 reference target and used in the combination describes the inverse of the characteristic as observed in the CD25 reference target. Thus, for example, a CD25 reference target may have a certain pattern of positive charge, a constraint related to charge is derived from said CD25 reference target, and the derived constraint describes a similar pattern but of neutral charge, or of negative charge. Thus, in some embodiments one or more inverse constraints are derived from the CD25 reference target and included in the combination. Such inverse constraints may be useful, for example, in selecting engineered polypeptides as control molecules for certain assays or panning methods, or as negative selection molecules in the programmable *in vitro* selection methods described herein.

[0083] In some embodiments, the combination of spatially-defined topological constraints comprises one or more non-reference derived topological constraints. In some embodiments, the one or more non-reference derived topological constraints enforces or stabilizes one or more secondary structural elements, enforces atomic fluctuations, alters peptide total hydrophobicity, alters peptide solubility, alters peptide total charge, enables detection in a labeled or label-free assay, enables detection in an in vitro assay, enables detection in an in vivo assay, enables capture from a complex mixture, enables enzymatic processing, enables cell membrane permeability, enables binding to a secondary target, or alters immunogenicity. In certain embodiments, the one or more non-reference derived topological constraints constrains one or more atoms or amino acids in the combination of constraints (or subsequently selected peptide) that were derived from the CD25 reference target. For example, in some embodiments, the combination of constraints includes a secondary structure that was derived from the CD25 reference target, and the combination of constraints also comprises a constraint that stabilizes the secondary structural element (e.g., through additional hydrogen bonding, or hydrophobic interactions, or side chain stacking, or a salt bridge, or a disulfide bond), wherein the stabilizing constraint is not present in the CD25 reference target. In another example, in some embodiments the combination of constraints (or subsequently selected peptide) comprises one or more atoms or amino acids that was derived from the CD25 reference target, and the combination of constraints also includes a constraint that enforces atomic fluctuations in at least a portion of the atoms or amino acids derived from the target reference, wherein the constraint is not present in the target reference. In some embodiments, one or more non-reference derived constraints is an inverse constraint. For example, in some embodiments, two combinations of constraints are constructed to select engineered polypeptides with inverse characteristics. In some such embodiments, a first combination of constraints will comprise one or more constraints derived from the CD25 reference target, and one or more constraints not derived from the CD25 reference target; and a second combination of constraints will comprise the same one or more constraints derived from the CD25 reference target, and the inverse of one or more of non-CD25 reference target constraints of the first combination.

b. CD25 reference target

[0084] Any suitable CD25 reference target may be used to derive one or more spatially-associated topological constraints for use in the methods provided herein. In some embodiments, the CD25 reference target is a full-length native protein. In other embodiments, the CD25 reference target is a portion of a full-length native protein. In still further embodiments, the CD25 reference target is a non-native protein, or portion thereof.

[0085] In some embodiments, a CD25 reference target is selected from:

Reference Target No.	CD25 Residues	Sequence
1	55-63	SWDNQCQCT
2	13-20:127-132	ATFKAMA:MVYYQC
3	5-17	DDPPEIPHATFKA
4	5-11:156-163	DDPPEIP:RWTQPQLI
5	77-89	QPEEQKERKTTEM
6	147-157	VCKMTHGKTRW
7	11-14	IPHA
8	44-56	YMLCTGSSSHSSW

[0086] For example, in some embodiments, the CD25 reference target is a portion of CD25, such as an epitope or a predicted epitope. In some embodiments, the methods provided herein may be used to select one or more engineered polypeptides that are immunogens, and which may be used to raise one or more antibodies that specifically bind to the protein from which the target reference is derived. In still further embodiments, the methods provided herein may be used to select one or more engineered polypeptides which in turn may be used to select one or more

binding partners of a protein of interest, such as an antibody, a Fab-displaying phage, or an scFv-displaying phage.

c. Comparison of Constraints

[0087] In some embodiments, the one or more constraints (e.g., reference-derived or non-reference derived) are determined by molecular simulation (e.g. molecular dynamics), or laboratory measurement (e.g. NMR), or a combination thereof. Once the constraints have been derived and combined, engineered polypeptide candidates are, in some embodiments, generated using a computational protein design (e.g., Rosetta). In some embodiments, other methods of sampling peptide space are used. Dynamics simulations may then be carried out on the candidate engineered polypeptides to obtain the parameters of constraints that have been selected. A covariance matrix of atomic fluctuations is generated for the CD25 reference target, covariance matrices are generated for the residues in each of the candidate engineered polypeptides, and these covariance matrices are compared to determine overlap. Principal component analysis is performed to compute the eigenvectors and eigenvalues for each covariance matrix - one covariance matrix for the CD25 reference target and one covariance for each of the candidate engineered polypeptides - and those eigenvectors with the largest eigenvalues are retained.

[0088] The eigenvectors describe the most, second-most, third-most, N-most dominant motion observed in a set of simulated molecular structures. Without wishing to be bound by any theory, if a candidate engineered polypeptide moves like the CD25 reference target, its eigenvectors will be similar to the eigenvectors of the CD25 reference target. The similarity of eigenvectors corresponds to their components (a 3D vector centered on each CA atom) being aligned, pointing in the same direction.

[0089] In some embodiments, this similarity between candidate engineered polypeptide and CD25 reference target eigenvectors is computed using the inner product of two eigenvectors. The inner product value is 0 if two eigenvectors are 90 degrees to each other or 1 if the two eigenvectors point precisely in the same direction. Without wishing to be bound by theory, since the ordering of eigenvectors is based on their eigenvalues, and eigenvalues may not necessarily be the same between two different molecules due to the stochastic nature by which molecular dynamics (MD) simulations sample the underlying energy landscape of those different

molecules, the inner product between multiple, differentially ranked eigenvectors is, in some embodiments, needed (e.g. eigenvector 1 of the engineered polypeptide by eigenvector 2, 3, 4, etc. of the CD25 reference target). In addition, molecular motions are complex and may involve more than one (or more than a few) dominant/principal modes of motion. Thus, in some embodiments, the inner product between all pairs of eigenvectors in a candidate engineered polypeptide and the CD25 reference target are computed. This results in a matrix of inner products the dimensions of which are determined by the number of eigenvectors analyzed. For example, for 10 eigenvectors, the matrix of inner products is 10 by 10. This matrix of inner products can be distilled into a single value by computing the root mean-square value of the 100 (if 10 by 10) inner products. This is the root mean square inner product (RMSIP). From this comparison, one or more candidate engineered polypeptides that have similarity with the defined combination of constraints are selected.

d. Additional Steps

[0090] In some embodiments, selection of one or more engineered polypeptides comprises one or more additional steps. For example, in some embodiments an engineered polypeptide candidate is selected based on similarity to the defined combination of spatially-associated topological constraints, as described herein, and then undergoes one or more analyses to determine one or more additional characteristics, and one or more structural adjustments to impart or enforce said desired characteristics. For example, in some embodiments, the selected candidate is analyzed, such as through molecule dynamics simulations, to determine overall stability of the molecule and/or propensity for a particular folded structure. In some embodiments, one or more modifications are made to the engineered polypeptide to impart or reinforce a desired level of stability, or a desired propensity for a desired folded structure. Such modifications may include, for example, the installation of one or more cross-links (such as a disulfide bond), salt bridges, hydrogen bonding interactions, or hydrophobic interactions, or any combinations thereof.

[0091] The methods provided herein may further comprise assaying one or more selected engineered polypeptides for one or more desired characteristics, such as desired binding

interactions or activity. Any suitable assay may be used, as appropriate to measure the desired characteristic.

[0092] In other aspects, provided herein are engineered polypeptides, such as engineered polypeptides selected through the methods described herein. In some embodiments, the engineered polypeptide has a molecular mass between 1 kDa and 10 kDa, and comprises up to 50 amino acids. In certain embodiments, the engineered polypeptide has a molecular mass between 2 kDa and 10 kDa, between 2 kDa and 10 kDa, between 3 kDa and 10 kDa, between 4 kDa and 10 kDa, between 5 kDa and 10 kDa, between 6 kDa and 10 kDa, between 7 kDa and 10 kDa, between 8 kDa and 10 kDa, between 9 kDa and 10 kDa, between 1 kDa and 9 kDa, between 1 kDa and 8 kDa, between 1 kDa and 7 kDa, between 1 kDa and 6 kDa, between 1 kDa and 5 kDa, between 1 kDa and 4 kDa, between 1 kDa and 3 kDa, or between 1 kDa and 2 kDa. In certain embodiments, the engineered polypeptide comprises up to 45 amino acids, up to 40 amino acids, up to 35 amino acids, up to 30 amino acids, up to 25 amino acids, up to 20 amino acids, at least 5 amino acids, at least 10 amino acids, at least 15 amino acids, at least 20 amino acids, at least 25 amino acids, at least 30 amino acids, at least 35 amino acids, or at least 40 amino acids.

[0093] In certain embodiments, the engineered polypeptide comprises a combination of spatially-associated topological constraints, wherein one or more of the constraints is a CD25 reference target-derived constraint. Any constraints described herein may be used in the combination, in some embodiments. In still further embodiments, between 10% to 98% of the amino acids of the engineered polypeptide meet the one or more CD25 reference target-derived constraints (e.g., if the engineered polypeptide comprises 50 amino acids, between 5 to 49 amino acids meet the one or more CD25 reference target-derived constraints). In some embodiments, between 20% to 98%, between 30% to 98%, between 40% to 98%, between 50% to 98%, between 60% to 98%, between 70% to 98%, between 80% to 98%, between 90% to 98%, between 10% to 90%, between 10% to 80%, between 10% to 70%, between 10% to 60%, between 10% to 50%, between 10% to 40%, between 10% to 30%, or between 10% to 20% of the amino acids of the engineered polypeptide meet the one or more CD25 reference target-derived constraints. In still further embodiments, the one or more amino acids that meet the one or more CD25 reference target-derived constraints have less than 8.0 Å, less than 7.5 Å, less than

7.0 Å, less than 6.5 Å, less than 6.0 Å, less than 5.5 Å, or less than 5.0 Å backbone root-mean-square deviation (RMSD) structural homology with the CD25 reference target. In some embodiments, the engineered polypeptide has a molecular mass of between 1 kDa and 10 kDa; comprises up to 50 amino acids; a combination of spatially-associated topological constraints, wherein one or more of the constraints is a CD25 reference target-derived constraint; between 10% to 98% of the amino acids of the engineered polypeptide meet the one or more CD25 reference target-derived constraints; and the amino acids that meet the one or more CD25 reference target-derived constraints have less than 8.0 Å backbone root-mean-square deviation (RMSD) structural homology with the CD25 reference target.

[0094] In some embodiments, the amino acids of the engineered polypeptide that meet the one or more CD25 reference target-derived constraints have between 10% and 90% sequence homology, between 20% and 90% sequence homology, between 30% and 90% sequence homology, between 40% and 90% sequence homology, between 50% and 90% sequence homology, between 60% and 90% sequence homology, between 70% and 90% sequence homology, or between 80% and 90% sequence homology with the CD25 reference target. In some embodiments, the amino acids that meet the one or more CD25 reference target-derived constraints have a van der Waals surface area overlap with the reference of between 30 Å² to 3000 Å², or between 100 Å² to 3000 Å², or between 250 Å² to 3000 Å², or between 500 Å² to 3000 Å², or between 750 Å² to 3000 Å², or between 1000 Å² to 3000 Å², or between 1250 Å² to 3000 Å², or between 1500 Å² to 3000 Å², or between 1750 Å² to 3000 Å², or between 2000 Å² to 3000 Å², or between 2250 Å² to 3000 Å², or between 2500 Å² to 3000 Å², or between 2750 Å² to 3000 Å².

[0095] The combination of constraints that the engineered polypeptide meets may comprise two or more, three or more, four or more, five or more, six or more, or seven or more CD25 reference target-derived constraints. The combination may comprise one or more constraints not derived from the CD25 reference target, as described elsewhere in the present disclosure. These reference-derived constraints, and non-reference derived constraints if present, may independently be any of the constraints described herein, such as any of the structural, dynamical, chemical, or functional characteristics described herein, or any combinations thereof.

[0096] In some embodiments, the engineered polypeptide comprises at least one structural difference when compared to the CD25 reference target. Such structural differences may include, for example, a difference in the sequence, number of amino acid residues, total number of atoms, total hydrophilicity, total hydrophobicity, total positive charge, total negative charge, one or more secondary structures, shape factor, Zernike descriptors, van der Waals surface, structure graph nodes and edges, volumetric surface, electrostatic potential surface, hydrophobic potential surface, local diameter, local surface features, skeleton model, charge density, hydrophilic density, surface to volume ratio, amphiphilicity density, or surface roughness, or any combinations thereof. In some embodiments, the difference in one or more characteristics (such as one or more characteristics described herein) is at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, at least 100%, or greater than 100% when compared to the characteristic in the CD25 reference target, as applicable to the type of characteristic. For example, in some embodiments the difference is the total number of atoms, and the engineered polypeptide has at least 10%, at least 20%, or at least 30% more atoms than the CD25 reference target, or at least 10%, at least 20%, or at least 30% fewer atoms than the CD25 reference target. In some embodiments, the difference is in total positive charge, and the total positive charge of the engineered polypeptide is at least 10%, at least 20%, at least 30%, at least 40%, or at least 50% larger (e.g., more positive) than the CD25 reference target, while in other embodiments the total positive charge of the engineered polypeptide is at least 10%, at least 20%, at least 30%, at least 40%, or at least 50% smaller (e.g., less positive) than the CD25 reference target.

[0097] In some embodiments, the combination of spatially-defined topological constraints includes one or more secondary structural elements not present in the CD25 reference target. Thus, in some embodiments, the engineered polypeptide comprises one or more secondary structural elements that are not present in the CD25 reference target. In some embodiments, the combination and/or engineered polypeptide comprises one secondary structural element, two secondary structural elements, three secondary structural elements, four secondary structural elements, or more than four secondary structural elements not found in the CD25 reference target. In some embodiments, each secondary structural element is independently selected from the group consisting of helices, sheets, loops, turns, and coils. In some embodiments, each

secondary structural element not present in the CD25 reference target is independently an α -helix, β -bridge, β -strand, 3_{10} helix, π -helix, turn, loop, or coil.

[0098] In certain embodiments, the CD25 reference target comprises one or more atoms associated with a biological response or a biological function (such as one described herein); the engineered polypeptide comprises one or more atoms associated with a biological response or a biological function (such as one described herein); and the atomic fluctuations of said atoms in the engineered polypeptide overlap with the atomic fluctuations of said atoms in the CD25 reference target. Thus, for example, in some embodiments the atoms themselves are different atoms, but their atomic fluctuations overlap. In other embodiments, the atoms are the same atoms, and their atomic fluctuations overlap. In still further embodiments, the atoms are independently the same or different. In some embodiments, the overlap is a root mean square inner product (RMSIP) greater than 0.25. In some embodiments, the overlap is a RMSIP greater than 0.3, greater than 0.35, greater than 0.4, greater than 0.45, greater than 0.5, greater than 0.55, greater than 0.6, greater than 0.65, greater than 0.7, greater than 0.75, greater than 0.8, greater than 0.85, greater than 0.9, or greater than 0.95. In certain embodiments, the RMSIP is calculated by:

$$\text{RMSIP} = \left(\frac{1}{10} \sum_{i=1}^{10} \sum_{j=1}^{10} (\mathbf{u}_i \cdot \mathbf{v}_j)^2 \right)^{1/2},$$

where $\mathbf{u}$ is the eigenvector of the engineered polypeptide topological constraints, and $\mathbf{v}$ is the eigenvector of the CD25 reference target topological constraints.

[0099] In some embodiments, the engineered polypeptide comprises atoms or amino acids (or combination thereof) associated with a biological response or biological function, and at least a portion of said atoms or amino acids or combination is derived from a CD25 reference target, and certain constraints of the set of atoms or amino acids in the engineered polypeptide and the set in the CD25 reference target can be described by a matrix. In some embodiments, the matrix is an LxL matrix. In other embodiments, the matrix is an SxSxM matrix. In still further embodiments, the matrix is an Lx2 phi/psi angle matrix

[0100] For example in some embodiments, the atomic fluctuations of the atoms or amino acids in the engineered polypeptide that are associated with a biological response or biological function are described by an $L \times L$ matrix; a portion of said atoms or amino acids are derived from the CD25 reference target; and the atomic fluctuations in the CD25 reference target of said portion are described by an $L \times L$ matrix. In some embodiments, the adjacency of each set (related to amino acid location) is described by corresponding $L \times L$ matrices. In certain embodiments, the mean percentage error (MPE) across all matrix elements (i, j) of the engineered polypeptide $L \times L$ atomic fluctuation or adjacency matrix is less than or equal to 75% relative to the corresponding (i, j) elements in the CD25 reference target atomic fluctuation or adjacency matrix, for the fraction of the engineered polypeptide derived from the CD25 reference target. In some embodiments, the MPE is less than 70%, less than 65%, less than 60%, less than 55%, less than 50%, less than 45%, or less than 40% relative to the corresponding elements in the CD25 reference target matrix, for the fraction of the engineered polypeptide derived from the CD25 reference target. In some embodiments, wherein the matrices represent atomic fluctuations, L is the number of amino acid positions and the (i, j) value in the atomic fluctuation matrix element is the sum of intra-molecular atomic fluctuations for the i^{th} and j^{th} amino acid respectively if the (i, j) atomic distance is less than or equal to 7 Å, or zero if the (i, j) atomic distance is greater than 7 Å or if (i, j) is on the diagonal. Alternatively, in some embodiments the atomic distance can serve as a weighting factor for the atomic fluctuation matrix element (i, j) instead of a 0 or 1 multiplier. In certain embodiments, the i^{th} and j^{th} atomic fluctuations and distances can be determined by molecular simulation (e.g. molecular dynamics) and/or laboratory measurement (e.g. NMR). In other embodiments, wherein the matrices represent adjacency, L is the number of amino acid positions and the value in adjacency matrix element (i, j) is the intra-molecular atomic distance between the i^{th} and j^{th} amino acid respectively if the atomic distance is less than or equal to 7 Å, or zero if the atomic distance is greater than 7 Å or if (i, j) is on the diagonal. Alternatively, in some embodiments the atomic distance can serve as a weighting factor for the adjacency matrix element (i, j) instead of a 0 or 1 multiplier. In certain embodiments, the i^{th} and j^{th} atomic distances could be determined by molecular simulation (e.g. molecular dynamics) and/or laboratory measurement (e.g. NMR).

[0101] In certain embodiments, the atoms or amino acids associated with a response or function in the engineered polypeptide have a topological constraint chemical descriptor vector and a mean percentage error (MPE) less than 75% relative to the reference described by the same chemical descriptor, for the fraction of the engineered polypeptide derived from the CD25 reference target, wherein each i^{th} element in the chemical descriptor vector corresponds to an amino acid position index. In some embodiments, the MPE is less than 70%, less than 65%, less than 60%, less than 55%, less than 50%, less than 45%, or less than 40% relative to the reference described by the same chemical descriptor, for the fraction of the engineered polypeptide derived from the CD25 reference target.

[0102] In still further embodiments, the matrix is an $L \times 2$ phi/psi angle matrix, and the atoms or amino acids associated with a response or function in the engineered polypeptide have an MPE less than 75% with respect to the reference phi/psi angles matrix in the fraction of the engineered polypeptide derived from the reference target, wherein L is the number of amino acid positions and phi, psi values are in dimensions $(L,1)$ and $(L,2)$ respectively. In some embodiments, the MPE is less than 70%, less than 65%, less than 60%, less than 55%, less than 50%, less than 45%, or less than 40% with respect to the reference phi/psi angles matrix in the fraction of the engineered polypeptide derived from the reference target. In some embodiments, the phi/psi values are determined by molecular simulation (e.g. molecular dynamics), knowledge-based structure prediction, or laboratory measurement (e.g. NMR).

[0103] In some embodiments, the matrix is an $S \times S \times M$ secondary structural element interaction matrix, and the atoms or amino acids associated with a response or function in the engineered polypeptide have less than 75% mean percentage error (MPE) relative to the reference secondary structural element relationship matrix, in the fraction of the engineered polypeptide derived from the reference target, where S is the number of secondary structural elements and M is the number of interaction descriptors. In some embodiments, the MPE is less than 70%, less than 65%, less than 60%, less than 55%, less than 50%, less than 45%, or less than 40% relative to the reference secondary structural element relationship matrix, in the fraction of the engineered polypeptide derived from the reference target. Interaction descriptors may include, for example, hydrogen bonding, hydrophobic packing, van der Waals interaction, ionic interaction, covalent bridge, chirality, orientation, or distance, or any combinations thereof.

In the secondary structural element interaction matrix index, $(i, j, m) = m^{\text{th}}$ interaction descriptor value between the i^{th} and j^{th} secondary structural elements.

[0104] Mean Percentage Error (MPE) for different matrices as described herein may be calculated by:

$$\text{Mean Percentage Error (MPE)} = \frac{100\%}{n} \sum_n^f \frac{|\text{ref}_n - \text{eng}_n|}{\text{ref}_n},$$

where n is the topological constraint vector or matrix position index for the engineered polypeptide (eng_n) and the corresponding reference (ref_n), summed up to vector or matrix position n .

[0105] In some embodiments, the engineered polypeptide has an MPE of less than 75% compared to the CD25 reference target. In certain embodiments, the engineered polypeptide has an MPE of less than 70%, less than 65%, less than 60%, less than 55%, less than 50%, less than 45%, or less than 40% compared to the CD25 reference target. In some embodiments, the MPE is determined by Total Topological Constraint Distance (TCD), topological clustering coefficient (TCC), Euclidean distance, power distance, Soergel distance, Canberra distance, Sorensen distance, Jaccard distance, Mahalanobis distance, Hamming distance, Quantitative Estimate of Likeness (QEL), or Chain Topology Parameter (CTP).

e. Secondary Structural Element

[0106] In some embodiments, at least a portion of the engineered polypeptide is topologically constrained to one or more secondary structural elements. In some embodiments, the atoms or amino acids associated with a biological response or biological function in the engineered polypeptide are topologically constrained to one or more secondary structural elements. In some embodiments, the secondary structural element is independently a sheet, helix, turn, loop, or coil. In some embodiments, the secondary structural element is independently an α -helix, β -bridge, β -strand, 3_{10} helix, π -helix, turn, loop, or coil. In certain embodiments, one or more of the secondary structural elements to which at least a portion of the engineered polypeptide is topologically constrained is present in the CD25 reference target. In some

embodiments, at least a portion of the engineered polypeptide is topologically constrained to a combination of secondary structural elements, wherein each element is independently selected from the group consisting of sheet, helix, turn, loop, and coil. In still further embodiments, each element is independently selected from the group consisting of an α -helix, β -bridge, β -strand, 3_{10} helix, π -helix, turn, loop, and coil.

[0107] In some embodiments, the secondary structural element is a parallel or anti-parallel sheet. In some embodiments, a sheet secondary structure comprises greater than or equal to 2 residues. In some embodiments, a sheet secondary structure comprises less than or equal to 50 residues. In still further embodiments, a sheet secondary structure comprises between 2 and 50 residues. Sheets can be parallel or anti-parallel. In some embodiments, a parallel sheet secondary structure may be described as having two strands i, j in a parallel (N-termini of i and j strands opposing orientation), and a pattern of hydrogen bonding of residues $i:j$. In some embodiments, an anti-parallel sheet secondary structure may also be described as having two strands i, j in an anti-parallel (N-termini of i and j strands same orientation), and a pattern of hydrogen bonding of residues $i:j-1, i:j+1$. In certain embodiments, the orientation and hydrogen bonding of strands can be determined by knowledge-based or molecular dynamics simulation and/or laboratory measurement.

[0108] In some embodiments, the secondary structural element is a helix. Helices may be right or left handed. In some embodiments, the helix has a residue per turn (residues/turn) value of between 2.5 and 6.0, and a pitch between 3.0 Å and 9.0 Å. In some embodiments, the residues/turn and pitch are determined by knowledge-based or molecular dynamics simulation and/or laboratory measurement.

[0109] In some embodiments, the secondary structural element is a turn. In some embodiments, a turn comprises between 2 to 7 residues, and 1 or more inter-residue hydrogen bonds. In some embodiments, the turn comprises 2, 3, or 4 inter-residue hydrogen bonds. In certain embodiments, the turn is determined by knowledge-based or molecular dynamics simulation and/or laboratory measurement.

[0110] In still further embodiments, the secondary structural element is a coil. In certain embodiments, the coil comprises between 2 to 20 residues and zero predicted inter-residue hydrogen bonds. In some embodiments, these coil parameters are determined by knowledge-based or molecular dynamics simulation and/or laboratory measurement.

[0111] In still further embodiments, the engineered polypeptide comprises one or more atoms or amino acids derived from the CD25 reference target, wherein said atoms or amino acids have a secondary structure. In some embodiments, these atoms or amino acids are associated with a biological response or biological function. In some embodiments, the secondary structure motif vector of the atoms or amino acids in the engineered polypeptide has a cosine similarity greater than 0.25 relative to the CD25 reference target secondary structure motif vector for the fraction of the engineered polypeptide derived from the CD25 reference target, wherein the length of the vector is the number of secondary structure motifs and the value at the i^{th} vector position defines the identity of the secondary structure motif (e.g. helix, sheet) derived from a lookup table. In some embodiments, each motif comprises two or more amino acids. In certain embodiments, motifs include, for example, α -helix, β -bridge, β -strand, 3_{10} helix, π -helix, turn, and loop. In some embodiments, the cosine similarity is greater than 0.3, greater than 0.35, greater than 0.4, greater than 0.45, or greater than 0.5 relative to the CD25 reference target secondary structure motif vector for the fraction of the engineered polypeptide derived from the CD25 reference target. Cosine similarity may be calculated by:

$$\text{Cosine Similarity} = \frac{\sum_{i=1}^n A_i B_i}{\sqrt{\sum_{i=1}^n A_i^2} \sqrt{\sum_{i=1}^n B_i^2}}$$

wherein A is the peptide vector of secondary structure motif identifiers, B is the reference vector of secondary structure motif identifiers, n is the length of the secondary structure motif vector, and i is the i^{th} secondary structure motif.

[0112] In some embodiments, one or more atoms or amino acids of the engineered polypeptide which are derived from the CD25 reference target can be compared to the corresponding CD25 reference target atoms or amino acids using a total topological constraint

distance (TCD). In some embodiments, the total TCD of said engineered polypeptide atoms or amino acids derived from the CD25 reference target is +/- 75% relative to the TCD distance of the corresponding atoms in the CD25 reference target, wherein two intra-molecule topological constraints are interacting if their pairwise distance is less than or equal to 7 Å. In some embodiments, the atoms or amino acids in the engineered polypeptide being compared are associated with a biological function or biological response. The $i^{\text{th}}, j^{\text{th}}$ pairwise distance of two atoms or amino acids can, in some embodiments, be determined by molecular simulation (e.g. molecular dynamics) and/or laboratory measurement (e.g. NMR). An exemplary equation for calculating total topological constraint distance (TCD) is:

$$\frac{1}{L^2} \sum_{i < j}^{i=1:L} S_{ij} \Delta_{ij}$$

where i, j are the intra-molecular position indices for amino acids (i, j), S_{ij} is the difference between constraints $S(i)$ and $S(j)$, $\Delta(i, j) = 1$ if amino acids (i, j) are within the 7 Å interaction threshold, and L is the number of amino acid positions in the peptide or the corresponding CD25 reference target. Alternatively, in some embodiments, $\Delta(i, j)$ can serve as a weighting factor for the S_{ij} difference instead of a 0 or 1 multiplier.

[0113] In some embodiments, one or more atoms or amino acids of the engineered polypeptide which are derived from the CD25 reference target can be compared to the corresponding CD25 reference target atoms or amino acids using a chain topology parameter (CTP). In some embodiments, the CTP of said engineered polypeptide atoms or amino acids is +/- 50% relative to the CTP of the corresponding atoms or amino acids in the CD25 reference target, wherein intra-chain topological interaction is a pairwise distance less than or equal to 7 Å. In some embodiments, the atoms or amino acids in the engineered polypeptide being compared are associated with a biological function or biological response. In some embodiments, $i^{\text{th}}, j^{\text{th}}$ pairwise distance can be determined by molecular simulation (e.g. molecular dynamics) and/or laboratory measurement (e.g. NMR). An exemplary equation for evaluating CTP is:

$$\text{Chain Topology Parameter (CTP)} = \frac{1}{L \cdot N} \sum_{i=1:L} \sum_{j < i} S_{ij}^2 \Delta_{ij},$$

where i, j are the position indices for amino acids (i, j), S_{ij} is the difference between topological constraints $S(i)$ and $S(j)$, $\Delta(i, j) = 1$ if amino acids (i, j) are within the 7 Å chain topological interaction threshold, L is the number of amino acid positions in the peptide or the corresponding CD25 reference target, and N is the total number of intra-chain contacts that meet the 7 Å topological interaction threshold in the engineered polypeptide or CD25 reference target. Alternatively, in some embodiments $\Delta(i, j)$ can serve as a weighting factor for the S_{ij} difference instead of a 0 or 1 multiplier.

[0114] In some embodiments, one or more atoms or amino acids of the engineered polypeptide which are derived from the CD25 reference target can be compared to the corresponding CD25 reference target atoms or amino acids using a quantitative estimate of likeness (QEL). In some embodiments, the QEL of said engineered polypeptide atoms or amino acids is +/- 50% relative to the QEL of the corresponding atoms or amino acids in the CD25 reference target. In some embodiments, the atoms or amino acids in the engineered polypeptide being compared are associated with a biological function or biological response. An exemplary equation for determining QEL is:

$$\text{Quantitative Estimate of Likeness (QEL)} = \exp\left(\frac{1}{n} \sum_{i=1}^n \ln di\right),$$

wherein di is a topological constraint for the i^{th} amino acid or atom position, or a composition function (e.g. linear regression function) that combines multiple topological constraints for the i^{th} amino acid or atom position, and n is the number of amino acid or atom positions in the peptide or the CD25 reference target.

[0115] In some embodiments, one or more atoms or amino acids of the engineered polypeptide which are derived from the CD25 reference target can be compared to the corresponding CD25 reference target atoms or amino acids using a topological clustering coefficient (TCC) vector and a mean percentage error (MPE). In some embodiments, the TCC

vector and MPE is less than 75% relative to the TCC of the corresponding atoms or amino acids in the CD25 reference target, wherein each element (i) of the vector is a topological clustering coefficient for the i^{th} amino acid position, intra-molecule clusters are defined by an interacting edge distance less than or equal to 7 Å, and two edges: i-j, j-l from the i^{th} amino acid position. In some embodiments, the atoms or amino acids in the engineered polypeptide being compared are associated with a biological function or biological response. In some embodiments, the i^{th} , j^{th} and l^{th} edge distance can be determined by molecular simulation (e.g. molecular dynamics) and/or laboratory measurement (e.g. NMR). An exemplary equation for evaluating the topological clustering coefficient for the i^{th} position is:

$$\text{Topological Clustering Coefficient for the } i^{\text{th}} \text{ position (TCC}_i\text{)} = \frac{\sum_{j,l=1:L} S_{ijl} \Delta_{ij} \Delta_{il} \Delta_{jl}}{N_c(N_c - 1)/2},$$

wherein $\Delta(i,j) = 1$, $\Delta(i,l) = 1$, $\Delta(j,l) = 1$ if intra-molecular amino acid positions: (i, j), (i, l), (j, l) are within the 7 Å interacting edge threshold respectively, S_{ijl} is the combination (e.g. sum) of topological constraints for the i^{th} , j^{th} and l^{th} amino acid, L is the number of amino acid positions in the peptide vector or corresponding CD25 reference target vector, N_c is the number of intra-molecular interacting amino acid positions for the i^{th} amino acid, meeting the 7 Å edge threshold and two edges: i-j, j-l from the i^{th} amino acid. Alternatively, in some embodiments, $\Delta(i,j)$, $\Delta(i,l)$ and $\Delta(j,l)$ can serve as weighting factors for the clustering coefficient vector element (i) instead of a 0 or 1 multiplier.

[0116] In still further embodiments, one or more atoms or amino acids of the engineered polypeptide which are derived from the CD25 reference target can be compared to the corresponding CD25 reference target atoms or amino acids using an LxM topological constraint matrix and mean percentage error (MPE) of: Euclidean distance, power distance, Soergel distance, Canberra distance, Sorensen distance, Jaccard distance, Mahalanobis distance, or Hamming distance across all M-dimensions. The LxM matrix element (l, m) contains the m^{th} constraint value for the l^{th} amino acid position, wherein L is the number of amino acid positions and M is the number of distinct topological constraints. In some embodiments, the MPE of the

engineered polypeptide LxM matrix is less than 75% relative to the matrix of the corresponding CD25 reference target atoms or amino acids. In some embodiments, the MPE is less than 70%, less than 65%, less than 60%, less than 55%, less than 50%, or less than 45%. In some embodiments, the atoms or amino acids in the engineered polypeptide being compared are associated with a biological function or biological response.

III. Programmable in vitro Selection

[0117] In other aspects, further provided herein are methods of using the engineered polypeptides described herein in selecting binding partners using a series of programmed selection steps, wherein at least one selection step includes evaluating the interactions of a pool of potential binding partners with an engineered polypeptide.

[0118] In some embodiments, provided herein are methods of steering the selection of a binding molecule using two or more selection molecules. In some embodiments, the methods include subjecting a pool of candidate binding molecules to at least one round of selection, wherein each round comprises at least one negative selection step wherein at least a portion of the pool is screened against a negative selection molecule, and at least one positive selection step wherein at least a portion of the pool is screened against a positive selection molecule. In some embodiments the method comprises at least two rounds, at least three rounds, at least four rounds, at least five rounds, at least six rounds, at least seven rounds, at least eight rounds, at least nine rounds, at least ten rounds, or more, wherein each round independently comprises at least one negative selection step and at least one positive selection step. In some embodiments, each round independently comprises more than one negative selection step, or more than one positive selection step, or a combination thereof. **FIG. 5** provides an exemplary schematic detailing three rounds of selection, wherein the first and third round comprise more than one negative selection step, and the first round further comprises more than one positive selection round. As shown in the scheme, two negative selection molecules (“baits”) are used in the first round, and three negative selection molecules are used in the third round. In addition, two positive selection molecules are used in the first round.

[0119] In some embodiments wherein the method comprises more than one round, each negative and positive selection molecule is independently chosen. In other embodiments, the same negative selection molecule, or the same positive selection molecule, or a combination thereof, may be used in more than one round. For example, in **FIG. 5**, the same negative selection molecules used in round 1 are used again in round 3, with an additional third negative selection molecule also included in round 3. The order of negative and positive selection steps may be, in certain embodiments, independently chosen within each round of selection. Thus, for example, in some embodiments, the method comprises one or more rounds of selection, wherein each round comprises first a negative selection step, and then a positive selection step. In other embodiments, the method comprises one or more rounds of selection, wherein each round comprises first a positive selection step, and then a negative selection step. In still further embodiments, the method comprises one or more rounds of selection, wherein each round independently comprise a negative selection step and a positive selection step, wherein in each round the negative selection step is independently before the positive selection step or after the positive selection step.

[0120] Such methods of selection use positive (+) and negative (-) steps to steer the library of candidate binding molecules towards and away from certain desired characteristics, such as binding specificity or binding affinity. By using multiple steps with both positive and negative selection molecules, the pool of candidates can be directed in a stepwise manner to select for characteristics that are desirable and against characteristics that are undesirable. Further, in some embodiments the order of each step within each round, and the order of the rounds relative to each other can direct the selection in different directions. Thus, for example, in some embodiments a method comprising one round with (+) selection followed by (-) selection will result in a different final pool of candidates than if (-) selection is first, followed by (+) selection. Extrapolating this out to methods comprising multiple rounds, the order of selection steps may result in a different final pool of selected candidates even if the same positive and negative selection molecules are used overall.

[0121] In some embodiments a selection molecule is used that has an inverse characteristic of another selection molecule. This may be useful, for example, to ensure that the candidate binding partners identified using the positive selection molecule (or excluded because of a negative

selection molecule) were identified (or excluded) because of a desired trait (or undesired trait), not because of a separate, unrelated binding interaction. To remove binding partners that are binding through unrelated interactions, an inverse selection molecule can be used that has similar or the same structure and characteristics as the selection molecule, except for the residues/structures conveying the desired trait (or undesired trait). For example, if interaction with a particular charge pattern in a positive selection molecule is desired, an inverse negative selection molecule may be used that has replaced the residues providing that charge pattern with uncharged residues, and/or residues of the opposite charge. Thus, for certain selection molecules, multiple different corresponding inverse selection molecules may be possible.

[0122] In the selection methods provided herein, at least one of the selection molecules is an engineered polypeptide as described herein. In some embodiments, more than one engineered polypeptide is used. In some embodiments, each engineered polypeptide is independently a positive or negative selection molecule. In certain embodiments, each selection molecule used in the one or more rounds of selection is independently an engineered polypeptide. In other embodiments, at least one molecule that is not an engineered polypeptide is used as a selection molecule. Such selection molecules that are not engineered polypeptides may comprise, for example, a naturally-occurring polypeptide, or a portion thereof. In other embodiments, one or more selection molecules that are not engineered polypeptides may comprise, for example, a non-naturally occurring polypeptide or portion thereof. For example, in some embodiments one or more selection molecules (e.g., positive selection molecule or negative selection molecule) is an immunogen, an antibody, cell-surface receptor, or a transmembrane protein, or a signaling protein, or a multiprotein complex, or a peptide-protein complex, or any portions thereof, or any combinations thereof. In some embodiments, one or more selection molecules is CD25 or a portion of any of CD25.

[0123] The positive and negative characteristics being selected for or against in each step may be selected from a variety of traits, and may be tailored depending on the desired features of the final one or more binding molecules obtained. Such desired features may depend, for example, on the intended use of the one or more binding molecules. For example, in some embodiments the methods provided herein are used to screen antibody candidates for one or more positive characteristics such as high specificity, and against one or more negative

characteristics such as cross-reactivity. It should be understood that what is considered a positive characteristic in one context might be a negative characteristic in another context, and vice versa. Thus, a positive selection molecule in one series of selection rounds may, in some embodiments, be a negative selection molecule in a different series of selection rounds, or in selecting a different type of binding molecule, or in selecting the same type of binding molecule but for a different purpose.

[0124] In some embodiments, each selection characteristic is independently selected from the group consisting of amino acid sequence, polypeptide secondary structure, molecular dynamics, chemical features, biological function, immunogenicity, CD25 reference target(s) multi-specificity, cross-species CD25 reference target reactivity, selectivity of desired CD25 reference target(s) over undesired reference target(s), selectivity of reference target(s) within a sequence and/or structurally homologous family, selectivity of reference target(s) with similar protein function, selectivity of distinct desired reference target(s) from a larger family of undesired targets with high sequence and/or structural homology, selectivity for distinct reference target alleles or mutations, selectivity for distinct reference target residue level chemical modifications, selectivity for cell type, selectivity for tissue type, selectivity for tissue environment, tolerance to reference target(s) structural diversity, tolerance to reference target(s) sequence diversity, and tolerance to reference target(s) dynamics diversity. In some embodiments, each selection characteristic is a different type of selection characteristic. In other embodiments, two or more selection characteristics are different characteristics but of the same type. For example, in some embodiments, two or more selection characteristics are polypeptide secondary structure, wherein one is a positive selection for a desired polypeptide secondary structure and one is a negative selection for an undesired polypeptide secondary structure. In some embodiments, two or more selection characteristics are selectivity for cell type, wherein a positive selection characteristic is selectivity for a specific desired cell type, and a negative selection characteristic is selectivity for a specific undesired cell type. In some embodiments, two or more, three or more, four or more, five or more, or six or more selection characteristics are of the same type.

[0125] In some embodiments, the selection characteristic is binding to an engineered polypeptide of the disclosure. For example, the engineered polypeptides shown in **FIG. 7, Table**

1, Table 8, and Table 9 may be used to select for antibodies (or other binding agents) that specifically bind to the epitopes shown in **FIG. 6** and **Table 7**. Illustrative selection strategies are provided in **Table 10**.

[0126] In yet another aspect, provided herein is a composition comprising two or more selection steering polypeptides, wherein each polypeptide is independently a positive selection molecule comprising one or more positive steering characteristics, or a negative selection molecule comprising one or more negative steering characteristics. Such characteristics may, in some embodiments, be selected from the group consisting of amino acid sequence, polypeptide secondary structure, molecular dynamics, chemical features, biological function, immunogenicity, reference target(s) multi-specificity, cross-species reference target reactivity, selectivity of desired reference target(s) over undesired reference target(s), selectivity of reference target(s) within a sequence and/or structurally homologous family, selectivity of reference target(s) with similar protein function, selectivity of distinct desired reference target(s) from a larger family of undesired targets with high sequence and/or structural homology, selectivity for distinct reference target alleles or mutations, selectivity for distinct reference target residue level chemical modifications, selectivity for cell type, selectivity for tissue type, selectivity for tissue environment, tolerance to reference target(s) structural diversity, tolerance to reference target(s) sequence diversity, and tolerance to reference target(s) dynamics diversity.

[0127] Thus, in further aspects, provided herein is a method of screening a library of binding molecules with a selection steering composition as described herein, wherein each round of selection comprises: a negative selection step of screening at least a portion of the pool against a negative selection molecule; and a positive selection step of screening at least a portion of the pool for a positive selection molecule; wherein the order of selection steps within each round, and the order of rounds, result in the selection of a different subset of the pool than an alternative order.

[0128] In some embodiments, the binding partners being evaluated using the composition of selection steering polypeptides as described herein, or the methods of screening as described herein, are a phage library, for example a Fab-containing phage library; or a cell library, for example a B-cell library or a T-cell library.

[0129] In some embodiments of the methods of screening provided herein, the methods comprise two or more, three or more, four or more, five or more, six or more, or seven or more rounds of selection. In some embodiments, wherein there is more than one round, each round comprises a different set of selection molecules. In other embodiments, wherein there is more than one round, at least two rounds comprise the same negative selection molecule, the same positive selection molecule, or both.

[0130] In some embodiments of the screening methods, the method comprises analyzing the subset of the pool prior to proceeding to the next round of selection. In certain embodiments, each subset pool analysis is independently selected from the group consisting of peptide/protein biosensor binding, peptide/protein ELISA, peptide library binding, cell extract binding, cell surface binding, cell activity assay, cell proliferation assay, cell death assay, enzyme activity assay, gene expression profile, protein modification assay, Western blot, and immunohistochemistry. In some embodiments, gene expression profile comprises full sequence repertoire analysis of the subset pool, such as next-generation sequencing. In some embodiments, statistical and/or informatic scoring, or machine learning training is used to evaluate one or more subsets of the pool in one or more selection rounds.

[0131] In some embodiments, the identity and/or order of positive and/or negative selection molecules for a subsequent round is determined by analyzing a subset pool from one selection round. In some embodiments, statistical and/or informatic scoring, or machine learning training, is used to evaluate one or more subsets of the pool in one or more selection rounds to determine the identity and/or order of the positive and/or negative selection molecules for a subsequent round (such as the next round, or a round further along in the program).

[0132] In still further embodiments, the methods of selection include modifying a subset pool obtained from a selection round before proceeding to the next selection round. Such modifications may include, for example, genetic mutation of the subset pool, genetic depletion of the subset pool (e.g., selecting a subset of the subset pool to move forward in selection), genetic enrichment of the subset pool (e.g., increasing the size of the pool), chemical modification of at least a portion of the subset pool, or enzymatic modification of at least a portion of the subset pool, or any combinations thereof. In some embodiments, statistical and/or informatic scoring, or

machine learning training is used to evaluate a subset pool and determine the one or more modifications to make prior to moving the modified subset pool forward in selection. In certain embodiments, such statistical and/or informatic scoring, or machine learning training, is also used to determine the identity and/or order of positive and/or negative selection molecules for a subsequent round of selection.

[0133] Any suitable assay may be used to evaluate the binding of a pool of binding partners with the selection molecules in each step. In some embodiments, binding is directly evaluated, for example by directly detecting a label on the binding partner. Such labels may include, for example, fluorescent labels, such as a fluorophore or a fluorescent protein. In other embodiments, binding is indirectly evaluated, for example using a sandwich assay. In a sandwich assay, a binding partner binds to the selection molecule, and then a secondary labeled reagent is added to label the bound binding partner. This secondary labeled reagent is then detected. Examples of sandwich assay components include His-tagged-binding partner detected with an anti-His-tag antibody or His-tag-specific fluorescent probe; a biotin-labeled binding partner detected with labeled streptavidin or labeled avidin; or an unlabeled binding partner detected with an anti-binding-partner antibody.

[0134] In some embodiments, the binding partners being selected in each step are identified based on the binding signal, or dose-response, using any number of available detection methods. These detection methods may include, for example, imaging, fluorescence-activated cell sorting (FACS), mass spectrometry, or biosensors. In some embodiments, a hit threshold is defined (for example the median signal), and any with signal above that signal is flagged as a putative hit motif.

IV. Use of Engineered polypeptides to Produce Antibodies

[0135] The engineered polypeptides provided herein, and identified by the methods provided herein, may be used, for example, to produce one or more antibodies. In some embodiments, the antibody is a monoclonal or polyclonal antibody. Thus, in some embodiments, provided herein is an antibody produced by immunizing an animal with an immunogen, wherein the immunogen is an engineered polypeptide as provided herein. In some embodiments, the animal is a human, a

rabbit, a mouse, a hamster, a monkey, etc. In certain embodiments, the monkey is a cynomolgus monkey, a macaque monkey, or a rhesus macaque monkey. Immunizing the animal with an engineered polypeptide can comprise, for example, administering at least one dose of a composition comprising the peptide and optionally an adjuvant to the animal. In some embodiments, generating the antibody from an animal comprises isolating a B cell which expresses the antibody. Some embodiments further comprise fusing the B cell with a myeloma cell to create a hybridoma which expresses the antibody. In some embodiments, the antibody generated using the engineered polypeptide can cross react with a human and a monkey, for example a cynomolgus monkey.

a. Characteristics of the Engineered polypeptide

[0136] The engineered polypeptides provided herein have one or more characteristics in common with CD25. In some embodiments, they exhibit at least one characteristic of the surface of CD25, for example the functional interface surface that binds with a binding partner of CD25. In some embodiments, the binding partner is an antibody that binds specifically to CD25. In some embodiments, the engineered polypeptide exhibits at least one characteristic of a portion of the surface of CD25 that is not known to interact to an antibody to CD25.

[0137] In some embodiments of certain types of characteristics, the engineered polypeptide presents a mimic of a functional interface of CD25 (such as a binding surface), but the characteristic shared by the engineered polypeptide may be best described as being shared with CD25 as a whole. For example, one characteristic that is shared may be binding between a binding partner of CD25 and CD25, wherein the binding occurs with a functional binding interface of CD25, but the structure and orientation of the functional binding interface is supported by the rest of the CD25 protein.

[0138] Such shared characteristics may include, for example, structural metrics, or functional metrics, or combinations thereof. The at least one shared characteristic may include, for example, one or more structural similarities, similarity of conformational entropy, one or more chemical descriptor similarities, one or more functional binding similarities, or one or more phenotypic similarities, or any combinations thereof. In certain embodiments, the engineered polypeptide

shares one or more of these characteristics with at least a portion of the surface of CD25, such as a functional interface, for example a binding surface.

[0139] In some embodiments, the engineered polypeptide has structural similarity to CD25 (or a portion of the surface of CD25, such as a binding surface), and this structural similarity is evaluated by backbone root-mean-square deviation (RMSD) or side-chain RMSD. RMSD evaluates the average distance between atoms, and can be applied to three-dimensional structures to compare how similar two separate structures are in three-dimensional space. In some embodiments, the RMSD of the backbone, or amino acid side chains, or both, between the engineered polypeptide and CD25 (or a functional interface of CD25) is lower than the RMSD between CD25 (or a functional interface of CD25) and a different molecule. In some embodiments, it is a portion of CD25 (or a portion of a functional interface of CD25) that is compared with the engineered polypeptide. The RMSD may be evaluated, for example, using the experimentally measured structure or the simulated structure of the engineered polypeptide; and the experimentally measured structure or the simulated structure of CD25 (or a functional interface thereof). In some embodiments, a engineered polypeptide is considered structurally similar to CD25 if the backbone of the engineered polypeptide has an average RMSD less than or equal to 6.0 Å relative to the backbone of an x-ray structure of CD25.

[0140] In some embodiments, the engineered polypeptide has similar conformational entropy to CD25 (or a portion of the surface of CD25, such as a binding surface), and this conformational entropy is evaluated, for example, using the experimentally measured structure or the simulated structure of the engineered polypeptide, and the experimentally measured structure or the molecular dynamics simulated motion of CD25 (or portion thereof). In such simulations, in some embodiments the experimentally measured structure or the molecular dynamics simulated motion of CD25 (or portion thereof, such as a portion of the binding surface) is used. In certain embodiments, the conformational entropy of the engineered polypeptide is considered similar to that of CD25 (or portion thereof) if an engineered polypeptide molecular dynamics ensemble run under standard physiological conditions has all states with all non-hydrogen atomic position RMSDs ≤ 6.0 Å relative to a known x-ray crystal structure of CD25 (or portion thereof).

[0141] In still other embodiments, the engineered polypeptide has one or more chemical descriptors similar to CD25 (or a portion thereof, such as the binding surface). In other embodiments, the engineered polypeptide has one or more chemical descriptors complementary to a binding partner of CD25 (e.g., an antibody to CD25). Such chemical descriptors (which may be similar or complementary) may include, for example, hydrophobicity patterns, H-bonding patterns, atomic volume/radii, charge patterns, or atomic occupancy patterns, or any combinations thereof. These chemical descriptors may, in some embodiments, be evaluated using the experimentally measured structure or the simulated structure of the engineered polypeptide, and the experimentally measured structure or the simulated structure of CD25 (or a portion thereof, such as the binding surface).

[0142] In still other embodiments, the engineered polypeptide has similar functional binding as CD25. For example, in some embodiments the engineered polypeptide has binding to a CD25 binding partner, or fragment thereof. In some embodiments, the binding partner is a fragment of the native binding partner, or is a modified native binding partner. Such modifications may include, for example, a fusion protein comprising at least a fragment of the native binding partner; labeling with a chromophore; labeling with a fluorophore; labeling with biotin; or labeling with a His-tag. In some embodiments, the engineered polypeptide has binding with a binding partner of CD25 that is within about two orders of magnitude, or within about one order of magnitude, of the binding of CD25 with a binding partner. In some embodiments, the similarity of binding is evaluated by comparing the binding constant (K_d), or the inhibitory constant (K_i), or the binding on-rate, or the binding off-rate, or the binding affinity of the binding pairs, or the Gibbs free energy of binding (ΔG). In some embodiments, the binding partner is an antibody to CD25.

[0143] In some embodiments, the binding constant (K_d) of the engineered polypeptide with a CD25 binding partner is within 1000-fold, within 800-fold, within 600-fold, within 400-fold, within 200-fold, within 100-fold, within 90-fold, within 80-fold, within 70-fold, within 60-fold, within 50-fold, within 40-fold, within 30-fold, within 20-fold, within 10-fold, within 8-fold, within 6-fold, within 4-fold, within 2-fold, within 1.5-fold, within 1.2-fold, or about the same as the K_d of CD25 with the binding partner. In other embodiments, the inhibitory constant (K_i) of the engineered polypeptide with a CD25 binding partner is within 1000-fold, within 800-fold,

within 600-fold, within 400-fold, within 200-fold, within 100-fold, within 90-fold, within 80-fold, within 70-fold, within 60-fold, within 50-fold, within 40-fold, within 30-fold, within 20-fold, within 10-fold, within 8-fold, within 6-fold, within 4-fold, within 2-fold, within 1.5-fold, within 1.2-fold, or about the same as the K_i of CD25 and the binding partner. In still further embodiments, the binding on-rate of the engineered polypeptide with a CD25 binding partner is similar to the binding on-rate of CD25 and the binding partner. In some embodiments, the binding on-rate of the engineered polypeptide with a CD25 binding partner is within 1000-fold, within 800-fold, within 600-fold, within 400-fold, within 200-fold, within 100-fold, within 90-fold, within 80-fold, within 70-fold, within 60-fold, within 50-fold, within 40-fold, within 30-fold, within 20-fold, within 10-fold, within 8-fold, within 6-fold, within 4-fold, within 2-fold, within 1.5-fold, within 1.2-fold, or about the same as the on-rate of CD25 and the binding partner. In other embodiments, the binding off-rate of the engineered polypeptide with a CD25 binding partner is similar to the binding off-rate of CD25 and the binding partner. In some embodiments, the binding off-rate of the engineered polypeptide with a CD25 binding partner is within 1000-fold, within 800-fold, within 600-fold, within 400-fold, within 200-fold, within 100-fold, within 90-fold, within 80-fold, within 70-fold, within 60-fold, within 50-fold, within 40-fold, within 30-fold, within 20-fold, within 10-fold, within 8-fold, within 6-fold, within 4-fold, within 2-fold, within 1.5-fold, within 1.2-fold, or about the same as the off-rate of CD25 and the binding partner. In still further embodiments, the binding affinity of the engineered polypeptide with a CD25 binding partner is similar to the binding affinity of CD25 and the binding partner. In some embodiments, the binding affinity of the engineered polypeptide with a CD25 binding partner is within 1000-fold, within 800-fold, within 600-fold, within 400-fold, within 200-fold, within 100-fold, within 90-fold, within 80-fold, within 70-fold, within 60-fold, within 50-fold, within 40-fold, within 30-fold, within 20-fold, within 10-fold, within 8-fold, within 6-fold, within 4-fold, within 2-fold, within 1.5-fold, within 1.2-fold, or about the same as the binding affinity of CD25 and the binding partner. In some embodiments, the Gibbs free energy of binding of the engineered polypeptide with a CD25 binding partner is within 1000-fold, within 800-fold, within 600-fold, within 400-fold, within 200-fold, within 100-fold, within 90-fold, within 80-fold, within 70-fold, within 60-fold, within 50-fold, within 40-fold, within 30-fold, within 20-fold, within 10-fold, within 8-fold, within 6-fold, within 4-fold, within 2-fold, within

1.5-fold, within 1.2-fold, or about the same as the Gibbs free energy of binding of CD25 and the binding partner. In some embodiments, the CD25 binding partner is an antibody of CD25.

[0144] In yet other embodiments, the engineered polypeptide shares sequence similarity with CD25, or a portion thereof (such as a binding surface of CD25). The similarity may be compared to the continuous amino acid sequence of CD25 (or portion thereof), or to a discontinuous sequence of CD25 (or portion thereof). For example, in certain embodiments, a binding surface of CD25 is formed by discontinuous amino acid sequences, and the engineered polypeptide has sequence similarity with at least a portion of the discontinuous sequences that form the surface. In other embodiments, the engineered polypeptide has sequence similarity with at least a portion of a continuous amino acid sequence that forms a binding surface of CD25. In some embodiments, the binding surface of CD25 comprises an epitope that binds to an antibody to CD25.

[0145] In some embodiments, the engineered polypeptide has a sequence that is at least 40% identical, at least 45% identical, at least 50% identical, at least 55% identical, at least 60% identical, at least 65% identical, at least 70% identical, at least 75% identical, at least 80% identical, at least 85% identical, or at least 90% identical, to a portion of the continuous sequence of CD25, for example a continuous sequence that forms a binding surface of CD25. In certain embodiments, the engineered polypeptide has a sequence that is at least 40% identical, at least 45% identical, at least 50% identical, at least 55% identical, at least 60% identical, at least 65% identical, at least 70% identical, at least 75% identical, at least 80% identical, at least 85% identical, or at least 90% identical, to a portion of the discontinuous sequence of CD25, for example the discontinuous sequence that forms a binding surface of CD25. In certain embodiments, the engineered polypeptide has a sequence that is at least 40% identical, at least 45% identical, at least 50% identical, at least 55% identical, at least 60% identical, at least 65% identical, at least 70% identical, at least 75% identical, at least 80% identical, at least 85% identical, or at least 90% identical, to a contiguous portion of a binding surface of CD25. In still further embodiments, the engineered polypeptide has a sequence that is at least 40% identical, at least 45% identical, at least 50% identical, at least 55% identical, at least 60% identical, at least 65% identical, at least 70% identical, at least 75% identical, at least 80% identical, at least 85% identical, or at least 90% identical, to two or more discontinuous portions of a binding surface of

CD25. In some embodiments, the engineered polypeptide has a sequence at least partly identical (as described herein) with a binding surface of CD25, wherein the binding surface comprises an epitope that binds to one or more antibodies to CD25.

[0146] In certain embodiments, sequence similarity of the engineered polypeptide and CD25 (or portion thereof) is evaluated using the peptide portion(s) of the engineered polypeptide, not including a linker, if present. In certain embodiments, one or more linking moieties are considered as well, for example if the engineered polypeptide comprises one or more linkers that comprise an amino acid.

b. Engineered Polypeptide

[0147] In some embodiments, the engineered polypeptide comprises more than one peptide, for example at least two peptides, or at least three peptides, or greater. In some embodiments, the engineered polypeptide comprises between 1 and 10 peptides, between 1 and 8 peptides, between 1 and 6 peptides, between 1 and 4 peptides, between 2 and 10 peptides, between 2 and 8 peptides, between 2 and 6 peptides, or between 2 and 4 peptides.

[0148] In some embodiments, the engineered polypeptide comprises between 2 to 100 amino acids, for example, between 2 to 80 amino acids, between 2 to 70 amino acids, between 2 to 60 amino acids, between 2 to 50 amino acids, between 2 to 40 amino acids, between 2 to 30 amino acids, between 2 to 25 amino acids, between 2 to 20 amino acids, between 2 to 15 amino acids, between 5 to 30 amino acids, between 5 to 25 amino acids, between 5 to 20 amino acids, between 5 to 15 amino acids, or between 9 and 15 amino acids.

[0149] In certain embodiments, the engineered polypeptide comprises greater than one peptide, for example at least two peptides, or at least three peptides, or at least four peptides, or greater, and each peptide independently comprises between 1 to 100 amino acids, or between 2 to 100 amino acids, for example, between 2 to 80 amino acids, between 2 to 70 amino acids, between 2 to 60 amino acids, between 2 to 50 amino acids, between 2 to 40 amino acids, between 2 to 30 amino acids, between 2 to 25 amino acids, between 2 to 20 amino acids, between 2 to 15 amino acids, between 5 to 30 amino acids, between 5 to 25 amino acids, between 5 to 20 amino acids, between 5 to 15 amino acids, or between 9 and 15 amino acids.

[0150] In some embodiments, the engineered polypeptide comprises only naturally occurring amino acids. In other embodiments, the engineered polypeptide comprises non-natural amino acids, for example a combination of naturally occurring and non-natural amino acids.

[0151] In some embodiments, wherein the engineered polypeptide comprises two or greater peptides, each peptide independently exhibits at least one characteristic of CD25, or a portion thereof (such as a binding surface). In some embodiments, each peptide independently exhibits 1 to 10, 1 to 9, 1 to 8, 1 to 7, 1 to 6, 1 to 5, 1 to 4, 1 to 3, or 1, or 2 characteristics of CD25, or a portion thereof. In some embodiments, the characteristics are shared with a portion of CD25 that interacts with an antibody of CD25.

[0152] In some embodiments, the engineered polypeptide has at least one characteristic that is complementary to a binding partner of CD25, for example an antibody of CD25.

[0153] In some embodiments, a peptide of the engineered polypeptide shares one or more structural similarities with CD25, or a portion thereof. The structural similarity may be, in some embodiments, evaluated by backbone RMSD or side-chain RMSD. For example, in certain embodiments, the RMSD of the backbone, or amino acid side chains, or both, between a peptide of the engineered polypeptide and CD25 (or a portion thereof) is lower than the RMSD between CD25 (or portion thereof) and a different molecule (such as a different peptide). In some embodiments, a portion of CD25 is compared with the peptide, for example a portion of the surface of CD25, such as a surface that interacts with an antibody to CD25. RMSD of structural similarity may be evaluated, for example, using the experimentally measured structure or the simulated structure of the peptide and the experimentally measured structure or the simulated structure of CD25 or portion thereof. In some embodiments, a peptide of the engineered polypeptide is considered structurally similar to CD25 (or portion thereof) if the backbone of the peptide has an average RMSD less than or equal to 6.0 Å relative to the backbone of a known x-ray structure of CD25, or the portion thereof.

[0154] In some embodiments, the engineered polypeptide has similar conformational entropy to CD25 or a portion thereof. In some embodiments, the experimentally measured structure or the molecular dynamics simulated motion of the peptide is used to compare the conformation

entropy with the experimentally measured structure or the simulated structure of CD25, or a portion thereof. The conformational entropy is considered similar, in some embodiments, if a peptide molecular dynamics ensemble run under standard physiological conditions has all states with all non-hydrogen atomic portions RMSDs ≤ 6.0 Å relative to a known x-ray crystal structure of CD25, or portion thereof. In some embodiments, a portion of CD25 is compared with the peptide, for example a surface portion of CD25 that interacts with an antibody of CD25.

[0155] In further embodiments, the similarity between a peptide of the engineered polypeptide and CD25 (or portion thereof) may be one or more chemical descriptors. In some embodiments, the peptide has one or more chemical descriptors in common with CD25 (or a portion thereof), or one or more chemical descriptors that is complementary to a binding partner of CD25 (for example, an antibody to CD25). Chemical descriptors may include, for example, hydrophobicity patterns, H-bonding patterns, atomic volume/radii, charge patterns, or atomic occupancy patterns, or any combinations thereof. In some embodiments, a peptide of the engineered polypeptide has one or more hydrophobicity patterns, H-bonding patterns, atomic volume/radii, charge patterns, or atomic occupancy patterns, or any combinations thereof, similar those in CD25 or a portion thereof, or which is complementary to a binding partner of CD25 (such as an antibody to CD25). In some embodiments, the similarity is having the same chemical descriptor in common, such as one or more of the same hydrophobicity patterns, H-bonding patterns, atomic volume/radii, charge patterns, or atomic occupancy patterns. Complementary chemical descriptors includes, for example, a peptide with a positive charge pattern that complements the negative charge pattern of a binding partner of CD25, such as an antibody to CD25. These chemical descriptors may, in some embodiments, be evaluated using an experimentally measured structure or a simulated structure of the peptide, and an experimentally measured structure or a simulated structure of CD25, or the CD25 binding partner (e.g., for complementary evaluation).

[0156] For example, in some embodiments, the engineered polypeptide binds binding partner of CD25 that is similar to the binding of CD25 with the binding partner (for example, IL-2). In some embodiments, the binding partner is the native binding partner, a fragment of a native binding partner, or a modified native binding partner or fragment thereof, or an antibody that binds specifically to CD25. In some embodiments, the binding partner binds under certain

circumstances but not others. In some embodiments, the binding partner binds under pathological conditions, or binds under non-pathological conditions. The binding partner may be, for example, constitutively expressed, or the product of a facultative gene, or comprise a protein or a fragment thereof. In certain embodiments, the binding partner is a fragment of a native binding partner, or is a modified native binding partner. Modifications may include, in some embodiments, a fusion protein comprising at least a fragment of the native binding partner; labeling with a chromophore; labeling with a fluorophore; labeling with biotin; or labeling with a His-tag.

[0157] In some embodiments, the engineered polypeptide has binding with a binding partner of CD25 that is within about two orders of magnitude, or within about one order of magnitude, of the binding of CD25 with the binding partner. In some embodiments, the similarity of binding is evaluated by comparing the binding constant (K_d), or the inhibitory constant (K_i), or the binding on-rate, or the binding off-rate, or the binding affinity of the binding pairs, or the Gibbs free energy of binding (ΔG). In some embodiments, the binding partner is an antibody to CD25.

[0158] In some embodiments, the binding constant (K_d) of the engineered polypeptide with a CD25 binding partner is within 1000-fold, within 800-fold, within 600-fold, within 400-fold, within 200-fold, within 100-fold, within 90-fold, within 80-fold, within 70-fold, within 60-fold, within 50-fold, within 40-fold, within 30-fold, within 20-fold, within 10-fold, within 8-fold, within 6-fold, within 4-fold, within 2-fold, within 1.5-fold, within 1.2-fold, or about the same as the K_d of CD25 with the binding partner. In other embodiments, the inhibitory constant (K_i) of the engineered polypeptide with a CD25 binding partner is within 1000-fold, within 800-fold, within 600-fold, within 400-fold, within 200-fold, within 100-fold, within 90-fold, within 80-fold, within 70-fold, within 60-fold, within 50-fold, within 40-fold, within 30-fold, within 20-fold, within 10-fold, within 8-fold, within 6-fold, within 4-fold, within 2-fold, within 1.5-fold, within 1.2-fold, or about the same as the K_i of CD25 and the binding partner. In still further embodiments, the binding on-rate of the engineered polypeptide with a CD25 binding partner is similar to the binding on-rate of CD25 and the binding partner. In some embodiments, the binding on-rate of the engineered polypeptide with a CD25 binding partner is within 1000-fold, within 800-fold, within 600-fold, within 400-fold, within 200-fold, within 100-fold, within 90-fold, within 80-fold, within 70-fold, within 60-fold, within 50-fold, within 40-fold, within 30-

fold, within 20-fold, within 10-fold, within 8-fold, within 6-fold, within 4-fold, within 2-fold, within 1.5-fold, within 1.2-fold, or about the same as the on-rate of CD25 and the binding partner. In other embodiments, the binding off-rate of the engineered polypeptide with a CD25 binding partner is similar to the binding off-rate of CD25 and the binding partner. In some embodiments, the binding off-rate of the engineered polypeptide with a CD25 binding partner is within 1000-fold, within 800-fold, within 600-fold, within 400-fold, within 200-fold, within 100-fold, within 90-fold, within 80-fold, within 70-fold, within 60-fold, within 50-fold, within 40-fold, within 30-fold, within 20-fold, within 10-fold, within 8-fold, within 6-fold, within 4-fold, within 2-fold, within 1.5-fold, within 1.2-fold, or about the same as the off-rate of CD25 and the binding partner. In still further embodiments, the binding affinity of the engineered polypeptide with a CD25 binding partner is similar to the binding affinity of CD25 and the binding partner. In some embodiments, the binding affinity of the engineered polypeptide with a CD25 binding partner is within 1000-fold, within 800-fold, within 600-fold, within 400-fold, within 200-fold, within 100-fold, within 90-fold, within 80-fold, within 70-fold, within 60-fold, within 50-fold, within 40-fold, within 30-fold, within 20-fold, within 10-fold, within 8-fold, within 6-fold, within 4-fold, within 2-fold, within 1.5-fold, within 1.2-fold, or about the same as the binding affinity of CD25 and the binding partner. In some embodiments, the Gibbs free energy of binding of the engineered polypeptide with a CD25 binding partner is within 1000-fold, within 800-fold, within 600-fold, within 400-fold, within 200-fold, within 100-fold, within 90-fold, within 80-fold, within 70-fold, within 60-fold, within 50-fold, within 40-fold, within 30-fold, within 20-fold, within 10-fold, within 8-fold, within 6-fold, within 4-fold, within 2-fold, within 1.5-fold, within 1.2-fold, or about the same as the Gibbs free energy of binding of CD25 and the binding partner. In some embodiments, the CD25 binding partner is an antibody of CD25.

[0159] In some embodiments, the engineered polypeptide has sequence similarity with CD25, or a portion thereof. In some embodiments, the engineered polypeptide has sequence similarity with a portion of the surface of CD25 that binds to an antibody of CD25. In certain embodiments, the sequence similarity is compared to the continuous amino acid sequence of CD25. In other embodiments, the sequence similarity is compared to a discontinuous sequence of CD25. For example, in certain embodiments, a binding surface of folded CD25 is formed by discontinuous amino acid sequences, and the engineered polypeptide has sequence similarity

with at least a portion of the discontinuous sequences that form the surface. In some embodiments, the engineered polypeptide has sequence similarity with at least a portion of a continuous amino acid sequence that forms a binding surface of CD25. In some embodiments, the engineered polypeptide has a sequence that is at least 50% identical, at least 55% identical, at least 60% identical, at least 65% identical, at least 70% identical, at least 75% identical, at least 80% identical, at least 85% identical, at least 90% identical, at least 95% identical, or at least 99% identical to at least a portion of a continuous sequence of CD25, such as a continuous sequence that forms a binding surface. In certain embodiments, the engineered polypeptide has a sequence that is at least 40% identical, at least 45% identical, at least 50% identical, at least 55% identical, at least 60% identical, at least 65% identical, at least 70% identical, at least 75% identical, at least 80% identical, at least 85% identical, or at least 90% identical, to at least a portion of the discontinuous sequence of CD25, for example the discontinuous sequence that forms a binding surface. In certain embodiments, the engineered polypeptide has a sequence that is at least 40% identical, at least 45% identical, at least 50% identical, at least 55% identical, at least 60% identical, at least 65% identical, at least 70% identical, at least 75% identical, at least 80% identical, at least 85% identical, or at least 90% identical, to a contiguous portion of CD25. In still further embodiments, the engineered polypeptide has a sequence that is at least 40% identical, at least 45% identical, at least 50% identical, at least 55% identical, at least 60% identical, at least 65% identical, at least 70% identical, at least 75% identical, at least 80% identical, at least 85% identical, or at least 90% identical, to two or more discontinuous portions of CD25. In some embodiments, for engineered polypeptides that comprise at least two peptides, two or more peptides of the engineered immunogen independently share sequence similarity with CD25, such as with a binding surface of CD25. In some embodiments, the portion of CD25 that shares sequence similarity with the engineered polypeptide is a surface that binds to an antibody to CD25.

c. Linking Moiety

[0160] The engineered polypeptides provided herein optionally comprise a linking moiety. When present, the linking moiety may be, for example, independently a cross-link or a linker.

[0161] In some embodiments, the engineered polypeptide comprises N number of peptides, and N-1 number of linking moieties; or N number of peptides, and N-1 number of linking moieties; or N number of peptides, and N number of linking moieties; or N number of peptides, and N+1 number of linking moieties; or N number of peptides, and N+2 number of linking moieties; or N number of peptides, and N-2 number of linking moieties, wherein N is 3 or larger.

[0162] In some embodiments, the engineered polypeptide comprises at least one linking moiety, at least two linking moieties, at least three linking moieties, at least four linking moieties, at least five linking moieties, at least six linking moieties, between one to six linking moieties, between one to five linking moieties, between one to four linking moieties, between one to three linking moieties, one linking moiety, or two linking moieties. In some embodiments, each linking moiety is independently a cross-link or a linker. In certain embodiments, each linking moiety is a cross-link. In other embodiments, each linking moiety is a linker. In still further embodiments, at least one linking moiety is a cross-link, and the remaining linking moieties are independently cross-links or a linkers. In other embodiments, at least one linking moiety is a linker, and the remaining linking moieties are independently cross-links or a linkers.

[0163] A cross-link includes, for example, a covalent bond between the side chain of one amino acid and a moiety of another amino acid. The amino acids may be independently natural or non-natural amino acids. In some embodiments, cross-links include a covalent bond between the side chains of two amino acids, or between the side chain of one amino acid and the amine or carboxyl group of another amino acid. A cross-link may form within one peptide or between two separate peptides. In some embodiments, the engineered polypeptides provided herein comprise mixture of both intra-peptide and inter-peptide cross-links. In some embodiments, the cross-link is a disulfide bond between two thiol groups of amino acid side chains, such as a disulfide bond between two cysteines. In some embodiments, the cross-link is an amide bond between an amine group and a carboxylic acid group of two amino acids, wherein at least one of the amine and the carboxylic acid group is located on a side chain of an amino acid (e.g., the amide bond is not a backbone amide bond). In some embodiments, the cross-link is an amide bond formed between diaminopimelic acid and aspartic acid. In some embodiments, an amide cross-link is a lactam. In some embodiments, the cross-link is an oxime. In some embodiments, the cross-link is a hydrazone. In some embodiments, a cross-link comprises a covalent bond between a side chain

of an amino acid and a moiety of another amino acid, wherein one or both of the side chain and the moiety are modified to form the covalent bond. Such modifications may include, for example, oxidation, reduction, reaction with a catalyst to form an intermediate, or other modifications known to one of skill in the art.

[0164] A linker includes, for example, a molecule that is covalently bonded to at least two sites of a peptide, or between at least two peptides. A linker may bond to two sites within one peptide or between two separate peptides, or a combination of both. For example, a linker that comprises at more than two peptide-attachment sites may form both intra-peptide and inter-peptide bonds. In engineered polypeptides comprising at least two peptides and at least one linker, the peptides and linker may be connected in a variety of different configurations. For example, an engineered polypeptide may have peptide-linker-peptide-etc. pattern, ending with a peptide. In some embodiments, an engineered polypeptide comprises a linker that forms a branching point, for example a linker that is independently attached to three peptides. In some embodiments, an engineered polypeptide comprises a linker with three peptide-attachment sites, wherein the linker is only attached to two peptides.

[0165] In some embodiments, a linker comprises one or more amino acids. Amino acids that form part of a linker may, in some embodiments, be identified separately from the the engineered polypeptide. In certain embodiments, the linker is a region that separates and presents peptides of the engineered polypeptide in a structural, chemical, and/or dynamical manner that reflects the structure and/or function of a functional interface of the interface protein. In still further embodiments, the linker does not have a function on its own when not connected to the peptides of engineered polypeptide, for example does not exhibit binding to a binding partner of CD25. In some embodiments, each linker independently comprises at least one, at least two, at least three, at least four, at least five, at least six, or more amino acids. In some embodiments, each linker independently comprises one amino acid, two amino acids, three amino acids, four amino acids, five amino acids, or six amino acids. Amino acids that form part of a linker may be, in some embodiments, naturally occurring amino acids or non-naturally occurring amino acids. Each linker may, in some embodiments, independently comprise one or more alpha-amino acids, one or more beta-amino acids, or one or more gamma-amino acids, or any combinations thereof. In certain embodiments, a linker independently comprises a cyclic beta residue. Cyclic beta

residues may include, for example, APC or ACPC. In still further embodiments, a linker may comprise one or more glycine residues, one or more serine residues, or one or more proline residues. In some embodiments, a linker has an amino acid sequence selected from the group consisting of AP, GP, GSG, (GGGS)_n, (GSG)_n, GGSGGGGS, GGGSGGGGS, (PGSG)_n, and PGSGSG, wherein n is an integer between 1 and 10. In some embodiments, the engineered polypeptide comprises at least one linker, wherein each linker does not comprise amino acids, or wherein each linker does not comprise natural amino acids, or wherein each linker comprises at least one non-natural amino acid.

[0166] In some embodiments, a linker comprises a polymer. In some embodiments, the polymer is polyethylene glycol (PEG). A linker comprising PEG may comprise, for example, at least 3 PEG monomer units, at least 4 PEG monomer units, at least 5 PEG monomer units, at least 6 PEG monomer units, at least 7 PEG monomer units, at least 8 PEG monomer units, at least 9 PEG monomer units, at least 10 PEG monomer units, at least 11 PEG monomer units, at least 12 PEG monomer units, or greater than 12 PEG monomer units. In some embodiments of a linker comprising PEG, the PEG comprises between 3 to 12 monomer units, between 3 to 6 monomer units, between 6 to 12 monomer units, or between 4 to 8 monomer units. In some embodiments, the engineered polypeptide comprises at least one linker comprising PEG₃ (comprising 3 monomer units), PEG₆, or PEG₁₂. In some embodiments, at least one linker is independently PEG₃, PEG₆, or PEG₁₂. In further embodiments, the linker comprises a multi-arm PEG. For example, in certain embodiments, at least one linker independently comprises a 4-arm PEG, or an 8-arm PEG. In certain embodiments, each arm independently comprises between 3 to 12 monomer units, or between 3 to 6 monomer units, or between 6 to 12 monomer units, or between 4 to 8 monomer units. In certain embodiments, each arm of the multi-arm PEG comprises the same number of monomer units, for example a 4- or 8-arm PEG wherein each arm comprises 3 monomer units, 6 monomer units, or 12 monomer units.

[0167] In other embodiments, a linker comprises a dendrimer. Dendrimers include, for example, molecules with a tree-like branching architecture, comprising a symmetric core from which molecular moieties radially extend, with branch points forming new layers in the molecule. Each new branch point introduces a new, larger layer, and these radial extensions often terminate in functional groups at the exterior terminal surface of the dendrimer. Thus,

increasing the number of branch points in turn amplifies the possible number of terminal functional groups at the surface.

[0168] In some embodiments, at least one linker comprises a small molecule that is not an amino acid or polymer. In some embodiments, at least one linker comprises a benzodiazepine. In some embodiments, the linker comprises a moiety that is the product of a sulfhydryl-maleimide reaction, which may be a pyrrolidine dione moiety (for example a pyrrolidine-2,5-dione moiety). In some embodiments, the linker comprises an amidine moiety. In some embodiments, the linker comprises a thioether moiety.

[0169] In some embodiments, at least one linker comprises *trans*-pyrrolidine-3,4-dicarboxamide.

[0170] In some embodiments, wherein the engineered polypeptide comprises at least two linkers (e.g., in embodiments wherein the engineered polypeptide comprises at least two linking moieties wherein each linking moiety is independently a linker or a cross-link, or wherein each linking moiety is independently a linker), each linker is independently any of the linkers described herein. For example, in some embodiments, each linker is independently a linker comprising one or more amino acids, a linker comprising a polymer, a linker comprising a dendrimer, or a linker comprising a small molecule that is not an amino acid or polymer.

[0171] The one or more linking moieties of the engineered polypeptide may impart a particular structural or functional characteristic of interest, or a combination thereof. For example, in some embodiments a linking moiety is present in the engineered polypeptide to impart a structural characteristic, or a functional characteristic, or a combination thereof. Such structural characteristics may include, for example, increased structural flexibility, decreased structural flexibility, a directional feature, increased length, or decreased length. Directional features that may be of interest may include, for example, a structural turn, or maintaining a linear structure. Functional characteristics may include, for example, enhanced solubility, one or more protonation sites, one or more proteolytic sites, one or more enzymatic modification sites, one or more oxidation sites, a label, or a capture handle. In some embodiments, a linker

comprises one or more functional characteristics, or one or more structural characteristics, or a combinations thereof.

[0172] In some embodiments, one or more linkers independently introduce a structural “turn” into the engineered polypeptide. Examples of such linker include Gly-Pro, Ala-Pro, and *trans*-pyrrolidine-3,4-dicarboxamide. In some embodiments, one or more linkers present in the engineered polypeptide increases structural flexibility of the engineered polypeptide, compared to the linker not being present, or the selection of a different linker. For example, a linker that is longer and/or less sterically hindered than another linker may, in some embodiments, result in the molecule having greater structural flexibility than if the linker were not present, or if another linker were used instead. In other embodiments, one or more linking moieties independently decreases structural flexibility in the engineered polypeptide, such as including a linker that is shorter and/or more sterically hindered than another linker, or a cross-link at a location or of a type that reduces flexibility of one or more peptides. The presence of a cross-link at a particular location between certain peptides, or between certain amino acid side chains, may result in the molecule having less structural flexibility than if the cross-link was at a different location or between different side chains (e.g., a disulfide or an amide cross-link), or if the cross-link were not present.

d. Additional Components

[0173] In some embodiments, the engineered polypeptides provided herein comprise one or more additional components. For example, in some embodiments, the engineered polypeptide comprises one or more moieties that attach the engineered polypeptide to a solid surface, such as a bead or flat surface. In some embodiments, the attachment moieties comprise a polymer (such as PEG), or biotin, or a combination thereof. In some embodiments, attaching the engineered polypeptide to a solid surface may, for example, enable assessment of one or more characteristics of the engineered polypeptide, such as assessment of binding with a binding partner of CD25 (for example, an antibody to CD25).

e. Sequence Similarity

[0174] In some embodiments, the engineered polypeptide provided herein has one of the sequences listed in **Table 1**:

Table 1

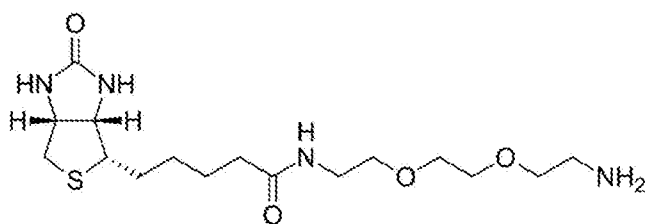
SEQ ID NO	Sequence
SEQ ID NO: 1	CDCQAQWTPGMRAPGYDPYCLNC
SEQ ID NO: 2	MVYCQPDCTAKCMHGCDRDTMKECCDRLK
SEQ ID NO: 3	DDCPEVPHATFKGPGQKWEGPGGGDCSK
SEQ ID NO: 4	DDCIEVPGPAECAERACRAQEERQRQPQCI
SEQ ID NO: 5	AEEKIKIEQKERKTTIKLAKEAK
SEQ ID NO: 6	CHLQIMTHGKIIYVPC
SEQ ID NO: 7	DDGDRCAKEHEIPHATGEECQKRDKS
SEQ ID NO: 8	CKQLVIYFTGNSSHSSVFYIYYDC
SEQ ID NO: 9	GSGDEDCKKFQSDDNWENYTSTRHLTFCDEKRS
SEQ ID NO: 10	GSGNEEIEKKIKDCTGNSSHSSWEEALECALKK
SEQ ID NO: 11	GSGDERIERLIKECTGNSSHSSWEEALECALRR
SEQ ID NO: 12	GSGSHPCAYWRWVIKMTHGKTRWVLELVFCYRD
SEQ ID NO: 13	GSGKCEEEAKKIASKMTHGKTREEEAEEYLKKC
SEQ ID NO: 14	GSGDDESEKRTTERDTRKCTKAKANDNQCPTE
SEQ ID NO: 15	GSGSSEWDKWVEEWYKKMCTEAKKNDNQCPTEK
SEQ ID NO: 16	GSGQCRVWVFRNGDKILYIYEDCDNDNQHQQTL

[0175] In some embodiments, the engineered polypeptide has at least 60% sequence similarity with any one of SEQ ID NOS: 1-21. In some embodiments, the engineered polypeptide has at least 70% sequence similarity with any one of SEQ ID NOS: 1-21. In some

embodiments, the engineered polypeptide has at least 80% sequence similarity with any one of SEQ ID NOS: 1-21. In some embodiments, the engineered polypeptide has at least 90% sequence similarity with any one of SEQ ID NOS: 1-21. In some embodiments, the engineered polypeptide has at least 95% sequence similarity with any one of SEQ ID NOS: 1-21. In some embodiments, the engineered polypeptide comprises any one of SEQ ID NOS: 1-21. In certain embodiments, the engineered polypeptide has any one of SEQ ID NOS: 1-21.

[0176] In some embodiments, the engineered polypeptide comprises any one of SEQ ID NOS: 1-21; and is modified at the N terminus, or the C terminus, or both. For example, in some embodiments the C terminus or the N terminus is covalently bonded to another molecule. In still further embodiments, the engineered polypeptide comprises any one of SEQ ID NOS: 1-21; and one or more amino acids at the N terminus or the C terminus, or both.

[0177] In some embodiments, the N-terminal molecule is a biotin-PEG₂:



[0178] In some embodiments, the C-terminal molecule is a linker followed by biotin (*e.g.* a –GSGSGK-Biotin). Other linkers suitable for attaching biotin to the C-terminus of the engineered polypeptide include GSG, GSS, GGS, GGSGGS, GSSGSS, GSGK, GSSK, GGSK, GGSGGSK, GSSGSSK, and the like.

V. Methods of Selecting an Engineered polypeptide

[0179] Further provided herein are methods of selecting an engineered polypeptide as described herein. Such methods may include, for example, using an iterative optimization of engineered polypeptide structural characteristics.

[0180] In some embodiments, one or more sections of CD25 are identified as the target interface. In some embodiments, at least a portion of the identified section(s) binds to an

antibody of CD25. Thus, for example, in some embodiments a portion of CD25 that is an epitope for one or more antibodies is identified as the target interface. In other embodiments, a section of CD25 is identified as the target interface that does not bind to an antibody, or for which it is unknown if antibody binding occurs. In certain embodiments, the crystal structure for at least a portion of CD25 is unknown, and the initial selection of a target interface includes molecular dynamics simulations of CD25 and CD25 binding. In some embodiments, one or more initial input sequences are obtained from the identified section or sections, wherein each sequence is independently continuous or discontinuous. In developing an engineered polypeptide candidate, at least some of the interface residues of each sequence are retained, and one or more linking moieties are incorporated into the sequence to provide desired structural and dynamic characteristics. In some embodiments, one or more non-interface residues are added to the sequence, or one or more residues in the input sequence are replaced with one or more non-interface residues, to achieve desired structural and dynamic characteristics relative to the cognate target structure and dynamics. In some embodiments, these non-interface residues are not from the target interface of CD25, or do not share one or more characteristics with the target interface of CD25, or share fewer characteristics and/or share characteristics less strongly with the target interface of CD25 than the retained interface residues. These intermediate, non-interface residues may, in some embodiments, form part or all of an amino acid linker.

[0181] Next, in some embodiments the initial design (or multiple designs) is produced and the molecular dynamics simulated to determine flexibility and overall stability of the design. If this initial design does not meet RMSD requirements, it may undergo iterative optimization of one or more linking moieties (such as one or more cross-links, or intermediate linker residues) using computational mutagenesis, in some embodiments. During this optimization, in some embodiments the interface residues are fixed while one or more of the linking moieties is changed, or removed, or added. The iterative optimization may be repeated until the engineered polypeptide RMSD interface residue positions relative to the target interface and structural order metric meet certain requirements (for example, ≤ 6.0 Å and ≥ 0.25 , respectively, wherein structural order is on a 0-1 normalized scale, where 1 = perfect structural stability).

[0182] In some embodiments, the intermediate structural stability residue regions can range from 1-50 amino acids in length. In certain embodiments, these intermediate structural stability

residue regions are linkers, for example amino acid linkers. In some embodiments, the relatively small size of an engineered polypeptide produced by certain embodiments of the methods provided herein (compared, for example, to approaches that graft an interface onto a large structurally stabilizing scaffold) may enable chemical synthesis of the molecule, in contrast to a larger molecule that may require an *in vitro* expression system. Furthermore, in some embodiments the methods provided herein enable the incorporation of non-natural amino acids into intermediate positions or the interface positions, which may allow for fine control of interface engineering with novel moieties and properties such as post-translational modifications, solubility, cell-permeability, enzyme reactivity, pH sensitivity, oxidation sensitivity, etc. In still further embodiments, an engineered polypeptide may be selected with a higher likelihood of species cross-reactivity or disease-related mutation reactivity in selected antibodies when the engineered polypeptide is used as an immunogen or epitope-bait.

[0183] In some embodiments, the optimized molecule is the engineered polypeptide provided herein. In other embodiments, the optimized molecule is a candidate engineered polypeptide that may undergo further evaluation, further adjustment, or be used to generate a peptide library or a candidate engineered polypeptide library, or any combinations thereof. In certain embodiments, the method further includes using the engineered polypeptide candidate to generate a peptide library, or an engineered polypeptide candidate library, and then contacting the library with a binding partner of CD25 (such as an antibody to CD25). The peptide library may include, for example, peptides which are smaller than and share at least some sequence similarity with the engineered polypeptide candidate, and in which certain residues are optionally replaced with other residues. An engineered polypeptide candidate library may include, for example, variations of the engineered polypeptide candidate.

[0184] In some embodiments, the peptides of the peptide library comprise between 2 to 15 amino acids, between 5 to 15 amino acids, between 10 to 15 amino acids, between 2 to 10 amino acids, or between 5 to 10 amino acids. In some embodiments, the total number of amino acids in each peptide of the library includes both the interface amino acids and structural amino acids, which may include, for example, linker amino acids. The engineered polypeptide candidate library may be prepared by, for example, varying one or more amino acids or linking moieties in the candidates to make new library members. The engineered polypeptide candidates in the

engineered polypeptide candidate library, in some embodiments, independently comprise between 5 to 40 amino acids, between 10 to 35 amino acids, between 15 to 35 amino acids, or between 20 to 30 amino acids. In some embodiments, the total number of amino acids in each engineered polypeptide candidate of the candidate library can, in some embodiments, include both the interface amino acids and structural amino acids, which may include, for example, linker amino acids. The peptide library and the engineered polypeptide candidate library can, in some embodiments, independently comprise between 5,000 and 100,000 members, between 5,000 and 80,000 members, between 5,000 and 60,000 members, between 5,000 and 40,000 members, between 5,000 and 30,000 members, between 10,000 and 25,000 members, between 15,000 and 20,000 members, or about 17,000 members (e.g., distinct peptides or distinct engineered polypeptide candidates). In some embodiments, multiple separate libraries are produced and evaluated. In certain embodiments, the library members do not comprise certain cross-links. For example, in some embodiments, a library is evaluated wherein the library members do not have disulfide cross-links.

[0185] In some embodiments, to produce candidates for a candidate library, one or more linking moieties is added or removed, or location changed, in the design of the original engineered polypeptide candidate. For example, in some embodiments, a disulfide cross-link is removed, or is added, or the location of which is moved. In other embodiments, a lactam cross-link is removed, or is added, or the location of which is moved. In some embodiments, one or more amino acid residues is replaced. The binding of a CD25 binding partner to the peptide library, or engineered polypeptide candidate library, or both (if present), can provide additional information that may be used to further refine the design of the engineered polypeptide, or to select an engineered polypeptide. Additional information from screening these libraries may, for example, be used to make changes to the engineered polypeptide, for example to increase binding affinity with a binding partner of CD25. The engineered polypeptide candidate library can, in some embodiments, provide additional information regarding the effect of certain linker moieties on binding interactions (including presence or location of such moieties), such as cross-links including disulfide bonds and lactams. The peptide or engineered polypeptide candidate libraries, or both, may in some embodiments be used to identify common motifs (e.g., amino acid patterns or linking moieties, or combinations thereof) that may increase binding affinity or

binding specificity for a binding partner of CD25, or provide other desired characteristics. Evaluating the binding of the cognate binding partner with the members of the peptide or the engineered polypeptide candidate libraries, or both, can provide additional structural and functional information, which may be used to further refine the engineered polypeptide design or to select an engineered polypeptide candidate.

a. Selection by Binding under Variable pH

[0186] In some embodiments, an engineered polypeptide is selected based, at least in part, on structural flexibility at physiological pH compared to structural flexibility at a lower pH. For example, CD25 may be overexpressed on tumor cells, and therefore binding of an antibody to CD25 with greater affinity in a tumor microenvironment may be desired in some embodiments. Therefore, in some embodiments, it may be desirable to select an engineered polypeptide that is more rigid at lower pH, or in which one or more amino acids have a particular orientation at lower pH, or has greater binding affinity or binding selectivity at lower pH, compared to the same engineered polypeptide at physiological pH. In many cancerous tumors, the growth rate of cancerous cells can outpace the oxygen supply available in portions of the tumor, resulting in a hypoxic microenvironment within the tumor. The level of oxygen in tissues can affect the pH of the tissue environment, and hypoxic levels can lead to decreased pH (including, for example, by the buildup of acidic metabolites from anaerobic glycolysis). Thus, in some embodiments, selecting an engineered polypeptide that has greater binding at low pH (e.g., has desirable structural characteristics that lead to binding interactions), but has reduced binding at physiological pH (e.g., has decreased, fewer, or no desirable structural characteristics that lead to binding interactions), can, in some embodiments, result in an engineered polypeptide that can produce an antibody with greater binding to the desired target in a tumor, compared to binding not in a tumor. Physiological pH is typically between about 7.35 and about 7.45, for example about 7.4. The pH of a tumor microenvironment may be, for example, less than about 7.45, less than about 7.45, between about 7.45 and about 6.0, between about 7.0 and about 6.0, between about 6.8 and about 6.2, between about 6.7 and about 6.3, about 6.4, about 6.5, about 6.6, about 6.7, about 6.8, about 6.9 or about 7.0. In some embodiments, an engineered polypeptide can be evaluated at different pHs using computational methods, for example molecular dynamics simulations. In other embodiments, an engineered polypeptide is selected based on differential

pH characteristics using an *in vitro* method. Suitable *in vitro* methods may include, for example, phage panning at different pHs. For example, an antibody phage display library can be used to pan one or more engineered polypeptides at physiological pH, and phage that bind at that pH can be discarded. Then, a second round of panning can be carried out at a lower pH, and phage that bind to the one or more engineered polypeptides at the lower pH can be selected. In some embodiments, engineered polypeptides which bind to no phage at a lower pH, or which bind to phage with similar affinity at both low and physiological pH, may be less desirable for use in generating an antibody that targets tumor cells.

b. Inverse Peptide Evaluation

[0187] In still further embodiments, selecting an engineered polypeptide may include comparing the binding of the engineered polypeptide to binding of an inverse engineered polypeptide. An inverse engineered polypeptide may be based on the engineered polypeptide, but replacing one or more of the interface-interacting amino acid residues (e.g., based on the surface of CD25) with an amino acid that exhibits an inverse characteristic. For example, an amino acid with a large, sterically bulky, hydrophobic side chain may be replaced with an amino acid that has a smaller side chain, or hydrophilic side chain, or a side chain that is both smaller and hydrophilic. In some embodiments, an amino acid with a hydrogen bond-donating side chain may be replaced with an amino acid that has a hydrogen bond-accepting side chain, or with an amino acid that has a side chain that does not hydrogen bond. Binding characteristics that may be compared using the engineered polypeptide and the inverse engineered polypeptide may include, in some embodiments, specificity and/or affinity. Comparing the binding characteristics of a engineered polypeptide with the binding characteristics of an inverse engineered polypeptide may, in some embodiments, help select engineered polypeptides in which the interface-interacting amino acids drive the binding interactions, rather than characteristics of a linking moiety such as a linker. Engineered polypeptides in which binding is driven by a linking moiety such as a linker may be less desirable in some embodiments as they may exhibit off-target binding, or other undesirable binding characteristics.

[0188] In further embodiments, the method further comprises modifying the selected engineered polypeptides.

c. Binding Evaluation

[0189] As described herein, in some embodiments, the method of selecting an engineered polypeptide provided herein comprises evaluating the binding of an engineered polypeptide candidate to a protein or fragment thereof, for example a binding partner of CD25 (such as an antibody to CD25). For example, in some embodiments, an engineered polypeptide candidate library or peptide library is screened for binding to a binding partner of CD25.

[0190] Binding of a protein or fragment thereof (e.g., a binding partner of CD25) with one or more peptides or engineered polypeptide candidates (such as a member of a library) may be evaluated in various ways. In some embodiments, binding is directly evaluated, for example by directly detecting a label on the protein or fragment thereof. Such labels may include, for example, fluorescent labels, such as a fluorophore or a fluorescent protein. In other embodiments, binding is indirectly evaluated, for example using a sandwich assay. In a sandwich assay, a peptide or engineered polypeptide candidate (such as a member of a library) binds to a binding partner, and then a secondary labeled reagent is added to label the bound binding partner. This secondary labeled reagent is then detected. Examples of sandwich assay components include His-tagged-binding partner detected with an anti-His-tag antibody or His-tag-specific fluorescent probe; a biotin-labeled binding partner detected with labeled streptavidin or labeled avidin; or an unlabeled binding partner detected with an anti-binding-partner antibody.

[0191] In some embodiments, peptides or engineered polypeptide candidates of interest are identified based on the binding signal, or dose-response, using any number of available detection methods. These detection methods may include, for example, imaging, fluorescence-activated cell sorting (FACS), mass spectrometry, or biosensors. In some embodiments, a hit threshold is defined (for example the median signal), and any with signal above that signal is flagged as a putative hit motif.

[0192] For the development of the combinatorial library, peptides identified from the peptide library based on binding with the protein or fragment thereof may, in some embodiments, be further clustered into distinct groups using sequence or structural information, or a combinations thereof. This grouping may be done, for example, using generally available sequence alignment, chemical descriptors, structural prediction, and entropy prediction informatics tools (e.g.

MUSCLE, CLUSTALW, PSIPRED, AMBER, Hydropathy Calculator, and Isoelectric Point Calculator) and clustering algorithms (e.g., K-Means, Gibbs, and Hierarchical). Clusters of motifs (e.g., structural or functional motifs) present in peptide hits can be identified from this analysis. Individual peptide motif hits can also be identified. Using these motif clusters and individual motifs, in some embodiments, design rules can be formulated that define one or more of sequence, structure, and chemical characteristics of the motifs that appear to drive the protein interactions at the target interface. In some embodiments, the structure of the target interface is not necessary for identification of these interface motif design rules. Rather, the design rules can, in some embodiments, be derived from analysis of peptides identified from screening the peptide library.

[0193] In some embodiments, the binding assay has a sensitivity dynamic range of about 10^5 . Thus, in some embodiments, an engineered polypeptide candidate is identified as of interest if it has a binding event with a CD25 binding partner that is within a 10^5 signal bracket of the native CD25:binding partner signal. The type of signal may be different depending on what type of assay is being used, or how it is being evaluated. For example, in some embodiments, the signal is response units in a sensorgram, fluorescence signal in an image-based readout, or enzymatic readout in an enzyme-based assay. The signal for binding events may be measured relative to CD25:binding partner signal.

[0194] In some embodiments, the engineered polypeptide candidate is modified prior to evaluating binding. For example, in some embodiments, biotin, PEG, or another attachment moiety, or combination thereof, is bonded to the C terminus or the N terminus of the peptide to enable it to be used with a binding evaluation system. For example, in some embodiments biotin-PEG12- is covalently attached to the N-terminus of the engineered polypeptide. In other embodiments, the engineered polypeptide candidate is modified at the C terminus with -GSGSGK-PEG4-biotin. In certain embodiments, such a biotin-modified engineered polypeptide candidate is then bound to a streptavidin bead through the biotin moiety, and the bead-supported immunogen is evaluated for binding to a binding partner of CD25.

VI. Use of Engineered polypeptides and CD25 antibodies

[0195] The engineered polypeptides provided herein, and identified by the methods provided herein, may be used, for example, to produce one or more antibodies that bind specifically to CD25. In some embodiments, the antibody is a monoclonal or polyclonal antibody.

[0196] The term “antibody,” as used herein, refers to a protein, or polypeptide sequences derived from an immunoglobulin molecule, which specifically binds to an antigen. Antibodies can be intact immunoglobulins of polyclonal or monoclonal origin, or fragments thereof and can be derived from natural or from recombinant sources.

[0197] The terms “antibody fragment” or “antibody binding domain” refer to at least one portion of an antibody, or recombinant variants thereof, that contains the antigen binding domain, *i.e.*, an antigenic determining variable region of an intact antibody, that is sufficient to confer recognition and specific binding of the antibody fragment to a target, such as an antigen and its defined epitope. Examples of antibody fragments include, but are not limited to, Fab, Fab', F(ab')₂, and Fv fragments, single-chain (sc)Fv (“scFv”) antibody fragments, linear antibodies, single domain antibodies (abbreviated “sdAb”) (either VL or VH), camelid VHH domains, and multi-specific antibodies formed from antibody fragments.

[0198] The term “scFv” refers to a fusion protein comprising at least one antibody fragment comprising a variable region of a light chain and at least one antibody fragment comprising a variable region of a heavy chain, wherein the light and heavy chain variable regions are contiguously linked via a short flexible polypeptide linker, and capable of being expressed as a single polypeptide chain, and wherein the scFv retains the specificity of the intact antibody from which it is derived.

[0199] “Heavy chain variable region” or “VH” (or, in the case of single domain antibodies, *e.g.*, nanobodies, “VHH”) with regard to an antibody refers to the fragment of the heavy chain that contains three CDRs interposed between flanking stretches known as framework regions, these framework regions are generally more highly conserved than the CDRs and form a scaffold to support the CDRs.

[0200] Unless specified, as used herein a scFv may have the VL and VH variable regions in either order, *e.g.*, with respect to the N-terminal and C-terminal ends of the polypeptide, the scFv may comprise VL-linker-VH or may comprise VH-linker-VL.

[0201] The term “antibody light chain,” refers to the smaller of the two types of polypeptide chains present in antibody molecules in their naturally occurring conformations. Kappa (“K”).

[0202] Thus, in some embodiments, provided herein is an antibody produced by immunizing an animal with an immunogen, wherein the immunogen is an engineered polypeptide as provided herein. In some embodiments, the animal is a human, a rabbit, a mouse, a hamster, a monkey, etc. In certain embodiments, the monkey is a cynomolgus monkey, a macaque monkey, or a rhesus macaque monkey. Immunizing the animal with an engineered polypeptide can comprise, for example, administering at least one dose of a composition comprising the immunogen and optionally an adjuvant to the animal. In some embodiments, generating the antibody from an animal comprises isolating a B cell which expresses the antibody. Some embodiments further comprise fusing the B cell with a myeloma cell to create a hybridoma which expresses the antibody. In some embodiments, the antibody generated using the engineered polypeptide can cross react with a human and a monkey, for example a cynomolgus monkey.

[0203] In certain embodiments, the method of generating an antibody further comprises determining one or more epitopes for the antibody. In some embodiments, the method comprises screening the antibody for binding to two or more epitopes, for example by contacting an epitope library with the antibody, and evaluating binding of the antibody to epitopes of the library. In certain embodiments, an antibody that binds to two or more epitopes is discarded. In some embodiments, the engineered polypeptide mimics one epitope of CD25. In other embodiments, the engineered polypeptide mimics two or more epitopes of CD25. In certain embodiments, screening an antibody for binding to two or more epitopes, wherein the engineered polypeptide mimics two or more epitopes of the CD25, comprises contacting an epitope library with the antibody, and evaluating binding of the antibody to epitopes of the library, and discarding one or more antibodies that binds to two or more epitopes, wherein the epitopes are not those mimicked by the engineered polypeptide.

[0204] In some embodiments, the antibody produced using an engineered polypeptide as provided herein binds specifically to CD25. In certain embodiments, the antibody does not block binding of IL-2 with CD25 when the antibody is bound to CD25.

[0205] In some embodiments, the antibody is a non IL-2-blocking antibody (a non IL-2 blocker) – that is, the binding of the antibody to CD25 does not disrupt or prevent binding of the IL-2 ligand to CD25 (the IL-2 alpha chain), and does not affect IL-2 mediated signal transduction, e.g. signaling through the IL-2/JAK3/STAT-5 signaling pathway. In some embodiments, the antibody does not disrupt the binding of IL-2 ligand to CD25 (IL-2 alpha chain), and binds to a different epitope than where the 7G7B6 antibody binds. In some embodiments, the antibody does not disrupt the binding of the IL-2 ligand to CD25 (IL-2 alpha chain), but does disrupt the trimerization of the beta, gamma, and alpha (CD25) chains of the IL-2 receptor.

[0206] In some embodiments, the antibody is an IL-2 blocking antibody, e.g., the antibody disrupts or prevents binding of the IL-2 ligand to the alpha, beta, and/or gamma chains of the receptor, and decreases or inhibits IL-2 mediated signal transduction. In certain embodiments, the antibody disrupts or prevents binding of the IL-2 ligand to CD25. In some embodiments, the antibody disrupts or prevents the binding of the IL-2 ligand to CD25, and binds to a different epitope than to which either daclizumab or basiliximab bind.

[0207] In some embodiments, the CD25 antibody is a partially blocking antibody, and partially, but not completely, disrupts binding of the IL-2 ligand to the alpha, beta, and/or gamma chains of the IL-2 receptor (CD25), and/or partially, but not completely decreases IL-2 mediated signal transduction.

[0208] In some embodiments, the antibody disrupts or prevents heterotrimerization of the alpha, beta, and gamma IL-2 chains. In some embodiments, the antibody does not block binding of the IL-2 ligand with CD25, but does disrupt or prevent heterotrimerization of the alpha, beta, and gamma IL-2R chains. In certain embodiments, the antibody selectively binds to Treg cells. In other embodiments, the antibody selectively binds to Teff cells.

[0209] In still further embodiments, whether an antibody produced using an engineered polypeptide as provided herein blocks binding of CD25 with IL-2 is evaluated. In some embodiments, an antibody that does not block CD25 binding with IL-2 is selected. In other embodiments, an antibody that does block binding of CD25 with IL-2 is selected. Such blocking or non-blocking may be evaluated, for example, by coupling CD25 to a biosensor tip, and evaluating binding by the antibody in the presence and absence IL-2. In some embodiments, the an antibody is expressed with a 6xHis tag that can be used with Ni-NTA in flow cytometry to evaluate binding of the antibody, and blocking or non-blocking of IL-2 binding to CD25. In certain embodiments, the binding of the antibody is evaluated at physiological pH (e.g., between about pH 7.3 and about pH 7.5, or about pH 7.4), and also at the pH of a tumor microenvironment (e.g., between about pH 6.4 and about pH 6.6, or about pH 6.5). In certain embodiments, the blocking/non-blocking activity is compared to the binding of an IL-2 blocker antibody (for example, daclizumab or baciliximab). In certain embodiments, the blocking/non-blocking activity is compared to the binding of an IL-2 non-blocker antibody (for example, antibody 7G7B6). In certain embodiments, the blocking/non-blocking activity is compared to both an IL-2 blocking antibody and an IL-2 non-blocking antibody.

[0210] In some embodiments, the antibody is an agonist antibody to CD25. In other embodiments, the antibody is an antagonist antibody to CD25.

[0211] In some embodiments, the antibody binds to CD25 in the trans orientation. In other embodiments the antibody binds to CD25 in the cis orientation. In still further embodiments, the antibody is capable of binding to CD25 in either the cis or the trans configuration.

[0212] The antibody clone of origin can be identified by the ID shown, *e.g.* the Clone ID in Table 2. For example, the antibody may comprise the heavy chain complementary determining regions of antibody clone “YU389-A01” as presented in row 1 of Table 2.

[0213] In some embodiments, the antibody has a CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3, each independently selected from those disclosed in **Table 2**.

Table 2

Clone ID	Heavy Chain CDR 1	Heavy Chain CDR 2	Heavy Chain CDR 3	Light Chain CDR 1	Light Chain CDR 2	Light Chain CDR 3
YU389-A01	GGTFSSYA	IIPIFGTA	AREMYYYYGMDV	QSISSY	AAS	QSYSTP PT
YU389-A02	GGTFSSYA	IIPIFGTA	AREMYYYYGMDV	QSISSY	AAS	QSYSTP PT
YU389-A03	GGSISSGGY Y	IYYSGST	ARGNLWSGYF	SSNIGNNF	DST	GSWDTN LSGYV
YU389-A05	GGTFSSYA	IIPIFGTA	AREMYYYYGMDV	QSISSY	AAS	QSYSTP PT
YU389-A07	GGTFSSYA	IIPIFGTA	AREMYYYYGMDV	QSISSY	AAS	QSYSTP PT
YU389-B11	GGTFSSYA	IIPIFGTA	AREMYYYYGMDV	QSISSY	AAS	QSYSTP PT
YU389-D07	GGTFSSYA	IIPIFGTA	AREMYYYYGMDV	QSISSY	AAS	QSYSTP PT
YU390-A11	GFTFSSYG	ISYDGSNK	AKELLEGAFDI	NIETKS	DDD	QVWDSS SGHREV
YU390-A12	GYTFTSY Y	INPSGGST	ARDRVTMVRGAL Y	KLGDY	KDN	QAWDSS TYV
YU390-B12	GFTFSSYG	ISYDGSNK	AKELLEGAFDI	NIETKS	DDD	QVWDSS SGHREV
YU390-C03	GGTFSSYA	IIPIFGTA	AREMYYYYGMDV	QSISSY	AAS	QSYSTP PT
YU390-C11	GYTFTSYG	ISAYNGNT	ARERSYYGMDV	QSVSNY	GAS	QQYNHW PPL
YU390-D01	GGTFSSYA	IIPIFGTA	AREMYYYYGMDV	QSISSY	AAS	QSYSTP PT
YU390-D03	GGTFSSYA	IMPIFDTA	ASWSERIGYQYGL DV	QTISQW	KAS	QQYSGD SMYT
YU390-D05	GGTFSSYA	IIPIFGTA	AREMYYYYGMDV	QSISSY	AAS	QSYSTP PT
YU390-D11	GYTFTSYG	ISAYNGNT	ARERSYYGMDV	QSVSNY	GAS	QQYNHW PPL
YU390-G03	GGTFSSYA	IIPIFGTA	AREMYYYYGMDV	QSISSY	AAS	QSYSTP PT
YU390-H11	GYTFTSYG	ISAYNGNT	ARERSYYGMDV	QSVSNY	GAS	QQYNHW PPL
YU392-A05	GYTFTSY Y	INPSGGST	ARDILGLDY	SSNIGSNY	RNN	AAWDDS LSGV
YU392-A07	GYTFTDY	VPEDGET	ATEDTAMGGIDY	SSNIGSNY	SNN	AAWDDS LNGV
YU392-A09	GYTFTDY	VPEDGET	ATEGRYGM DV	NFNIGNNL	AND	ATWDDS LSGV
YU392-B11	GYTFTDY	VPEDGET	AVEGGRAPGTYYY DSSGLAY	SSNIGSNY	SNN	ATWDDS LSGV
YU393-A01	GGSISSGGY S	IYHSGST	ARAGYYYGMDV	RNIWSY	GAS	QQSHSTP IT
YU393-A02	GGTFSSYA	IIPIFGTA	ARDLGT MVRGVIE PYYFDY	QSISSW	DAF	QQYNSY SRT

Clone ID	Heavy Chain CDR 1	Heavy Chain CDR 2	Heavy Chain CDR 3	Light Chain CDR 1	Light Chain CDR 2	Light Chain CDR 3
YU393-A03	GGSISSSNW	IYHSGST	ARGVRGTGFDP	QSVSSR	GAS	QQYTNW PQT
YU393-A04	GYTFTSYG	ISAYNGNT	ARDRNGYFQH	QTISGL	GAS	LQYDRY SGA
YU393-A08	GFTFSSYG	ISYDGSNK	AKDLLGELSFFDY	DIESEM	DDS	QVWHHT NDHVL
YU393-A09	GYSFTSYW	IYPGDSDT	ARLENNWDYGGW FDP	NIGSKS	DDS	QVWDSS SDHWV
YU393-A11	GYSFTSYW	IYPGDSDT	ARLENNWDYGGW FDP	NIGSKS	DDS	QVWDSS SDHWV
YU393-B02	GGTFSSYA	IPIFGTA	ARDRSYYGMDV	QSIGNY	AAT	QQSKQIP YT
YU393-B03	GGTFSSYA	IPIFGTA	ARDKGYYGMDV	QGISSW	AVS	QQSYSLP LT
YU393-B04	GGTFSSYA	IPIFGTA	ARDRSYYGMDV	QSIGNY	AAT	QQSKQIP YT
YU393-B05	GFTFSNYG	ISHDGHVK	AKEISPRSSVGWPL DY	QSVSSTY	GAS	QQFDISG GLI
YU393-B06	GFTFSSSA	ISYDGSNK	ARDFWSGYNELGG MDV	QDISNY	DAS	QQYDNL PLT
YU393-B07	GFTFSSYW	IKQDGSEK	ARTWFGEFFDY	NIESES	DDS	QVWDSS SDHTVA
YU393-B08	GYTFTSYG	ISAYNGNT	ARVIGGWFDY	SSDVGAY NY	GVS	SSYTTTD TFV
YU393-C02	GFIFSRHA	ISYDGSNK	ARGRLAYGDTEGF DY	QDINNY	DAS	QQYDNL PYT
YU393-C03	GYTFNNYG	ISVYNGDI	ARDILRGESSILDH	QGISNS	AAS	QQYYSTP PH
YU393-C05	GGTFSSYA	IPIFGTA	ARDRYYYGMDV	QSISSY	AAS	QQSYSTP LT
YU393-C07	GFTFSSYA	ISYDGSNK	ARDLLGSGYDIIDY	NIGSKS	DDS	QVWDSS SDHVV
YU393-C08	GYTFTSYG	ISAYNGNT	ARVWGKNGDFDY	SSNIGNNY	DNN	GTWDSS LSAYV
YU393-D03	GYTFTTYA	INTNTGDP	ARDRFHYGMDV	EGIRTS	GAS	QQTHTW PWT
YU393-D04	GYTFTSYG	ISAYNGNT	ARDRGDY	QGTSSW	AAS	QQANSFP LT
YU393-D05	GFTFNNAW	IKSKTDGG TT	TTEGVLLSFGGAP FDY	QSISSY	AAS	QQSYSTP YT
YU393-D07	GFTFSSYE	ISSSGSTI	ARRRRGGGFDY	SSDVGGY NY	DVS	SSYTSSS TYV
YU393-E04	GFTFSSYW	IKQDGSEK	AREKGSWFDP	QSVSNYY	GAS	QRYGSSP R
YU393-E05	GGTFSSYA	IPIFGTA	ARDKGYYGMDV	QGINSY	AAS	QQVHSFP FT
YU393-E07	GFTFSSYG	ISSRGSTI	ARDRGDRVGGLVF DY	NIGSKS	DDS	QVWDSS SDHVV
YU393-F03	GYSFTTYW	IYPGDSDT	ARQVAGGLDY	QAVRID	GAS	LQHNTFP YT

Clone ID	Heavy Chain CDR 1	Heavy Chain CDR 2	Heavy Chain CDR 3	Light Chain CDR 1	Light Chain CDR 2	Light Chain CDR 3
YU393-F04	GYTFTSYG	ISAYNGNT	ARDRGYYGMDV	QSI SRY	AAS	QQSHSTP LT
YU393-F06	GYSFTSYW	IYPGDSDT	FRFGEGFDY	QSIGYW	RAS	QQYNSY PFT
YU393-F07	GYSFTTYW	IYPGDSDT	ARQVAGGLDY	SSNVGSN Y	RNN	AAWDDS LSGVV
YU393-G01	GYSFNTYW	IYPSDSDT	ARDGGYYFDD	QSVSSTY	GTS	QQYNSSP LMYT
YU393-G03	GGTFSSYA	IIPFGTA	ARDKGYGMDV	QSIKNY	AAS	QQTYSTP LT
YU393-G04	GYTFTSYG	ISAYNGNT	ARDFRMDV	QDIKRR	DAS	QQANTFP QT
YU393-G07	GFTFRRYW	IKQDGSEK	ARDAYAYGLDV	SGSIASSY	EDN	QSYDGSS VV
YU393-G08	GYSFTSYW	IYPGDSDT	ARLENNWDYGGW FDP	NIGSKS	DDS	QVWDSS SDHWV
YU393-G11	GYSFTSYW	IYPGDSDT	ARLENNWDYGGW FDP	NIGSKS	DDS	QVWDSS SDHWV
YU393-G12	GYSFTSYW	IYPGDSDT	ARLENNWDYGGW FDP	NIGSKS	DDS	QVWDSS SDHWV
YU393-H03	GGSISSN W	IYHSGST	ARDLMNYGMDV	QSISSY	AAS	QQSYSTP PT
YU393-H07	GFTFSSYA	ISYDGSNK	ARDLLGSGYDIIDY	NIGSKS	DDS	QVWDSS SDHVV
YU393-H09	GYSFTSYW	IYPGDSDT	ARLENNWDYGGW FDP	NIGSKS	DDS	QVWDSS SDHWV
YU394-A01	GFTFSSYW	IKQDGSEK	AREYDYG DYVFDY	NSNVGN Y	DND	GSWEAR ESV FV
YU394-A02	GYSFTSYW	IYPGDSDT	ARLENNWDYGGW FDP	NIGSKS	DDS	QVWDSS SDHWV
YU394-A07	GYSFTSYW	IYPGDSDT	ARLENNWDYGGW FDP	NIGSKS	DDS	QVWDSS SDHWV
YU394-A09	GGTFSSYA	IIPFGTA	AREMYYYYGMDV	QSISSY	AAS	QQSYSTP PT
YU394-C01	GYSFTSYW	IYPGDSDT	ARLENNWDYGGW FDP	NIGSKS	DDS	QVWDSS SDHWV
YU394-E02	GYSFTSYW	IYPGDSDT	ARLENNWDYGGW FDP	NIGSKS	DDS	QVWDSS SDHWV
YU394-H01	GYSFTSYW	IYPGDSDT	ARLENNWDYGGW FDP	NIGSKS	DDS	QVWDSS SDHWV
YU394-H03	GYSFTSYW	IYPGDSDT	ARLENNWNYGGW FDP	NIGSKS	DDS	QVWDSS SDHWV
YU394-H04	GYSFTSYW	IYPGDSDT	ARLENNWDYGGW FDP	NIGSKS	DDS	QVWDSS SDHWV
YU394-H05	GYSFTSYW	IYPGDSDT	ARLENNWNYGGW FDP	NIGSKS	DDS	QVWDSS SDHWV
YU394-H07	GGTFSSYA	IIPFGTA	ARDYYYYGMDV	QSI SRY	GAS	QQT YND PPT
YU395-A02	GGTFSSYA	IIPFGTA	AREMYYYYGMDV	QSISSY	AAS	QQSYSTP PT

Clone ID	Heavy Chain CDR 1	Heavy Chain CDR 2	Heavy Chain CDR 3	Light Chain CDR 1	Light Chain CDR 2	Light Chain CDR 3
YU395-B12	GYTFSSYG	ISAYNGNT	ARDIGYYYGMDV	SLRSYY	GKN	NSRDSSG NHVV
YU395-C06	GGTFSSYA	IPIFGTA	AREMYYYYGMDV	QSIISNY	AAS	QQSYSTP PT
YU395-C08	GGTFSSYA	IPIFGTA	AREMYYYYGMDV	QSISSY	AAS	QQSYSTP PT
YU395-D05	GGTFSSYA	IPIFGTA	AREMYYYYGMDV	QSIISNY	AAS	QQSYSTP PT
YU396-B12	GYSFSTYW	IYPGDSDT	ARVGDGYSLDY	KLGERF	QYI	QTDWDSI VV
YU396-C03	GFTFSSYG	ISYDGSNK	AKAITSIEPY	SGSVSTSY Y	NTD	VLYMGS GIWV
YU396-C12	GYSFSTYW	IYPGDSDT	ARVGDGYSLDY	SSNIGRNY	RNH	ATWDDA LSGWV
YU396-G10	GGTFSSYA	IPIFGTA	AREMYYYYGMDV	QSISSY	AAS	QQSYSTP PT
YU396-H12	GFAFSSYG	ISYDGSNK	AKGQGDGMDV	SSDVGGY NY	GVS	SSYTSSS TLVV
YU397-A01	GYKFANY W	IYPGDSDT	ARLGWGMVDV	QSISSY	AAS	QQSYSTP WT
YU397-A02	GYTFKNFG	ISGRKGNT	ARVWGDITLGYG MDV	QDISNY	DAS	QQYDNL PLT
YU397-A03	GFTFSSYE	ISSSGSTI	ARRRGGGFDY	SSDVGGY NY	DVS	SSYTSSS TWV
YU397-B01	GYSFTSYW	IYPGDSDT	AIPWDAELGNYGM DV	QSISSY	AAS	LQDYNV PPA
YU397-B02	GGTFSSYA	IPIFGTA	ARGRWGLGDY	EDIRMY	EGS	QQYYDD PQ
YU397-D01	GGSISSN W	IYHSGST	ARARGGRYFDY	QGISTY	AAS	QQLNGY PTT
YU398-A11	GFTFSSYG	ISYDGSNK	AKGQGDGMDV	SSNVGSRT	SNN	AAWDDS LIGHV
YU398-E10	GFTFSSYS	ISSSSSYI	ARDQLAARRGYGY GMDV	NIGTKS	DDS	QVWDSS SDHVV
YU400-A05	GFTFSSYG	ISYDGSNK	AKGDVNYGMDV	NIGSKT	DGR	QVWDTS GDLHWA
YU400-A12	GGSISSN W	IYHSGST	ARDFYGGSGSYPN GYGYGMDV	QSINSY	TAS	QQSYTTP LT
YU400-B07	GFTFSSYG	ISYDGSNK	AKGDVNYGMDV	NIGSKS	DDT	QVWDSS SDLLWV
YU400-D09	GGTFSSYA	IPIFGTA	ARDFNPFSITIFEMD V	SSNIGNNY	DNN	GTWDSS LSALV
YU400-F07	GFTFSSYG	ISYDGSNK	AKGDVNYGMDV	NIGSKT	DGR	QVWDTS GDLHWA
YU400-H08	GFTFSSYG	ISYDGSNK	AKGDVNYGMDV	NIGSKT	DGR	QVWDTS GDLHWA
YU401-A11	GFTFSSYG	ISYDGSNK	ANLAMGQYFDY	SSNIGSNT	SNN	AAWDDS LNGPV
YU401-B01	GGTFSSYA	IPIFGTA	AREMYYYYGMDV	QSIITY	AAS	QQSYSTP PT

Clone ID	Heavy Chain CDR 1	Heavy Chain CDR 2	Heavy Chain CDR 3	Light Chain CDR 1	Light Chain CDR 2	Light Chain CDR 3
YU401-D11	GFTFSSYG	ISYDGSNK	ANLAMGQYFDY	SSNIGSNT	SNN	AAWDDS LNGPV
YU401-E11	GFTFSSYA	ISYDGSNK	ARDLGEAKSSSPHE PDY	QSLHSD GKTY	EVS	MQTKQL PLT
YU401-F11	GFTFSSYA	ISYDGSNK	ARDLGEAKSSSPHE PDY	QSLHSD GKTY	EVS	MQTKQL PLT
YU401-G07	GFTFSSYG	ISYDGSNK	AKGDVNYGMDV	NIGSKT	DGR	QVWDT GDLHWA
YU402-A02	GDSISSSY Y	INHSGST	ARDQEMYFDY	QGISSW	AAS	QQANSFP PT
YU402-A11	GGISRSN W	IYHTGST	ARGKGSYAFDI	GGNIARN Y	EDD	QSYDGN NHMV
YU402-D10	GFTFSSYG	ISYDGNNK	AKGYSSSPGDY	SSDVGAY NY	DVS	SSYTSSS TLWV
YU403-G05	GGISRSN W	IYHTGST	ARGKGSYAFDI	GGNIARN Y	EDD	QSYDGN NHMV

[0214] In some embodiments, the CDR-H1 is selected from: GGTFSSYA, GGSISSGGYY, GFTFSSYG, GYTFTSY, GYTFTSYG, GYTFTDYY, GGSISSGGYS, GGSISSNW, GYSFTSYW, GFTFSNYG, GFTFSSA, GFTFSSYW, GFIFSRHA, GYTFNNYG, GFTFSSYA, GYTFTTYA, GYTFNNAW, GFTFSSYE, GYSFTTYW, GYSFNTYW, GFTFRRYW, GYSFSTYW, GFAFSSYG, GYKFANYW, GYTFKNFG, GFTFSSYS, GDSISSSSYY, and GGSISRSNW;

[0215] In some embodiments, the CDR-H2 is selected from: IPIFGTA, IPIFGTA, IYSGST, ISYDGSNK, INPSGGST, ISAYNGNT, IMPIFDA, VDPEDGET, IYHSGST, IYPGSDT, ISHDGHVK, IKQDGSEK, ISVYNGDI, INTNTGDP, IKSKTDGGTT, ISSSGSTI, ISSRGSTI, IYPSDSDT, ISGRKGNT, ISSSSSYI, INHSGST, IYHTGST, and ISYDGNNK;

[0216] In some embodiments, the CDR-H3 is selected from: AREMYYYYGMDV, AREMYYYYGMDV, ARGNLWSGYF, AKELLEGAFFDI, ARDRVTMVRGALAY, ARERSYYGMDV, ASWSERIGYQYGLDV, ARDILGLDY, ATEDTAMGGIDY, ATEGRYGMDV, AVEGGRAPGTYYYDSSGLAY, ARAGYYYGMDV, ARDLGTMVRGVIEPYFDY, ARGVRGTGFDP, ARDRNGYFQH, AKDLLGELSFFDY, ARLENNWDYGGWFDP, ARDRSYYGMDV, ARDKGYGMDV, AKEISPRSSVGWPLDY, ARDFWSGYNELGGMDV, ARTWFGEFFDY, ARVIGGWFP, ARGRLAYGDTEGFDY,

ARDILRGESSILDH, ARDRYYYGMDV, ARDLLGSGYDIIDY, ARVWGKNGDFDY, ARDRFHYGMDV, ARDRGDY, TTEGVLLSFGGAPFDY, ARRRGGGFDY, AREKGSWFDP, ARDRGDRVGGGLVFDY, ARQVAGGLDY, ARDRGYYGMDV, FRFGEFDFY, ARDGGYYFDD, ARDFRMDV, ARDAYAYGLDV, ARDLMNYGMDV, AREYDYGDYVFDY, ARLENNWNYGGWFDP, ARDYYYYGMDV, ARDIGYYYGMDV, ARVGDGYSLDY, AKAITSIPEY, AKGQGDGMDV, ARLGWGMDV, ARVWGDTTLGYGMDV, AIPWDAELGNYGMDV, ARGRWSGLGDY, ARARGGRYFDY, ARDQLAARRGYYYGMDV, AKGDVNYGMDV, ARDFYYGSGSYPNGYYYGMDV, ARDFNPFSITIFEMDV, ANLAMGQYFDY, ARDLGEAKSSSPHEPDY, ARDQEMYFFDY, ARGKGSYAFDI, and AKGYSSSPGDY;

[0217] In some embodiments, the CDR-L1 is selected from: QSISSY, QSISSY, SSNIGNNF, QSISNY, NIETKS, KLGDY, QSVSNY, QTISQW, SSNIGSNY, NFNIGNNL, RNIWSY, QSISSW, QSVSSR, QTISGL, DIESEM, NIGSKS, QSIGNY, QGISSW, QSVSSTY, QDISNY, NIESES, SSDVGAYNY, QDINNY, QGISNS, SSNIGNNY, EGIRTS, QGTSSW, SSDVGGYNY, QSVSNY, QGINSY, QAVRID, QSISRY, QSIGYW, SSNVGSNY, QSIKNY, QDIKRR, SGSIASSY, NSNVGNYY, SLRSYY, KLGERF, SGSVSTSY, SSNIGRNY, EDIRMY, QGISTY, SSNVGSRT, NIGTKS, NIGSKT, QSINSY, SSNIGSNT, QSIITY, QSLLHSDGKTY, and GGNIARNY.

[0218] In some embodiments, the CDR-L2 is selected from: AAS, AAS, DST, DDD, KDN, GAS, KAS, RNN, SNN, AND, DAF, DDS, AAT, AVS, DAS, GVS, DNN, DVS, RAS, GTS, EDN, DND, GKN, QYI, NTD, RNH, EGS, DGR, TAS, DDT, EVS, and EDD.

[0219] In some embodiments, the CDR-L3 is selected from: QQSYSTPPT, QQSYSTPPT, GSWDTNLSGYV, QVWDSSSGHREV, QAWDSSTYV, QQYNHWPPL, QQYSGDSMYT, AAWDDSLSGVV, AAWDDSLNGVV, ATWDDSLSGVV, QQSHSTPIT, QQYNSYSRT, QQYTNWPQT, LQYDRYSGA, QVWHTTNDHVL, QVWDSSSDHWV, QQSKQIPYT, QQSYSLPLT, QQFDISGGLI, QQYDNLPLT, QVWDSSSDHTVA, SSYTTTDTFV, QQYDNLPLYT, QQYYSTPPH, QQSYSTPLT, QVWDSSSDHVV, GTWDDSSLAYV, QQTHTWPWT, QQANSFPLT, QQSYSTPYT, SSYTSSSTYV, QRYGSSPR, QQVHSFPFT, LQHNTFPYT, QQSHSTPLT, QQYNSYPFT, QQYNSSPLMYT, QQTYSTPLT,

QQANTFPQT, QSYDGSSVV, GSWEARESVFV, QQTYNDPPT, NSRDSSGNHV, QTWGDSIVV, VLYMGSGIWV, ATWDDALSGWV, SSYTSSSTLVV, QQSYSTPWT, SSYTSSSTWV, LQDYNYP, QQYYDDPQ, QQLNGYPTT, AAWDDSLIGHV, QVWDTSGDLHWA, QQSYTTPLT, QVWDSSSDLLWV, GTWDSSLSALV, AAWDDSLNGPV, MQTKQLPLT, QQANSFPPT, QSYDGNNHVM, and SSYTSSSTLVV.

[0220] In some embodiments, the antibody has a CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3, each independently selected from those disclosed in **Table 3A** and **Table 3B**. It is possible to combine the CDRs from different antibodies in any combination to generate new antibodies. Gene synthesis and high-throughput screening technologies enable the skilled person to test all combinations of six CDRs without undue experimentation.

Table 3A

VH_CDR1	VH_CDR2	VH_CDR3
GGTFSSYA	IIPIFGTA	AREMYYYYGMDV
GGTFSSYA	IIPIFGTA	AREMYYYYGMDV
GGSISSGGYY	IYYSGST	ARGNLWSGYF
GGTFSSYA	IIPIFGTA	AREMYYYYGMDV
GGTFSSYA	IIPIFGTA	AREMYYYYGMDV
GGTFSSYA	IIPIFGTA	AREMYYYYGMDV
GGTFSSYA	IIPIFGTA	AREMYYYYGMDV
GFTFSSYG	ISYDGSNK	AKELLEGAFDI
GYTFTSY	INPSGGST	ARDRVMTVRGALAY
GFTFSSYG	ISYDGSNK	AKELLEGAFDI
GGTFSSYA	IIPIFGTA	AREMYYYYGMDV
GYTFTSYG	ISAYNGNT	ARERSYYGMDV
GGTFSSYA	IIPIFGTA	AREMYYYYGMDV
GGTFSSYA	IMPIFDTA	ASWSERIGYQYGLDV
GGTFSSYA	IIPIFGTA	AREMYYYYGMDV
GYTFTSYG	ISAYNGNT	ARERSYYGMDV
GGTFSSYA	IIPIFGTA	AREMYYYYGMDV
GYTFTSYG	ISAYNGNT	ARERSYYGMDV
GGTFSSYA	IIPIFGTA	AREMYYYYGMDV
GYTFTSY	INPSGGST	ARDILGLDY
GYSFTSYW	IYPGSDT	ARLENNWDYGGWFD
GYTFTDYY	VDPEDGET	ATEDTAMGGIDY

VH_CDR1	VH_CDR2	VH_CDR3
GYTFTDYY	VDPEDGET	ATEGRYGM DV
GYTFTDYY	VDPEDGET	AVEGGRAPGTYYYYDSSGLAY
GGTFSSYA	IIPIFGTA	AREMYYYYGM DV
GGSISSSNW	IYHSGST	ARGVIAAAGTYFDY
GGSISSSNW	IYHSGST	ARERTHYYYGMDI
GYSFTSYW	IYPGDS DT	ARLENNWDYGGWFDP
GGTFSSYA	IIPIFGTA	ARDGAGNYDILTGD RSEDYYYYYYGM DV
GGSISSGGYS	IYHSGST	ARAGYYYGM DV
GGSISSGGYY	IYYS GST	ARDSSSGPYGM DV
GGSISSSNW	IYHSGST	ARVNYGDYDWYFDL
GGTFSSYA	IIPIFGTA	ARDLGTMVRGVIEPY YFDY
GGSISSSNW	IYHSGST	ARGVRGTGFDP
GYTFTSYG	ISAYNGNT	ARDRNGYFQH
GFTFSSYG	ISYDGSNK	AKDLLGELSFFDY
GYSFTSYW	IYPGDS DT	ARLENNWDYGGWFDP
GGTFSSYA	IIPIFGTA	ARDRSYYGM DV
GGTFSSYA	IIPIFGTA	ARDKGY YGM DV
GGTFSSYA	IIPIFGTA	ARDRSYYGM DV
GFTFSNYG	ISHDGHVK	AKEISPRSSVGWPLDY
GFTFSSSA	ISYDGSNK	ARDFWSGYNELGGMDV
GFTFSSYW	IKQDGSEK	ARTWFGEFFDY
GYTFTSYG	ISAYNGNT	ARVIGGW FDP
GFIFSRHA	ISYDGSNK	ARGRLAYGDTEGFDY
GYTFNNYG	ISVYNGDI	ARDILRGESSILDH
GGTFSSYA	IIPIFGTA	ARDRIYYGM DV
GFTFSSYA	ISYDGSNK	ARDLLGSGYDIIDY
GYTFTSYG	ISAYNGNT	ARVWGKNGDFDY
GYTFTTYA	INTNTGDP	ARDRFHYGM DV
GYTFTSYG	ISAYNGNT	ARDRGDY
GFTFNNAW	IKSKTDGGTT	TTEGVELLSFGGAPFDY
GFTFSSYE	ISSSGSTI	ARRRGGGFDY
GFTFSSYW	IKQDGSEK	AREKGSWFDP
GGTFSSYA	IIPIFGTA	ARDKGY YGM DV
GFTFSSYG	ISSRGSTI	ARDRGDRVGGLVFDY
GYSFTTYW	IYPGDS DT	ARQVAGGLDY
GYTFTSYG	ISAYNGNT	ARDRGYYGM DV
GYSFTSYW	IYPGDS DT	FRFGEGFDY
GYSFTTYW	IYPGDS DT	ARQVAGGLDY
GYSFNTYW	IYPSDSDT	ARDGGYYFDD
GGTFSSYA	IIPIFGTA	ARDKGY YGM DV

VH_CDR1	VH_CDR2	VH_CDR3
GYTFTSYG	ISAYNGNT	ARDFRMDV
GFTFRRYW	IKQDGSEK	ARDAYAYGLDV
GYSFTSYW	IYPGDSDT	ARLENNWDYGGWFDP
GYSFTSYW	IYPGDSDT	ARLENNWDYGGWFDP
GYSFTSYW	IYPGDSDT	ARLENNWDYGGWFDP
GGSISSSNW	IYHSGST	ARDLMNYGMDV
GFTFSSYA	ISYDGSNK	ARDLLGSGYDIIDY
GYSFTSYW	IYPGDSDT	ARLENNWDYGGWFDP
GFTFSSYW	IKQDGSEK	AREYDYGDYVFDY
GYSFTSYW	IYPGDSDT	ARLENNWDYGGWFDP
GYSFTSYW	IYPGDSDT	ARLENNWDYGGWFDP
GYTFTGYG	INPNSGDT	AILEYSSSGAEYFQH
GGTFSSYA	IIPIFGTA	AREMYYYYGMDV
GYSFTSYW	IYPGDSDT	ARLENNWDYGGWFDP
GYTFTTYA	ISAYNGNT	ARGGLGGDDAFDI
GGTFSSYA	ISAYNGNT	AREPLRYYYYYGMDV
GYSFTSYW	IYPGDSDT	ARLENNWDYGGWFDP
GYSFTSYW	IYPGDSDT	ARLENNWDYGGWFDP
GYSFTSYW	IYPGDSDT	ARLENNWNYGGWFDP
GYSFTSYW	IYPGDSDT	ARLENNWDYGGWFDP
GYSFTSYW	IYPGDSDT	ARLENNWNYGGWFDP
GGTFSSYA	IIPIFGTA	ARDYYYYGMDV
GGTFSSYA	IIPIFGTA	AREMYYYYGMDV
GGSISSSSYY	IYYSGST	ARLSRYYYYGMDV
GYTFTSYG	ISAYNGNT	ARDIGYYYGMDV
GGTFSSYA	IIPIFGTA	AREMYYYYGMDV
GGTFSSYA	IIPIFGTA	AREMYYYYGMDV
GGTFSSYA	IIPIFGTA	AREMYYYYGMDV
GFTFSNAW	IKSKNDGGTT	TTAPSLMDV
GYSFSTYW	IYPGDSDT	ARVGDGYSLDY
GFTFSSYG	ISYDGSNK	AKAITSIEPY
GYSFSTYW	IYPGDSDT	ARVGDGYSLDY
GGTFSSYA	IIPIFGTA	AREMYYYYGMDV
GFTFSSYA	ISGSGGST	AKNPYSNYVYWFDP
GFAFSSYG	ISYDGSNK	AKGQGDGMDV
GYKFANYW	IYPGDSDT	ARLGWGMDV
GYTFKNFG	ISGRKGNT	ARVWGDTTLGYGMDV
GFTFSSYE	ISSSGSTI	ARRRGGGFDY
GYSFTSYW	IYPGDSDT	AIPWDAELGNYGMDV
GGTFSSYA	IIPIFGTA	ARGRWSGLGDY

VH_CDR1	VH_CDR2	VH_CDR3
GGSISSSNW	IYHSGST	ARARGGRYFDY
GFTFSSYG	ISYDGSNK	AKGQGDGMDV
GFTFSSYS	ISSSSSYI	ARDQLAARRGYYYGMDV
GFDNFNWWYG	IWYDGSNE	ARDRRGSGWYFYFDY
GFTFSSYG	ISYDGSNK	AKGDVNYGMDV
GFTFSSYG	ISYDGSDK	AKDLSGLPIIDY
GGSISSSNW	IYHSGST	ARDFYYGSGSYPNGYYYGMDV
GFTFSSYG	ISYDGSNK	AKGDVNYGMDV
GGTFSSYA	IPIFGTA	ARDNFNPFITIFEMDV
GFTFSSYG	ISYDGSNK	AKGDVNYGMDV
GFTFSSYG	ISYDGSNK	AKGDVNYGMDV
GFTFSSYG	ISYDGSNK	ANLAMGQYFDY
GGTFSSYA	IPIFGTA	AREMYYYYGMDV
GFTFGDYA	INTDGSIT	ARDSHTVYYGSGSQDY
GFTFSSYG	ISYDGSNK	ANLAMGQYFDY
GFTFSSYA	ISYDGSNK	ARDLGEAKSSSPHEPDY
GFTFSSYA	ISYDGSNK	ARDLGEAKSSSPHEPDY
GFTFSSYG	ISYDGSNK	AKGDVNYGMDV
GDSISSSSYY	INHSGST	ARDQEMYFYFDY
GGSISRSNW	IYHTGST	ARGKGSYAFDI
GFTFSSYG	ISYDGSDK	AKDLSGLPIIDY
GFTFSSYG	ISYDGNNK	AKGYSSSPGDY
GGSISRSNW	IYHTGST	ARGKGSYAFDI

Table 3B

VL_CDR1	VL_CDR2	VL_CDR3
QSISSY	AAS	QSYSTPPT
QSISSY	AAS	QSYSTPPT
SSNIGNNF	DST	GSWDTNLSGYV
QSISSY	AAS	QSYSTPPT
QSISSY	AAS	QSYSTPPT
QSISSY	AAS	QSYSTPPT
QSISSY	AAS	QSYSTPPT
NIETKS	DDD	QVWDSSSGHREV
KLGDKY	KDN	QAWDSSTYV
NIETKS	DDD	QVWDSSSGHREV
QSISSY	AAS	QSYSTPPT

VL_CDR1	VL_CDR2	VL_CDR3
QSVSNY	GAS	QQYNHWPPL
QSISSY	AAS	QQSYSTPPT
QTISQW	KAS	QQYSGDSMYT
QSISSY	AAS	QQSYSTPPT
QSVSNY	GAS	QQYNHWPPL
QSISSY	AAS	QQSYSTPPT
QSVSNY	GAS	QQYNHWPPL
QSISSY	AAS	QQSYSTPPA
QSISSY	AAS	QQSYSTPPA
SSNIGSNY	RNN	AAWDDSLSGVV
NIGSKS	DDS	QVWDSSSDHWV
SSNIGSNY	SNN	AAWDDSLNGVV
NFNIGNNL	AND	ATWDDSLSGVV
SSNIGSNY	SNN	ATWDDSLSGVV
QSIISNY	AAS	QQSYSTPPT
RPNVASNS	SDN	ETWDDSLRGVV
SSNIGSNT	SNN	AAWDDSLNGYV
NIGSKS	DDS	QVWDSSSDHWV
YSNIGSNT	SDN	ATWDDSLNGPV
RNIWSY	GAS	QQSHSTPIT
NIGSQS	DDY	QIWDSSSAHVV
SSNIGSNF	SNN	AAWDDSLRSYV
QSISSW	DAF	QQYNSYSRT
QSVSSR	GAS	QQYTNWPQT
QTISGL	GAS	LQYDRYSGA
DIESEM	DDS	QVWHTTNDHVL
NIGSKS	DDS	QVWDSSSDHWV
QSIGNY	AAT	QQSKQIPYT
QGISSW	AVS	QQSYSLPLT
QSIGNY	AAT	QQSKQIPYT
QSVSSTY	GAS	QQFDISGGLI
QDISNY	DAS	QQYDNLPLT
NIESES	DDS	QVWDSSSDHTVA
SSDVGAYNY	GVS	SSYTTTDTFV
QDINNY	DAS	QQYDNLPLYT
QGISNS	AAS	QQYYSTPPH
QSISSY	AAS	QQSYSTPLT
NIGSKS	DDS	QVWDSSSDHVV
SSNIGNNY	DNN	GTWDSSLSAYV
EGIRTS	GAS	QQTHTWPWT

VL_CDR1	VL_CDR2	VL_CDR3
QGTSSW	AAS	QQANSFPLT
QSISSY	AAS	QQSYSTPYT
SSDVGGYNY	DVS	SSYTSSSTYV
QSVSNNY	GAS	QRYGSSPR
QGINSY	AAS	QQVHSFPFT
NIGSKS	DDS	QVWDSSSDHVV
QAVRID	GAS	LQHNTFPYT
QSISSY	AAS	QQSHSTPLT
QSIGYW	RAS	QQYNSYPFT
SSNVGSNY	RNN	AAWDDSLSGVV
QSVSSTY	GTS	QQYNSSPLMYT
QSIKNY	AAS	QQTYSTPLT
QDIKRR	DAS	QQANTFPQT
SGSIASSY	EDN	QSYDGSSVV
NIGSKS	DDS	QVWDSSSDHWV
NIGSKS	DDS	QVWDSSSDHWV
NIGSKS	DDS	QVWDSSSDHWV
QSISSY	AAS	QQSYSTPPT
NIGSKS	DDS	QVWDSSSDHVV
NIGSKS	DDS	QVWDSSSDHWV
NSNVGNNY	DND	GSWEARESFFV
NIGSKS	DDS	QVWDSSSDHWV
NIGSKS	DDS	QVWDSSSDHWV
QSVSSN	AAS	QQYNNWWT
QSISSY	AAS	QQSYSTPPT
NIGSKS	DDS	QVWDSSSDHWV
QSISSH	AAS	QQSYSTPPT
QSISSY	AAS	QQSYSTPWT
NIGSKS	DDS	QVWDSSSDHWV
NIGSKS	DDS	QVWDSSSDHWV
NIGSKS	DDS	QVWDSSSDHWV
NIGSKS	DDS	QVWDSSSDHWV
NIGSKS	DDS	QVWDSSSDHWV
QSISSY	GAS	QQTYNDPPT
QSISSY	AAS	QQSYSTPPT
SSNIGNNY	DNN	GTWDSSLSAWV
SLRSYY	GKN	NSRDSSGNHVV
QSISSY	AAS	QQSYSTPPT
QSISSY	AAS	QQSYSTPPT
QSISSY	AAS	QQSYSTPPT

VL_CDR1	VL_CDR2	VL_CDR3
NIGSKS	DDS	QVWDSSSDHPVV
KLGERF	QYI	QTWDGSIVV
SGSVSTSY	NTD	VLYMGSGIWV
SSNIGRNY	RNH	ATWDDALSGWV
QSISSY	AAS	QQSYSTPPT
SGRIASNY	QDD	QSYDSTTLV
SSDVGGYNY	GVS	SSYTSSSTLVV
QSISSY	AAS	QQSYSTPWT
QDISNY	DAS	QQYDNLPLT
SSDVGGYNY	DVS	SSYTSSSTWV
QSISSY	AAS	LQDYNYPPIA
EDIRMY	EGS	QQYYDDPQ
QGISTY	AAS	QQLNGYPTT
SSNVGSRT	SNN	AAWDDSLIGHV
NIGTKS	DDS	QVWDSSSDHVV
SSDVGGYNY	EVS	SSYTSSSTPV
NIGSKT	DGR	QVWDTSGDLHWA
SSDVGGYNY	EVS	SSYTSSSTLV
QSINSY	TAS	QQSYTTPLT
NIGSKS	DDT	QVWDSSSDLLWV
SSNIGNNY	DNN	GTWDSSLSALV
NIGSKT	DGR	QVWDTSGDLHWA
NIGSKT	DGR	QVWDTSGDLHWA
SSNIGSNT	SNN	AAWDDSLNGPV
QSIITY	AAS	QQSYSTPPT
SSDVGGYNY	EVS	SSYTSSSTLV
SSNIGSNT	SNN	AAWDDSLNGPV
QSLHSDGKTY	EVS	MQTKQLPLT
QSLHSDGKTY	EVS	MQTKQLPLT
NIGSKT	DGR	QVWDTSGDLHWA
QGISSW	AAS	QQANSFPPT
GGNIARNY	EDD	QSYDGNNHMOV
SSDVGGYNY	EVS	SSYTKNNSVV
SSDVGAYNY	DVS	SSYTSSSTLWV
GGNIARNY	EDD	QSYDGNNHMOV

[0221] In some embodiments, the antibody has the six CDRs of any one of the combinations provided in **Table 4**.

Table 4

Combination #	VH_CDR1	VH_CDR2	VH_CDR3	VL_CDR1	VL_CDR2	VL_CDR3
1.	GGTFSSYA	IIPIFGTA	AREMYYY YGMDV	QSISSY	AAS	QQSYSTPP T
2.	GGTFSSYA	IIPIFGTA	AREMYYY YGMDV	QSISSY	AAS	QQSYSTPP T
3.	GGSISSGGY Y	IYYSGST	ARGNLWS GYFF	SSNIGNNF	DST	GSWDTNLS GYV
4.	GGTFSSYA	IIPIFGTA	AREMYYY YGMDV	QSISSY	AAS	QQSYSTPP T
5.	GGTFSSYA	IIPIFGTA	AREMYYY YGMDV	QSISSY	AAS	QQSYSTPP T
6.	GGTFSSYA	IIPIFGTA	AREMYYY YGMDV	QSISSY	AAS	QQSYSTPP T
7.	GGTFSSYA	IIPIFGTA	AREMYYY YGMDV	QSISSY	AAS	QQSYSTPP T
8.	GFTFSSYG	ISYDGSNK	AKELLEGA FDI	NIETKS	DDD	QVWDSSS GHREV
9.	GYTFTSYY	INPSGGST	ARDRVMT VRGALAY	KLGDKY	KDN	QAWDSST YV
10.	GFTFSSYG	ISYDGSNK	AKELLEGA FDI	NIETKS	DDD	QVWDSSS GHREV
11.	GGTFSSYA	IIPIFGTA	AREMYYY YGMDV	QSISSY	AAS	QQSYSTPP T
12.	GYTFTSYY	ISAYNGNT	ARERSYYG MDV	QSVSNY	GAS	QQYNHWP PL

Combination #	VH_CDR1	VH_CDR2	VH_CDR3	VL_CDR1	VL_CDR2	VL_CDR3
13.	GGTFSSYA	IIPIFGTA	AREMYYY YGMDV	QSISSY	AAS	QQSYSTPP T
14.	GGTFSSYA	IMPIFDTA	ASWSERIG YQYGLDV	QTISQW	KAS	QQYSGDS MYT
15.	GGTFSSYA	IIPIFGTA	AREMYYY YGMDV	QSISSY	AAS	QQSYSTPP T
16.	GYTFTSYG	ISAYNGNT	ARERSYYG MDV	QSVSNY	GAS	QQYNHWP PL
17.	GGTFSSYA	IIPIFGTA	AREMYYY YGMDV	QSISSY	AAS	QQSYSTPP T
18.	GYTFTSYG	ISAYNGNT	ARERSYYG MDV	QSVSNY	GAS	QQYNHWP PL
19.	GGTFSSYA	IIPIFGTA	AREMYYY YGMDV	QSISSY	AAS	QQSYSTPP A
20.	GGTFSSYA	IIPIFGTA	AREMYYY YGMDV	QSISSY	AAS	QQSYSTPP A
21.	GYTFTSY	INPSGGST	ARDILGLD Y	SSNIGSNY	RNN	AAWDDSL SGVV
22.	GYSFTSYW	IYPGDSDT	ARLENNW DYGGWFD P	NIGSKS	DDS	QVWDSSS DHWV
23.	GYTFTDYY	VPEDGET	ATEDTAM GGIDY	SSNIGSNY	SNN	AAWDDSL NGVV
24.	GYTFTDYY	VPEDGET	ATEGRYG MDV	NFNIGNNL	AND	ATWDDSL GVV
25.	GYTFTDYY	VPEDGET	AVEGGRAP GTYYYDSS GLAY	SSNIGSNY	SNN	ATWDDSL GVV

Combination #	VH_CDR1	VH_CDR2	VH_CDR3	VL_CDR1	VL_CDR2	VL_CDR3
26.	GGTFSSYA	IIPIFGTA	AREMYYY YGMDV	QSISSNY	AAS	QQSYSTPP T
27.	GGSISSSNW	IYHSGST	ARGVIAAA GTYFDY	RPNVASNS	SDN	ETWDDSLR GVV
28.	GGSISSSNW	IYHSGST	ARERTHY YGMDI	SSNIGSNT	SNN	AAWDDSL NGYV
29.	GYSFTSYW	IYPGDSDT	ARLENNW DYGGWFD P	NIGSKS	DDS	QVWDSSS DHWV
30.	GGTFSSYA	IIPIFGTA	ARDGAGN YDILTGDR SEDY YGMDV	YSNIGSNT	SDN	ATWDDSL NGPV
31.	GGSISSGGY S	IYHSGST	ARAGYYY GMDV	RNIWSY	GAS	QQSHSTPIT
32.	GGSISSGGY Y	IYYSGST	ARDSSSGP YGMDV	NIGSQS	DDY	QIWDSSSA HVV
33.	GGSISSSNW	IYHSGST	ARVNYGD YDWYFDL	SSNIGSNF	SNN	AAWDDSL RSYV
34.	GGTFSSYA	IIPIFGTA	ARDLGTM VRGVIEPY YFDY	QSISSW	DAF	QQYNSYSR T
35.	GGSISSSNW	IYHSGST	ARGVRGT GFDP	QSVSSR	GAS	QQYTNWP QT
36.	GYTFTSYG	ISAYNGNT	ARDRNGY FQH	QTISGL	GAS	LQYDRYSG A
37.	GFTFTSYG	ISYDGSNK	AKDLLGEL SFFDY	DIESEM	DDS	QVWHTTN DHVL
38.	GYSFTSYW	IYPGDSDT	ARLENNW DYGGWFD P	NIGSKS	DDS	QVWDSSS DHWV

Combination #	VH_CDR1	VH_CDR2	VH_CDR3	VL_CDR1	VL_CDR2	VL_CDR3
39.	GGTFSSYA	IPIFGTA	ARDRSYY GMDV	QSIGNY	AAT	QQSKQIPY T
40.	GGTFSSYA	IPIFGTA	ARDKGY GMDV	QGISSW	AVS	QQSYSLPL T
41.	GGTFSSYA	IPIFGTA	ARDRSYY GMDV	QSIGNY	AAT	QQSKQIPY T
42.	GFTFSNYG	ISHDGHVK	AKEISPRSS VGWPLDY	QSVSSTY	GAS	QQFDISGG LI
43.	GFTFSSSA	ISYDGSNK	ARDFWSG YNELGGM DV	QDISNY	DAS	QQYDNLPL T
44.	GFTFSSYW	IKQDGSEK	ARTWFGEF FDY	NIESES	DDS	QVWDSSS DHTVA
45.	GYTFTSYG	ISAYNGNT	ARVIGGW DP	SSDVGAY NY	GVS	SSYTTTDT FV
46.	GFIFSRHA	ISYDGSNK	ARGRLAY GDTEGFDY	QDINNY	DAS	QQYDNLPL YT
47.	GYTFNNYG	ISVYNGDI	ARDILRGE SSILDH	QGISNS	AAS	QQYYSTPP H
48.	GGTFSSYA	IPIFGTA	ARDRYYY GMDV	QSISSY	AAS	QQSYSTPL T
49.	GFTFSSYA	ISYDGSNK	ARDLLGSG YDIIDY	NIGSKS	DDS	QVWDSSS DHVV
50.	GYTFTSYG	ISAYNGNT	ARVWGKN GDFDY	SSNIGNNY	DNN	GTWDSSLS AYV
51.	GYTFTTYA	INTNTGDP	ARDRFHY GMDV	EGIRTS	GAS	QQTHTWP WT

Combination #	VH_CDR1	VH_CDR2	VH_CDR3	VL_CDR1	VL_CDR2	VL_CDR3
52.	GYTFTSYG	ISAYNGNT	ARDRGDY	QGTSSW	AAS	QQANSFPL T
53.	GFTFNNAW	IKSKTDGG TT	TTEGVELL SFGGAPFD Y	QSISSY	AAS	QQSYSTPY T
54.	GFTFSSYE	ISSSGSTI	ARRRGGGF DY	SSDVGGY NY	DVS	SSYTSSSTY V
55.	GFTFSSYW	IKQDGSEK	AREKGSW FDP	QSVSNY	GAS	QRYGSSPR
56.	GGTFSSYA	IIPIFGTA	ARDKGYG GMDV	QGINSY	AAS	QQVHSFPF T
57.	GFTFSSYG	ISSRGSTI	ARDRGDR VGGLVFD Y	NIGSKS	DDS	QVWDSSS DHVV
58.	GYSFTTYW	IYPGDSDT	ARQVAGG LDY	QAVRID	GAS	LQHNTFPY T
59.	GYTFTSYG	ISAYNGNT	ARDRGYY GMDV	QSISSY	AAS	QQSHSTPL T
60.	GYSFTSYW	IYPGDSDT	FRFGEGFD Y	QSIGYW	RAS	QQYNSYPF T
61.	GYSFTTYW	IYPGDSDT	ARQVAGG LDY	SSNVGSNY	RNN	AAWDDSL SGVV
62.	GYSFNTYW	IYPSDSDT	ARDGGYY FDD	QSVSSTY	GTS	QQYNSSPL MYT
63.	GGTFSSYA	IIPIFGTA	ARDKGYG GMDV	QSIKNY	AAS	QQTYSTPL T
64.	GYTFTSYG	ISAYNGNT	ARDFRMD V	QDIKRR	DAS	QQANTFPQ T

Combination #	VH_CDR1	VH_CDR2	VH_CDR3	VL_CDR1	VL_CDR2	VL_CDR3
65.	GFTFRRYW	IKQDGSEK	ARDAYAY GLDV	SGSIASSY	EDN	QSYDGSSV V
66.	GYSFTSYW	IYPGDSDT	ARLENNW DYGGWFD P	NIGSKS	DDS	QVWDSSS DHWV
67.	GYSFTSYW	IYPGDSDT	ARLENNW DYGGWFD P	NIGSKS	DDS	QVWDSSS DHWV
68.	GYSFTSYW	IYPGDSDT	ARLENNW DYGGWFD P	NIGSKS	DDS	QVWDSSS DHWV
69.	GGSISSSNW	IYHSGST	ARLDMNY GMDV	QSISSY	AAS	QQSYSTPP T
70.	GFTFSSYA	ISYDGSNK	ARDLLGSG YDIIDY	NIGSKS	DDS	QVWDSSS DHWV
71.	GYSFTSYW	IYPGDSDT	ARLENNW DYGGWFD P	NIGSKS	DDS	QVWDSSS DHWV
72.	GFTFSSYW	IKQDGSEK	AREYDYG DYVFDY	NSNVGNN Y	DND	GSWEARES VFV
73.	GYSFTSYW	IYPGDSDT	ARLENNW DYGGWFD P	NIGSKS	DDS	QVWDSSS DHWV
74.	GYSFTSYW	IYPGDSDT	ARLENNW DYGGWFD P	NIGSKS	DDS	QVWDSSS DHWV
75.	GYTFTGY	INPNSGDT	AILEYSSSG AEYFQH	QSVSSN	AAS	QQYNNW WT
76.	GGTFSSYA	IIPIFGTA	AREMYYY YGMDV	QSISSY	AAS	QQSYSTPP T
77.	GYSFTSYW	IYPGDSDT	ARLENNW DYGGWFD P	NIGSKS	DDS	QVWDSSS DHWV

Combination #	VH_CDR1	VH_CDR2	VH_CDR3	VL_CDR1	VL_CDR2	VL_CDR3
78.	GYTFTTYA	ISAYNGNT	ARGGLGG DDAFDI	QSISSH	AAS	QQSYSTPP T
79.	GGTFSSYA	ISAYNGNT	AREPLRY YYGMDV	QSISSY	AAS	QQSYSTPW T
80.	GYSFTSYW	IYPGDSDT	ARLENNW DYGGWFD P	NIGSKS	DDS	QVWDSSS DHWV
81.	GYSFTSYW	IYPGDSDT	ARLENNW DYGGWFD P	NIGSKS	DDS	QVWDSSS DHWV
82.	GYSFTSYW	IYPGDSDT	ARLENNW NYGGWFD P	NIGSKS	DDS	QVWDSSS DHWV
83.	GYSFTSYW	IYPGDSDT	ARLENNW DYGGWFD P	NIGSKS	DDS	QVWDSSS DHWV
84.	GYSFTSYW	IYPGDSDT	ARLENNW NYGGWFD P	NIGSKS	DDS	QVWDSSS DHWV
85.	GGTFSSYA	IPIFGTA	ARDYYYY GMDV	QSISSY	GAS	QQTYNDPP T
86.	GGTFSSYA	IPIFGTA	AREMY YGM DV	QSISSY	AAS	QQSYSTPP T
87.	GGSISSSSYY	IYYSGST	ARLSRY YGM DV	SSNIGNNY	DNN	GTWDSSLS AWV
88.	GYTFTSYG	ISAYNGNT	ARDIGY YGM DV	SLRSY	GKN	NSRDSSGN HVV
89.	GGTFSSYA	IPIFGTA	AREMY YGM DV	QSISSY	AAS	QQSYSTPP T
90.	GGTFSSYA	IPIFGTA	AREMY YGM DV	QSISSY	AAS	QQSYSTPP T

Combination #	VH_CDR1	VH_CDR2	VH_CDR3	VL_CDR1	VL_CDR2	VL_CDR3
91.	GGTFSSYA	IIPIFGTA	AREMYYY YGMDV	QSISSNY	AAS	QQSYSTPP T
92.	GFTFSNAW	IKSKNDGG TT	TTAPSLMD V	NIGSKS	DDS	QVWDSSS DHPVV
93.	GYSFSTYW	IYPGDSDT	ARVGDGY SLDY	KLGERF	QYI	QTDWGSIV V
94.	GFTFSSYG	ISYDGSNK	AKAITSIEP Y	SGSVSTSY Y	NTD	VLYMGSGI WV
95.	GYSFSTYW	IYPGDSDT	ARVGDGY SLDY	SSNIGRNY	RNH	ATWDDAL SGWV
96.	GGTFSSYA	IIPIFGTA	AREMYYY YGMDV	QSISSY	AAS	QQSYSTPP T
97.	GFTFSSYA	ISGSGGST	AKNPYSNY VYWFDV	SGRIASNY	QDD	QSYDSTTL V
98.	GFAFSSYG	ISYDGSNK	AKGQGDG MDV	SSDVGGY NY	GVS	SSYTSSSTL VV
99.	GYKFANYW	IYPGDSDT	ARLGWGM DV	QSISSY	AAS	QQSYSTPW T
100.	GYTFKNFG	ISGRKGNT	ARVWGD TLGYGMD V	QDISNY	DAS	QQYDNLPL T
101.	GFTFSSYE	ISSSGSTI	ARRRGGGF DY	SSDVGGY NY	DVS	SSYTSSST WV
102.	GYSFTSYW	IYPGDSDT	AIPWDAEL GNYGMDV	QSISSY	AAS	LQDYNYP A
103.	GGTFSSYA	IIPIFGTA	ARGRWG LGDY	EDIRMY	EGS	QQYYDDP Q

Combination #	VH_CDR1	VH_CDR2	VH_CDR3	VL_CDR1	VL_CDR2	VL_CDR3
104.	GGSISSSNW	IYHSGST	ARARGGR YFDY	QGISTY	AAS	QQLNGYPT T
105.	GFTFSSYG	ISYDGSNK	AKGQGDG MDV	SSNVGSRT	SNN	AAWDDSLI GHV
106.	GFTFSSYS	ISSSSSYI	ARDQLAA RRGYYYG MDV	NIGTKS	DDS	QVWDSSS DHVV
107.	GFDFNWYG	IWYDGSNE	ARDRRGSG WYEIFDY	SSDVGGY NY	EVS	SSYTSSSTP V
108.	GFTFSSYG	ISYDGSNK	AKGDVNY GMDV	NIGSKT	DGR	QVWDTS DLHWA
109.	GFTFSSYG	ISYDGSDK	AKDLSGLP IIDY	SSDVGGY NY	EVS	SSYTSSSTL V
110.	GGSISSSNW	IYHSGST	ARDFYYGS GSYPNGYY YGMDV	QSINSY	TAS	QQSYTTPL T
111.	GFTFSSYG	ISYDGSNK	AKGDVNY GMDV	NIGSKS	DDT	QVWDSSS DLLWV
112.	GGTFSSYA	IPIFGTA	ARDFNPFSI TIFEMDV	SSNIGNNY	DNN	GTWDSSLS ALV
113.	GFTFSSYG	ISYDGSNK	AKGDVNY GMDV	NIGSKT	DGR	QVWDTS DLHWA
114.	GFTFSSYG	ISYDGSNK	AKGDVNY GMDV	NIGSKT	DGR	QVWDTS DLHWA
115.	GFTFSSYG	ISYDGSNK	ANLAMGQ YFDY	SSNIGSNT	SNN	AAWDDSL NGPV
116.	GGTFSSYA	IPIFGTA	AREMYYY YGMDV	QSIITY	AAS	QQSYSTPP T

Combination #	VH_CDR1	VH_CDR2	VH_CDR3	VL_CDR1	VL_CDR2	VL_CDR3
117.	GFTFGDYA	INTDGSIT	ARDSHTVY YGSGSQDY	SSDVGGY NY	EVS	SSYTSSSTL V
118.	GFTFSSYG	ISYDGSNK	ANLAMGQ YFDY	SSNIGSNT	SNN	AAWDDSL NGPV
119.	GFTFSSYA	ISYDGSNK	ARDLGEA KSSSPHEP DY	QSLHSDG KTY	EVS	MQTKQLPL T
120.	GFTFSSYA	ISYDGSNK	ARDLGEA KSSSPHEP DY	QSLHSDG KTY	EVS	MQTKQLPL T
121.	GFTFSSYG	ISYDGSNK	AKGDVNY GMDV	NIGSKT	DGR	QVWDTSG DLHWA
122.	GDSISSSSY	INHSGST	ARDQEMY YFDY	QGISSW	AAS	QQANSFPP T
123.	GGISRSNW	IYHTGST	ARGKGSY AFDI	GGNIARNY	EDD	QSYDGNN HNV
124.	GFTFSSYG	ISYDGSDK	AKDLSGLP IIDY	SSDVGGY NF	EVS	SSYTKNNS VV
125.	GFTFSSYG	ISYDGNNK	AKGYSSSP GDY	SSDVGAY NY	DVS	SSYTSSSTL WV
126.	GGISRSNW	IYHTGST	ARGKGSY AFDI	GGNIARNY	EDD	QSYDGNN HNV

[0222] In some embodiments, the antibody is an scFv selected from **Table 5**, or any antibody having an antigen-binding domain derived from the scFv's in **Table 5**. In embodiments, the full length heavy chain and light chain variable regions are extracted from the scFv sequences in Table 5 and used to generate soluble Fab fragments, monoclonal antibodies, bispecific antibodies, or any other type of antibody known in the art. Where an scFv in Table 5 is a VH:VL scFv, it is possible to reverse the order of the heavy and light chains to generate a VL:VH scFv.

Where an scFv in Table 5 is a VL:VH scFv, it is possible to reverse the order of the heavy and light chains to generate a VH:VL scFv.

Table 5

Clone ID	scFv sequence
YU389-A01	PGSSVKVSCKASGGTFSSYAISWVRQAPGQGLEWMGGIPIFGTANYAQ KFQGRVTITADESTSTAYMELSSLRSEDNAVYYCAREMYYYYGMDVW GQGTTVTVSSCAREMYYYYGMDVWDIQMTQSPSSLSASVGDRVTITC RASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTL TISSLQPEDFATYYCQQSYSTPPTFGQGTKVEIKCQQSYSTPPTF
YU389-A02	PGSSVKVSCKASGGTFSSYAISWVRQAPGQGLEWMGGIPIFGTANYAQ KFQGRVTITADESTSTAYMELSSLRSEDNAVYYCAREMYYYYGMDVW GQGTTVTVSSCAREMYYYYGMDVWEIVMTQSPSSLSASVGDRVTITCR ASQSISSYLNWYQQKPGKAPKLLTYAASSLQSGVPSRFSGSGSGTDFTL TISSLQPEDFATYYCQQSYSTPPTFGPGTKVDIKCQQSYSTPPTF
YU389-A03	PSQTLSTCTVSGGSISSGGYYWSWIRQHPGKGLEWIGYIYYSGSTYYN PSLKSRTISVDTSKNQFSLKLSSVTAADNAVYYCARGNLWSGYYFWG QGTLTVTVSSCARGNLWSGYYFWQSVLTQPPSVSAAPGQKVTISCSGSSS NIGNNFVSWYQQVPGTAPKLLTYDSTKRPAGIPDRFSGSKSGTSATLEIA GLQTGDEADYYCGSWDTNLSGYVFGTGTKVTVLCGSWDTNLSGYVF
YU389-A04	PGSSVKVSCKASGGTFSSYAISWVRQAPGQGLEWMGGIPIFGTANYAQ KFQGRVTITADESTSTAYMELSSLRSEDNAVYYCAREMYYYYGMDVW GQGTTVTVSSCAREMYYYYGMDVWDIQMTQSPSSLSASVGDRVTITC RASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTL TISSLQPEDFATYYCQQSYSTPPTFGQGTKVEIKCQQSYSTPPTF
YU389-A05	PGSSVKVSCKASGGTFSSYAISWVRQAPGQGLEWMGGIPIFGTANYAQ KFQGRVTITADESTSTAYMELSSLRSEDNAVYYCAREMYYYYGMDVW GQGTTVTVSSCAREMYYYYGMDVWDIQMTQSPSSLSASVGDRVTITC

Clone ID	scFv sequence
	RASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTL TISSLQPEDFATYYCQQSYSTPPTFGQGTKVETNCQQSYSTPPTF
YU389-A07	PGSSVKVSCKASGGTFSSYAISWVRQAPGQGLEWMGGIPIFGTANYAQ KFQGRVTITADESTSTAYMELSSLRSEDVAVYYCAREMYYYYGMDVW GQGTTVTVSSCAREMYYYYGMDVWDIQMTQSPSSLSASVGDRVTITC RASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTL TISSLQPEDFATYYCQQSYSTPPTFGQGTKVETKCQQSYSTPPTF
YU389-B11	PGSSVKVSCKASGGTFSSYAISWVRQAPGQGLEWMGGIPIFGTANYAQ KFQGRVTITADESTSTAYMELSSLRSEDVAVYYCAREMYYYYGMDVW GQGTTVTVSSCAREMYYYYGMDVWEIVMTQSPSSLSASVGDRVTITCR ASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLT ISSLQPEDFATYYCQQSYSTPPTFGQGTKLEIKCQQSYSTPPTF
YU389-D07	PGSSVKVSCKASGGTFSSYAISWVRQAPGQGLEWMGGIPIFGTANYAQ KFQGRVTITADESTSTAYMELSSLRSEDVAVYYCAREMYYYYGMDVW GQGTTVTVSSCAREMYYYYGMDVWDIQMTQSPSSLSASVGDRVTITC RASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFT LTISSLQPEDFATYYCQQSYSTPPTFGQGTKLEIKCQQSYSTPPTF
YU390-A11	PGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVISYDGSNKYY ADSVKGRFTISRDNKNTLYLQMNSLRAEDTAVYYCAKELLEGAFDIW GQGTMTVTVSSCAKELLEGAFDIWSYVLTQPPSLSVAPGQTARITCGGD NIETKSVHWYQQRPGQAPVLVYDDDDRPSGIPERFSGSNSGNTATLTI SRVEAGDEADYYCQVWDSSSGHREVFGGRTKPALLCQVWDSSSGHRE VF
YU390-A12	PGASVKVSCKASGYTFTSYMHWRQAPGQGLEWMGIINPSGGSTSY AQKFQGRVTMTRDTSTSTVYMELSSLRSEDVAVYYCARDRTVMVRGA LAYWGQGTLLTVSSCARDRTVMVRGALAYWSYELTQPPSVSVSPGHT ATITCSGEKLGDKYVYWYQQKPGQSPLLVMYKDNKRPSATPERFSGSN

Clone ID	scFv sequence
	SGDTATLTIRGTQAMDEADYYCQAWDSSTYVFGSGTKVTVLCQAWDS STYVF
YU390-B12	PGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVISYDGSNKYY ADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAKELLEGAFDIW GQGTMTVTVSSCAKELLEGAFDIWSYVLTQPPSLSVAPGQTARITCGGD NIETKSVHWYQQRPQGAPVLVYDDDDRPSGIPERFSGSNSGNTATLTI SRVEAGDEADYYCQVWDSSSGHREVF VF
YU390-C03	PGSSVKVSCKASGGTFSSYAISWVRQAPGQGLEWMGGIPIFGTANYAQ KFQGRVTITADESTSTAYMELSSLRSED TAVYYCAREMYYYYGMDVW GQGTTVTVSSCAREMYYYYGMDVWDIQMTQSPSSLSASVGDRVITC RASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTL TISSLQPEDFATYYCQQSYSTPPTFGQGPKVEIKCQQSYSTPPTF
YU390-C11	PGASAKVSCKASGYTFTSYGISWVRQAPGQGLEWMGWISAYNGNTNY AQKLQGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCARERSYYGMDV WGQGTTVTVSSCARERSYYGMDVWTQSPATLSVSPGESATLSCRASQS VSNYLAWYQQKPGQAPRLLIYGASTRATGIPARFSGSGSGTEFTLTISL QSEDFAVYYCQQYNHWPPPLFGGGTKVETKCQQYNHWPPPLF
YU390-D01	PGSSVKVSCKASGGTFSSYAISWVRQAPGQGLEWMGGIPIFGTANYAQ KFQGRVTITADESTSTAYMELSSLRSED TAVYYCAREMYYYYGMDVW GQGTTVTVSSCAREMYYYYGMDVWDIQMTQSPSSLSASVGDRVITC RASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTL TISSLQPEDFATYYCQQSYSTPPTFGQGPKVELKCQQSYSTPPTF
YU390-D03	PGSSVKVSCKVSGGTFSSYAISWVRQAPGQGLEWMGGIMPIFDTAEYA QKFQGRVTITADESTSTAYMELSTLRSED TAVYYCASWSERIGYQYGL DVWGQGTTVTVSSCASWSERIGYQYGLDVWDIRMTQSPSTLSASVGD RVSITCRASQTISQWLAWFHQKPGKAPKLLIYKASRLESGVSSRFSGSGS

Clone ID	scFv sequence
	GTEFTLTITSLQPDDIGTYYCQQYSGDSMYTFGQGTRLEIRCQQYSGDS MYTF
YU390-D05	PGSSVKVSCKASGGTFSSYAISWVRQAPGQGLEWMGGIPIFGTANYAQ KFQGRVTITADESTSTAYMELSSLRSEDVAVYYCAREMYYYYGMDVW GQGTTVTVSSCAREMYYYYGMDVWDIQMTQSPSSLSASVGDRVTITC RASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTL TISSLQPEDFATYYCQQSYSTPPTFGQGTKVETCQQSYSTPPTF
YU390-D11	PGASAKVSCKASGYTFTSYGISWVRQAPGQGLEWMGWISAYNGNTNY AQKLQGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCARERSYYGMDV WGQGTTVTVSSCARERSYYGMDVWTQSPATLSVSPGESATLSCRASQS VSNYLAWYQQKPGQAPRLLIYGASTRATGIPARFSGSGSGTEFTLTISL QSEDFAVYYCQQYNHWPPPLFGGGTKVEIKCQQYNHWPPPLF
YU390-G03	PGSSVKVSCKASGGTFSSYAISWVRQAPGQGLEWMGGIPIFGTANYAQ KFQGRVTITADESTSTAYMELSSLRSEDVAVYYCAREMYYYYGMDVW GQGTTVTVSSCAREMYYYYGMDVWDIQMTQSPSSLSASVGDRVTITC RASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTL TISSLQPEDFATYYCQQSYSTPPTFGQGTKVELKCQQSYSTPPTF
YU390-H11	PGASAKVSCKASGYTFTSYGISWVRQAPGQGLEWMGWISAYNGNTNY AQKLQGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCARERSYYGMDV WGQGTTVTVSSCARERSYYGMDVWTQSPATLSVSPGESATLSCRASQS VSNYLAWYQQKPGQAPRLLIYGASTRATGIPARFSGSGSGTEFTLTISL QSEDFAVYYCQQYNHWPPPLFGGGNGGEIKCQQYNHWPPPLF
YU392-A05	PGASVKVSCKASGYTFTSYMHWRQAPGQGLEWMGIINPSGGSTSY AQKFQGRVTMTRDTSTSTVYMELSSLRSEDVAVYYCARDILGLDYWG QGTLLTVTVSSCARDILGLDYWQPGLTQPPSASETPGQRTISCSGSSSNIG SNVYVYWYQQLPGTAPKLLIYRNNQRPSGVPGRFSGSKSGTSASLAISGL RSEDEADYYCAAWDDSLSGVVFVGGGKLTVC AAWDDSLSGVVF

Clone ID	scFv sequence
YU392-A07	PGATVKISCKVSGYTFTDYMHVWVQQAPGKGLEWMGLVDPEDGETIY AEKFQGRVTITADTSTDTAYMELSSLRSEDVAVYYCATEDTAMGGIDY WGQGTLLTVSSCATEDTAMGGIDYWQPVLTQSPSASGTPGQRTISCS GSSSNIGSNYVYWYQQLPGTAPKLLIYSNNQRPSGVPDRFSGSKSGTSA SLAISGLQSEDEADYYCAAWDDSLNGVVFVGGGTKLTVLCAAWDDSLN GVVF
YU392-A09	PGATVKISCKVSGYTFTDYMHVWVQQAPGKGLEWMGLVDPEDGETIY AEKFQGRVTITADTSTDTAYMELSSLRSEDVAVYYCATEGRYGMDVW GQGTLLTVSSCATEGRYGMDVWQAVLTQPPSVSGTPGQRTISCSGNN FNIGNNLVYWYQQLPGTAPKLLIYANDERPSGVPDRFSGSKSGTSASLA ISGLRSEDDADYYCATWDDSLSGVVFVGGGTKLTALCATWDDSLSGVV F
YU392-B11	PGATVKISCKVSGYTFTDYMHVWVQQAPGKGLEWMGLVDPEDGETIY AEKFQGRVTITADTSTDTAYMELSSLRSEDVAVYYCAVEGGRAPGTYY YDSSGLAYWGQGTLLTVSSCAVEGGRAPGTYYDYDSSGLAYWQAGLT QPPSASGTPGQRTISCSGSSSNIGSNYVYWYQQLPGTAPKLLIYSNNQR PSGVPDRFSGSKSGTSASLAISGLRSEDEADYYCATWDDSLSGVVFVGGG TKLTVLCATWDDSLSGVV
YU393-A01	PSQTLSTCAVSGGSISSGGYSWSWIRQPPGKGLEWIGYIYHSGSTYYNP SLKSRVTISVDRSKNQFSLKLSSVTAADTAVYYCARAGYYYGMDVWG QGTTTVTVSSCARAGYYYGMDVWDIVMTQTPSSLSASVGDRVAITCQA SRNIWSYVNWYQQKPGEAPRLLIYGASTLQRGVPSRFSGSGSGTGTFTLT INSLQPEDFATYFCQQSHSTPITFGGGTRVDIKCQQSHSTPITF
YU393-A02	PGSSVKVSCKASGGTFSSYAIWVRQAPGQGLEWMGGIPIFGTANYAQ KFQGRVTITADKSTSTAYMELSSLRSDDTAVYYCARDLGTMRGVIEP YYFDYWGGTLLTVSSCARDLGTMRGVIEPYFDYWDIQTQSPST LSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLLIYDAFSLSGVP

Clone ID	scFv sequence
	SRFSGSGSGTEFTLTISLQPDDEFATYYCQQYNSYSRTEFGQGTKVEIKCQ QYNSYSRTE
YU393-A03	PSGTLSTCAVSGSGSISSSNWWSWVRQPPGKGLEWIGEIIYHSGSTNYP SLKSRVTISVDKSKNQFSLKLSSVTAADTAVYYCARGVRGTGFDPWGQ GTLVTVSSCARGVRGTGFDPWQTQSPGTLSPGERATLSCRASQSVSSR LAWYQQKPGQAPRLLIYGASTRATGIPARFSGSGSGTEFTLTISLQSED FAVYFCQQYTNWPQTFGQGTKVEIKCQQYTNWPQTF
YU393-A04	PGASVKVSCKASGYTFTSYGISWVRQAPGQGLEWMGWISAYNGNTNY AQKLQGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCARDNRNGYFQH WGQGTLLTVSSCARDNRNGYFQHWDIVMTQTPSTLSASVGDRVTITCRA SQTISGLLAWYQQKPGKAPNLLIYGASNSQSGVPSRFTGSGSGTEFTLTI TNLQPDDEFATYYCLQYDRYSGAFGQGTKLEIKCLQYDRYSGAF
YU393-A08	PGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVISYDGSNKYY ADSVKGRFTISRDNKNTLYLQMNSLRAEDTAVYYCAKDLLGELSFFD YWGQGTLLTVSSCAKDLLGELSFFDYWSVLTQPPSVSVAPGQTARIPC GGDDIESEMWHWYQQKPGQAPVLVYDDSVRPSGIPERFSGSNSGNTA TLISGVEAGDEAAYYCQVWHTTNDHVLFGGGTNLTVLCQVWHTTND HVL
YU393-A09	PGDLWKISCKGSGYSFTSYWIGWVRQMPGKGLEWMGIIYPGDSSTRYS PSFQQQVTISADKSISTAYLQWSSLKASDTAMYYCARLENNWDYGGW FDPWGQGTLLTVSSCARLENNWDYGGWFDPWSYVLTQPPSVSVAPGQ TARITCGGNNIGSKSVHWYQQKPGQAPVLVYDDSDRPSGIPERFSGSN SGNTATLTISRVEAGDEADYYCQVWDSSSDHWVFGGGTKLTVLCQVW DSSSDHWVF
YU393-A11	PGESLKISCKGSGYSFTSYWIGWVRQMPGKGLEWMGIIYPGDSSTRYSP SFQQQVTISADKSISTAYLQWSSLKASDTAMYYCARLENNWDYGGWF DPWGQGTLLTVSSCARLENNWDYGGWFDPWSYVLTQPPSVSVAPGQT ARITCGGNNIGSKSVHWYQQKPGQAPVLVYDDSDRPSGIPERFSGSNS

Clone ID	scFv sequence
	GNTATLTISRVEAGDEADYYCQVWDSSSDHWVFGGGKLTVLCQVW DSSSDHWVF
YU393-B02	PGSSVKVSCKASGGTFSSYAIWVRQAPGQGLEWMGGIPIFGTANYAQ KFQGRVTITADKSTSTAYMELSSLRSEDNAVYYCARDRSYYGMDVWG QGTTVTVSSCARDRSYYGMDVWDIRLTQSPSSLSASVGDRVITICRASQ SIGNYNWYQQRLGEAPKVLIIYAATRLQRGVPSRFSASASGTDFTLTIS LQPEDFTTYCQQSKQIPYTFGGGKLTQIKCQQSKQIPYTF
YU393-B03	PGSSVKVSCKASGGTFSSYAIWVRQAPGQGLEWMGGIPIFGTANYAQ KFQGRVTITADKSTSTAYMELSSLRSEDNAVYYCARDKGYGMDVWG QGTTVTVSSCARDKGYGMDVWDIQTQSPSSVSASVGDRVITICRAS QGISSWLAWYQQKPGKAPKLLIYAVSSLQSGVPSRFSGSGSGTDFTLTIS SLQPEDFATYYCQSYSLPLTFGGGTEVLKICQQSYSLPLTF
YU393-B04	PGSSVKVSCKASGGTFSSYAIWVRQAPGQGLEWMGGIPIFGTANYAQ KFQGRVTITADESTSTAYMELSSLRSEDNAVYYCARDRSYYGMDVWG QGTTVTVSSCARDRSYYGMDVWDIQTQSPSSLSASVGDRVITICRAS QSIGNYNWYQQRLGEAPKVLIIYAATRLQRGVPSRFSAGASGTDFTLTI SSLQPEDFTTYCQQSKQIPYTFGGGKLTQIKCQQSKQIPYTF
YU393-B05	PGRSLRLSCAASGFTFSNYGMHWVRQAPGKGLEWVAVISHDGHVKW HGDSVKGRFTISRDNKNTLYLQLDSLRTEDNAVYYCAKEISPRSSVGW PLDYWGQGTLVTVSSCAKEISPRSSVGWPLDYWTQSPGTLSPGERAT LSCRADQSVSSTYLAWYQQRPGQAPRLIIYGASNRATGIPDRFSGSGSG SDFTLTISRLEPEDFNAVYYCQQFDISGGLIFGPGTKVDIKCQQFDISGGLIF
YU393-B06	PGRSLRLSCAASGFTFSSSAMHWVRQAPGKGLEWVAVISYDGSNKYY ADSVKGRFTISRDKAKNSLYLQMNSLRAEDNAVYYCARDFWSGYNEL GGMDVWGQGTTVTVSSCARDFWSGYNELGGMDVWEIVMTQSPSSLS ASVGDRVITICQASQDISYNWYQQKPGKAPKLLIYDASNLETGVPSR FSGSGSGTDFTFTISLQPEDATYYCQQYDNLPLTFGGGKVEIKCQQY DNLPLTF

Clone ID	scFv sequence
YU393-B07	PGGSLRLSCAASGFTFSSYWMSWVRQAPGKGLEWVANIKQDGSEKYY VDSVKGRFTISRDNKNSLYLQMNSLRAEDTAVYYCARTWFGFFDY WGQGTLLTVSSCARTWFGFFDYWSVLTQPPSVSVAPGQTARVTCGG NNIESESVHWYQQKPGQAPVLLVYDDSAARPSGIPERFSGSNSGNTATLT ISRVEAGDEADYYCQVWDSSSDHTVAFGGGTKLAVLCQVWDSSSDHT VAF
YU393-B08	PGASVKVSCKASGYTFTSYGISWVRQAPGQGLEWMGWISAYNGNTNY AQKLQGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCARVIGGWFDPW GQGTLLTVSSCARVIGGWFDPWQSALTQPASVSGSPGQSITISCTGTSSD VGAYNYVSWYQQQPGKAPELMIYGVSHRPSRVSNRFSGSKSGNTASLT ISGLQTEDEADYYCSSYTTTDTFVLGSGTKVTVLCSSYTTTDTFVL
YU393-C02	PGRSLRLSCAASGFIFSRHAMHWVRQAPDKGLEWVAVISYDGSNKYY ADSVKGRFTISRDNPKNTLYLQMNSLRAEDTAVYYCARGRLAYGDTE GFDYWQGTLLTVSSCARGRLAYGDTEGFDYWDIVMTQSPSSLSASV GDRVITTCQASQDINNYLSWFQHKPGKAPKLLIYDASDLETGVPSRFSG SGSGPEFSFTITNLQPEDVATYYCQYDNLPTYTFGQGTKVEIRCQYDN LPYTF
YU393-C03	PGASVKVSCKASGYTFNNYGLAWVRQAPGQGLEWMGWISVYNGDIN YAQKFQGRVTMTTDRATRTAYMELRSLISDDTAVYYCARDILRGESSIL DHWGQGTLLTVSCARDILRGESSILDHWDIVMTQSPSSLSASVGDRVIT TCRASQGISNSLAWYQQKPGKAPKLLLYAASRLESGVPSRFSGSGSGTD YTLTISSLQPEDFATYYCQYYSTPPHFGGGTKVEIKCQYYSTPPHF
YU393-C05	PGSSVKVSCKASGGTFSSYAIWVRQAPGQGLEWMGGHIPIFGTANYAQ KFQGRVTITADESTSTAYMELSSLRSDDTAVYYCARDRIYYGMDVWG QGTTTVTVSSCARDRIYYGMDVWAIKMTQSPSSLSASVGDRVITTCRAS QSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTIS SLQPEDFATYYCQSYSTPLTFGGGTKVEIKCQSYSTPLTF

Clone ID	scFv sequence
YU393-C07	PGRSLRLSCAASGFTFSSYAMHWVRQAPGKGLEWVAVISYDGSNKYY ADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCARDLLGSGYDII DYWGQGTLVTVSSCARDLLGSGYDII DYWSYVLTQPPSVSVAPGQTAR ITCGGNNIGSKSVHWYQQKPGQAPVLVYDDSDRPSGIPERFSGSNSGN TATLTISRVEAGDEADYYCQVWDSSSDHVVFVGGGTKLTVLCQVWDSS SDHVVF
YU393-C08	PGASVKVSCKASGYTFTSYGISWVRQAPGQGLEWMGWISAYNGNTNY AQKLQGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCARVWGKNGDF DYWGQGTLVTVSSCARVWGKNGDFDYWQSVLTQPPSVSAAPGQKVTI SCSGSSNIGNNYVSWYQQLPGTAPKLLIYDNNKRPSGIPDRFSGSKSGT SATLGITGLQTGDEADYYCGTWDSLSAYVFGTGTKVTVLCGTWDSLS SAYVF
YU393-D03	PGASVKVSCKASGYTFTTYAMNWVRQAPGQGLEWMGGINTNTGDPT YAQGSTGRFVFSSDTSVSTAYLQISSLPEDTAVYYCARDRFHYGMDV WGQGTTVTVSSCARDRFHYGMDVWTQSPDTLSVSPGDGATLSCRASE GIRTSVAWYQQRPGQAPRLLIYGASTRAAGVPARFSGSGSGTEFTLTIS LQSDDFAVYYCQQTHTWPWTFGQGTKAEIKCQQTHTWPWTF
YU393-D04	PGASVKVSCKASGYTFTSYGISWVRQAPGQGLEWMGWISAYNGNTNY AQKLQGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCARDRGDYWGQ GTLVTVSSCARDRGDYWDIQMTQSPSSVSASVGDRVTITCRASQGTSS WLAWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISLQP EDFATYYCQQANSFPLTFGGGTKVEIKCQQANSFPLTF
YU393-D05	PGGSLRLSCAASGFTFNNAWMSWVRQAPGKGLEWVGRIKSKTDGGTT DYGAPVKGRFTISRDDSKNTLYLQMNSLKTEDTAVYYCTTEGVLLSF GGAPFDYWGQGTLVTVSSCTTEGVLLSF GGAPFDYWDIQMTQSPSSL SASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPS RFSGSGSGTDFTLTISLQPEDFATYYCQQSYSTPYTFGQGTKLEIKCQQ SYSTPYTF

Clone ID	scFv sequence
YU393-D07	PGGSLRLSCAASGFTFSSYEMNWVRQAPGKGLEWVSYISSSGSTIYYAD SVKGRFTISRDNKNSLYLQMNSLRAEDTAVYYCARRRGGGFDYWGQ GTLVTVSSCARRRGGGFDYWQSALTQPASVSGSPGQSITISCTGTSSDV GGYNYVSWYQQHPGKAPKLMYDVSNRPSGVSNRFSGSKSGNTASLTI SGLQAEDADYYCSSYTSSSTYVFGTGTKVTVLCSSYTSSSTYVF
YU393-E04	PGGSLRLSCAASGFTFSSYWMSWVRQAPGKGLEWVANIKQDGSEKYY VDSVGGRTISRDNKNSLYLQMNSLRAEDTAVYYCAREKGSWFDPW GQGTLVTVSSCAREKGSWFDPWTSQPGTSLSPGERATLSCRASQSVSN NYLAWYQQKPGQAPRLLIYGASSRATGIPDRFSGNGSGTDFTLTISRLEP EDFAVYYCQRYGSSPRFGGGTKVEIKCQRYGSSPRF
YU393-E05	PGSSVKVSKASGGTFSSYAIWVRQAPGQGLEWMGGIPIFGTANYAQ KFQGRVTITADKSTSTAYMELSSLRSEDVAVYYCARDKGYYGMDVWG QGTTVTVSSCARDKGYYGMDVWMTQSPSFLSASVGDRVTITCRASQGI NSYLVWYKQKPGKAPDLLIYAASLTQSGVPSRFSGSGSGTDFTLTISLQ PEDFATYYCQQVHSFPFTFGPGTKVEIKCQQVHSFPFTF
YU393-E07	PGGSLRLSCAASGFTFSSYGINWVRQAPGKGLEWVSYISSRGSTILYADS VKGRFTISRDNARNVHLQMNSLRDEDTAVYYCARDRGDRVGGLVFD YWGQGSLLTVSSCARDRGDRVGGLVFDYWVLTQPPSVSVAPGQTARI TCGNNIGSKSVHWYQQKPGQAPVLVYDDSDRPSGIPERFSGSNSGN TATLTISRVEAGDEADYYCQVWDSSSDHVVFVGGGKLTVLCQVWDSS SDHVVF
YU393-F03	PGESLKISCKGSGYSFTTYWIAWVRQMPGKGLEWMGHIYPGDSDDTYSP SFQGQVTISADKSITTTYLQWSSLKASDTAMYYCARQVAGGLDYWGQ GTLVTVSSCARQVAGGLDYWDIVLTQSPSSLSASVGDRVTITCRASQAV RIDLSWYQQKPGKAPERLIFGASGLQRGVPSRFSGSGSGTEFTLTISLQ EDFATYYCLQHNTFPYTFGQGTKLEIKCLQHNTFPYTF
YU393-F04	PGASVKVSKASGYTFTSYGISWVRQAPGQGLEWMGWISAYNGNTNY AQLQGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCARDRGYYGMD

Clone ID	scFv sequence
	VWGQGTTVTVSSCARDRGYYGMDVWDIQMTQSPSSLSASVGDRVITIT CRASQISRYLNWYQQKPGKDPKLLIYAASSLQSGVPSRFSGSGSGTDF TLTISSLQPEDFATYYCQQSHSTPLTFGGGKVEIKCQQSHSTPLTF
YU393-F06	PGESLKISCKGSGYSFTSYWIGWVRQMPGKGLEWMGHIYPGDSDDTRYSP SFQGGQVTISADKSISTAYLQWSSLKASDTAMYYCFRFGEGFDYWGGQT LTVTVSSCFRFGEGFDYWMTQSPSTLSASVGDRVITITCRASQSIGYWLA WYQQRPGRAPKLLMYRASNLKSGVPSRFSGSGSGTEFTLTISSLQPDFF ATYYCQQYNSYPFTFGPGTKVDIKCQQYNSYPFTF
YU393-F07	PGESLKISCKGSGYSFTTYWIAWVRQMPGKGLEWMGHIYPGDSDDTTYSP SFQGGQVTISADKSITTTYLQWSSLKASDTAMYYCARQVAGGLDYWGQ GTLTVTVSSCARQVAGGLDYWQSVLTQPPSASGTPGQRTVITSCGSSSNV GSNYVSWYQQLPGTAPKLLIQRNRRPSGVPDRFSGSGSKSGTSASLAISG LRSEDEADYYCAAWDDSLSGVVFGGGTKLTVLCAAWDDSLSGVVF
YU393-G01	PGESLKISCKSSGYSFNTYWIGWVRQMPGKGLEWMGHIYPSDSDTRYSP SFQGGQVTISADKSINTAYLQWSSLKASDSAMYYCARDGGYYFDDWGQ GTLTVTVSSCARDGGYYFDDWTQSPGTLSPGERATLSCRASQSVSSTY LAWYQQKPGQAPRLLIYGTSTRATGIPDRFSGSGSGTDFTLTISRLEPED FAVYYCQQYNSSPLMYTFGQGTRLEIKCQQYNSSPLMYTF
YU393-G03	PGSSVKVSKKASGGTFSSYAISWVRQAPGQGLEWMGGIPIFGTANYAQ KFQGRVTITADKSTSTAYMELSSLRSEDYAVYYCARDKGYGMDVWG QGTTTVTVSPCARDKGYGMDVWDIVMTQSPSSLSASIGDRVITITCRAS QSIKNYLNWYQQKPGKAPKLLIYAASSLQNGVPSRFSGSGSGTDFTVTI SSLQPEDFAIYYCQQTYSTPLTFGGGTNVEIKCQQTYSTPLTF
YU393-G04	PGSSVKVSKKASGYTFTSYGISWVRQAPGQGLEWMGWISAYNGNTNY AQKLQGRVTMTTDTSTSTAYMELRGLRSDDTAVYYCARDFRMDVWG QGTTTVTVSSCARDFRMDVWDIRLTQSPSSVASSVGDSVTVTICRASQDIK RRLAWYLQKPGQAPKLLIFDASRLHTGVPSRFSGSGSGTDFTLIINSLQP EDFGTYCQQANTFPQTFGQGTKEIKCQQANTFPQTF

Clone ID	scFv sequence
YU393-G07	PGGSLRLSCAASGFTFRRYWMTWVRQAPGKGLEWVANIKQDGSEKYY VDSVKGRFAVSRDNANNSLYLRMNSLRAEDTAVYYCARDAYAYGLD VWGQGTAVTVSSCARDAYAYGLDVWVLTQPHSVSESPGKTVTISCTGS SGSIASSYVHWYQQRPGRVPTPIYEDNQRPSGVPDRFSGSIDSSNSAS LTISGLKTEDEADYYCQSYDGSSVVFGGGKLTVLCQSYDGSSVVF
YU393-G08	PGDLRKISCKGSGYSFTSYWIGWVRQMPGKGLEWMGHIYPGDS DTRY S PSFQGGVTVISADKSISTAYLQWSSLKASDTAMY YCARLENNWDYGGW FDPWGQGT LVT VSSCARLENNWDYGGWFDPWSYVLTQPPSVSVAPGQ TARITCGGNNIGSKSVHWYQQKPGQAPVLV VYDDSDRPSGIPERFSGSN SGNTATLTISRVEAGDEADYYCQVWDSSSDHWVF GGGTKLTVLCQVW DSSSDHWVF
YU393-G11	PGNLWKISCKGSGYSFTSYWIGWVRQMPGKGLEWMGHIYPGDS DTRY S PSFQGGVTVISADKSISTAYLQWSSLKASDTAMY YCARLENNWDYGGW FDPWGQGT LVT VSSCARLENNWDYGGWFDPWSYVLTQPPSVSVAPGQ TARITCGGNNIGSKSVHWYQQKPGQAPVLV VYDDSDRPSGIPERFSGSN SGNTATLTISRVEAGDEADYYCQVWDSSSDHWVF GGGTKLTVLCQVW DSSSDHWVF
YU393-G12	PGNLLKISCKGSGYSFTSYWIGWVRQMPGKGLEWMGHIYPGDS DTRY S PSFQGGVTVISADKSISTAYLQWSSLKASDTAMY YCARLENNWDYGGW FDPWGQGT LVT VSSCARLENNWDYGGWFDPWSYVLTQPPSVSVAPGQ TARITCGGNNIGSKSVHWYQQKPGQAPVLV VYDDSDRPSGIPERFSGSN SGNTATLTISRVEAGDEADYYCQVWDSSSDHWVF GGGTKLTVLCQVW DSSSDHWVF
YU393-H03	PSGTLSTCAVSGGSISSSNWWSWVRQPPGKGLEWIGE IYHSGSTNYP SLKSRVTISVDKSKNQFSLKLSSVTAADTAVYYCARDLMNYGMDVWG QGTTVT VSSCARDLMNYGMDVWMTQSPSSLSASVGD RVTITCRASQSI SSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSLQ PEDFATYYCQSYSTPPTFGGQTKVEIKCQSYSTPPTF

Clone ID	scFv sequence
YU393-H07	PGRSLRLSCAASGFTFSSYAMHWVRQAPGKGLEWVAVISYDGSNKYY ADSVKGRFTISRDSKNTLYLQMNSLRAEDTAVYYCARDLLGSGYDIID YWGQGTLLTVSSCARDLLGSGYDIIDYWVLTQSPSVSVAPGKTARITC GGNNIGSKSVHWYQQKPGQAPVLVYDDSDRPSGIPERFSGSNSGNTA TLTISRVEAGDEADYYCQVWDSSSDHWVFVGGGTKLTVLCQVWDSSSD HVVVF
YU393-H09	PGDL*KISCKGSGYSFTSYWIGWVRQMPGKGLEWMGHIYPGDS DTRYSP SFQGGVTISADKSISTAYLQWSSLKASDTAMYYCARLENNWDYGGWF DPWGQGTLLTVSSCARLENNWDYGGWFD PWSYVLTQPPSVSVAPGQT ARITCGGNNIGSKSVHWYQQKPGQAPVLVYDDSDRPSGIPERFSGSNS GNTATLTISRVEAGDEADYYCQVWDSSSDHWVFVGGGTKLTVLCQVW DSSSDHWVF
YU394-A01	PGGSLRLSCAASGFTFSSYWMSWVRQAPGKGLEWVANIKQDGSEKYY VDSVKGRFTISRDNKNSLYLQMNSLRAEDTAVYYCAREYDYGDYVF DYWGQGTLLTVSSCAREYDYGDYVFDYWYELTQPPSMSATPGQKVTI TCSGSNSNVGNNYVSWYQQVPGTAPKLLIYDNDRRPSGIPDRFSGAKS GTSATLGITGLQTGDEADYYCGSWEARES VFVFGGGTKLTVCGSWEAR ESVFVF
YU394-A02	PGDLLKISCKGSGYSFTSYWIGWVRQMPGKGLEWMGHIYPGDS DTRY S PSFQGGVTISADKSISTAYLQWSSLKASDTAMYYCARLENNWDYGGW FDPWGQGTLLTVSSCARLENNWDYGGWFD PWSYVLTQPPSVSVAPGQ TARITCGGNNIGSKSVHWYQQKPGQAPVLVYDDSDRPSGIPERFSGSN SGNTATLTISRVEAGDEADYYCQVWDSSSDHWVFVGGGTKLTVLCQVW DSSSDHWVF
YU394-A07	RGDLLKISCKGSGYSFTSYWIGWVRQMPGKGLEWMGHIYPGDS DTRY S PSFQGGVTISADKSISTAYLQWSSLKASDTAMYYCARLENNWDYGGW FDPWGQGTLLTVSSCARLENNWDYGGWFD PWSYVLTQPPSVSVAPGQ TARITCGGNNIGSKSVHWYQQKPGQAPVLVYDDSDRPSGIPERFSGSN

Clone ID	scFv sequence
	SGNTATLTISRVEAGDEADYYCQVWDSSSDHWVFVGGGKLTVLCQVW DSSSDHWVF
YU394-A09	PGSSVKVSCKASGGTFSSYAIWVRQAPGQGLEWMGGIPIFGTANYAQ KFQGRVTITADESTSTAYMELSSLRSEDVAVYYCAREMYYYYGMDVW GQGTTVTVSSCAREMYYYYGMDVWDIVMTQSPSSLSASVGDRTITC RASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTL TISSLQPEDFATYYCQQSYSTPPTFGQGTKVEIKCQQSYSTPPTF
YU394-C01	PGDPLKISCKGSGYSFTSYWIGWVRQMPGKGLEWMGGIYPGDSSTRYS PSFQQQVTISADKSISTAYLQWSSLKASDTAMYYCARLENNWDYGGW FDPWGQGTLLTVSSCARLENNWDYGGWFDPWSYVLTQPPSVSVAPGQ TARITCGGNNIGSKSVHWYQQKPGQAPVLLVYDDSDRPSGIPERFSGSN SGNTATLTISRVEAGDEADYYCQVWDSSSDHWVFVGGGKLTVLCQVW DSSSDHWVF
YU394-E02	PGDFLKISCKGSGYSFTSYWIGWVRQMPGKGLEWMGGIYPGDSSTRYS PSFQQQVTISADKSISTAYLQWSSLKASDTAMYYCARLENNWDYGGW FDPWGQGTLLTVSSCARLENNWDYGGWFDPWSYVLTQPPSVSVAPGQ TARITCGGNNIGSKSVHWYQQKPGQAPVLLVYDDSDRPSGIPERFSGSN SGNTATLTISRVEAGDEADYYCQVWDSSSDHWVFVGGGKLTVLCQVW DSSSDHWVF
YU394-H01	PGEFRKISCKGSGYSFTSYWIGWVRQMPGKGLEWMGGIYPGDSSTRYSP SFQQQVTISADKSISTAYLQWSSLKASDTAMYYCARLENNWDYGGWF DPWGQGTLLTVSSCARLENNWDYGGWFDPWSYVLTQPPSVSVAPGQT ARITCGGNNIGSKSVHWYQQKPGQAPVLLVYDDSDRPSGIPERFSGSNS GNTATLTISRVEAGDEADYYCQVWDSSSDHWVFVGGGKLTVLCQVW DSSSDHWVF
YU394-H03	RGDLLKISCKGSGYSFTSYWIGWVRQMPGKGLEWMGGIYPGDSSTRYS PSFQQQVTISADKSISTAYLQWSSLKASDTAMYYCARLENNWNYGGW FDPWGQGTLLTVSSCARLENNWNYGGWFDPWVLTQPPSVSVAPGQTA

Clone ID	scFv sequence
	RITCGGNNIGSKSVHWYQQKPGQAPVLVYDDSDRPSGIPERFSGSNSG NTATLTISRVEAGDEADYYCQVWDSSSDHWVFVGGGTKLTVLCQVWDS SSDHWVF
YU394-H04	RGNLLKISCKGSGYSFTSYWIGWVRQMPGKGLEWMGHIYPGDS DTRYSP PSFQQQVTISADKSISTAYLQWSSLKASDTAMYYCARLENNWDYGGW FDPWGQGT LVT VSSCARLENNWDYGGWFDPWSYVLTQPPSVSVAPGQ TARITCGGNNIGSKSVHWYQQKPGQAPVLVYDDSDRPSGIPERFSGSN SGNTATLTISRVEAGDEADYYCQVWDSSSDHWVFVGGGTKLTVLCQVW DSSSDHWVF
YU394-H05	PGESLKISCKGSGYSFTSYWIGWVRQMPGKGLEWMGHIYPGDS DTRYSP SFQQQVTISADKSISTAYLQWSSLKASDTAMYYCARLENNWNYGGWF DPWGQGT LVT VSSCARLENNWNYGGWFDPWVLTQPPSVSVAPGQTA RITCGGNNIGSKSVHWYQQKPGQAPVLVYDDSDRPSGIPERFSGSNSG NTATLTISRVEAGDEADYYCQVWDSSSDHWVFVGGGTKLTVLCQVWDS SSDHWVF
YU394-H07	PGASVKVSCKASGGTFSSYAISWVRQAPGQGLEWMGGIPIFGTANYAQ KFQGRVTITADESTSTAYMELSSLRSED TAVYYCARDY YYYGMDVWG QGTTVT VSSCARDY YYYGMDVWDIRMTQSPSSLSASVGDRVITICRAS QSISRYVNWYQQKPGKAPNLLIYGASNLESGVPSRFSGSGSGTDFTLTN SSLQPEDFASYCQQTYN DPPTFGGGTRMEIKCQQTYN DPPTF
YU395-A02	PGSSVKVSCKASGGTFSSYAISWVRQAPGQGLEWMGGIPIFGTANYAQ KFQGRVTITADESTSTAYMELSSLRSED TAVYYCAREMY YYYGMDVW GQGTTVT VSSCAREMY YYYGMDVWDIVMTQSPSSLSASVGDRVITIC RASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTL TISSLQPEDFATYYCQQS YSTPPTFGQGPKVEIKCQQS YSTPPTF
YU395-B12	PGASVKVSCKASGYTFTSYGISWVRQAPGQGLEWMGWISAYNGNTNY AQKLQGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCARDIGY YYYGMD VWGQGTTVT VSSCARDIGY YYYGMDVWSSELTQDPAVSVALGQTVRIT

Clone ID	scFv sequence
	CQGDSLRSYYASWYQQEPGQAPVLVIYGKNNRPSGISDRFSGSSSGNTA SLTITGAQAEDEADYYCNSRDSSGNHVVFVGGGTRLTVLCNSRDSSGNH VVF
YU395-C06	PGSSVKVSCKASGGTFSSYAISWVRQAPGQGLEWMGGIPIFGTANYAQ KFQGRVTITADESTSTAYMELSSLRSEDVAVYYCAREMYYYYGMDVW GQGTTVTVSSCAREMYYYYGMDVWDIQMTQSPSSLSASVGDRVITC RASQSIISNYLNWYQQKPKGAPKLLIYAASSLQSGVPSRFSGSGSGTDFT LTISSLQPEDFATYYCQSYSTPPTFGQGTKLETKCQSYSTPPTF
YU395-C08	PGSSVKVSCKASGGTFSSYAISWVRQAPGQGLEWMGGIPIFGTANYAQ KFQGRVTITADESTSTAYMELSSLRSEDVAVYYCAREMYYYYGMDVW GQGTTVTVSSCAREMYYYYGMDVWDIVMTQSPSSLSASVGDRVITC RASQSIISNYLNWYQQKPKGAPKLLIYAASSLQSGVPSRFSGSGSGTDFTL TISSLQPEDFATYYCQSYSTPPTFGQGTKVELKCQSYSTPPTF
YU395-D05	PGSSVKVSCKASGGTFSSYAISWVRQAPGQGLEWMGGIPIFGTANYAQ KFQGRVTITADESTSTAYMELSSLRSEDVAVYYCAREMYYYYGMDVW GQGTTVTVSSCAREMYYYYGMDVWDIQMTQSPSSLSASVGDRVITC RASQSIISNYLNWYQQKPKGAPKLLIYAASSLQSGVPSRFSGSGSGTDFT LTISSLQPEDFATYYCQSYSTPPTFGQGPKLEIKCQSYSTPPTF
YU396-B12	SGESLKISCKGSGYSFSTYWIGWVRQMPGKGLEWMGLIYPGDSSTRYS PSFQQQVTISADKSISTAYLQWSSLKASDTAMYYCARVGDGYSLDYWG QGTLTVTVSSCARVGDGYSLDYWSVLTQPPSVSVSPGQTASITCSGHKLG ERFAYWYQQKPGQSPVLVINQYIRRPSPGIPERFSGSNSGSTATLTISGTQ AMDEADYYCQTDWGSIVVFVGGGTKLTVLCQTDWGSIVVF
YU396-C03	PGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVISYDGSNKYY ADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAKAITSIEPYWG QGTLTVTVSSCAKAITSIEPYWQTVVTQEPSFSVSPGGTVTLTCGLSSGSV STSYYPWYQQTPGQAPRTLIYNTDTRSSRPDRFSGSIVGNKAALTITG AQADDES DYCVLYMGSGIWFVGGGTKLTVLCVLYMGSGIWFV

Clone ID	scFv sequence
YU396-C12	SGESLKISCKGSGYSFSTYWIGWVRQMPGKGLEWMGLIYPGDS DTRYSPSFQGGV TISADKSISTAYLQWSSLKASDTAMY YCARVGDGYSLDYWGQGT LVTVSSCARVGDGYSLDYWQPVLTQPPSASGTPGQRVTISCSGGSSNIGRNYVY WYQQLPGTAPNLLISR NHQRPSGVPDRFSGSRSDTSASLAISGLRSEDEADYYCATWDDALSGWVFGGGTKLTVLCATWDDALSGWVF
YU396-G10	PGSSVKVSC KASGGTFSSY AISWVRQAPGQGLEWMGGIPIFGTANYAQKFQGRVTITADESTSTAYMELSSLRSEDTAVYYCAREMYYYYGMDVWGQGT TTVTVSSCAREMYYYYGMDVWDIVMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSTPPTFGQGTKVETKCQQSYSTPPTF
YU396-H12	PGRSLRLSCAASGFAFSSYGMHWVRQAPGKGLEWVAVISYDGSNKYYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAKGQGDGMDVWGQGT TTVTVSSCAKGQGDGMDVWQSALTQPPSASGSPGQSVTISCTGTSSDVGGYNYVSWYQQHPGKAPKLMLYGVSNRPSGISSRFSGSKSGNTASLTISGLQA EDEADYYCSSYTSSSTLVVFGGGTKLTVLCSSYTSSSTLVVF
YU397-A01	PGESLQISCKGSGYKFANYWIGWVRQMPGKGLEWMGHIYPGDS DTRYSPSFQGGV TISADKSISTAYLQWSSLKASDTAMY YCARLGWGM DVWGQGTTTVTVSSCARLGWGM DVWDIVMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPNLIYAASSLRSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSTPWTFGQGTKVEIKCQQSYSTPWTF
YU397-A02	PGASVKVSC KASGYTFKNFGISWVRRAPGQGPEWMGWISGRKGNTIYAQKFQGRVTMTTDTSTTTAYMELRSLRSDDTAVYYCARVWGD TTLGYGMDVWGQGT TTVTVSSCARVWGD TTLGYGMDVWDIQMTQSPSSLSASVGDRVTITCQASQDISNYLNWYQQKPGKAPKLLIYDASNLETGVPSRFSGSGSGTDFTFTISSLQPEDATYYCQQYDNLPLTFGGG TKVEIKCQQYDNLPLTF

Clone ID	scFv sequence
YU397-A03	PGGSLRLSCAASGFTFSSYEMNWVRQAPGKGLEWVSYISSSGSTIYYAD SVKGRFTISRDNANKNSLYLQMNSLRAEDTAVYYCARRRGGGFDYWGQ GTLVTVSSCARRRGGGFDYWQSALTQPASVSGSPGQSITISCTGTSSDV GGYNYVSWYQQHPGKAPKLMYDVSNRPSGVSNRFSGSKSGNTASLTI SGLQAEDADYYCSSYTSSSTWVFGGGTKLTVLCSSYTSSSTWVF
YU397-B01	PGESLKISCKGSGYSFTSYWIGWVRQMPGKGLEWMGHIYPGDS DTRYSP SFQGQVTISADKSISTAYLQWSSLKASDTAMYYCAIPWDAELGNYGMD VWGQGT TVTVSSCAIPWDAELGNYGMDVWDIQMTQSPSSLSASVGDR VTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSG TDFTLTISLQPEDFATYYCLQDYNYPFAFGQGTKVEIKCLQDYNYPFA F
YU397-B02	PGSSVKVSCKASGGTFSSYAIWVRQAPGQGLEWMGGHIPIFGTANYAQ KFQGRVTITADKSTSTAYMELSSLRSED TAVYYCARGRW SGLGDYWG QGTLVTVSSCARGRW SGLGDYWMTQSPSSLSASVGDRVTITCQASEDI RMYLGWYQQKAGRAPKLLIFEGSSLEPGVPSRFSGSGSGTHFTFTISLQ PDDFATYYCQQYYDDPQFGGGTKVVLKCQQYYDDPQF
YU397-D01	PSGTLSTCAVSGGSISSSNWWSWVRQPPGKGLEWIGEIYHSGSTNYP SLKSRVTISVDKSKNQFSLKLSSVTAADTAVYYCARARGGRYFDYWGQ GTLVTVSSCARARGGRYFDYWDIVLTQSPSFLSASVGDRVTITCRASQG ISTYLAWYQQKPGTAPKVL MYAASTLHSGVPSRFSGSGSGTEFTLTISL QPEDFAIYYCQQLNGYPTTFGGGTRVEIKCQQLNGYPTTF
YU398-A11	PGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVISYDGSNKYY ADSVKGRFTISRDNANKNTLYLQMNSLRAEDTAVYYCAKGQGDGMDV WGQGT TVTVSSCAKGQGDGMDVWYELTQPPSASGTPGQRTISCSGSS SNVGSRTVSWFQQLPGTAPKLLIYSNNLRPSGV PDRFSGSKSGTSASLAI SGLQSEDEADYYCAAWDDSLIGHVFGTGKVTTVCAAWDDSLIGHVF
YU398-E10	PGGSLRLSCAASGFTFSSYSMNWVRQAPGKGLEWVSSISSSSSYIYYAD SVKGRFTISRDNANKNSLYLQMNSLRAEDTAVYYCARDQLAARRGYYY

Clone ID	scFv sequence
	GMDVWGQGTTVTVSSCARDQLAARRGYYYGMDVWVLTQPPSVSVAP GQTATIACGGNNIGTKSVHWYQQKPGQAPVLVYDDSDRPSGIPERFS GSNSGNTATLTISRVEAGDEADYYCQVWDSSSDHVVFVGGGTKLTVLCQ VWDSSSDHVVF
YU400-A05	PGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVISYDGSNKYY ADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAKGDVNYGMDV WGQGTTVTVSSCAKGDVNYGMDVWSYVLTQPPSVSVAPGQTARISCG GSNIGSKTVNWYRKAGQAPVLVYDGRDRPSGIPERFSGSNSGNAAT LIISRVEVGDEADYYCQVWDTSGDLHWAFGGGTKLTVLCQVWDTSGD LHWAF
YU400-A12	PSGTLSTCAVSGGSISSSNWWSWVRQPPGKGLEWIGEIYHSGSTNYP SLKSRVTISVDKSKNQFSLKLSSVTAADTAVYYCARDFFYGGSGSYPNG YYYGMDVWGQGTTVTVSSCARDFFYGGSGSYPNGYYYGMDVWDIVM TQSPSSLSASLGDRVTITCRASQSINSYLNWYQQKPGKAPRLLIYTASTL QSGVPSRFSGSGAGTDFTLTISSLQPEDVATYYCQQSYTTPLTFGGGTK MEIKCQQSYTTPLTF
YU400-B07	PGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVISYDGSNKYY ADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAKGDVNYGMDV WGQGTTVTVSSCAKGDVNYGMDVWSYVLTQPPSVSVAPGKTARITCG GNNIGSKSVHWYQQKPGQAPVLVYDDTD RPSGIPERFSGSNSGNTAT LTISRVEAGDEADYYCQVWDSSSDLLWVFVGGGTKLAVLCQVWDSSD LLWVF
YU400-D09	PGSSVKVSKASGGTFSSYAIWVRQAPGQGLEWMGGIPIFGTANYAQ KFQGRVTITADESTSTAYMELSSLRSEDTAVYYCARDFNPF SIFEMDV WGQGTTVTVSSCARDFNPF SIFEMDVWQSVLTQPPSVSAAPGQKVTI SCSGSSSNIGNNYVSWYQQLPGTAPKLLIYDNNKRPSGIPDRFSGSKSGT SATLGITGLQTGDEADYYCGTWDSLSALVFVGGGTKLTVLCGTWDSLS SALVF

Clone ID	scFv sequence
YU400-F07	PGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVISYDGSNKYY ADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAKGDVNYGMDV WGQGT TTVTVSSCAKGDVNYGMDVWSYVLTQPPSVSVAPGQTARISCG GSNIGSKTVNWYRKKAGQAPVLVVDGRDRPSGIPERFSGSNSGNAAT LIISRVEVGDEADYYCQVWDTSGDLHWAFGGRTKLTRCQVWDTSGDL HWAF
YU400-H08	PGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVISYDGSNKYY ADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAKGDVNYGMDV WGQGT TTVTVSSCAKGDVNYGMDVWSYVLTQPPSVSVAPGQTARISCG GSNIGSKTVNWYRKKAGQAPVLVVDGRDRPSGIPERFSGSNSGNAAT LIISRVEVGEGGQY*LQVWDTSGDLHWAFGGGTKLTVLLQVWDTSGD LHWAF
YU401-A11	PGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVISYDGSNKYY ADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCANLAMGQYFDY WGQGT LTVTVSSCANLAMGQYFDYWQAVLTQPPSASGTPGQRTVITCS GSSSNIGSNTVNWYQQLPGTAPKLLIYSNNQRPSGVPDRFSGSKSGTSA SLAISGLQSEDEADYYCAAWDDSLNGPVFGGGTKLTVLCAAWDDSLN GPVF
YU401-B01	PGSSVKVSKASGGTFSSYAIWVRQAPGQGLEWMGGIPIFGTANYAQ KFQGRVTITADESTSTAYMELSSLRSED TAVYYCAREMYYYYGMDVW GQGT TTVTVSSCAREMYYYYGMDVWDIVMTQSPSSLSASVGDRVITC RASQSIITYLNWYQQKPGKVPKLLIYAASSLQSGVPSRFSGSGSGTDFTL TISSLQPEDFATYYCQQSYSTPPTFGQG TKLEIKCQQSYSTPPTF
YU401-D11	PGGSLRFSCAASGFTFSSYGMHWVRQAPGKGLEWVAVISYDGSNKYY ADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCANLAMGQYFDY WGQGT LTVTVSSCANLAMGQYFDYWQAVLTQPPSASGTPGQRTVITCS GSSSNIGSNTVNWYQQLPGTAPKLLIYSNNQRPSGVPDRFSGSKSGTSA

Clone ID	scFv sequence
	SLAISGLQSEDEADYYCAAWDDSLNGPVFGGGTKLTVLCAAWDDSLN GPVF
YU401-E11	PGRSLRLSCAASGFTFSSYAMHWVRQAPGKGLEWVAVISYDGSNKYY ADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCARDLGEAKSSSP HEPDYWGQGTLVTVSSCARDLGEAKSSSPHEPDYWLTQSPLSLSVTPG QPASISCKSSQSLLHSDGKTYLDWYLQKPGQPPQLLIYEVS NRFSGVPD RFSGSGSGTDFTLKISRVEAEDVGIYYCMQTKQLPLTFGGGPKLEICMQ TKQLPLTF
YU401-F11	PGRSLRLSCAASGFTFSSYAMHWVRQAPGKGLEWVAVISYDGSNKYY ADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCARDLGEAKSSSP HEPDYWGQGTLVTVSSCARDLGEAKSSSPHEPDYWLTQSPLSLSVTPG QPASISCKSSQSLLHSDGKTYLDWYLQKPGQPPQLLIYEVS NRFSGVPD RFSGSGSGTDFTLKISRVEAEDVGIYYCMQTKQLPLTFGGGPKLEICMQ TKQLPLTF
YU401-G07	LGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVISYDGSNKYY ADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAKGDVNYGMDV WGQGTITVTVSSCAKGDVNYGMDVWSYVLTQPPSVSVAPGQTARISCG GSNIGSKTVNWYRK KAGQAPVLVVDGRDRPSGIPERFSGSNSGNAAT LIISRVEVGDEADYYCQVWDTSGDLHWAFFGGGTKLTVLCQVWDTSGD LHWAFF
YU402-A02	PSETLSLTCTVSGDSISSSSYWSWIRQPPGKGLEWIGEINHSGSTNYPNPS LKSRTISVDTSKNQFSLKLSSVTAADTAVYYCARDQEMYYFDYWGGQ GTLVTVSSCARDQEMYYFDYWDIQMTQSPSSVSASVGDRVTITCRASQ GISSWLAWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTIS LQPEDFATYYCQQANSFPPTFGPGTKVDIKCQQANSFPPTF
YU402-A11	PSGTLSTCDVSGGSISRSNWWIWRQPPGKGLEWIGEIYHTGSTNYPNPS SLKRRVTISVDKSKNQFSLNLSSVTAADTAVYYCARGKGSYAFDIWGL GTMVTVSSCARGKGSYAFDIWVLTQPHSVSESPGKTVTISCTGSGGNIA

Clone ID	scFv sequence
	RNYVQWYQHRPGRAPSTVIYEDDRPSGVPDRFSGSTDISSNSASLTISG LKTEDEADYYCQSYDGNNHMVFGGGTRVTVLCQSYDGNNHMV
YU402-D10	PGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVISYDGNKYY TDSVKGRFTISRDNKNTVYLQMNSLRAEDTAVYYCAKGYSSSPGDY WGQGTLLTVSSCAKGYSSSPGDYWQSALTQPASVSGSPGQSITISCTGT SSDVGAYNYVSWYQQYPGKAPKLMYDVSNRPSGVSDRFSGSKSGNT ASLTISGLQAEDEADYYCSSYTSSSTLWVFGGGTKLTALCSSYTSSSTL WVF
YU403-G05	PSGDLSLTCDVSGGSISRSNWWIWRQPPGKGLEWIGEYHTGSTNYP SLKRRVTISVDKSKNQFSLNLSSVTAADTAVYYCARGKGSYAFDIWGL GTMVTVSSCARGKGSYAFDIWVLTQPHSVSESPGKTVTISCTGSGGNIA RNYVQWYQHRPGRAPSTVIYEDDRPSGVPDRFSGSTDISSNSASLTISG LKTEDEADYYCQSYDGNNHMVFGGGTRVTVLCQSYDGNNHMV
YU391-B12	QMQLVQSGAEVKKPGSSVKVSCKASGGTFSSYAISWVRQAPGQGLEW MGHIPIFGTANYAQKFQGRVTITADESTSTAYMELSSLRSEDTAVYYC AREMYYYYGMDVWGQGTITVTVSSDIQMTQSPSSLSASVGDRVTITCR ASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLT ISSLPEDFATYYCQSYSTPPAFGQGTKLEIK
YU392-E05	QVQLQESGPGLVKPSGTLSTCTVSGGSISSSNWWSWVRQPPGKGLEW IGEYHSGSTNYPNPSLKSRVTISVDKSKNQFSLKLSSVTAADTAVYYCAR GVIAAAGTYFDYWQGTLLTVSSQAVLTQPPSASGTPGQRTISCSGSR PNVASNSVNWYQQFPGTAPRLLIYSDNQRPSGVDPDRFSGSKSGTSASLA ISGLQFEDEADYYCETWDDSLRGVVFGGGTKVTVL
YU392-E06	QLQLQESGPGLVKPSGTLSTCAVSGGSISSSNWWSWVRQPPGKGLEW IGEYHSGSTNYPNPSLKSRVTISVDKSKNQFSLKLSSVTAADTAVYYCAR ERTHYYYGMDIWGQGTITVTVSSQSVLTQPPSTSGTPGQRTISCSGSSS NIGSNTVNWYHQLPGTAPRLLIYSNNQRPSGVDPDRFSGSKSGTSASLAL SGLQSEDEGDYYCAAWDDSLNGYVFGTGKTVTVL

Clone ID	scFv sequence
YU392-G08	EVRLGQSGPELKNPGDFRKISCKGSGYSFTSYWIGWVRQMPGKGLEW MGHIYPGDS DTRYSPSFQGGQVTISADKSISTAYLQWSSLKASDTAMYYC ARLENNWDYGGWFDPPWGQGT LVTVSSSYVLTQPPSVSVAPGQTARIT CGGNNIGSKSVHWYQQKPGQAPV L VVYDDSDRPSGIPERFSGSNSGNT ATLTISRVEAGDEADYYCQVWDSSSDHWVFGGGTKLTVL
YU392-G09	QVQLVQSGAEVKKPGSSVKVSCASGGTFSSYAISWVRQAPGQGLEW MGHIPIFGTANYAQKFQGRVTITADESTSTAYMELSSLRSEDTAVYYC ARDGAGNYDILTGDRSEDIY YYYGMDVWGQGT TTVTVSSSYELTQPPS ASGAPGQRV SISC SGGYSNIGSNTVNWYQQLPGAAPKFLIYSDNQRPSG VPDRFSGSKSGTSASLAISGLQSEDEADYYCATWDDSLNGPVFGGGTK LTVL
YU392-G12	QVQLQESGSLVKPSQTL SLTCAVSGGSISSGGYSWSWIRQPPGKGLEW IGYIYHSGSTYYNPSLKSRVTISVDRSKNQFSLKLSSVTAADTAVYYCA RAGYYYGMDVWGQGT TTVTVSSDIVMTQTPSSLSASVGDRVAITCQAS RNIWSYVNWYQQKPGEAPRL LIYGASTLQRGVPSRFSGSGSGTGFTLTI NSLQPEDFATYFCQQSHSTPITFGGGTRVDIK
YU392-H02	QLQLQESGPGLVNLSQTL SLTCTVSGGSISSGGYYWSWIRQHPGKGLE WIGYIYSGSTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYC ARDSSSGPYGMDVWGQGT TTVTVSSQSVLTQPPSVSVAPGQTARVTCG GSNIGSQSVHWYQQKPGQAPV L VVYDDYDRPSGIPERFSGSNSGNTAT LTITRVDAGDEADYYCQIWDSSSAHV VFGGGTKLTVL
YU392-H04	QVQLQESGPGLVKPSGTL SLTCAVSGGSISSSNWWSWVRQPPGKGLEW IGEYIYHSGSTNYNPSLKSRVTISVDKSKNQFSLKLSSVTAADTAVYYCAR VNYGDYDWYFDLWGRGTLVTVSSQPVL TQPPSASGTPGQRVTISCSGS SSNIGSNFVTWYQQLPGTAPKLLIYSNNQRPSGVSDRFSASKSGTSASLA ISRLQSQDEAEYYCAAWDDSLRSYVFGSGTKVTVV
YU394-D08	QVQLGESGAEVKKPGSSVKVSCASGGTFSSYAISWVRQAPGQGLEW MGWISAYNGNTNYAQKLQGRVTMTTDTSTSTAYMELRSLRSDDTAVY

Clone ID	scFv sequence
	YCAREPLRYYYYYGMDVWGQGTTVTVSSDIQMTQSPSSLSASVGDRV TITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGT DFTLTISLQPEDFATYYCQQSYSTPWTFGQGTKVEIK

[0223] In some embodiments, the antibody has a CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3, each independently selected from those disclosed in **Table 14A** and **Table 14B**. In some embodiments, the antibody has a CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3, each independently selected from any one clone listed in **Table 14A** and **Table 14B**. In some embodiments, the antibody has a CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3, each independently selected from those disclosed, in groups, in **Table 15A** and **Table 15B**. The disclosure provides antibodies having CDRs from individual clones or from matching any one CDR with any other five CDRs. The antibodies identified in **Table 14A** and **Table 14B** are derived from mouse phage-display library. Known methods may be used to convert these CDRs into humanized or chimeric antibodies.

VII. Use of CD25 antibodies

[0224] In some embodiments, the CD25 antibodies provided herein are useful for therapeutics., e.g. for use in proliferative diseases or disorders such as cancer or for use in autoimmune diseases.

[0225] Accordingly provided herein are methods of treating a cancer comprising administering to a subject in need thereof a therapeutically effective amount of a therapeutic CD25 antibody. In some embodiments, the cancer is a primary cancer. In some embodiments, the cancer is a metastatic cancer. In some embodiments, the cancer involves a solid tumor; in other embodiments, the cancer involves a liquid tumor, e.g. a blood based cancer. In exemplary embodiments, the CD25 antibody is a non-IL-2 blocking antibody.

[0226] Accordingly provided herein are methods of treating an autoimmune-related disease or disorder comprising administering to a subject in need thereof a therapeutically effective

amount of a therapeutic CD25 antibody. In exemplary embodiments, the CD25 antibody is a non IL-2 blocking antibody.

[0227] As used herein, a subject refers to any animal classified as a mammal, including humans, domestic and farm animals, and zoo, sport, or pet animals, such as dogs, horses, rabbits, cattle, pigs, hamsters, gerbils, mice, ferrets, rats, cats, and the like. Subjects may be male or female.

[0228] The administration of any of the therapeutic CD25 antibodies provided herein may be administered in combination with other known drugs/treatments (e.g. small molecule drugs, or biologics). The administration may be sequential or concurrent.

[0229] In vivo administration of the therapeutic CD25 antibodies described herein may be carried out intravenously, intratumorally, intracranially, intralesionally (e.g. intralesional injection, direct contact diffusion), intracavitary (intraperitoneal, intrapleural, intrauterine, intrarectal), intraperitoneally, intramuscularly, subcutaneously, topically, orally, transdermally, by implantation, by inhalation, intrathecally, intraventricularly, or intranasally. In an exemplary embodiment, the route of administration is by intravenous injection.

[0230] A therapeutically effective amount of the therapeutic antibody generally will be administered. The appropriate dosage of the therapeutic antibody may be determined based on the severity of the disease, the clinical condition of the subject, the subject's clinical history and response to the treatment, and the discretion of the attending physician.

VIII. Diagnostic Uses

[0231] The CD25 antibodies provided herein may be used for diagnostic and detection purposes. Depending on the application, the CD25 antibody may be detected and quantified *in vivo* or *in vitro*.

[0232] The CD25 antibodies provided herein are amendable for use in a variety of immunoassays. These immunoassays include, but are not limited to enzyme-linked immunosorbent assay (ELISA), Western blot, radioimmunoassay (RIA), flow cytometry, a radioimmunoassay, an immunofluorescence assay, spectrophotometry, radiography,

electrophoresis , high performance liquid chromatography (HPLC), or thin layer chromatography (TLC).

[0233] The CD25 antibodies provided herein may be comprise a detectable label, for example detectable by spectroscopic, photochemical, biochemical, immunochemical, fluorescent, electrical, optical or chemical methods. Useful labels in the present invention include, but are not limited to fluorescent dyes, radiolabels, enzymes, colorimetric lables, avidin or biotin.

[0234] In some embodiments, the CD25 antibody is radiolabeled with an isotope, useful for imaging by nuclear medicine equipment (SPECT, PET, or scintigraphy).

VIII. Pharmaceutical Compositions

[0235] The disclosure provides compositions comprising therapeutic CD25 antibodies, In some embodiments the composition is sterile. The pharmaceutical compositions generally comprise an effective amount of the therapeutic antibody in a pharmaceutically acceptable excipient.

IX. Kits and Articles of Manufacture

[0236] The disclosure also provides for kits comprising any of the CD25 antibodies described herein, e.g. for either therapeutic or diagnostic uses. In some embodiments, the kits further contain a component selected from any of secondary antibodies, reagents for immunohistochemistry analysis, pharmaceutically acceptable excipient and instruction manual and any combination thereof. In some embodiments, the kit comprises any one or more of the therapeutic compositions described herein, with one or more pharmaceutically acceptable excipients.

[0237] The present application also provides articles of manufacture comprising any one of the therapeutic or diagnostic compositions or kits described herein. Examples of an article of manufacture include vials (e.g. sealed vials).

[0238] The description provided herein sets forth numerous exemplary configurations, methods, parameters, and the like. It should be recognized, however, that such description is not intended as a limitation on the scope of the present disclosure, but is instead provided as a description of exemplary embodiments.

EXAMPLES

[0239] The following Examples are merely illustrative and are not meant to limit any aspects of the present disclosure in any way.

Example 1: Development of Engineered Immunogens Sharing Characteristics of CD25

[0240] A crystal structure of CD25 was obtained. A number of the crystal structures available for CD25 are missing a mobile loop section of the protein. Molecular dynamics simulations were performed to gain a greater understanding of this mobile loop, and binding interactions of CD25 with IL-2.

[0241] Different sections of CD25 were selected as inputs for developing an engineered immunogen. Some of these areas are shown in **FIG. 34B** and **FIG. 34C**. These inputs were used with the ROSETTA program to improve to the overall desirable structural and dynamic properties of the interfacial residues. This process made changes to the structural (non-interface) parts of the segment to stabilize and recapitulate the structure, conformation, dynamics and other properties of the interface residues in-context of the native CD25 from which they were derived. The stability and flexibility of the segment under development was also analyzed, and the sequence adjusted if needed to change these parameters. For example, the N or the C terminus can be extended by the addition of one or more amino acids to add desired properties. The effect of cross-linking on the engineered immunogen candidates was also evaluated, using disulfide bonds forming between the side chains of different amino acid residues. At each stage of design engineering – amino acid addition, crosslinking, and structural residue optimization – the native scoring and energy functions of the ROSETTA program were used to quantitatively evaluate each of the many design candidates. Those candidates possessing the best ROSETTA energies are carried forward to subsequent stages of design, and ultimately forward to evaluation and validation by molecular dynamics simulation. In addition to evaluating these parameters at

physiological pH (e.g., around pH 7.4), parameters were also evaluated in some instances at tumor microenvironment pH (e.g., around pH 6.5).

[0242] Quantitative metrics for ranking the different designs using molecular dynamics (MD) simulation included similarity to CD25, evaluated through RMSD; and structural flexibility of the candidates. **FIG. 33A** and **FIG. 33B** show exemplary comparisons of stability vs. RMSD at physiological pH for exemplary engineered immunogens developed using the input sections indicated in **FIG. 32** (left arrow for **FIG. 33A**, right arrow for **FIG. 33B**). **FIG. 33C** is an exemplary comparison of stability vs. RMSD at tumor microenvironment pH for the exemplary immunogen of **FIG. 33B**. A representative scoring algorithm is presented below.

$$\text{Score}_{\text{similarity+flexibility}} = \frac{\sum(a_i f_i)}{f_0}, a_i = \begin{cases} 0, & \text{rmsd}_i > k_{\text{max}}(\text{\AA}) \\ 1, & \text{rmsd}_i \leq k_{\text{max}}(\text{\AA}) \end{cases}$$

f_i = Fraction of ensemble

k_{max} = Similarity cutoff

[0243] Structural similarity was calculated using root mean square deviation (RMSD) between the atomic coordinates of each peptide conformation in the MD ensemble and the reference structure after RMS alignment to the reference structure. The RMSD was computed using the computationally designed engineered immunogen candidate structure as the reference structure or by using the experimentally characterized (e.g., X-ray crystal structure) structure as the reference. In these simulations, the functional interface residues of the candidate (in some simulations) and all residues including the structural residues of the candidate (in other simulations) were compared to the reference.

[0244] The ensemble of conformations sampled by MD were clustered into groups (clusters) structurally similar to each other based on RMSD. Disorder was evaluated as the fraction of the conformations in the MD ensemble that could not be grouped into a cluster of similar conformations due to structural dissimilarity (e.g., high RMSD) to all other conformations in the ensemble. Thus, an engineered immunogen candidate with more disorder than an alternative

candidate was more flexible. Order was evaluated as the fraction of the conformations in the MD ensemble that were grouped into a cluster of similar conformations (low RMSD). An engineered immunogen candidate with more order than an alternate candidate was less flexible when a higher fraction of its ensemble of conformations fell into fewer clusters than the alternate candidate.

[0245] The clusters populated by an engineered immunogen candidate were compared with a reference structure using RMSD. If the RMSD of a cluster was below a threshold value of 4 Angstroms, the cluster was considered ordered (*e.g.*, low flexibility) and similar to the reference (structural similarity). An engineered immunogen candidate with a high fraction of its ensemble meeting this criterion of low flexibility and high structural similarity is predicted to be more active than an alternate candidate with a low fraction of its ensemble meeting this criterion of low flexibility and high structural similarity.

[0246] This quantitative analysis was combined with qualitative analysis of the MD trajectories regarding biophysical, biological and physical-chemical interactions, and used to select given immunogen candidates to evaluate *in vitro*. **Table 6** below lists eleven engineered immunogens prepared as described above.

Table 6. Engineered Immunogens

Label	Sequence	Cross-Link	SEQ ID NO:
13_131_CYN	TVYPQPDATAKCVHGCDPREYTKAVEDAK	C12-C16	17
11_14_CYN	DWGDDCKKKHEITHATGDYCEKLDKS	C6-C20	18
6_163_CYN	DDCIKVTGPAECAERACRAQEERQRQPQCI	C3-C17	19
57_63	CDCQAQWTPGMRAPGYDPYCLNCGS	C1-C23, C3-C20	20
13_131	MVYCQPDCTAKCMHGCDRDTMKECCDRLK	C12-C16, C8-C25, C4-C24	2
6_130	DDCPEVPHATFKGPGQKWEGPGGGDCSK	C3-C26	3
6_163	DDCIEVPGPAECAERACRAQEERQRQPQCI	C3-C17, C12-C29	4
77_89	AEEKIKIEQKERKTTIKLAKEAK	none	5
147_156	CHLQIMTHGKIIVPCGS	C1-C23	21
11_14	DDGDRCakeHEIPHATGEECQKRDKS	C6-C23	7
44_56	CKQLVIYFTGNSSHSSVFYIYDC	C1-C24	8

Example 2: Evaluation of Engineered Immunogens *in vitro*

[0247] The binding of the engineered immunogens prepared in Example 1 are evaluated using an antibody to CD25. The engineered immunogens are modified on the C-terminus with a –GSGSGK-biotin group, and then bound separately to a streptavidin-coated biosensor tip. Buffer containing the CD25 antibody is flowed over the tip during an association phase of 300 seconds, and then the flowed solution is switched to buffer without the CD25 antibody and the dissociation from the biosensor tip will be measured. A control is also run where the tip does not have any engineered immunogen or protein initially bound, to evaluate any background binding of the CD25 antibody to the tip. A second control is performed where full length CD25 is biotinylated and bound to the biosensor tip, to demonstrate the binding level of the CD25 antibody to full length CD25. The data obtained from these biosensor experiments is used to qualitatively rank binding of the engineered immunogens.

Example 3: Evaluation of Engineered Immunogens with Phage Panning

[0248] Engineered immunogens provided herein are evaluated using phage panning techniques.

[0249] Mouse HuCD25 immunized phage libraries are transformed by electroporation in TG1 and phage propagated with the addition of CM13 using standard Phage Display protocols. TG1 cultures secreting phage are PEG precipitated with PEG/NaCl after incubation on ice for one hour. Exemplary libraries that may be used include 7807, 7808, 7809, and 7810.

[0250] *Tumor microenvironment (TME) pH subtractive selections:* Phage panning is carried out physiological pH and TME pH. To deplete antibodies that bind with high affinity to full-length CD25 at physiological pH, subtractive panning is first carried out by counter-selection of 3×10^{11} pfu phage (1000-fold representation of a 3×10^8) at pH 7.4 by absorption for 1 hour on ELISA plates coated with 10 ug/ml full-length CD25 (400 nM) in PBST pH 7.4. Resulting phage supernatant is collected and pH is adjusted to pH 6.5 with PBST. Subsequent phage panning selections are carried out at pH 6.5.

[0251] Panning selections are pre-cleared with 25 microliters streptavidin Dynabeads with no antigen after a one hour incubation. Phage are then added to new pre-blocked Eppendorf LoBind tube. Biotinylated engineered immunogens (such as those described in Example 1) are added at 100 nM concentration (in some cases, additional 500 mMNaCl was added to reduce non-specific binding of immunogen to phage) for 40 min to one hour. Samples are then incubated with 25 microliters streptavidin beads or streptavidin coated plates at RT for one hour. Samples are pelleted and washed using magnet/magnetic beads or with plates, washed 7-10 times with PBST. Tubes are changed twice to remove residual phage.

[0252] To elute phage, 50-800 μ L glycine pH 2.2 is added to the beads and plates, respectively, and incubated for no more than ten minutes, then neutralized with high pH Tris 9.0. Eluted phage is added to 1-5 ml TG1 freshly grown (OD600 ~ 0.5), and incubated for 20-30 minutes.

[0253] Fractional log dilution series are plated, and the remainder transferred to 25 ml 2 x YT. 1 ml glycerol stock is saved for a subsequent panning round, and helper phage/IPTG added at OD600 ~0.5.

[0254] The selection against the engineered immunogen at pH 6.5 with counter-selection at pH 7.4 is carried out once more. The periplasmic extracts are subsequently evaluated using phage ELISA and octet screening.

[0255] To ensure that fab phage also bind full-length CD25 in addition to the engineered immunogen, a final selection with full-length CD25 can optionally be carried out, with full-length CD25 in place of the engineered immunogen (2 rounds selection against engineered immunogen, then 1 round selection against full length CD25).

[0256] To carry out selection with full-length CD25, after preclearing the panning selections with 25 microliters streptavidin Dynabeads, and adding phage to new pre-blocked Eppendorf LoBind tubes, biotinylated full-length CD25 is added at 100 nm concentration for one hour. The samples are then incubated with 25 microliters streptavidin beads at RT for one hour. Pelletting, washing, and elution steps are followed as described above.

Example 4: Phage ELISA protocol and Biosensor/Octet Screening

[0257] *ELISA/Extract Preparation:* Phage ELISA and periplasmic extract preparation for Fab Octet screening are conducted.

[0258] The CD25 antigen is diluted, added to the ELISA plate wells, and incubated. Following the incubation, wells are washed twice with PBS, then blocked by adding BSA followed by incubation for 2 hours at 25°C. Phage are diluted two-fold in 1xPBST 1.0% BSA, pH 6.5, 50 microliters are added per and incubated for 5 minutes at room temperature. The blocking solution is shaken out of the wells, and 50 µL of the dilute phage preparation is added to each well, and incubated for 1 hour at room temperature. The ELISA plate wells are washed 3-5 times with 200 microliters PBST pH 6.5. HRP-conjugated anti-M13 antibodies are diluted (Abcam, ab50370) 1:5000 with 1xPBST 1.0% BSA pH 6.5. 50 microliters of diluted secondary antibody conjugate is added to each well, and incubated for 1 hour at room temperature. ELISA plate wells are washed 3-5 times with 200 microliters PBST pH 6.5. The ECL Lumo substrate is prepared (e.g. Supersignal ELISA Pico Chemiluminescent Substrate) as described, into a 1:1 mixture. 50 microliters substrate solution is added to each well, incubated at room temperature for 5 to 60 minutes before reading.

[0259] Colonies are inoculated in 0.03-4 ml 2xYT 0.2% Glucose with 0.1 ml overnight culture (1 ml cultures in 96-well plate or 4 ml cultures in 14-ml falcon tubes). They are incubated at 250-700 rpm at 37°C until the OD600 ~0.5-1.0. Cultures are induced with 50-400 µL 0.025-0.1M IPTG. In some cases, the temperature is reduced to 30°C with shaking at 250 rpm. They are then incubated overnight. 1-4 ml cultures are harvested by pelleting 3400 rcf for 10-15 minutes. The supernatant is discarded. Cultures are resuspended with 50-75 µL PPB buffer (30 mM Tris-HCl, pH 8.0, 1 mM EDTA, 20% Sucrose) with 1x Halt Protease Inhibitor and incubated on a rocking platform for 15 minutes at room temperature or 4°C for 10 min. Then, cultures are resuspended with 150-225 µL of cold ddH2O with 1x Halt Protease Inhibitor and incubated on a rocking platform for one hour at room temperature or 4°C for 1-2 hours. The lysate suspension was spun at 15000 rcf for 10-15 min at 4°C. Supernatant is collected and diluted.

[0260] *Fab Expression and Purification Protocol:* Cell cultures are inoculated, grown up overnight, and then induced with 50 μ L of 25mM-1M IPTG. The temperature was reduced to 30°C and rpm to 150. Incubation was done overnight. 50 ml cultures or plates were harvested by pelleting 3400 rcf for 15 minutes. The supernatant was discarded. Cell pellets from 50 mL cultures were placed in a -80°C freezer for 1 hour, while cultures grown in plates had 75 μ L of PPB added with 1x Halt protease inhibitor, EDTA-free (Thermo Fisher Scientific) and vortexed. Plates are shaken at 4°C for 10 minutes at 1000 rpm. The volume of 225 μ L of cold water with 1x Halt protease inhibitor, EDTA-free (Thermo Fisher Scientific) is added to each well. Samples were mixed and shaken at 4°C for 1-2 hours at max speed i.e. 1000 rpm. Plates are spun at 3500 rpm for 10 mins at 4°C. The supernatant (PPE) is transferred to fresh plates and stored at -20°C. Cell pellets from the 50 mL cultures are removed from the freezer and 5 ml PBS, 10 mM Imidazole is added with 2.5 mg/ml lysozyme and 1x Halt protease inhibitor, EDTA-free (Thermo Fisher Scientific). After pellets are thawed at room temperature for 30 minutes and lysates were centrifuged for 15 minutes at 3400 rcf. The supernatant is removed and pellet discarded. 500 μ L Ni-NTA resin was added (pre-washed and pelleted) or a Ni-NTA spin column was used for Fab purification. Incubate with cleared lysate for 30 min – 1 hr. This was spun at 1500 rcf. These were washed 5 times with 1 ml PBS, 10 mM Imidazole. Buffer was discarded after each spin. 1 ml PBS, 200 mM Imidazole were added and mixed, incubated for 30 minutes and spun at 1500 rcf for 15 minutes. The eluted protein was stored at 4°C or 20°C after determining protein concentration. Zeba columns were used for desalting/buffer exchange.

[0261] *Octet/Biosensor Screening:* For Octet Koff rate screening in raw supernatants, 50 μ L of lysate is used in 384-well Pall ForteBio Octet plates. Data is collected on an Octet RED 384 (MD ForteBio). Briefly, Human CD25 is coupled to AR2G tips (1 μ g/ml). For data collection, baseline is assessed in PBST 1% BSA buffer for 60 seconds. Tips are then moved to 50 μ L lysate and association measured for 300 seconds. Finally, tips are moved to PBST 1% BSA buffer. Tips are then regenerated with 200 mM Tris-Glycine, pH 2.5 and neutralized with PBST, 1% BSA. For data analysis, double referencing (no CD25 on tip as well as blank reference well) is performed on Octet HT 11.0 software for reference subtraction.

Example 5: Evaluation of Antibodies Generated from Immunogens

[0262] Antibodies are produced by immunizing mice with the engineered immunogens described herein. These antibodies are evaluated for cross-reactivity, cross-blocking, affinity, and off-rate estimation.

[0263] *Protocol for cross-reactivity determination by Biosensor (Octet Red 384, Pall Forte Bio):* This protocol is used to determine the ability of individual test clones (anti-human CD25 mouse monoclonals) to bind the target (antigen) from human, cynomolgous monkey, and mouse species. The target proteins are either covalently coupled via primary amines to dextran coated sensor tips or by affinity capturing the 6X-His tagged target proteins on anti-6X-His monoclonal antibody coated sensor tip. The monoclonal supernatants, in solution, are made to bind to the antigen on the biosensor tip. The net binding signal is the binding signal with the subtraction of corresponding signal with blank media or buffer binding to blank or antigen coated tips. A signal > 3X background binding is considered as real binding event.

[0264] *Protocol for cross-blocking by Biosensor:* This method is to determine if the individual test clones (anti-human CD25 mouse monoclonals) are able to cross-block control antibodies. Cross-blocking may indicate that the test clones recognize an epitope that overlaps with the corresponding epitopes of the control antibodies. Additionally, this might imply that the test antibodies could have similar functional properties as the control antibodies. For this protocol, the control antibodies are covalently coupled via primary amines to dextran coated sensor tips. The target antigens, in solution, are made to bind to the control antibodies. Following this step, the test antibody, in solution, is made to bind to the antigen in a sandwich format. If the test antibody can bind to the antigen, it indicates that it does not cross-block the control antibody, while a non-binding may be interpreted as an ability to cross-block the control antibody.

[0265] *Protocol for affinity determination by Biosensor:* This method is used to determine the affinities of the individual test clones with antigens, when the concentration of the test antibodies is known. A capture molecule, such as Protein G or anti-mouse IgG-monoclonal or anti-human IgG-monoclonal is coated on the biosensor tip. Test clones are captured on the capture molecule coated surface. To these test clones, antigens in solution are made to associate

and dissociate for time periods ranging from 60 to 600 seconds for association phase and 60 to 1800 seconds for dissociation phase. The result data (or 'sensograms') are then fit using either a 1:1 Langmuir model or 2:1 heterogeneous model. The former assumes that the interacting pairs are homogenous if a 2:1 model for fitting the data results in a better fit, it indicates that the clones require further sub-cloning due to inherent heterogeneity. The data curve fits provide the dissociation constant as a ratio of the on and off-rate constants

[0266] *Protocol for off-rate estimation by Biosensor:* This method is used to estimate the dissociation rate constant of test clones when the concentration of antibodies is not known or if the test clones require further subcloning. A capture molecule, such as Protein G or anti-mouse IgG-monoclonal or anti-human IgG-monoclonal is coated on the biosensor tip. Test clones are captured on the capture molecule coated surface. To these test clones, antigens in solution are made to associate and dissociate for time periods ranging from 60 to 600 seconds for association phase and 60 to 1800 seconds for dissociation phase. The result data (or 'sensograms') are then fit using either a 1:1 Langmuir model or 2:1 heterogeneous model. The former assumes that the interacting pairs are homogenous if a 2:1 model for fitting the data results in a better fit, it indicates that the clones require further sub-cloning due to inherent heterogeneity. The data is fit only for the off-rate constant and not the on-rate (or association) rate constant. This provides the estimates of off-rate constant, which can be used to rank-order the test clones.

Example 6: Selection of Engineered Polypeptides using a CD25 Portion as the Reference Target

[0267] The sequence and three dimensional (3D) structure of CD25 was retrieved from the protein databank (PDB) (PDB ID NO: 2ERJ, chain A):

ELCDDDPPEIPHATFKAMAYKEGTMLNCECKRGFRRIKSGSLYMLCTGSSSHSSWDNQC
QCTSSATRSTTKQVTPQPEEQKERKTTEMQSPMQPVDQASLPGHCREPPPWENEATERI
YHFVVGQMVYYQCVQGYRALHRGPAESVCKMTHGKTRWTQPQLICTG

[0268] As shown in **FIG. 6**, a putative therapeutic epitopes of CD25 were identified as reference targets for engineered polypeptide selection. Residues positions with respect to SEQ ID NO: 1) and epitope sequences are provided in **Table 7**.

Table 7

Epitope #	Epitope ID	Epitope Positions	Epitope Sequence
1	_55-63_	55-63	SWDNQCQCT
2	_13-20_127-132_	13-20:127-132	ATFKAMA . . . MVYYQC
3	_6-17_	5-17	DDPPEIPHATFKA
4	_5-11_156-163_	5-11:156-163	DDPPEIP . . . RWTQPQLI
5	_77-89_	77-89	QPEEQKERKTTEM
6	_147-157_	147-157	VCKMTHGKTRW
7	_11-14_	11-14	IPHA
8	_44-56_	44-56	YMLCTGSSSHSSW

[0269] Atomic distance and amino acid descriptor topology were determined. The atomic distance and amino acid descriptor topology of the reference target were obtained using dynamic simulations, and a covariance matrix of atomic fluctuations was generated for the epitope in the reference target. Next, different engineered polypeptide candidates were generated using computational protein design (*e.g.*, Rosetta), dynamics simulations performed on the candidates, and the atomic distance and amino acid descriptor topologies determined. A covariance matrix of atomic fluctuations was generated for the reference target epitope, and for the residues in the candidates corresponding to the residues in the epitope of the reference target.

[0270] Principal component analysis was performed to compute the eigenvectors and eigenvalues for each covariance matrix—one covariance matrix for each reference target and one covariance for each of the candidates—and only those eigenvectors with the largest eigenvalues are retained. Eigenvectors describe the most, second-most, third-most, N-most dominant motion observed in a set of simulated molecular structures. If a candidate moves like the reference epitope, its eigenvectors will be similar to the eigenvectors of the reference target (epitope). The similarity of eigenvectors corresponds to their components (a 3D vector centered on each CA

atom) being aligned – pointing in the same direction. This similarity between candidates and reference target eigenvectors was computed using the inner product of two eigenvectors. The inner product value was 0 if two eigenvectors are 90 degrees to each other or 1 if the two eigenvectors point precisely in the same direction.

[0271] Since the ordering of eigenvectors is based on their eigenvalues, and eigenvalues may not necessarily be the same between two different molecules due to the stochastic nature by which molecular dynamics simulations sample the underlying energy landscape of those different molecules, the inner product between multiple, differentially ranked eigenvectors was needed (*e.g.*, eigenvector 1 of the candidate by eigenvector 2, 3, 4, etc. of the reference target). In addition, without wishing to be bound by any theory, molecular motions are complex and may involve more than one (or more than a few) dominant/principal modes of motion.

[0272] To solve these two challenges, the inner product between all pairs of eigenvectors in the candidates and the reference target were computed. This resulted in a matrix of inner products the dimensions of which were determined by the number of eigenvectors analyzed – for 10 eigenvectors, the matrix of inner products is 10 by 10. This matrix of inner products was distilled into a single value by computing the root mean-square value of the inner products. This is the root mean square inner product (RMSIP).

[0273] Principal component analysis (PCA) reduces the $3L \times 3L$ dimensional coordinate covariance matrices (L being number of atoms) into sets of eigenvectors, Φ (reference target) and Ψ (MEM), and eigenvalues, Λ . The set Φ contains N eigenvectors ϕ_i for the reference target and the set Ψ contains N eigenvectors ψ_j for the MEM, where eigenvectors are ordered in their respective sets by their associated eigenvalues. The eigenvector with the largest eigenvalue accounts for the largest fraction of total coordinate covariation. The inner product of each ϕ_i and ψ_j eigenvector is computed to compare the similarity of motion between the reference target and the MEM. The root mean square of all inner product combinations of ϕ_i and ψ_j eigenvectors renders the total similarity of motion of the engineered polypeptide candidate (MEM) to the reference target (RMSIP).

[0274] As shown in **FIG. 7**, in each engineered polypeptide, epitope residues (gold) and position in the in 3D space by addition of scaffold residues (grey) selected by this computational design procedure. Residues positions with respect to PDB ID NO: 2ERJ, chain A, and epitope sequences are provided in **Table 8** and **Table 9**. Crosslink positions refer to the expected occurrence of intracellular disulfide bond formation in each MEM sequence.

Table 8

MEM ID	N-Terminal Linker	MEM Sequence (N→C)	C-Terminal Linker	Crosslink Positions	Epitope #
57_63	—	CDCQAQWTPGMR APGYDPYCLNC	GSGSGK- Biotin	C1-C23, C3-C20	1
13_131	—	MVYCQPDCTAKC MHGCDRDTMKEC CDRLK	GSGSGK- Biotin	C12-C16, C8-C25, C4-C24	2
6_130	—	DDCPEVPHATFKG PGQKWEGPGGGD CSK	GSGSGK- Biotin	C3-C26	3
6_163	—	DDCIEVPGPAECA ERACRAQEERQRQ PQCI	GSGSGK- Biotin	C3-C17, C12-C29	4
77_89	—	AEEEEKIKIEQKERK TTIKLAKEAK	GSGSGK- Biotin	none	5
147_156	—	CHLQIMTHGKIIYV PC	GSGSGK- Biotin	C1-C23	6
11_14	—	DDGDRCAKEHEIP HATGEECQKRDKS	GSGSGK- Biotin	C6-C20	7
44_56	—	CKQLVIYFTGNSS HSSVFYIYYDC	GSGSGK- Biotin	C1-C24	8
6_130_J1	Biotin- PEG2	GSGDEDCKKFQSD DNWENYTSTRHLT FCDEKRS	—	C7-C28	3

MEM ID	N-Terminal Linker	MEM Sequence (N→C)	C-Terminal Linker	Crosslink Positions	Epitope #
44_56_J1	Biotin-PEG2	GSGNEEIEKKIKDC TGNSSHSSWEEAL ECALKK	—	C14-C29	8
44_56_J2	Biotin-PEG2	GSGDERIERLIKEC TGNSSHSSWEEAL ECALRR	—	C14-C29	8
147_157_J1	Biotin-PEG2	GSGSHPCAYWRW VIKMTHGKTRWV LELVFCYRD	—	C7-C30	6
147_157_J2	Biotin-PEG2	GSGKCEEEAKKIA SKMTHGKTREEEA EEYLKKC	—	C5-C33	6
33_63_J1	Biotin-PEG2	GSGDDESEKRTTE RDTRKCTKAKAN DNQCQPTTE	—	C19-C29	1
33_63_J2	Biotin-PEG2	GSGSSEWDKWVE EWYKKMCTEAKK NDNQCQPTK	—	C19-C29	1
33_63_J3	Biotin-PEG2	GSGQCRVWVERN GDKILYIYEDCDN DNQHQQTL	—	C5-C22	1

*Biotin-PEG2=Biotin-Poly-ethyleneglycol(2)

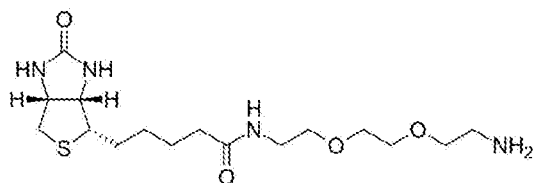


Table 9

MEM ID	Epitope #		CD25 Interface Residues (bold and underline: <u>X</u>) MEM Scaffold Residues (plain text: X)
57_63	1		C <u>D</u> C <u>Q</u> A <u>Q</u> <u>W</u> T PGMRAPGYDPYCLNC
13_131	2		<u>M</u> <u>V</u> <u>Y</u> C <u>Q</u> PDC <u>T</u> <u>A</u> <u>K</u> <u>C</u> <u>M</u> HGCDRDTMKECCDRLK
6_130	3		<u>D</u> <u>D</u> C <u>P</u> <u>E</u> V <u>P</u> <u>H</u> <u>A</u> <u>T</u> <u>F</u> <u>K</u> GPGQKWE GPGGGDCSK
6_163	4		<u>D</u> <u>D</u> C <u>I</u> <u>E</u> <u>V</u> <u>P</u> GPAECAERACRAQEER <u>R</u> <u>Q</u> <u>R</u> <u>Q</u> <u>P</u> <u>Q</u> <u>C</u> <u>I</u>
77_89	5		AE <u>E</u> <u>E</u> K <u>I</u> <u>K</u> <u>I</u> E <u>Q</u> <u>K</u> <u>E</u> <u>R</u> <u>K</u> <u>T</u> <u>T</u> IKLAKEAK
147_156	6		CHLQI <u>M</u> <u>T</u> <u>H</u> <u>G</u> <u>K</u> IIYVPC
11_14	7		DDGDRCAKEH <u>E</u> <u>I</u> <u>P</u> <u>H</u> <u>A</u> <u>T</u> GEECQKRDKS
44_56	8		CKQLVIYF <u>T</u> <u>G</u> <u>N</u> <u>S</u> <u>S</u> HSSVFYIYYDC
6_130_J1	3		GSGDEDCKKFQSD <u>D</u> <u>N</u> <u>W</u> <u>E</u> <u>N</u> <u>Y</u> <u>T</u> <u>S</u> <u>T</u> <u>R</u> <u>H</u> <u>L</u> <u>T</u> <u>F</u> CDEKRS
44_56_J1	8		GSGNEEIEKKIKDC <u>T</u> <u>G</u> <u>N</u> <u>S</u> <u>S</u> <u>H</u> <u>S</u> <u>S</u> <u>W</u> E EALECALKK
44_56_J2	8		GSGDERIERLIKEC <u>T</u> <u>G</u> <u>N</u> <u>S</u> <u>S</u> <u>H</u> <u>S</u> <u>S</u> <u>W</u> E EALECALRR
147_157_J1	6		GSGSHPCAYWRWVI <u>K</u> <u>M</u> <u>T</u> <u>H</u> <u>G</u> <u>K</u> <u>T</u> <u>R</u> <u>W</u> VLELVFCYRD
147_157_J2	6		GSGKCEEEAKKIAS <u>K</u> <u>M</u> <u>T</u> <u>H</u> <u>G</u> <u>K</u> <u>T</u> <u>R</u> <u>E</u> <u>E</u> <u>E</u> <u>E</u> <u>A</u> <u>E</u> <u>E</u> <u>Y</u> <u>L</u> <u>K</u> <u>K</u> <u>C</u>
33_63_J1	1		GSGDDESEKRTTERDTRKCTKAKAND <u>D</u> <u>N</u> <u>Q</u> <u>C</u> <u>Q</u> <u>P</u> <u>T</u> <u>E</u>

MEM ID	Epitope #		CD25 Interface Residues (bold and underline: <u>X</u>) MEM Scaffold Residues (plain text: X)
33_63_J2	1		GSGSSEWDKWVEEWYKKMCTEAKKN <u>DNQCQP</u> <u>TK</u>
33_63_J3	1		GSGQCRVWVFRNGDKILYIYEDCDN <u>DNQHQQ</u> <u>TL</u>

Example 7: Selection of Antibodies Using MEM Programmed *In Vitro* Selection

[0275] Thirty-two different panning strategies (S1-S32) were devised, each comprising three rounds, of positive selection (**Table 10**). Each program used at least one engineered polypeptide as a selection molecule. A conventional selection was also included using conventional methods (CD25 as the positive target). Bovine serum albumin (BSA) was used a negative target selecting against non-specific binding.

[0276] The panning protocol began with a human naïve scFv library, and panning was performed in solution, with the selection molecules bound to biotin (but still in solution). For each round, the starting pool was combined with the negative selection molecule (BSA) first in solution, and then a streptavidin-coated substrate (*e.g.*, magnetic beads) was applied to the mixture to bind the negative selection molecules. Thus, any phage in the pool that was bound to the negative selection molecule was also bound to the streptavidin-coated support. The remaining solution was removed, and this flow through was then taken on to the positive selection step. The flow through was combined with positive selection molecule (antigen 1), allowed to bind, and then a streptavidin-coated solid substrate applied to the mixture. In this step, the bound phage were retained while the remaining unbound phage were removed. Then the bound phage were eluted. *E. coli* were transfected with the eluted phage using a 30 minute cultivation, the transfected cells were split for next-generation sequencing and DNA isolation for analysis, and then the phage amplified for use in the subsequent panning round. For each panning program, in each round negative selection was performed first, and positive selection second.

Table 10

Strategy	Round 1 Antigen	Round 2 Antigen	Round 3 Antigen
S1	57_63	CD25	57_63
S2	57_63	CD25	CD25
S3	13_131	CD25	13_131
S4	13_131	CD25	CD25
S5	6_130	CD25	6_130
S6	6_130	CD25	CD25
S7	6_163	CD25	6_163
S8	6_163	CD25	CD25
S9	77_89	CD25	77_89
S10	77_89	CD25	CD25
S11	147_156	CD25	147_156
S12	147_156	CD25	CD25
S13	11_14	CD25	11_14
S14	11_14	CD25	CD25
S15	44_56	CD25	44_56
S16	44_56	CD25	CD25
S17	6_130_J1	CD25	6_130_J1
S18	6_130_J1	CD25	CD25
S19	44_56_J1	CD25	44_56_J1
S20	44_56_J1	CD25	CD25
S21	44_56_J2	CD25	44_56_J2
S22	44_56_J2	CD25	CD25
S23	147_157_J1	CD25	147_157_J1
S24	147_157_J1	CD25	CD25
S25	147_157_J2	CD25	147_157_J2
S26	147_157_J2	CD25	CD25

Strategy	Round 1 Antigen	Round 2 Antigen	Round 3 Antigen
S27	33_63_J1	CD25	33_63_J1
S28	33_63_J1	CD25	CD25
S29	33_63_J2	CD25	33_63_J2
S30	33_63_J2	CD25	CD25
S31	33_63_J3	CD25	33_63_J3
S32	33_63_J3	CD25	CD25
S33	CD25	CD25	CD25

Primary ELISA Screen and Hit Selection

[0277] 384 clones for each strategy were selected for ELISA response analysis to full-length CD25 after three rounds of panning (**FIG. 9**). Data are shown with the sorted strategies ordered by epitope (**FIG. 6**). At least one strategy for each epitope yielded clones capable of binding to CD25. It was observed that different strategies using the same engineered polypeptides enrich distinct high-affinity clonal subsets (**FIG. 10**, black bars). As shown in **Table 11**, most MEM-programmed selection strategies produced anti-CD25 hits more productively than conventional full-length panning.

Table 11

Strategy	CD25 Epitope	Anti-Hu CD25 % Hit Rate
S16	8	65.0
S2	1	59.0
S12	6	51.0
S6	4	46.0
S10	5	30.0
S33	Full-length CD25	19.0
S4	3	17.0
S14	7	16.0

[0278] Of the hits 1475 were selected for further characterization because they met one of two criteria in ELISA: 1) >10:1 signal to noise (s/n) in full-length CD25 ELISA; or 2) >3:1 s/n in MEM ELISA and >5:1 s/n in CD25 ELISA.

Confirmatory Testing by Biolayer Interferometry

[0279] The affinity of the different scFv antibodies were evaluated on a FortéBio® Octet RED384™ biolayer interferometry instrument, using a single-cycle kinetics assay design. His-tagged scFv's were immobilized on anti-his biosensor (Fortebio® HIS1K). Full-length CD25 analyte was washed over the sensor tip and the binding of the molecules in the analyte to the scFv's recorded. Each assay was run in duplicate. Controls were also run, using just a buffer (to control for sensor drift) and a separate control of purified polyclonal IgG isotype antibodies from human serum (to control for non-specific IgG binding).

[0280] As shown in **FIG. 11**, biolayer interferometry of 1475 anti-CD25 scFv's identified by phage display panning. Shows that 1433 hits (97%) are confirm to bind CD25. The observed K_D range of the hits was 10-200 nM, with a median K_D of 28.5 nM. As shown in **FIG. 11**, most screening strategies generated scFv with high affinity for CD25. Only scFv's having k_{off} less than $10^{-3}/s$ are shown. Approximate K_D values are given on the y-axis. As shown in **FIG. 12**, most of the panning strategies resulted in at least one hit that has k_{off} of less than $10^{-3}/s$.

Confirmatory Testing by Flow Cytometry

[0281] The CD25 specificity the different scFv antibodies were evaluated on flow cytometer using cells that express CD25 [CD25(+)] or do not express CD25 [CD25(-)]. As shown in **FIG. 13**, of 1248 scFv hits analyzed in this assay, 1160 (93%) bind specifically to CD25(+) cells.

Sequence Analysis of Hits

[0282] Next generation sequencing was performed on each round of panned phage. As shown in **FIG. 15**, MEM-steered panning focuses CDR diversity of antibody libraries in a

strategy-dependent manner. Each round of selection decreased repertoire diversity (**FIG. 16**) and focused CDR length to preferred lengths for each MEM (**FIG. 17**).

[0283] Individual scFv's were sequenced using Sanger sequencing methods. Complete protein sequences for each scFv are provided in **Table 5**. Immunoglobulin gene usage and complementarity determining regions are provided in **Table 12** and **Table 2**, respectively.

Table 12

Clone ID	VH Germline	DH Germline	JH Germline	VL Germline	VJ Germline
YU389-A01	IGHV1-69*01	IGHD2-8*01	IGHJ6*01	IGKV1-39*01	IGKJ1*01
YU389-A02	IGHV1-69*12	IGHD2-8*01	IGHJ6*01	IGKV1-39*01	IGKJ3*01
YU389-A03	IGHV4-31*03	IGHD3-3*01	IGHJ5*02	IGLV1-51*01	IGLJ1*01
YU389-A05	IGHV1-69*12	IGHD2-8*01	IGHJ6*01	IGKV1-39*01	IGKJ1*01
YU389-A07	IGHV1-69*01	IGHD2-8*01	IGHJ6*01	IGKV1-39*01	IGKJ1*01
YU389-B11	IGHV1-69*12	IGHD2-8*01	IGHJ6*01	IGKV1-39*01	IGKJ2*02
YU389-D07	IGHV1-69*01	IGHD2-8*01	IGHJ6*01	IGKV1-39*01	IGKJ2*02
YU390-A11	IGHV3-30*18	IGHD6-19*01	IGHJ3*02	IGLV3-21*02	IGLJ3*01
YU390-A12	IGHV1-46*01	IGHD3-10*01	IGHJ4*02	IGLV3-1*01	IGLJ1*01
YU390-B12	IGHV3-30*18	IGHD6-19*01	IGHJ3*02	IGLV3-21*02	IGLJ3*01
YU390-C03	IGHV1-69*12	IGHD2-8*01	IGHJ6*01	IGKV1-39*01	IGKJ1*01
YU390-C11	IGHV1-18*01	IGHD2-15*01	IGHJ6*01	IGKV3-15*01	IGKJ4*01
YU390-D01	IGHV1-69*01	IGHD2-8*01	IGHJ6*01	IGKV1-39*01	IGKJ1*01
YU390-D03	IGHV1-69*01	IGHD3-22*01	IGHJ6*01	IGKV1-5*03	IGKJ2*01
YU390-D05	IGHV1-69*12	IGHD2-8*01	IGHJ6*01	IGKV1-39*01	IGKJ1*01
YU390-D11	IGHV1-18*01	IGHD2-15*01	IGHJ6*01	IGKV3-15*01	IGKJ4*01
YU390-G03	IGHV1-69*12	IGHD2-8*01	IGHJ6*01	IGKV1-39*01	IGKJ1*01
YU390-H11	IGHV1-18*01	IGHD2-15*01	IGHJ6*01	IGKV3-15*01	IGKJ4*01
YU392-A05	IGHV1-46*01	IGHD1-26*01	IGHJ4*02	IGLV1-47*01	IGLJ3*01
YU392-A07	IGHV1-69-2*01	IGHD5-5*01	IGHJ4*02	IGLV1-44*01	IGLJ3*01
YU392-A09	IGHV1-69-2*01	IGHD2-15*01	IGHJ6*01	IGLV1-47*01	IGLJ3*01
YU392-B11	IGHV1-69-2*01	IGHD3-22*01	IGHJ4*02	IGLV1-47*02	IGLJ3*01
YU393-A01	IGHV4-30-2*01	IGHD3-10*01	IGHJ6*01	IGKV1-39*01	IGKJ4*01
YU393-A02	IGHV1-69*14	IGHD3-10*01	IGHJ4*02	IGKV1-5*01	IGKJ1*01
YU393-A03	IGHV4-4*02	IGHD3-10*01	IGHJ5*02	IGKV3-15*01	IGKJ1*01

Clone ID	VH Germline	DH Germline	JH Germline	VL Germline	VJ Germline
YU393-A04	IGHV1-18*01	IGHD1-1*01	IGHJ1*01	IGKV1-5*03	IGKJ1*01
YU393-A08	IGHV3-30*18	IGHD3-16*02	IGHJ4*02	IGLV3-21*02	IGLJ3*01
YU393-A09	IGHV5-51*03	IGHD1-7*01	IGHJ5*02	IGLV3-21*02	IGLJ3*02
YU393-A11	IGHV5-51*01	IGHD1-7*01	IGHJ5*02	IGLV3-21*02	IGLJ3*02
YU393-B02	IGHV1-69*14	IGHD2-2*01	IGHJ6*01	IGKV1-39*01	IGKJ2*01
YU393-B03	IGHV1-69*14	IGHD2-8*01	IGHJ6*01	IGKV1-12*01	IGKJ4*01
YU393-B04	IGHV1-69*01	IGHD2-2*01	IGHJ6*01	IGKV1-39*01	IGKJ2*01
YU393-B05	IGHV3-30*18	IGHD6-19*01	IGHJ4*02	IGKV3-20*01	IGKJ3*01
YU393-B06	IGHV3-30-3*01	IGHD3-3*01	IGHJ6*01	IGKV1-33*01	IGKJ4*01
YU393-B07	IGHV3-7*01	IGHD3-10*01	IGHJ4*02	IGLV3-21*02	IGLJ3*01
YU393-B08	IGHV1-18*01	IGHD3-22*01	IGHJ5*02	IGLV2-14*01	IGLJ1*01
YU393-C02	IGHV3-30-3*01	IGHD4-17*01	IGHJ4*02	IGKV1-33*01	IGKJ2*01
YU393-C03	IGHV1-18*01	IGHD3-10*02	IGHJ4*02	IGKV1-NL1*01	IGKJ4*01
YU393-C05	IGHV1-69*12	IGHD3-10*01	IGHJ6*01	IGKV1-39*01	IGKJ4*01
YU393-C07	IGHV3-30-3*01	IGHD5-12*01	IGHJ4*02	IGLV3-21*02	IGLJ3*01
YU393-C08	IGHV1-18*04	IGHD2-8*01	IGHJ4*02	IGLV1-51*01	IGLJ1*01
YU393-D03	IGHV7-4-1*02	IGHD2-21*01	IGHJ6*01	IGKV3-15*01	IGKJ1*01
YU393-D04	IGHV1-18*04	IGHD1-26*01	IGHJ4*02	IGKV1-12*01	IGKJ4*01
YU393-D05	IGHV3-15*01	IGHD3-10*01	IGHJ4*02	IGKV1-39*01	IGKJ2*01
YU393-D07	IGHV3-48*03	IGHD2-15*01	IGHJ4*02	IGLV2-14*01	IGLJ1*01
YU393-E04	IGHV3-7*01	IGHD3-10*01	IGHJ5*02	IGKV3-20*01	IGKJ4*01
YU393-E05	IGHV1-69*06	IGHD2-8*01	IGHJ6*01	IGKV1-9*01	IGKJ3*01
YU393-E07	IGHV3-48*02	IGHD5-12*01	IGHJ4*02	IGLV3-21*02	IGLJ3*01
YU393-F03	IGHV5-51*03	IGHD6-19*01	IGHJ4*02	IGKV1-17*01	IGKJ2*01
YU393-F04	IGHV1-18*04	IGHD3-10*01	IGHJ6*01	IGKV1-39*01	IGKJ4*01
YU393-F06	IGHV5-51*01	IGHD3-16*01	IGHJ4*02	IGKV1-5*03	IGKJ3*01
YU393-F07	IGHV5-51*03	IGHD6-19*01	IGHJ4*02	IGLV1-47*01	IGLJ3*01
YU393-G01	IGHV5-51*01	IGHD2-8*02	IGHJ4*02	IGKV3-20*01	IGKJ2*01
YU393-G03	IGHV1-69*06	IGHD2-8*01	IGHJ6*01	IGKV1-39*01	IGKJ4*01
YU393-G04	IGHV1-18*01	IGHD3-3*01	IGHJ6*01	IGKV1-12*01	IGKJ1*01
YU393-G07	IGHV3-7*01	IGHD2-8*02	IGHJ6*01	IGLV6-57*02	IGLJ3*01
YU393-G08	IGHV5-51*03	IGHD1-7*01	IGHJ5*02	IGLV3-21*02	IGLJ3*02
YU393-G11	IGHV5-51*01	IGHD1-7*01	IGHJ5*02	IGLV3-21*02	IGLJ3*02
YU393-G12	IGHV5-51*03	IGHD1-7*01	IGHJ5*02	IGLV3-21*02	IGLJ3*02

Clone ID	VH Germline	DH Germline	JH Germline	VL Germline	VJ Germline
YU393-H03	IGHV4-4*02	IGHD2-8*01	IGHJ6*01	IGKV1-39*01	IGKJ1*01
YU393-H07	IGHV3-30-3*01	IGHD5-12*01	IGHJ4*02	IGLV3-21*03	IGLJ3*01
YU393-H09	IGHV5-51*03	IGHD1-7*01	IGHJ5*02	IGLV3-21*02	IGLJ3*02
YU394-A01	IGHV3-7*01	IGHD4-17*01	IGHJ4*02	IGLV1-51*01	IGLJ3*02
YU394-A02	IGHV5-51*03	IGHD1-7*01	IGHJ5*02	IGLV3-21*02	IGLJ3*02
YU394-A07	IGHV5-51*03	IGHD1-7*01	IGHJ5*02	IGLV3-21*02	IGLJ3*02
YU394-A09	IGHV1-69*01	IGHD2-8*01	IGHJ6*01	IGKV1-39*01	IGKJ1*01
YU394-C01	IGHV5-51*03	IGHD1-7*01	IGHJ5*02	IGLV3-21*02	IGLJ3*02
YU394-E02	IGHV5-51*03	IGHD1-7*01	IGHJ5*02	IGLV3-21*02	IGLJ3*02
YU394-H01	IGHV5-51*03	IGHD1-7*01	IGHJ5*02	IGLV3-21*02	IGLJ3*02
YU394-H03	IGHV5-51*03	IGHD1-7*01	IGHJ5*02	IGLV3-21*02	IGLJ3*02
YU394-H04	IGHV5-51*03	IGHD1-7*01	IGHJ5*02	IGLV3-21*02	IGLJ3*02
YU394-H05	IGHV5-51*03	IGHD1-7*01	IGHJ5*02	IGLV3-21*02	IGLJ3*02
YU394-H07	IGHV1-69*13	IGHJ6*01	IGKV1-39*01	IGKJ4*01	
YU395-A02	IGHV1-69*01	IGHD2-8*01	IGHJ6*01	IGKV1-39*01	IGKJ1*01
YU395-B12	IGHV1-18*01	IGHD3-16*02	IGHJ6*01	IGLV3-19*01	IGLJ3*01
YU395-C06	IGHV1-69*01	IGHD2-8*01	IGHJ6*01	IGKV1-39*01	IGKJ2*02
YU395-C08	IGHV1-69*01	IGHD2-8*01	IGHJ6*01	IGKV1-39*01	IGKJ1*01
YU395-D05	IGHV1-69*01	IGHD2-8*01	IGHJ6*01	IGKV1-39*01	IGKJ2*02
YU396-B12	IGHV5-51*01	IGHD2-21*01	IGHJ4*02	IGLV3-1*01	IGLJ3*01
YU396-C03	IGHV3-30*18	IGHD3-9*01	IGHJ4*02	IGLV8-61*01	IGLJ3*02
YU396-C12	IGHV5-51*01	IGHD2-21*01	IGHJ4*02	IGLV1-47*01	IGLJ3*02
YU396-G10	IGHV1-69*12	IGHD2-8*01	IGHJ6*01	IGKV1-39*01	IGKJ1*01
YU396-H12	IGHV3-30*18	IGHD3-9*01	IGHJ6*01	IGLV2-14*01	IGLJ3*01
YU397-A01	IGHV5-51*03	IGHD6-19*01	IGHJ6*01	IGKV1-39*01	IGKJ1*01
YU397-A02	IGHV1-18*01	IGHD3-3*01	IGHJ6*01	IGKV1-33*01	IGKJ4*02
YU397-A03	IGHV3-48*03	IGHD2-15*01	IGHJ4*02	IGLV2-14*01	IGLJ3*02
YU397-B01	IGHV5-51*03	IGHD3-10*01	IGHJ6*01	IGKV1-39*01	IGKJ1*01
YU397-B02	IGHV1-69*14	IGHD2-2*01	IGHJ4*02	IGKV1-33*01	IGKJ4*01
YU397-D01	IGHV4-4*02	IGHD2-15*01	IGHJ4*02	IGKV1-9*01	IGKJ4*01
YU398-A11	IGHV3-30*18	IGHD3-9*01	IGHJ6*01	IGLV1-44*01	IGLJ1*01
YU398-E10	IGHV3-21*01	IGHD6-6*01	IGHJ6*01	IGLV3-21*02	IGLJ3*01
YU400-A05	IGHV3-30*18	IGHD3-10*01	IGHJ6*01	IGLV3-21*02	IGLJ3*02
YU400-A12	IGHV4-4*02	IGHD3-10*01	IGHJ6*01	IGKV1-39*01	IGKJ4*01

Clone ID	VH Germline	DH Germline	JH Germline	VL Germline	VJ Germline
YU400-B07	IGHV3-30*18	IGHD3-10*01	IGHJ6*01	IGLV3-21*03	IGLJ3*02
YU400-D09	IGHV1-69*01	IGHD3-3*01	IGHJ6*01	IGLV1-51*01	IGLJ3*01
YU400-F07	IGHV3-30*18	IGHD3-10*01	IGHJ6*01	IGLV3-21*02	IGLJ3*02
YU400-H08	IGHV3-30*18	IGHD3-10*01	IGHJ6*01	IGLV3-21*02	IGLJ3*02
YU401-A11	IGHV3-30*18	IGHD3-16*01	IGHJ4*02	IGLV1-44*01	IGLJ3*01
YU401-B01	IGHV1-69*01	IGHD2-8*01	IGHJ6*01	IGKV1-39*01	IGKJ2*02
YU401-D11	IGHV3-30*18	IGHD3-16*01	IGHJ4*02	IGLV1-44*01	IGLJ3*01
YU401-E11	IGHV3-30*01	IGHD6-6*01	IGHJ4*02	IGKV2D-29*01	IGKJ4*01
YU401-F11	IGHV3-30*01	IGHD6-6*01	IGHJ4*02	IGKV2D-29*01	IGKJ4*01
YU401-G07	IGHV3-30*18	IGHD3-10*01	IGHJ6*01	IGLV3-21*02	IGLJ3*02
YU402-A02	IGHV4-39*07	IGHD6-13*01	IGHJ4*02	IGKV1-12*01	IGKJ3*01
YU402-A11	IGHV4-4*02	IGHD2-8*01	IGHJ3*02	IGLV6-57*02	IGLJ3*01
YU402-D10	IGHV3-30*18	IGHD6-6*01	IGHJ4*02	IGLV2-14*01	IGLJ3*02
YU403-G05	IGHV4-4*02	IGHD2-8*01	IGHJ3*02	IGLV6-57*02	IGLJ3*01

[0284] Analysis of the CDRs and germline usages suggest that the 1475 scFv's sequenced represent at least 126 distinct clones. The set includes 40 different VH+JH frameworks choices, and 35 VL+JL framework choices. Unique CDR sequences include:

CDR-H1	GGTFSSYA, GGSISSGGYY, GFTFSSYG, GYTFTSY, GYTFTSYG, GYTFTDYY, GGSISSGGYS, GGSISSSNW, GYSFTSYW, GFTFSNYG, GFTFSSSA, GFTFSSYW, GFIFSRHA, GYTFNNYG, GFTFSSYA, GYTFTTYA, GFTFNNAW, GFTFSSYE, GYSFTTYW, GYSFNTYW, GFTFRRYW, GYSFSTYW, GFAFSSYG, GYKFANYW, GYTFKNFG, GFTFSSYS, GDSISSSSYY, and GGSISRSNW
CDR-H2	IIPIFGTA, IIPIFGTA, IYYSGST, ISYDGSNK, INPSGGST, ISAYNGNT, IMPIFDTA, VDPEDGET, IYHSGST, IYPGSDST, ISHDGHVK, IKQDGSEK, ISVYNGDI, INTNTGDP, IKSKTDGGTT, ISSSGSTI, ISSRGSTI, IYPSDSDT, ISGRKGNT, ISSSSSYI, INHSGST, IYHTGST, and ISYDGNNK

CDR-H3	AREMYYYYGMDV, AREMYYYYGMDV, ARGNLWSGYF, AKELLEGAFDI, ARDRVMTVRGALAY, ARERSYYGMDV, ASWSERIGYQYGLDV, ARDILGLDY, ATEDTAMGGIDY, ATEGRYGMDV, AVEGGRAPGTYYYDSSGLAY, ARAGYYYGMDV, ARDLGTMVRGVIEPYFDY, ARGVRGTGFDP, ARDRNGYFQH, AKDLLGELSFFDY, ARLENNWDYGGWFDP, ARDRSYYGMDV, ARDKGYYGMDV, AKEISPRSSVGWPLDY, ARDFWSGYNELGGMDV, ARTWFGEFFDY, ARVIGGWFP, ARGRLAYGDTEGFDY, ARDILRGESSILDH, ARDRYYYGMDV, ARDLLGSGYDIIDY, ARVWGKNGDFDY, ARDRFHYGMDV, ARDRGDY, TTEGVLLSFGGAPFDY, ARRRGGGFDY, AREKGSWFDP, ARDRGDRVGGVFDY, ARQVAGGLDY, ARDRGYGMDV, FRFGEGFDY, ARDGGYYFDD, ARDFRMDV, ARDAYAYGLDV, ARDLMNYGMDV, AREYDYGDYVFDY, ARLENNWNYGGWFDP, ARDYYYYGMDV, ARDIGYYYGMDV, ARVGDGYSLDY, AKAITSIPEY, AKGQGDGMDV, ARLGWGMDV, ARVWGDTTLGYGMDV, AIPWDAELGNYGMDV, ARGRWSGLGDY, ARARGGRYFDY, ARDQLAARRGYGMDV, AKGDVNYGMDV, ARDFYGSYSPNGYYYGMDV, ARDFNPFSITIFEMDV, ANLAMGQYFDY, ARDLGEAKSSSPHEPDY, ARDQEMYYFDY, ARGKGSYAFDI, and AKGYSSSPGDY
CDR-L1	QSISSY, QSISSY, SSNIGNNF, QSISSY, NIETKS, KLGDY, QSVSNY, QTISQW, SSNIGSNY, NFNIGNNL, RNIWSY, QSISSW, QSVSSR, QTISGL, DIESEM, NIGSKS, QSIGNY, QGISSW, QSVSSTY, QDISNY, NIESES, SSDVGAYNY, QDINNY, QGISNS, SSNIGNNY, EGIRTS, QGTSSW, SSDVGGYNY, QSVSNY, QGINSY, QAVRID, QSISSY, QSIGYW, SSNVGSNY, QSIKNY, QDIKRR, SGSIASSY, NSNVGNYY, SLRSYY, KLGERF, SGSVSTSY, SSNIGRNY, EDIRMY, QGISTY, SSNVGSRT, NIGTKS, NIGSKT, QSINSY, SSNIGSNT, QSITY, QSLHSDGKTY, and GGNIARNY

CDR-L2	AAS, AAS, DST, DDD, KDN, GAS, KAS, RNN, SNN, AND, DAF, DDS, AAT, AVS, DAS, GVS, DNN, DVS, RAS, GTS, EDN, DND, GKN, QYI, NTD, RNH, EGS, DGR, TAS, DDT, EVS, and EDD
CDR-L3	QQSYSTPPT, QQSYSTPPT, GSWDTNLSGYV, QVWDSSSGHREV, QAWDSSTYV, QQYNHWPPL, QQYSGDSMYT, AAWDDSLSGVV, AAWDDSLNGVV, ATWDDSLSGVV, QQSHSTPIT, QQYNSYSRT, QQYTNWPQT, LQYDRYSGA, QVWHTTNDHVL, QVWDSSSDHWV, QQSKQIPYT, QQSYSLPLT, QQFDISGGLI, QQYDNLPLT, QVWDSSSDHTVA, SSYTTTDTFV, QQYDNLPLYT, QQYYSTPPH, QQSYSTPLT, QVWDSSSDHVV, GTWDSSLSAYV, QQTHTWPWT, QQANSFPLT, QQSYSTPYT, SSYTSSSTYV, QRYGSSPR, QQVHSFPFT, LQHNTFPYT, QQSHSTPLT, QQYNSYPFT, QQYNSSPLMYT, QQTYSTPLT, QQANTFPQT, QSYDGSSVV, GSWEARESVFV, QQTYNDPPT, NSRDSSGNHVV, QTWGDSIVV, VLYMGSGIWV, ATWDDALSGWV, SSYTSSSTLVV, QQSYSTPWT, SSYTSSSTWV, LQDYNYPFA, QQYYDDPQ, QQLNGYPTT, AAWDDSLIGHV, QVWDTSGDLHWA, QQSYTTPLT, QVWDSSSDLLWV, GTWDSSLSALV, AAWDDSLNGPV, MQTKQLPLT, QQANSFPPT, QSYDGNNHNV, and SSYTSSSTLWV

[0285] Sequence analysis applied to scFv's directed to individual target epitopes identifies common CDR usage patterns within each set of antibody:

[0286] For CD25 epitope 1 (55-63), CDRs used include:

CDR-H1	CDR-H2	CDR-H3	CDR-L1	CDR-L2	CDR-L3
GFTFSSYG	ISYDGSNK	AKGDVNYGMDV	NIGSKS	DDT	QVWDSSSDLLWV
			NIGSKT	DGR	QVWDTSGDLHWA
	ISYDGNNK	AKGYSSSPGDY	SSDVGAYNY	DVS	SSYTSSSTLWV
GGTFSSYA	IIPIFGTA	ARDFNPFSTIFEMDV	SSNIGNNY	DNN	GTWDSSLSALV
GGSISSSNW	IYHSGST	ARDFYYGSGSYPNNGYYYGMDV	QSINSY	TAS	QQSYTTPLT

GYSFNTYW	IYPSDSDT	ARDGGYYFDD	QSVSSTY	GTS	QQYNSSPLMYT
GGTFSSYA	IIPIFGTA	ARDYYYYGMDV	QSISSY	GAS	QQTYNDPPT
		AREMYYYYGMDV	QSISSY	AAS	QQSYSTPPT
			QSISSY		
			QSIITY		
			QSISSY		
GGSISRSNW	IYHTGST	ARGKGSYAFDI	GGNIARNY	EDD	QSYDGNHNMV

[0287] For CD25 epitope 2 (13-20:127-132), CDRs used include:

CDR-H1	CDR-H2	CDR-H3	CDR-L1	CDR-L2	CDR-L3
GFTFSSYG	ISYDGSNK	ANLAMGQYFDY	SSNIGSNT	SNN	AAWDDSLNGPV
GFTFSSYA		ARDLGEAKSSSPHEPDY	QSLHSDGKTY	EVS	MQTKQLPLT
GDSISSSSYY	INHSGST	ARDQEMYYFDY	QGISSW	AAS	QQANSFPPT
GGTFSSYA	IIPIFGTA	AREMYYYYGMDV	QSISSY	AAS	QQSYSTPPT

[0288] For CD25 epitope 3 (5-17), CDRs used include:

CDR-H1	CDR-H2	CDR-H3	CDR-L1	CDR-L2	CDR-L3
GFTFSSYG	ISYDGSNK	AKAITSIEPY	SGSVSTSY	NTD	VLYMGSGI WV
GFTFSSYG	ISYDGSNK	AKELLEGAFDI	NIETKS	DDD	QVWDDSSSGHREV
GGTFSSYA	IIPIFGTA	AREMYYYYGMDV	QSISSY	AAS	QQSYSTPPT
			QSISSY		

[0289] For CD25 epitope 4 (5-11:156-163), CDRs used include:

CDR-H1	CDR-H2	CDR-H3	CDR-L1	CDR-L2	CDR-L3
GGTFSSYA	IIPIFGTA	AREMYYYYGMDV	QSISSY	AAS	QQSYSTPPT
GYTFTSYG	ISAYNGNT	ARERSYYGMDV	QSVSNY	GAS	QQYNHWPL

[0290] For CD25 epitope 5 (77-89), CDRs used include:

CDR-H1	CDR-H2	CDR-H3	CDR-L1	CDR-L2	CDR-L3
GFTFSSYG	ISYDGSNK	AKELLEGAFDI	NIETKS	DDD	QVWDDSSSGHREV
GYTFTSYG	INPSGGST	ARDRTMVRGALAY	KLGDY	KDN	QAWDSSTYV

[0291] For CD25 epitope 6 (147-157), CDRs used include:

CDR-H1	CDR-H2	CDR-H3	CDR-L1	CDR-L2	CDR-L3
GFTFSSYG	ISYDGSNK	AKGQGDGMDV	SSNVGSRT	SNN	AAWDDSLIGHV
GGSISSGGYS	IYHSGST	ARAGYYYGMDV	RNIWSY	GAS	QQSHSTPIT
GYTFSSYG	ISAYNGNT	ARDIGYYYGMDV	SLRSYY	GKN	NSRDSSGNHVV
GYTFSSYY	INPSGGST	ARDILGLDY	SSNIGSNY	RNN	AAWDDSLSGVV
GGTFSSYA	IIPIFGTA	AREMYYYYGMDV	QSISSY	AAS	QQSYSTPPT
			QSISSY		
GFTFSSYW	IKQDGSEK	AREYDYG DYVFDY	NSNVGNYY	DND	GSWEARES VFV
GYSFTSYW	IYPGDS DT	ARLENNWDYGGWFDP	NIGSKS	DDS	QVWDSSSDHWV
	IYPGDS DT				
GYTFDYY	VDPEDGET	ATEDTAMGGIDY	SSNIGSNY	SNN	AAWDDSLNGVV
		ATEGRYGMDV	NFNIGNNL	AND	ATWDDSLSGVV
		AVEGGRAPGTYYYDSSGLAY	SSNIGSNY	SNN	

[0292] For CD25 epitope 7 (11-14), CDRs used include:

CDR-H1	CDR-H2	CDR-H3	CDR-L1	CDR-L2	CDR-L3
GGTFSSYA	IIPIFGTA	AREMYYYYGMDV	QSISSY	AAS	QQSYSTPPT

[0293] For CD25 epitope 8 (44-56), CDRs used include:

CDR-H1	CDR-H2	CDR-H3	CDR-L1	CDR-L2	CDR-L3
GYSFTSYW	IYPGDS DT	AIPWDAELGNYGMDV	QSISSY	AAS	LQDYNYP PA
GFAFSSYG	ISYDGSNK	AKGQGDGMDV	SSDVGGYNY	GVS	SSYTSSSTLVV
GGSISSSNW	IYHSGST	ARARGGRYFDY	QGISTY	AAS	QQLNGYPTT
GGTFSSYA	IIPIFGTA	AREMYYYYGMDV	QSISSY	AAS	QQSYSTPPT
			QSISSY		
		ARGRWGLGDY	EDIRMY	EGS	QQYYDDPQ
GYKFANYW	IYPGDS DT	ARLGWGMDV	QSISSY	AAS	QQSYSTPWT
GFTFSSYE	ISSSGSTI	ARRRGGGFDY	SSDVGGYNY	DVS	SSYTSSSTWV
GYSFSTYW	IYPGDS DT	ARVGDGYS LDY	SSNIGRNY	RNH	ATWDDALSGWV
			KLGERF	QYI	QTWDGSIVV
GYTFKNFG	ISGRKGNT	ARVWGDTTLGYGMDV	QDISNY	DAS	QQYDNLPLT
GFTFSSYG	ISYDGSNK	AKDLLGELSFFDY	DIESEM	DDS	QVWHTTNDHVL
GFTFSNYG	ISHDGHVK	AKEISPRSSVGWPLDY	QSVSSTY	GAS	QQFDISGLI
GFTFRRYW	IKQDGSEK	ARDAYAYGLDV	SGSIASSY	EDN	QSYDGSSVV
GYTFSSYG	ISAYNGNT	ARDFRMDV	QDIKRR	DAS	QQANTFPQT
GFTFSSSA	ISYDGSNK	ARDFWSGYNELGGMDV	QDISNY		QQYDNLPLT

GYTFNNYG	ISVYNGDI	ARDILRGESSILDH	QGISNS	AAS	QQYYSTPPH
GGTFSSYA	IIPIFGTA	ARDKGYYGMDV	QSIKNY		QQTYSTPLT
			QGINSY		QQVHSFPFT
			QGISSW	AVS	QQSYSLPLT
		ARDLGTMRGVIEPYFDY	QSISSW	DAF	QQYNSYSRT
GFTFSSYA	ISYDGSNK	ARDLLGSGYDIIDY	NIGSKS	DDS	QVWSSSDHVV
GGSISSSNW	IYHSGST	ARDLMNYGMDV	QSISSY	AAS	QQSYSTPPT
GFTFSSYS	ISSSSSYI	ARDQLAARRGYYYGMDV	NIGTKS	DDS	QVWSSSDHVV
GYTFTTYA	INTNTGDP	ARDRFHYGMDV	EGIRTS	GAS	QQTHTWPWT
GFTFSSYG	ISSRGSTI	ARDRGDRVGGLVFDY	NIGSKS	DDS	QVWSSSDHVV
GYTFTSYG	ISAYNGNT	ARDRGDY	QGTSSW	AAS	QQANSFPLT
		ARDRGYYGMDV	QSIERY		QQSHSTPLT
		ARDRNGYFQH	QTISGL	GAS	LQYDRYSGA
GGTFSSYA	IIPIFGTA	ARDRSYYGMDV	QSIGNY	AAT	QQSKQIPYT
		ARDRYYYGMDV	QSISSY	AAS	QQSYSTPLT
GFTFSSYW	IKQDGSEK	AREKGSWFDP	QSVSNY	GAS	QRYGSSPR
GFIFSRHA	ISYDGSNK	ARGRLAYGDTEGFDY	QDINNY	DAS	QQYDNLPLYT
GGSISSSNW	IYHSGST	ARGVRGTGFDP	QSVSSR	GAS	QQYTNPQT
GYSFTTYW	IYPGSDST	ARQVAGGLDY	SSNVGSNY	RNN	AAWDDSLSGVV
			QAVRID	GAS	LQHNTFPYT
GFTFSSYE	ISSSGSTI	ARRRGGGFDY	SSDVGGYNY	DVS	SSYTSSSTYV
GFTFSSYW	IKQDGSEK	ARTWFGEFFDY	NIESES	DDS	QVWSSSDHTVA
GYTFTSYG	ISAYNGNT	ARVIGGWFPD	SSDVGAYNY	GVS	SSYTSTDFTV
		ARVWGKNGDFDY	SSNIGNNY	DNN	GTWSSSLAYV
GYSFTSYW	IYPGSDST	FRFEGGFDY	QSIGYW	RAS	QQYNSYPFT
GFTFNNAW	IKSKTDGGTT	TTEGVVLLSFGGAPFDY	QSISSY	AAS	QQSYSTPYT

Example 8: Confirmation of Epitope Specificity by Competitive Binding

[0294] 126 anti-CD25 clones were subjected to epitope resolution with a four-target competitive binding assay, as depicted in **FIG. 18**. The binding sites for IL-2, daclizumab, and basiliximab shown in the figure are based on X-ray crystallographic structure determination. The binding site for 7G7B6 is based on peptide mapping.

[0295] Cross-competition assays were performed in the classical sandwich format, involves immobilizing the first antibody onto the biosensor, followed by incubation with the antigen, and then the second sandwiching antibody. His-tagged scFv were expressed and purified *in situ* on the biosensor using His-tag capture from supernatant. Biosensor His-tag capture was normalized across scFv clones by monitoring the tip loading response to a consistent level across all scFv

measurements. The scFv's were each individually captured to an anti-His biosensor (Fortebio HIS1K). A baseline measurement was taken in running buffer. Then CD25 was captured to the antibodies. Finally each of various competitive analytes were added, including IL-2, 7G7B6, Basiliximab, or Daclizumab. The competitive analyte can bind the captured CD25 only if competitive analyte's binding epitope does not overlap that of immobilized scFv.

[0296] As shown in **FIG. 19**, the full-length CD25 panning clones are dominated by IL-2 interface epitope. Most clones are blocked by IL-2, daclizumab, and basiliximab, but not 7G7B6.

[0297] As shown in **FIG. 20**, the 147-157 epitope MEM-steered clones primarily bind at the intended epitope. Most clones are blocked by daclizumab but not by IL-2, basiliximab, or 7G7B6.

[0298] As shown in **FIG. 21**, the 6-17 epitope MEM-steered clones primarily bind at the intended epitope. Most clones are blocked by 7G7B6 but not by IL-2, daclizumab, or basiliximab.

[0299] As shown in **FIG. 22**, the 13-20:127-132 epitope MEM-steered clones primarily bind at the intended epitope. Most clones are blocked by 7G7B6 but not by IL-2, daclizumab, or basiliximab.

[0300] As shown in **FIG. 23**, the 44-56 epitope MEM-steered clones primarily bind at the intended epitope. The clones divided into two profiles. In profile 1, clones are blocked by 7G7B6 but not by IL-2, daclizumab, or basiliximab. In profile 2, clones are blocked by IL-2, daclizumab, and basiliximab, but not 7G7B6. These blocking profiles indicate binding to the intended epitope from different approach angles.

[0301] As shown in **FIG. 24**, the 55-63 epitope MEM-steered clones primarily bind at the intended epitope. The clones divided into three profiles. In profile 1, clones are blocked by 7G7B6 but not by IL-2, daclizumab, or basiliximab. In profile 2, clones are blocked by IL-2, daclizumab, and basiliximab, but not 7G7B6. These blocking profiles indicate binding to the intended epitope from different approach angles. In profile 3, clones are blocked by IL-2 and

7G7B6, but not daclizumab or basiliximab. These blocking profiles indicate binding to the intended epitope from different approach angles.

Example 9: Mapping of Functional Epitopes by Alanine Mutagenesis

[0302] Alanine mutations were designed to confirm or reject that MEM-steered clones bin the intended epitopes (**FIG. 25**). Alanine mutagenesis was selected as an orthogonal method for binning antibodies because it operates on the functional epitope, rather than the structural epitope defined by competition assays. Various pairs of surface-accessible residues were selected for mutagenesis. Computational modeling is used to confirm that the alanine mutations selected for use in these assays do not impact global or local stability. For example, **FIG. 26** shows results for modeling of alanine mutations within the 145-157 epitope. For each mutant and wild-type: RMSD from 3 independent 100 ns MD simulations in explicit solvent for each of 8 different starting apo-CD25 configurations using the crystal structure as the reference. As shown in **FIGS. 27-29**, alanine mutant versions of CD25 have the binding responses to basiliximab, daclizumab, and 7G7B6, respectively.

[0303] As intended, binding scFv hits from *in vitro* selection with the 147-157 epitope-targeted engineered polypeptides are consistent with specificity for the intended portion of CD25.

[0304] Each of 117 scFv's from the screening campaign were tested against four alanine mutations pairs (**FIG. 31**). Functional epitope diversity is observed. MEM-steered hits have distinct in-epitope alanine substitution position sensitivity.

Example 10: Confirmatory Testing of Antibodies in Immunoglobulin G (IgG1) Format

[0305] Thirty antibodies were selected for additional testing as full-length immunoglobulins. The heavy and light chain sequences were cloned into human immunoglobulin G (IgG1) format and expressed and purified. Binding to CD25 was assessed by Octet® as shown in **Table 13**.

Table 13: Human IgG1 Clone Selection/Epitope Details and Biophysical Measurements

Sample_ID	Biosensor Measured CD25 Affinity	Epitope	Selection R1_Antigen	Selection R2_Antigen	Selection R3_Antigen
YU390-B12	1.366E-08	_77-89_	77_89	CD25	77_89
YU397-F01	7.053E-08	_44-56_	44_56	CD25	CD25
YU397-D01	3.857E-09	_44-56_	44_56	CD25	CD25
YU398-A11	1.209E-08	_147-157_	147_156	CD25	CD25
YU404-H01	5.179E-08	_55-63_	57_63	CD25	CD25
YU400-B07	5.775E-08	_55-63_	57_63	CD25	57_63
YU400-D09	5.455E-08	_55-63_	57_63	CD25	57_63
YU401-B01	7.038E-08	_55-63_	57_63	CD25	CD25
YU401-G07	1.535E-08	_55-63_	57_63	CD25	57_63
YU404-C02	1.262E-08	_55-63_	57_63	CD25	CD25
YU403-G07	2.956E-08	_55-63_	57_63	CD25	CD25
YU403-G05	3.193E-08	_55-63_	57_63	CD25	CD25
YU391-B12	4.581E-08	_77-89_	77_89	CD25	CD25
YU400-A03	1.022E-08	_147-157_	147_156	CD25	CD25
YU400-D02	1.011E-08	_147-157_	147_156	CD25	CD25
YU392-A09	1.237E-08	_147-157_	147_156	CD25	147_156
YU392-B11	6.558E-08	_147-157_	147_156	CD25	147_156
YU392-B12	4.04E-08	_147-157_	147_156	CD25	CD25
YU392-E05	1.612E-08	_147-157_	147_156	CD25	147_156
YU392-E06	8.301E-09	_147-157_	147_156	CD25	147_156
YU392-G08	8.259E-09	_147-157_	147_156	CD25	147_156
YU389-A03	9.546E-09	_6-17_	6_130	CD25	CD25
YU392-G09	2.019E-08	_147-157_	147_156	CD25	147_156
YU392-G12	2.571E-08	_147-157_	147_156	CD25	CD25
YU392-H02	1.055E-08	_77-89_	77_89	CD25	CD25
YU392-H04	9.098E-09	_147-157_	147_156	CD25	147_156
YU402-F01	6.303E-09	_13-20_127-132_	13_131	CD25	CD25
YU389-B11	1.418E-07	_6-17_	6_130	CD25	CD25
YU394-D08	4.432E-08	_11-14_	11_14	CD25	11_14

Sample_ID	Biosensor Measured CD25 Affinity	Epitope	Selection R1_Antigen	Selection R2_Antigen	Selection R3_Antigen
YU390-A11	1.327E-08	_6-17_	6_130	CD25	CD25

Example 11: Panning Biased Library of Mouse Antibody Sequences

[0306] A phage-display library was generated from the immunoglobulin genes of a mouse immunized with full-length CD25. This library, biased towards CD25-binding antibodies, was panned against the indicated engineered polypeptides, yielding the complementarity determining region sequences indicated in **Table 14A** and **Table 14B**.

Table 14A

ID	Epitope	H_FR1_AA	H_CDR1_AA	H_FR2_AA	H_CDR2_AA	H_FR3_AA	H_CDR3_AA	H_FR4_AA
M1	33_6 3	EVRLQSGAELVRSGA SVKLSCTAS	GFNIKD YY	IHWVKQRPEQGL EWIGW	IDPDNGE T	EYAPKFGKATMTADTSSNTAHLQ LSSLTSEDIAVYYC	TVFWYGNYY AGFAY	WGQGITLV TV
M2	33_6 3	EVRLQSGAELVRSGA SVKLSCTAS	GFNIKD YY	IHWVKQRPEQGL EWIGW	IDPDNGE T	EYAPKFGKATMTADTSSNTAHLQ LSSLTSEDIAVYYC	TVFWYGNYY AGFAY	WGQGITLV TV---
M3	44_5 6	EVRLQSGAELVRSGA SVKLSCTAS	GFNIKD YY	IHWVKQRPEQGL EWIGW	IDPDNGE T	EYAPKFGKATMTADTSSNTAHLQ LSSLTSEDIAVYYC	TVFWYGNYY AGFAY	WGQGITLV TV---
M4	44_5 6	EVRLQSGAELVRSGA SVKLSCTAS	GFNIKD YY	IHWVKQRPEQGL EWIGW	IDPDNGE T	EYAPKFGKATMTADTSSNTAHLQ LSSLAPEDIAVYYC	TVFWYGNYY AGFAY	WGQGITLV TVSS
M5	147_156	QAYLQSGAELVRSGA SVKLSCTAS	GFNIKD YY	IHWVKQRPEQGL EWIGW	IDPDNGE T	EYAPKFGKATMTADTSSNTAHLQ LSSLTSEDIAVYYC	TVFWYGNYY AGFAY	WGQGITLV TV---
M6	44_5 6	QAYLQSGAELVRSGA SVKLSCTAS	GFNIKD YY	IHWVKQRPEQGL EWIGW	IDPDNGE T	EYAPKFGKATMTADTSSNTAHLQ LSSLTSEDIAVYYC	TVFWYGNYY AGFAY	WGQGITLV TVSS
M7	6_13 0	QAYLQSGAELVRSGA SVKLSCTAS	GFNIKD YY	IHWVKQRPEQGL EWIGW	IDPDNGE T	EYAPKFGKATMTADTSSNTAHLQ LSSLTSEDIAVYYC	TVFWYGNYY AGFAY	WGQGITLV TVSS
M8	6_16 3	EVLLQSGAELVRSGA SAKLSCTAS	GFNIKD YY	IHWVKQRPEQGL EWIGW	IDPDNGE T	EYAPKFGKATMTADTSSNTAHLQ LSSLTSEDIAVYYC	TVFWYGNYY AGFAY	WGQGITLV TVSS
M9	147_157	EVRLQSGAELVRSGA SVKLSCTAS	GFNIKD YY	IHWVKQRPEQGL EWIGW	IDPDNGE TEYAP	KFQKATMTADTSSNTAHLQLSSL TSEDIAVYYC	TVFWYGNYY AGFAY	WGQGITLV TVSS
M10	147_157	QAYLQSGAELVRSGA SVKLSCTAS	GFNIKD YY	IHWVKQRPEQGL EWIGW	IDPDNGE TEYAP	KFQKATMTADTSSNTAHLQLSSL TSEDIAVYYC	TVFWYGNYY AGFAY	WGQGITLV TVSA
M11	147_157	EVRLQSGAELVRSGA SVKLSCTAS	GFNIKD YY	IHWVKQRPEQGL EWIGW	IDPDNGE TEYAP	KFQKATMTADTSSNTAHLQLSSL TSEDIAVYYC	TVFWYGNYY AGFAY	WGQGITLV TVSA
M12	33_6 3	EVRLQSGAELVRSGA SVKLSCTAS	GFNIKD YY	IHWVKQRPEQGL EWIGW	IDPDNGE TEYAP	KFQKATMTADTSSNTAHLQLSSL TSEDIAVYYC	TVFWYGNYY AGFAY	WGQGITLV TVSA
M13	33_6 3	EVRLQSGAELVRSGA SVKLSCTAS	GFNIKD YY	IHWVKQRPEQGL EWIGW	IDPDNGE TEYAP	KFQKATMTADTSSNTAHLQLSSL TSEDIAVYYC	TVFWYGNYY AGFAY	WGQGITLV TVSA
M14	33_6 3	EVRLQSGAELVRSGA SVKLSCTAS	GFNIKD YY	IHWVKQRPEQGL EWIGW	IDPDNGE TEYAP	KFQKATMTADTSSNTAHLQLSSL TSEDIAVYYC	TVFWYGNYY AGFAY	WGQGITLV TVSS
M15	33_6 3	EVRLQSGAELVRSGA SVKLSCTAS	GFNIKD YY	IHWVKQRPEQGL EWIGW	IDPDNGE TEYAP	KFQKATMTADTSSNTAHLQLSSL TSEDIAVYYC	TVFWYGNYY AGFAY	WGQGITLV TVSS
M16	33_6 3	QAYLQSGAELVRSGA SVKLSCTAS	GFNIKD YY	IHWVKQRPEQGL EWIGW	IDPDNGE TEYAP	KFQKATMTADTSSNTAHLQLSSL TSEDIAVYYC	TVFWYGNYY AGFAY	WGQGITLV TVSA
M17	33_6 3	QAYLQSGAELVRSGA SVKLSCTAS	GFNIKD YY	IHWVKQRPEQGL EWIGW	IDPDNGE TEYAP	KFQKATMTADTSSNTAHLQLSSL TSEDIAVYYC	TVFWYGNYY AGFAY	WGQGITLV TVSA

M18	44__5 6	QAYLQSGAELVRSGA SVKLSCTAS	GFNIKD YY	IHWVKORPEQGL EWIGW	IDPDNGE TEYAP	KFQKATMTADTSSNTAHLQLSSL TSEDIAVYYC	TVFWYGNYY AGEFAY	WGQGTILV TVSA
M19	44__5 6	EVHLQSGAELVRSGA SVKLSCTAS	GFNIKD YY	IHWVKORPEQGL EWIGW	IDPDNGE TEYAP	KFQKATMTADTSSNTAHLQLSSL TSEDIAVYYC	TVFWYGNYY AGEFAY	WGAGTSL TVSS
M20	33__6 3	QVQLQOPGAELVRPGA SVKLSCKAS	GYTFTS YW	MHWVKORPQGGL EWIGI	IHPDSE TRLNQ	KFKDKATLTVDKSSSTAYMQLSSP TSEDSAVYYC	ARSRGIPFA Y	WGQGTILV TVSA
M21	33__6 3	QVQLQOPGADLMKPGA SVKISCKAS	GYTFSN YW	IEWIKORPGHGL EWVGE	ILPGSGF TNYNE	NFKGKATFTADTSSNTTYMQLSSL TSEDSAVYYC	ARGGTSVVH FDY	WGQGTSL TVSS
M22	44__5 6	EVRLQSGADLMKPGA SVKISCKAS	GYTFSN YW	IEWIKORPGHGL EWVGE	ILPGSGF TNYNE	NFKGKATFTADTSSNTTYMQLSSL TSEDSAVYYC	ARGGTSVVH FDY	WGQGTIV TVSS
M23	44__5 6	EVRLQSGADLMKPGA SVKISCKAS	GYTFSN YW	IEWIKORPGHGL EWIGE	ILPGSGF TNYNE	NFKGKATFTADTSSNTTYMQLSSL SSEDSAVYYC	SRGGTSFVH FDY	WGQGTIL TVSS
M24	6__13 0	QIQLQOPGAELAKPGA SVKMSCKAS	GYTFTR YW	MRWVKORPQGDL EWIGY	INPGSDY T	DYNEKFKDKATLTADKSSSTAYMQ LSSLISDDSAVYYC	ARXGYFDY	WGRGTIV TVSS
M25	33__6 3	QVQLQSGAELAKPGA SVKMSCKAS	GYTFNR FW	IHWIRORPGQSL EWIGY	INPNSDY T	EYNQMFEDRATLTADTSSTAYIQ LSSLISEDASVYYC	ARGTIIDY	WGQGTIL TVSS
M26	6__16 3	QVQLQSGAELAKPGA SVKMSCKAS	GYTFNR FW	IHWIRORPGQSL EWIGY	INPNSDY T	EYNQMFEDRATLTADTSSTAYIQ LSSLISEDASVYYC	ARGTIIDY	WGQGTIL TVSS
M27	33__6 3	QVQLQSGAELAKPGA SVKMSCKAS	GYTFTR YW	IHWVKORPGQDL EWIGY	INERTDY T	EYNQKFKDKATLTADKSSSTAYMQ LSSLISDDSAVYYC	ARHGYFDY	WGQGTIL TVSS
M28	33__6 3	QVQLQOPGAELAKPGA SVKMSCKAS	GYTFTR YW	IHWVKORPGQDL EWIGY	INERTDY T	EYNQKFKDKATLTADKSSSTAYMQ LSSLISDDSAVYYC	ARHGYFDY	WGQGTIL TVSS
M29	33__6 3	QIQLQOPGAELAKPGA SVKMSCKAS	GYTFTR YW	MHWVKORPGQDL EWIGY	INERTDY T	EYNQKFKDKATLTADKSSSTAYMQ LSSLISDDSAVYYC	ARHGYFDY	WGQGTIV TVSS
M30	33__6 3	QIQLQSGAELAKPGA SVKMSCKAS	GYTFTR YW	MHWVKORPGQDL EWIGY	INERTDY T	EYNQKFKDKATLTADKSSSTAYMQ LSSLISDDSAVYYC	ARHGYFDY	WGQGTSL TVSS
M31	44__5 6	QVQLQOPGAELAKPGA SVKMSCKAS	GYTFTR YW	IHWVKORPGQDL EWIGY	INERTDY T	EYNQKFKDKATLTADKSSSTAYMQ LSSLISDDSAVYYC	ARHGYFDY	WGQGTIL TVSS
M32	44__5 6	QVQLQOPGAELAKPGA SVKMSCKAS	GYTFTR YW	IHWVKORPGQDL EWIGY	INERTDY T	EYNQKFKDKATLTADKSSSTAYMQ LSSLISDDSAVYYC	ARHGYFDY	WGQGTIL TVSS
M33	44__5 6	QVQLQOPGAELAKPGA SVKMSCKAS	GYTFTR YW	IHWVKORPGQDL EWIGY	INERTDY T	EYNQKFKDKATLTADKSSSTAYMQ LSSLISDDSAVYYC	ARHGYFDY	WGQGTIL TVSS
M34	44__5 6	QVQLQOPGAELAKPGA SVKMSCKAS	GYTFTR YW	IHWVKORPGQDL EWIGY	INERTDY T	EYNQKFKDKATLTADKSSSTAYMQ LSSLISDDSAVYYC	ARHGYFDY	WGQGTIL TVSS
M35	44__5 6	QVQLQOPGAELAKPGA SVKMSCKAS	GYTFTR YW	IHWVKORPGQDL EWIGY	INERTDY T	EYNQKFKDKATLTADKSSSTAYMQ LSSLISDDSAVYYC	ARHGYFDY	WGQGTIL TVSS
M36	44__5 6	QVQLQOPGAELAKPGA SVKMSCKAS	GYTFTR YW	IHWVKORPGQDL EWIGY	INERTDY T	EYNQKFKDKATLTADKSSSTAYMQ LSSLISDDSAVYYC	ARHGYFDY	WGQGTIL TVSS

M37	44__5 6	QVQLQQPGAELAKPGA SVKMSCKAS	GYTFTR YW	IHWVKQRPQQDL EWIGY	INPRTDY T	EYNQKFKDKATLTADKSSSTAYMQ LSSLTSDDSAVYYC	ARHGYFDY	WGQGTTL TVSS
M38	44__5 6	QVQLQQPGAELAKPGA SVKMSCKAS	GYTFTR YW	IHWVKQRPQQDL EWIGY	INPRTDY T	EYNQKFKDKATLTADKSSSTAYMQ LSSLTSDDSAVYYC	ARHGYFDY	WGQGTTL TVSS
M39	44__5 6	QVQLQQPGAELAKPGA SVKMSCKAS	GYTFTR YW	IHWVKQRPQQDL EWIGY	INPRTDY T	EYNQKFKDKATLTADKSSSTAYMQ LSSLTSDDSAVYYC	ARHGYFDY	WGQGTTL TVSS
M40	44__5 6	QVQLQQPGAELAKPGA SVKMSCKAS	GYTFTR YW	IHWVKQRPQQDL EWIGY	INPRTDY T	EYNQKFKDKATLTADKSSSTAYMQ LSSLTSDDSAVYYC	ARHGYFDY	WGQGTTL TVSS
M41	44__5 6	QVQLQQSGAELAKPGA SVKMSCKAS	GYTFTR YW	MHWVKQRPQQDL EWIGY	INPRTDY T	EYNQKFKDKATLTADKSSSTAYMQ LSSLTSDDSAVYYC	ARHGYFDY	WGQGTTL TVSS
M42	44__5 6	QVQLQQSGAELAKPGA SVKMSCKAS	GYTFTR YW	MHWVKQRPQQDL EWIGY	INPRTDY T	EYNQKFKDKATLTADKSSSTAYMQ LSSLTSDDSAVYYC	ARHGYFDY	WGQGTTL TVSS
M43	44__5 6	QVQLQQPGAELAKPGA SVKMSCKAS	GYTFTR YW	MHWVKQRPQQDL EWIGY	INPRTDY T	EYNQKFKDKATLTADKSSSTAYMQ LSSLTSDDSAVYYC	ARHGYFDY	WGQGTTL TVSS
M44	44__5 6	QVQLQQSGAELAKPGA SVKMSCKAS	GYTFTR YW	IHWVKQRPQQDL EWIGY	INPRTDY T	EYNQKFKDKATLTADKSSSTAYMQ LSSLTSDDSAVYYC	ARHGYFDY	WGQGTTL TVSS
M45	44__5 6	QVQLQQPGAELAKPGA SVKMSCKAS	GYTFTR YW	MHWVKQRPQQDL EWIGY	INPRTDY T	EYNQKFKDKATLTADKSSSTAYMQ LSSLTSDDSAVYYC	ARHGYFDY	WGQGTTL TVSS
M46	44__5 6	QVQLQQSGAELAKPGA SVKMSCKAS	GYTFTR YW	IHWVKQRPQQDL EWIGY	INPRTDY T	EYNQKFKDKATLTADKSSSTAYMQ LSSLASDDSAVYYC	ARHGYFDY	WGQGTTL TV----
M47	57__6 3	QVQLQQPGAELAKPGA SVKMSCKAS	GYTFTR YW	IHWVKQRPQQDL EWIGY	INPRTDY T	EYNQKFKDKATLTADKSSSTAYMQ LSSLTSDDSAVYYC	ARHGYFDY	WGQGTTL TVSS
M48	6__13 0	QVQLQQPGAELAKPGA SVKMSCKAS	GYTFTR YW	IHWVKQRPQQDL EWIGY	INPRTDY T	EYNQKFKDKATLTADKSSSTAYMQ LSSLTSDDSAVYYC	ARHGYFDY	WGQGTTL TVSS
M49	6__13 0	QVQLQQPGAELAKPGA SVKMSCKAS	GYTFTR YW	MHWVKQRPQQDL EWIGY	INPRTDY T	EYNQKFKDKATLTADKSSSTAYMQ LSSLTSDDSAVYYC	ARHGYFDY	WGQGTTL TVSS
M50	6__13 0	QVQLQQSGAELAKPGA SVKMSCKAS	GYTFTR YW	IHWVKQRPQQDL EWIGY	INPRTDY T	EYNQKFKDKATLTADKSSSTAYMQ LSSLASDDSAVYYC	ARHGYFDY	WGQGTTL TV---
M51	6__16 3	QVQLQQSGAELAKPGA SVKMSCKAS	GYTFTR YW	MHWVKQRPQQDL EWIGY	INPRTDY T	EYNQKFKDKATLTADKSSSTAYMQ LSSLTSDDSAVYYC	ARHGYFDY	WGQGTTL TVSS
M52	6__16 3	QVQLQQSGAELAKPGA SVKMSCKAS	GYTFTR YW	MHWVKQRPQQDL EWIGY	INPRTDY T	EYNQKFKDKATLTADKSSSTAYMQ LSSLTSDDSAVYYC	ARHGYFDY	WGQGTTL TVSS
M53	57__6 3	QVQLQQPGAELAKPGA SVKMSCKAS	GYTFTR YW	IHWVKQRPQQDL EWIGY	INPRTDY T	EYNQKFKDKATLTANKSSSTAYMQ LSSLTSDDSAVYYC	ARHXYFDY	WGQGTTL TVSS
M54	33__6 3	QVQLQQSGAELAKPGA SVKMSCKAS	GYTFTR YW	MHWVKQRPQQDL EWIGY	INPRTDY TEYNQ	KFKDKATLTADKSSSTAYMQLSSL TSDDSAVYYC	AIHGYFDY	WGQGTTL TVSS
M55	147__ 157	QVQMKQSGAELAKPGA SVKMSCKAS	GYTFTR YW	IHWVKQRPQQDL EWIGY	INPRTDY TEYNQ	KFKDKATLTADKSSSTAYMQLSSL TSDDSAVYYC	ARHGYFDY	WGQGTSL TVSS

M56	147__ 157	QVQLQSGAEELAKPGA SVKMSCKAS	GYTFTR YW	MHWVKQRPQGDL EWIGY	INPRTDY TEYNQ	KFKDKATLTADKSSSTAYMQLSSL TSDDSAVYYC	ARHGFDY	WGQGTTL TVSS
M57	147__ 157	QVQLQSGAEELAKPGA SVKMSCKAS	GYTFTR YW	IHWVKQRPQGDL EWIGY	INPRTDY TEYNQ	KFKDKATLTADKSSSTAYMQLSSL TSDDSAVYYC	ARHGFDY	WGQGTTL TVSS
M58	33__ 3	QIQLKESGAELAKPGA SVKMSCKAS	GYTFTR YW	IHWVKQRPQGDL EWIGY	INPRTDY TEYNQ	KFKDKATLTADKSSSTAYMQLSSL TSDDSAVYYC	ARHGFDY	WGQGTTL TVSS
M59	33__ 3	QVQLQSGAEELAKPGA SVKMSCKAS	GYTFTR YW	MHWVKQRPQGDL EWIGY	INPRTDY TEYNQ	KFKDKATLTADKSSSTAYMQLSSL TSDDSAVYYC	ARHGFDY	WGQGTTL TVSS
M60	33__ 3	QIQLQPPGAELAKPGA SVKMSCKAS	GYTFTR YW	MHWVKQRPQGDL EWIGY	INPRTDY TEYNQ	KFKDKATLTADKSSSTAYMQLSSL TSDDSAVYYC	ARHGFDY	WGQGTTL TVSS
M61	33__ 3	QIQLQSGAEELAKPGA SVKMSCKAS	GYTFTR YW	IHWVKQRPQGDL EWIGY	INPRTDY TEYNQ	KFKDKATLTADKSSSTAYMQLSSL TSDDSAVYYC	ARHGFDY	WGQGTTL TVSS
M62	33__ 3	QVQLQSGAEELAKPGA SVKMSCKAS	GYTFTR YW	IHWVKQRPQGDL EWIGY	INPRTDY TEYNQ	KFKDKATLTADKSSSTAYMQLSSL ASDDSAVYYC	ARHGFDY	WGQGTTL TVSS
M63	33__ 3	QIQLQSGAEELAKPGA SVKMSCKAS	GYTFTR YW	IHWVKQRPQGDL EWIGY	INPRTDY TEYNQ	KFKDKATLTADKSSSTAYMQLSSL TSDDSAVYYC	ARHGFDY	WGQGTTL TVSS
M64	33__ 3	QVQLQPPGAELAKPGA SVKMSCKAS	GYTFTR YW	IHWVKQRPQGDL EWIGY	INPRTDY TEYNQ	KFKDKATLTADKSSSTAYMQLSSL TSDDSAVYYC	ARHGFDY	WGQGTTL TVSS
M65	33__ 3	QIQLQSGAEELAKPGA SVKMSCKAS	GYTFTR YW	IHWVKQRPQGDL EWIGY	INPRTDY TEYNQ	KFKDKATLTADKSSSTAYMQLSSL TSDDSAVYYC	ARHGFDY	WGQGTTL TVSS
M66	33__ 3	QIQLQPPGAELAKPGA SVKMSCKAS	GYTFTR YW	MHWVKQRPQGDL EWIGY	INPRTDY TEYNQ	KFKDKATLTADKSSSTAYMQLSSL TSDDSAVYYC	ARHGFDY	WGQGTTL TVSS
M67	33__ 3	QVQLQPPGAELAKPGA SVKMSCKAS	GYTFTR YW	IHWVKQRPQGDL EWIGY	INPRTDY TEYNQ	KFKDKATLTADKSSSTAYMQLSSL TSDDSAVYYC	ARHGFDY	WGQGTTL TVSS
M68	33__ 3	QIQLQPPGAELAKPGA SVKMSCKAS	GYTFTR YW	IHWVKQRPQGDL EWIGY	INPRTDY TEYNQ	KFKDKATLTADKSSSTAYMQLSSL TSDDSAVYYC	ARHGFDY	WGQGTTL TVSS
M69	33__ 3	QIQLQSGAEELAKPGA SVKMSCKAS	GYTFTR YW	MHWVKQRPQGDL EWIGY	INPRTDY TEYNQ	KFKDKATLTADKSSSTAYMQLSSL TSDDSAVYYC	ARHGFDY	WGQGTTL TVSS
M70	33__ 3	QIQLQSGAEELAKPGA SVKMSCKAS	GYTFTR YW	MHWVKQRPQGDL EWIGY	INPRTDY TEYNQ	KFKDKATLTADKSSSTAYMQLSSL TSDDSAVYYC	ARHGFDY	WGQGTTL TVSS
M71	33__ 3	QVQLQPPGAELAKPGA SVKMSCKAS	GYTFTR YW	IHWVKQRPQGDL EWIGY	INPRTDY TEYNQ	KFKDKATLTADKSSSTAYMQLSSL TSDDSAVYYC	ARHGFDY	WGQGTTL TVSS
M72	33__ 3	QIQLQSGAEELAKPGA SVKMSCKAS	GYTFTR YW	MHWVKQRPQGDL EWIGY	INPRTDY TEYNQ	KFKDKATLTADKSSSTAYMQLSSL TSDDSAVYYC	ARHGFDY	WGQGTTL TVSS
M73	44__ 6	QVQLQPPGAELAKPGA SVKMSCKAS	GYTFTR YW	IHWVKQRPQGDL EWIGY	INPRTDY TEYNQ	KFKDKATLTADKSSSTAYMQLSSL TSDDSAVYYC	ARHGFDY	WGQGTTL TVSS
M74	44__ 6	EVHLQSGAEELAKPGA SVKMSCKAS	GYTFTR FW	MHWVKQRPQGDL EWIGY	INPRTDY I	EYNQMFEDRATLTADKSSSTAYMQLSSL LTSLSDDSAVYYC	ARGTIIDY	WGQGTTL TVSS

M75	6__16 3	QVQLQQSGAELAKPGA SVKMSCKAS	GYTFNR FW	MHWVKQRPQGGL EWIGV	INPSTGY I	EHNQKFKDKATLTADKSSSTAYMQ LSSLTSEDSAYYC	ARGTVVDY	WGQGTTL TVSS
M76	147__ 157	QVQLVETGGGLVQPGG SRGLSCEGS	GFTFSG FW	MSWVRQTPGKTL EWIGD	INSDGSA INYAP	SIKDRFTIFRDNDRKSTLYLQMSNV RSEDATAYFC	MRVDGYWY FDV	WGAGTIV TVSS
M77	44__5 6	QVQLQQSGAGLVRPGV SLKISCKGS	GYTFD YA	MHWVRQTHAKSL KWIGV	INTYSGD A	IYNQKFKGKATMTVDKSSNTAYRE LAKLTSEDSAYYC	ARGVSFDY	WGQGTIV TVSS
M78	33__6 3	QIQLQQSGAELVRPGV SLKISCKGS	GYTFD YA	MHWVRQSHAKSL EWIGV	INTYSGD A	IYNQKFKGKATMTVDKSSSTAYLE LARLTSDDSAYYC	ARGVTEDY	WGQGTSL TVSS
M79	57__6 3	QVQLQQSGAELVRPGV SLKISCKGS	GYTFD YA	MHWVRQSHAKSL EWIGV	INTYSGD A	IYNQKFKGKATMTVDKSSSTAYLE LARLTSDDSAYYC	ARGVTEDY	WGQGTIV TVSS
M80	44__5 6	QVQLQQSGAELVRPGV SLKISCKGS	GYTFD YA	MHWVRP SHAKSL EWIGV	ISTYSGD A	IYNQKFKGKATMTVDKSSSTAYLE LARLTSDDSAYYC	ARGVPPDY	WAQSTIL TVSS
M81	147__ 156	QIQLQQSGAELVRPGV SLKISCKGS	GYTFD YA	MHWVRQSHAKSL EWIGV	ISTYSGD A	IYNQKFKGKATMTVDKSSSTAYLE LARLTSDDSAYYC	ARGVTEDI	WGQGTSL TVSS
M82	33__6 3	QVQLQQSGAELVRPGV SLKISCKGS	GYTFD YA	MHWVRQSHAKSL EWIGV	ISTYSGD A	IYNQKFKGKATMTVDKSSSTAYLE LARLTSDDSAYYC	ARGVTEDY	WGQGTTL TVSS
M83	33__6 3	QVQLQQPGAELVRPGV SLKISCKGS	GYTFD YA	MHWVRQSHAKSL EWIGV	ISTYSGD A	IYNQKFKGKATMTVDKSSSTAYLE LARLTSDDSAYYC	ARGVTEDY	WGQGTIV TVSS
M84	33__6 3	QIQLQQPGAELVRPGV SLKISCKGS	GYTFD YA	MHWVRQSHAKSL EWIGV	ISTYSGD A	IYNQKFKGKATMTVDKSSSTAYLE LARLTSDNSAYYC	ARGVTEDY	WGQGTIV TVSS
M85	33__6 3	QVQLQQSGAELVRPGV SLKISCKGS	GYTFD YA	MHWVRQSHAKSL EWIGV	ISTYSGD A	IYNQKFKGKATMTVDKSSSTAYLE LARLTSDDSAYYC	ARGVTEDY	WGQGTIV TVSS
M86	33__6 3	QIQLQQSGAELVRPGV SLKISCKGS	GYTFD YA	MHWVRQSHAKSL EWIGV	ISTYSGD A	IYNQKFKGKATMTVNKSSSTAYLE LARLTSDDSAYYC	ARGVTEDY	WGQGTSL TVSS
M87	33__6 3	QVQLIQSGAELVRPGV SLKISCKGS	GYTFD YA	MHWVRQSHAKSL EWIGV	ISTYSGD A	IYNQKFKGKATMTVDKSSSTAYLE LARLTSDDSAYYC	ARGVTEDY	WGQGTIV TVSS
M88	33__6 3	QVQLQQSGAELVRPGV SLKISCKGS	GYTFD YA	MHWVRQSHAKSL EWIGV	ISTYSGD A	IYDQKFQKGKATMTVDKSSSTAYLG LARLTSDDSAYYC	ARGVTEDY	WGQGTIV TVSS
M89	33__6 3	QVQLQQSGAELVRPGV SLKISCKGS	GYTFD YA	MHWVRQSHAKSL EWIGV	ISTYSGD A	IYNQKFKGKATMTVDKSSSTAYLE LARLTSDDSAYYC	ARGVTEDY	WGQGTIV TVSS
M90	33__6 3	QVQLQQPGAELVRPGV SLKISCKGS	GYTFD YA	MHWVRQSHAKSL EWIGV	ISTYSGD A	IYNQKFKGKATMTVDKSSSTAYLE LARLTSDDSAYYC	ARGVTEDY	WGQGTIV TVSS
M91	33__6 3	QVQLQQSGAELVRPGV SLKISCKGS	GYTFD YA	MHWVRQSHAKSL EWIGV	ISTYSGD A	IYNQKFKDKATMTVDKSSSTAYLE LARLTSEDSAYYC	ARGVTEDY	WGQGTTL TVSS
M92	33__6 3	QVQLQQSGAELVRPGV SLKISCKGS	GYTFD YA	MHWVRQSHAKSL EWIGV	ISTYSGD A	IYNQKFKGKATMTVDKSSSTAYLE LARLTSDDSAYYC	ARGVTEDY	WGQGTSL TVSS
M93	33__6 3	QIQLQQSGAELVRPGV SLKISCKGS	GYTFD YA	MHWVRQSHAKSL EWIGV	ISTYSGD A	IYNQKFKGKATMTVDKSSSTAYLE LARLTSDDSAYYC	ARGVTEDY	WGQGTSL TVSS

M94	33__6 3	QVQLQQSGAELVRPGV SLKISCKGS	GYFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD A	IYNQKFKGKATMTVDKSSSTAYLE LARLTSEDSAIYYC	ARGVTFDY	WGQGTTL TVSS
M95	44__5 6	QVQLQQSGAELVRPGV SLKISCKGS	GYFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD A	IYNQKFKGKATMTVDKSSSTAYLE LARLTSEDSAIYYC	ARGVTFDY	WGQGTSL TVSS
M96	44__5 6	QVQLQQSGAELVRPGV SLKISCKGS	GYFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD A	IYNQKFKGKATMTVDKSSSTAYLE LARLTSEDSAIYYC	ARGVTFDY	WGQGTSL TVSS
M97	44__5 6	QVQLQQSGAELVRPGV SLKISCKGS	GYFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD A	IYNQKFKGKATMTVDKSSSTAYLE LARLTSEDSAIYYC	ARGVTFDY	WGQGTTL TVSS
M98	147__ 156	QVQLQQSGAELVRPGV SLKISCKGS	GYFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD A	IYNQKFKGKATMTVDKSSSTAYLE LARLTSDHSAIYYC	ARGVTFDY	WGQGTIV TVSS
M99	147__ 156	QVQLQQSGAELVRPGV SLKISCKGS	GYFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD A	IYNQKFKGKATMTVDKSSSTAYLE LARLTSEDSAIYYC	ARGVTFDY	WGQGTSL TVSS
M10 0	147__ 156	QVQLQQSGAELMRPGV SLKISCKGS	GYFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD A	IYNQKFKGKATMTVDKSSSTAYLE LARLTSEDSAIYYC	ARGVTFDY	WGQGTTL TVSS
M10 1	44__5 6	QVQLQQSGAELVRPGV SLKISCKGS	GYFTD YA	MHWVRQSHAKSP EWIGV	ISTYSGD A	IYNQKFKGKATMTVDKSSSTAYLE LARLTSEDSAIYYC	ARGVTFDY	WGQGTTL TVSS
M10 2	57__6 3	QVQLQQSGAELVRPGV SLKISCKGS	GYFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD A	IYNQKFKGKATMTVDKSSSTAYLE LARLTSEDSAIYYC	ARGVTFDY	WGQGTIV TVSS
M10 3	57__6 3	QVQMQQSGAELVRPGV SLKISCKGS	GYFTD YA	MQWVRQSHAKSL EWIGV	ISTYSGD A	IYNQKFKSKATMTVDKSSSTAYLE LARLTSEDSAIYYC	ARGVTFDY	WGQGTIV TVSS
M10 4	6__13 0	QVQLQQSGAGLVRPGV SLKISCKGS	GYFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD A	IYNQKFKGKATMTVDKSSSTAYLE LARLTSEDSAIYYC	ARGVTFDY	WGQGTIV TVSS
M10 5	6__13 0	QVQLQQSGAELVRPGV SLKISCKGS	GYFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD A	IYNQKFKGKATMTVDKSSSTAYLE LARLTSEDSAIYYC	ARGVTFDY	WGQGTSL TV---
M10 6	6__13 0	QVQLQQSGAELVRPGV SLKISCKGS	GYFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD A	IYNQKFKGKATMTVDKSSSTAYLE LARLTSEDSAIYYC	ARGVTFDY	WGQGTTL TVSS
M10 7	6__13 0	QAYLQQSGAELVRPGV SLKISCKGS	GYFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD A	IYNQKFKGKATMTVDKSSSTAYLE LARLTSEDSAIYYC	ARGVTFDY	WGQGTTL TVSS
M10 8	6__16 3	QVQLQQSGAELVRPGV SLKISCKGS	GYFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD A	IYNQKFKGKATMTVDKSSSTAYLE LARLTSEDSAIYYC	ARGVTFDY	WGQGTIV TVSS
M10 9	77__8 9	QVQLQQSGAELVRPGV SLKISCKGS	GYFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD A	IYNQKFKGKATMTVDKSSSTAYLE LARLTSEDSAIYYC	ARGVTFDY	WGQGTIV TVSS
M11 0	77__8 9	QVQLQQSGAELVRPGV SLKISCKGS	GYFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD A	IYNQKFKGKATMTVDKSSSTAYLE LARLTSEDSAIYYC	ARGVTFDY	WGQGTIV TVSS
M11 1	77__8 9	QVQLQQSGAELVRPGV SLKISCKGS	GYFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD A	IYNQKFKGKATMTVDKSSSTAYLE LARLTSEDSAIYYC	ARGVTFDY	WGQGTTL TVSS
M11 2	77__8 9	QAYLQQSGAELVRPGV SLKISCKGS	GYFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD A	IYNQKFKGKATMTVDKSSSTAYLE LARLTSEDSAIYYC	ARGVTFDY	WGQGTTL TVSS

M11 3	77__8 9	QVQLQQSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD A	LYNQKFKGKATMTVDKSSSTAYLE LARLTSDSAIYYC	ARGVTFDY	WGQGTTL TVSS
M11 4	57__6 3	QIQLQQPGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIVV	ISTYSGD A	IYNQKFKGKATMTVDKSSITAYLE LARLTSDSAVYYC	ARXVTFDY	WGQGTIV TVSS
M11 5	44__5 6	QVQMQQSGAELVRPGV SLKISCKGS	GYTFTD YA	MQWVRQSHAKSL EWIGV	ISTYSGD A	IYNQKFKSKATMTVDKSSSTAYLE LARLTSEDSAIYYC	ATGVTFDY	WGQGTIV TVSS
M11 6	57__6 3	QIQLQQSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD A	IYNQKFKGKATMTVDKSSNTAYLE LARLTSDSAIYYC	ATGVTFDY	WGQGTIL TVSS
M11 7	147__ 157	QVQLQQSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD AIYNQ	KFKGKATMTVDKSSSTAYLELARL TSDDSAIYYC	ARGVTFDY	WGQGTIV TVSS
M11 8	147__ 157	QVQLQQSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD AIYNQ	KFKGKATMTVDKSSSTAYLELARL TSDDSAIYYC	ARGVTFDY	WGQGTIV TVSS
M11 9	147__ 157	QVQLQQSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD AIYNQ	KFKGKATMTVDKSSSTAYLELARL TSDDSAIYYC	ARGVTFDY	WGQGTIV TVSS
M12 0	147__ 157	EVQLQQSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD AIYNQ	KFKGKATMTVDKSSSTAYLELARL TSDDSAIYYC	ARGVTFDY	WGQGTTL TVSS
M12 1	147__ 157	QVQLQQSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD AIYNQ	KFKGKATMTVDKSSSTAYLELARL TSDDSAIYYC	ARGVTFDY	WGQGTIV TVSS
M12 2	147__ 157	QVQLQQSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD AIYNQ	KFKGKATMTVDKSSSTAYLELARL TSEDSAIYYC	ARGVTFDY	WGQGTTL TVSS
M12 3	147__ 157	QVQLQQSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD AIYNQ	KFKDKATMTVDKSSSTAYLELARL TSEDSAIYYC	ARGVTFDY	WGQGTTL TVSS
M12 4	147__ 157	QIQLQQSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD AIYNQ	KFKGKATMTVDKSSSTAYLELARL TSDDSAIYYC	ARGVTFDY	WGQGTSL TVSA
M12 5	147__ 157	QVQLQQPGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD AIYNQ	KFKGKATMTVDKSSSTAYLELARL TSDDSAIYYC	ARGVTFDY	WGQGTIV TVSS
M12 6	147__ 157	QVQLQQPGAELVRPGV SLKISCKGS	GYTFTD YA	MQWVRQSHAKSL EWIGV	ISTYSGD AIYNQ	KFKGKATMTVDKSSSTAYLELARL TSEDSAIYYC	ARGVTFDY	WGQGTIV TVSS
M12 7	147__ 157	QVQLQQPGAELVRPGV SLKISCKGS	GYTFTD YA	MQWVRQSHAKSL EWIGV	ISTYSGD AIYNQ	KFKGKATMTVDKSSSTAYLELARL TSEDSAIYYC	ARGVTFDY	WGQGTIV TVSS
M12 8	147__ 157	QVQLQQSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD AIYNQ	KFKGKATMTVDKSSSTAYLELARL TSDDSAIYYC	ARGVTFDY	WGQGTIV TVSS
M12 9	147__ 157	QVQLQQSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD AIYNQ	KFKGKATMTVDKSSSTAYLELARL TSDDSAIYYC	ARGVTFDY	WGQGTIV TVSS
M13 0	147__ 157	QVQLQQSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL KWIGV	ISTYSGD AIYNQ	KFKGKATMTVDKSSSTAYLELARL TSDDSAIYYC	ARGVTFDY	WGQGTIV TVSS
M13 1	33__6 3	QVQMQQSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD AIYNQ	KFKGKATMTVDKSSSTAYLELARL TSDDSAIYYC	ARGVTFDY	WGQGTIV TVSS

M13 2	33__6 3	QVQLQQSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD AIYNQ	KFKGKATMTVDKSSSTAYLELARL TSDDSAIYYC	ARGVTFDY	WGQGTIV TVSS
M13 3	33__6 3	QIQLQQSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD AIYNQ	KFKGKATMTVDKSSSTAYLELARL TSDDSAIYYC	ARGVTFDY	WGQGTSL TVSS
M13 4	33__6 3	QVQLQQSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD AIYNQ	KFKGKATMTVDKSSSTAYLELARL TSDDSAIYYC	ARGVTFDY	WGQGTIV TVSS
M13 5	33__6 3	QVQLQQSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSP EWIGV	ISTYSGD AIYNQ	KFKGKATMTVDKSSSTAYLELARL TSDDSAIYYC	ARGVTFDY	WGQGTIL TVSS
M13 6	33__6 3	QVQLQQSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD AIYNQ	KFKGKATMTVDKSSSTAYLELARL TSDDSAIYYC	ARGVTFDY	WGQGTIV TVSS
M13 7	33__6 3	QIQLQQSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD AIYNQ	KFKGKATMTVDKSSSTAYLELARL TSDDSAIYYC	ARGVTFDY	WGQGTSL TVSS
M13 8	33__6 3	QVQLQQSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD AIYNQ	KFKGKATMTVDKSSSTAYLELARL TSDDSAIYYC	ARGVTFDY	WGQGTIV TVSS
M13 9	33__6 3	QVQLQQSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD AIYNQ	KFKGKATMTVDKSSSTAYLELARL TSDDSAIYYC	ARGVTFDY	WGQGTIL TVSS
M14 0	33__6 3	QVQLQQSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD AIYNQ	KFKGKATMTVDKSSSTAYLELARL TSDDSAIYYC	ARGVTFDY	WGQGTIV TVSS
M14 1	33__6 3	QIQLQQSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD AIYNQ	KFKGKATMTVDKSSSTAYLELARL TSDDSAIYYC	ARGVTFDY	WGQGTSL TVSS
M14 2	33__6 3	QVQLQQSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD AIYNQ	KFKGKATMTVDKSSSTAYLELARL TSDDSAIYYC	ARGVTFDY	WGQGTSL TVSS
M14 3	33__6 3	QVQLQQSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD AIYNQ	KFKGKATMTVDKSSSTAYLELARL TSDDSAIYYC	ARGVTFDY	WGQGTIV TVSS
M14 4	33__6 3	QVQLQQSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD AIYNQ	KFKGKATMTVDKSSSTAYLELARL TSDDSAIYYC	ARGVTFDY	WGQGTIV TVSS
M14 5	33__6 3	QAYLQQSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD AIYNQ	KFKGKATMTVDKSSSTAYLELARL TSDDSAIYYC	ARGVTFDY	WGQGTIL TVSS
M14 6	33__6 3	QVQLQQSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD AIYNQ	KFKGKATMTVDKSSSTAYLELARL TSDDSAIYYC	ARGVTFDY	WGQGTIL TVSS
M14 7	33__6 3	QVQLQQSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD AIYNQ	KFKGKATMTVDKSSSTAYLELARL TSDDSAIYYC	ARGVTFDY	WGQGTSL TVSS
M14 8	33__6 3	QVQMKQSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD AIYNQ	KFKGKATMTVDKSSSTAYLELARL TSDDSAIYYC	ARGVTFDY	WGQGTIL TVSS
M14 9	33__6 3	QVQLQQSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD AIYNQ	KFKGKATMTVDKSSSTAYLELARL TSDDSAIYYC	ARGVTFDY	WGQGTIL TVSS
M15 0	33__6 3	QAYLQQSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD AIYNQ	KFKGKATMTVDKSSSTAYLELARL TSDDSAIYYC	ARGVTFDY	WGQGTIL TVSS

M15 1	33__6 3	QAYLQOSGAELVRPGV SLKISCKGS	GYTFTD YA	VQWVRQSHAKSL EWIGV	ISTYSGD AIYNQ	KFKGKATMTVDKSSSTAYLELARL TSEDSAIYYC	ARGVTFDY	WGQGTTL TVSS
M15 2	33__6 3	QVQLQOSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD AIYNQ	KFKGKATMTVDKSSSTAYLELARL TSDDSAIYYC	ARGVTFDY	WGQGTIV TVSS
M15 3	33__6 3	QVQLQOSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD AIYNQ	KFKGKATMTVDKSSSTAYLELARL TSDDSAIYYC	ARGVTFDY	WGQGTIV TVSS
M15 4	33__6 3	QVQLQOSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD AIYNQ	KFKGKATMTVDKSSSTAYLELARL TSEDSAIYYC	ARGVTFDY	WGQGTTL TVSS
M15 5	44__5 6	QVQLQOSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD AIYNQ	KFKGKATMTVDKSSSTAYLELARL TSDDSAIYYC	ARGVTFDY	WGQGTSL TVSS
M15 6	44__5 6	QVQLQOSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD AIYNQ	KFKGKATMTVDKSSSTAYLELARL TSDDSAIYYC	ARGVTFDY	WGQGTIV TVSS
M15 7	44__5 6	QVQLQOSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD AIYNQ	KFKGKATMTVDKSSSTAYLELARL TSDDSAIYYC	ARGVTFDY	WGQGTIV TVSS
M15 8	44__5 6	QVQMKQSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD AIYNQ	KFKGKATMTVDKSSSTAYLELARL TSDDSAIYYC	ARGVTFDY	WGQGTIV TVSS
M15 9	44__5 6	QVQMKQSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD AIYNQ	KFKGKATMTVDKSSSTAYLELARL TSDDSAIYYC	ARGVTFDY	WGQGTIV TVSS
M16 0	44__5 6	QVQMKQSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD AIYNQ	KFKGKATMTVDKSSSTAYLELARL TSDDSAIYYC	ARGVTFDY	WGQGTIV TVSS
M16 1	44__5 6	QAYLQOSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD AIYNQ	KFKGKATMTVDKSSSTAYLELARL TSEDSAIYYC	ARGVTFDY	WGQGTTL TVSS
M16 2	44__5 6	QVQLQOSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD AIYNQ	KFKGKATMTVDKSSSTAYLELARL TSDDSAIYYC	ARGVTFDY	WGQGTSL TVSA
M16 3	44__5 6	QVQLQOPGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD AIYNQ	KFKGKATMTVDKSSSTAYLELARL TSDDSAIYYC	ARGVTFDY	WGQGTIV TVSS
M16 4	44__5 6	QVQLQOPGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD AIYNQ	KFKGKATMTVDKSSSTAYLELARL TSDDSAIYYC	ARGVTFDY	WGQGTIV TVSS
M16 5	44__5 6	QAYLQOSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD AIYNQ	KFKGKATMTVDKSSSTAYLELARL TSEDSAIYYC	ARGVTFDY	WGQGTTL TVSS
M16 6	44__5 6	QVQMKQSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD AIYNQ	KFKGKATMTVDKSSSTAYLELARL TSDDSAIYYC	ARGVTFDY	WGQGTIV TVSS
M16 7	44__5 6	QVQMKQSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD AIYNQ	KFKGKATMTVDKSSSTAYLELARL TSDDSAIYYC	ARGVTFDY	WGQGTIV TVSS
M16 8	44__5 6	QVQLQOSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD AIYNQ	KFKGKATMTVDKSSSTAYLELARL TSDDSAIYYC	ARGVTFDY	WGQGTTL TVSS
M16 9	44__5 6	QVQLQOSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD AIYNQ	KFKGKATMTVDKSSSTAYLELARL TSDDSAIYYC	ARGVTFDY	WGQGTIV TVSS

M17 0	44__5 6	QVQLQQSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD ALYNQ	KFKGKATMTVDKSSSTAYLELARL TSDDSAIYYC	ARGVTFDY	WGQGTIV TVSS
M17 1	44__5 6	QVQLQQSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD ALYNQ	KFKGKATMTVDKSSSTAYLELARL TSDDSAIYYC	ARGVTFDY	WGQGTIV TVSS
M17 2	44__5 6	QVQLQQSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD ALYNQ	KFKGKATMTVDKSSSTAYLELARL TSDDSAIYYC	ARGVTFDY	WGQGTIV TVSS
M17 3	33__6 3	QVQLQQSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD ALYNQ	KFKGKATMTVDKSSSTAYLELARL TSDDSAIYYC	ARGVTFDY	WGQGTIV TVSS
M17 4	33__6 3	QVQLQQSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD ALYNQ	KFKGKATMTVDKSSSTAYLELARL TSDDSAIYYC	ARGVTFDY	WGQGTIV TVSS
M17 5	33__6 3	QVQLQQSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD ALYNQ	KFKGKATMTVDKSSSTAYLELARL TSDDSAIYYC	ARGVTFDY	WGQGTIV TVSS
M17 6	44__5 6	QVQLQQSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD ALYNQ	KFKGKATMTVDKSSSTAYLELARL TSDDSAIYYC	ARGVTFDY	WGQGTIV TVSS
M17 7	44__5 6	QVQLQQSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD ALYNQ	KFKGKATMTVDKSSSTAYLELARL TSDDSAIYYC	ARGVTFDY	WGQGTIV TVSS
M17 8	44__5 6	QVQLQQSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD ALYNQ	KFKGKATMTVDKSSSTAYLELARL TSDDSAIYYC	ARGVTFDY	WGQGTIV TVSS
M17 9	44__5 6	QVQLQQSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD ALYNQ	KFKGKATMTVDKSSSTAYLELARL TSDDSAIYYC	ARGVTFDY	WGQGTIV TVSS
M18 0	44__5 6	QVQLQQSGAELVRPGV SLKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD ALYNQ	KFKGKATMTVDKSSSTAYLELARL TSDDSAIYYC	ARGVTFDY	WGQGTIV TVSS
M18 1	33__6 3	QVQLQQSGAELVRPGV SVKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD V	SYNQKFKGKATMTVDKSSSTAYME LARLTSDDSAIYYC	ARGVTFDY	WGQGTIV TVSS
M18 2	33__6 3	QVQLQQSGAELVRPGV SVKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD V	SYNQKFKGKATMTVDKSSSTAYME LARLTSDDSAIYYC	ARGVTFDY	WGQGTIV TVSS
M18 3	33__6 3	QVQLQQSGAELVRPGV SVKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD V	SYNQKFKGKATMTVDKSSSTAYME LARLTSDDSAIYYC	ARGVTFDY	WGQGTIV TVSS
M18 4	33__6 3	QVQLQQSGAELVRPGV SVKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD V	SYNQKFKGKATMTVDKSSSTAYME LARLTSDDSAIYYC	ARGVTFDY	WGQGTIV TVSS
M18 5	44__5 6	QVQLQQSGAELVRPGV SVKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD V	SYNQKFKGKATMTVDKSSSTAYME LARLTSDDSAIYYC	ARGVTFDY	WGQGTIV TVSS
M18 6	6__13 0	QVQLQQSGAELVRPGV SVKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD V	SYNQKFKGKATMTVDKSSSTAYME LARLTSDDSAIYYC	ARGVTFDY	WGQGTIV TVSS
M18 7	6__13 0	QVQLQQSGAELVRPGV SVKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD V	SYNQKFKGKATMTVDKSSSTAYME LARLTSDDSAIYYC	ARGVTFDY	WGQGTIV TVSS
M18 8	6__16 3	QVQLQQSGAELVRPGV SVKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD V	SYNQKFKGKATMTVDKSSSTAYME LARLTSDDSAIYYC	ARGVTFDY	WGQGTIV TVSS

M18 9	6__16 3	EVHLQOSGAELVRPGV SVKISCKGS	GYTFTD YA	MHWVKQSHAKSL EWIGV	ISTYSGD V	SYNQKFKGKATMTVDKSSSTAYME LARLTSEDSAIYYC	ARGVTFTDS	WGQGTIV TVSS
M19 0	77__ 9	QIQLQOSGAELVRPGV SVKISCKGS	GYTFTD YA	MHWVKQSHAKSL EWIGV	ISTYSGD V	SYNQKFKGKATMTVDKSSSTAYME LARLTSEDSAIYYC	ARGVTFTDS	WGQGTSL TVSS
M19 1	77__ 9	QVQLQOSGAELVRPGV SVKISCKGS	GYTFTD YA	MHWVKQSHAKSL EWIGV	ISTYSGD V	SYNQKFKGKATMTVDKSSSTAYME LARLTSEDSAIYYC	ARGVTFTDS	WGQGTIV TVSS
M19 2	57__ 3	QIQLQOSGAELVRPGV SVKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD V	SYNQKFKGKATMTVDKSSSTAYME LARLTSEDSAIYYC	ATXVTFTDS	WGQGTIL TVSS
M19 3	147__ 157	QVQLQOSGAELVRPGV SVKISCKGS	GYTFTD YA	MHWVKQSHAKSL EWIGV	ISTYSGD V	KFKGKATMTVDKSSSTAYMELARL TSEDSAIYYC	ARGVTFTDS	WGQGTSL TVSS
M19 4	33__ 3	QVQLQOSGAELVRPGV SVKISCKGS	GYTFTD YA	MHWVKQSHAKSL EWIGV	ISTYSGD V	KFKGKATMTVDKSSSTAYMELARL TSEDSAIYYC	ARGVTFTDS	WGQGTSL TVSS
M19 5	44__ 6	QVQLQOSGAELVRPGV SVKISCKGS	GYTFTD YA	MHWVKQSHAKSL EWIGV	ISTYSGD V	KFKGKATMTVDKSSSTAYMELARL TSEDSAIYYC	ARGVTFTDS	WGQGTSL TVSS
M19 6	44__ 6	QVQLQOSGAELVRPGV SVKISCKGS	GYTFTD YA	MHWVKQSHAKSL EWIGV	ISTYSGD V	KFKGKATMTVDKSSSTAYMELARL TSEDSAIYYC	ARGVTFTDS	WGQGTSL TVSS
M19 7	44__ 6	QVQLQOSGAELVRPGV SVKISCKGS	GYTFTD YA	MHWVKQSHAKSL EWIGV	ISTYSGD V	KFKGKATMTVDKSSSTAYMELARL TSEDSAIYYC	ARGVTFTDS	WGQGTSL TVSS
M19 8	147__ 157	QAYLQOSGAELVRPGV SVKISCKGS	GYTFTD YA	MHWVKQSHAKSL EWIGV	ISTYSGD V	KFKD KATMTVDKSSSTAYMELARL TSEDSAIYYC	ARGVTFTDS	WGQGTIL TVSS
M19 9	147__ 157	QIQLQOSGAELVRPGV SVKISCKGS	GYTFTD YA	MHWVKQSHAKSL EWIGV	ISTYSGD V	KFKGKATMTVDKSSSTAYMELARL TSEDSAIYYC	ARGVTFTDS	WGQGTIV TVSS
M20 0	33__ 3	QVQLQOPGAELVRPGV SVKISCKGS	GYTFTD YA	MHWVKQSHAKSL EWIGV	ISTYSGD V	KFKGKATMTVDKSSSTAYMELARL TSEDSAIYYC	ARGVTFTDS	WGQGTIL TVSS
M20 1	33__ 3	QVQLQOSGAELVRPGV SVKISCKGS	GYTFTD YA	MHWVKQSHAKSL EWIGV	ISTYSGD V	KFKGKATMTVDKSSSTAYMELARL TSEDSAIYYC	ARGVTFTDS	WGQGTSL TVSS
M20 2	33__ 3	QVQLQOSGAELVRPGV SVKISCKGS	GYTFTD YA	MHWVKQSHAKSL EWIGV	ISTYSGD V	KFKGKATMTVDKSSSTAYMELARL TSEDSAIYYC	ARGVTFTDS	WGQGTIV TVSS
M20 3	33__ 3	QVQLQOSGAELVRPGV SVKISCKGS	GYTFTD YA	MHWVKQSHAKSL EWIGV	ISTYSGD V	KFKGKATMTVDKSSSTAYMELARL TSEDSAIYYC	ARGVTFTDS	WGQGTIL TVSS
M20 4	33__ 3	QVQLQOSGAELVRPGV SVKISCKGS	GYTFTD YA	MHWVKQSHAKSL EWIGV	ISTYSGD V	KFKGKATMTVDKSSSTAYMELARL TSEDSAIYYC	ARGVTFTDS	WGQGTIV TVSS
M20 5	33__ 3	QAYLQOSGAELVRPGV SVKISCKGS	GYTFTD YA	MHWVKQSHAKSL EWIGV	ISTYSGD V	KFKGKATMTVDKSSSTAYMELARL TSEDSAIYYC	ARGVTFTDS	WGQGTIV TVSS
M20 6	33__ 3	QVQMOSGAELVRPGV SVKISCKGS	GYTFTD YA	MHWVKQSHAKSL EWIGV	ISTYSGD V	KFKGKATMTVDKSSSTAYMELARL TSEDSAIYYC	ARGVTFTDS	WGQGTIV TVSS
M20 7	33__ 3	QAYLQOSGAELVRPGV SVKISCKGS	GYTFTD YA	MHWVKQSHAKSL EWIGV	ISTYSGD V	KFKGKATMTVDKSSSTAYMELARL TSEDSAIYYC	ARGVTFTDS	WGQGTIL TVSS

M20 8	33__6 3	QIQLQSGAELVRPGV SVKISCKGS	GYTFTD YA	MQWVKQSHAKSL EWIGV	ISTYSGD VSYNQ	KFKGKATMTVDKSSNTAYMELARL TSEDSAIYYC	ARGVTFTDS	WGQGTTL TVSS
M20 9	33__6 3	QIQLQSGAELVRPGV SVKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD VSYNQ	KFKGKATMTVDKSSSTAYMELARL TSEDSAIYYC	ARGVTFTDS	WGQGTIV TVSS
M21 0	33__6 3	QAYLQSGAELVRPGV SVKISCKGS	GYTFTD YA	MHWVKQSHAKSL EWIGV	ISTYSGD VSYNQ	KFKGKATMTVDKSSSTAYMELARL TSEDSAIYYC	ARGVTFTDS	WGQGTTL TVSS
M21 1	33__6 3	QVQLQSGAELVRPGV SVKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD VSYNQ	KFKGKATMTVDKSSSTAYMELARL TSEDSAIYYC	ARGVTFTDS	WGQGTIV TVSS
M21 2	33__6 3	QAYLQSGAELVRPGV SVKISCKGS	GYTFTD YA	MHWVRQSHAKSL EWIGV	ISTYSGD VSYNQ	KFKGKATMTVDKSSSTAYMELARL TSEDSAIYYC	ARGVTFTDS	WGQGTIV TVSS
M21 3	44__5 6	EVLQSGAELVRPGV SVKISCKGS	GYTFTD YA	MHWVKQSHAKSL EWIGV	ISTYSGD VSYNQ	KFKGKATMTVDKSSSTAYMELARL TSEDSAIYYC	ARGVTFTDS	WGQGTIV TVSS
M21 4	44__5 6	QAYLQSGAELVRPGV SVKISCKGS	GYTFTD YA	MHWVKQSHAKSL EWIGV	ISTYSGD VSYNQ	KFKGKATMTVDKSSSTAYMELARL TSEDSAIYYC	ARGVTFTDS	WGQGTIV TVSS
M21 5	44__5 6	QAYLQSGAELVRPGV SVKISCKGS	GYTFTD YA	MHWVKQSHAKSL EWIGV	ISTYSGD VSYNQ	KFKGKATMTVDKSSSTAYMELARL TSEDSAIYYC	ARGVTFTDS	WGQGTTL TVSS
M21 6	44__5 6	QAYLQSGAELVRPGV SVKISCKGS	GYTFTD YA	MHWVKQSHAKSL EWIGV	ISTYSGD VSYNQ	KFKGKATMTVDKSSSTAYMELARL TSEDSAIYYC	ARGVTFTDS	WGQGTTL TVSS
M21 7	44__5 6	QVQLQSGAELVRPGV SVKISCKGS	GYTFTD YA	MHWVKQSHAKSL EWIGV	ISTYSGD VSYNQ	KFKGKATMTVDKSSSTAYMELARL TSEDSAIYYC	ARGVTFTDS	WGQGTIV TVSS
M21 8	33__6 3	QIQLQSGAELVRPGV SVKISCKGS	GYTFTD YA	MHWVKQSHAKSL EWIGV	ISTYSGD VSYNQ	KFKGKATMTVDKSSSTAYMELARL TSEDSAIYYC	ARGVTSDS	WGQGTSL TVSS
M21 9	6__16 3	QVQLQSGAELVRPGT SVKISCKAS	GYTFTK YW	LGWVKQRPBGHL EWIGD	IYPGGDY T	NYNEKFKGKATLTADTSSSTAYMQ LSSLISED SAVYFC	ARVTPAS	WGQGTIV TVSS
M22 0	33__6 3	QVQLQSGAELVRPGT SVKISCKAS	GYTFTN YW	LGWVKQRPBGHL EWIGD	IYPGGDY T	NYNEKFKGKATLTADTSSSTAYMQ LSSLISED SAVYFC	ARVTPSS	WGQGTTL TVSS
M22 1	33__6 3	QVQLQSGAELVRPGT SVKISCKAS	GYTFTN YW	LGWVKQRPBGHL EWIGD	IYPGGDY T	NYNEKFKGKATLTADTSSSTAYMQ LSSLISED SAVYFC	ARVTPSS	WGQGTTL TVSS
M22 2	33__6 3	QVQLQSGAELVRPGT SVKISCKAS	GYTFTN YW	LGWVKQRPBGHL EWIGD	IYPGGDY T	NYNEKFKGKATLTADTSSSTAYMQ LSSLISED SAVYFC	ARVTPSS	WGQGTTL TVSS
M22 3	44__5 6	QIQLQSGAELVRPGT SVKISCKAS	GYTFTK YW	LGWVKQRPBGHL EWIGD	IYPGGDY TNVNE	KFKGKATLTADTSSSTAYMQ LSSL TSEDSAVYFC	ARVTPAS	WGQGTSL TVSS
M22 4	147__ 157	QVQLQSGAELVRPGT SVKISCKAS	GYTFTN YW	LGWVKQRPBGHL EWIGD	IYPGGDY TNVNE	KFKGKATLTADTSSSTAYMQ LSSL TSEDSAAVYFC	ARVTPSS	WGQGTIV TVSS
M22 5	147__ 157	QVQLQSGAELVRPGT SVKISCKAS	GYTFTN YW	LGWVKQRPBGHL EWIGD	IYPGGDY TNVNE	KFKGKATLTADTSSSTAYMQ LSSL TSEDSAVYFC	ARVTPSS	WGQGTTL TVSS
M22 6	33__6 3	QVQLQSGAELVRPGT SVKISCKAS	GYTFTN YW	LGWVKQRPBGHL EWIGD	IYPGGDY TNVNE	KFKGKATLTADTSSSTAYMQ LSSL TSEDSAVYFC	ARVTPSS	WGQGTTL TVSS

M22 7	33__6 3	QVQLQQSGAELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGDY TNVNE	KFKGKATLTADTSSSTAYMQLSSL TSSEDSAVYFC	ARVTPSS	WGQGTTL TVSS
M22 8	44__5 6	QVQLQQSGAELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGDY TNVNE	KFKGKATLTADTSSSTAYMQLSSL TSSEDSAVYFC	ARVTPSS	WGQGTTL TVSS
M22 9	33__6 3	QVQLQQSGAELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY A	NYNEKFKGKATLTADTSSSTAYMQ LSSLTSEDSAVYFC	ARVTPAS	WGQGTIV TVSS
M23 0	147__ 157	QVQLQQSGAELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY T	NYNEKFKGKATLTADTSSSTAYMQ LSSLTSEDSAVYFC	ARVTPAS	WGQGTIL TVSS
M23 1	147__ 157	QVQLQQSGAELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY T	NYNEKFKGKATLTADTSSSTAYMQ LSSLTSEDSAVYFC	ARVTPAS	WGQGTIL TVSS
M23 2	33__6 3	QVQLQQSGAELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY T	NYNEKFKGKATLTADTSSSTAYMQ LSSLTSEDSAVYFC	ARVTPAS	WGQGTIL TVSS
M23 3	33__6 3	QVQLQQSGAELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY T	NYNEKFKGKATLTADTSSSTAYMQ LSSLTSEDSAVYFC	ARVTPAS	WGQGTSL TVSS
M23 4	33__6 3	QVQLQQSGAELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY T	NYNEKFKGKATLTADTSSSTAYMQ LSSLTSEDSAVYFC	ARVTPAS	WGQGTIV TVSS
M23 5	33__6 3	QVQLQQSGAELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY T	NYNEKFKGKATLTADTSSSTAYMQ LSSLTSEDSAVYFC	ARVTPAS	WGQGTIL TVSS
M23 6	33__6 3	QVQLQQSGAELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY T	NYNEKFKGKATLTADTSSSTAYMQ LSSLTSEDSAVYFC	ARVTPAS	WGQGTIV TVSS
M23 7	33__6 3	QVQLQQSGAELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY T	NYNEKFKGKATLTADTSSSTAYMQ LSSLTSEDSAVYFC	ARVTPAS	WGQGTSL TVSS
M23 8	33__6 3	QVQLQQSGAELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY T	NYNEKFKGKATLTADTSSSTAYMQ LSSLTSEDSAVYFC	ARVTPAS	WGQGTIL TVSS
M23 9	33__6 3	QVQLQQSGAELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY T	NYNEKFKGKATLTADTSSSTAYMQ LSSLTSEDSAVYFC	ARVTPAS	WGQGTIL TVSS
M24 0	33__6 3	QVQLQQSGAELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY T	NYNEKFKGKATLTADTSSSTAYMQ LSSLTSEDSAVYFC	ARVTPAS	WGQGTIV TVSS
M24 1	33__6 3	QVQLQQSGAELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY T	NYNEKFKGKATLTADTSSSTAYMQ LSSLTSEDSAVYFC	ARVTPAS	WGQGTSL TVSS
M24 2	44__5 6	QVQLQQSGAELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY T	NYNEKFKGKATLTADTSSSTAYMQ LSSLTSEDSAVYFC	ARVTPAS	WGQGTSL TVSS
M24 3	44__5 6	QVQLQQSGAELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY T	NYNEKFKGKATLTADTSSSTAYMQ LSSLTSEDSAVYFC	ARVTPAS	WGQGTIV TVSS
M24 4	6__13 0	QVQLQQSGAELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY T	NYNEKFKGKATLTADTSSSTAYMQ LSSLTSEDSAVYFC	ARVTPAS	WGQGTSL TVSS
M24 5	6__13 0	QVQLQQSGAELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY T	NYNEKFKGKATLTADTSSSTAYMQ LSSLTSEDSAVYFC	ARVTPAS	WGQGTIV TVSS

M24 6	6_16 3	QIQLQSGAELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY T	NYNEKFKGKATLTADTSSSTAYMQ LSSLTSEDSAVYFC	ARVTPAS	WGQGTTL TVSS
M24 7	6_16 3	QVQLQPGAEELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY T	NYNEKFKGKATLTADTSSSTAYMQ LSSLTSEDSAVYFC	ARVTPAS	WGQGTSL TVSS
M24 8	6_16 3	QVQLQSGAEELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY T	NYNEKFKGKATLTADTSSSTAYMQ LSSLTSEDSAVYFC	ARVTPAS	WGQGTSL TVSS
M24 9	6_16 3	QVQLQSGAEELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY T	NYNEKFKGKATLTADTSSSTAYMQ LSSLTSEDSAVYFC	ARVTPAS	WGQGTTL TVSS
M25 0	6_16 3	QVQLQSGAEELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY T	NYNEKFKGKATLTADTSSSTAYMQ LSSLTSEDSAVYFC	ARVTPAS	WGQGTTL TVSS
M25 1	77_8 9	QVQLQSGAEELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY T	NYNEKFKGKATLTADTSSSTAYMQ LSSLTSEDSAVYFC	ARVTPAS	WGQGTTL TVSS
M25 2	77_8 9	QVQLQSGAEELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY T	NYNEKFKGKATLTADTSSSTAYMQ LSSLTSEDSAVYFC	ARVTPAS	WGQGTTL TVSS
M25 3	77_8 9	QVQLQSGAEELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY T	NYNEKFKGKATLTADTSSSTAYMQ LSSLTSEDSAVYFC	ARVTPAS	WGQGTTL TVSS
M25 4	77_8 9	QVQLQSGAEELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY T	NYNEKFKGKATLTADTSSSTAYMQ LSSLTSEDSAVYFC	ARVTPAS	WGQGTTL TVSS
M25 5	77_8 9	QIQLQSGAEELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY T	NYNEKFKGKATLTADTSSSTAYMQ LSSLTSEDSAVYFC	ARVTPAS	WGQGTTL TVSS
M25 6	77_8 9	QIQLQSGAEELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY T	NYNEKFKGKATLTADTSSSTAYMQ LSSLTSEDSAVYFC	ARVTPAS	WGQGTTL TVSS
M25 7	77_8 9	QIQLQSGAEELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY T	NYNEKFKGKATLTADTSSSTAYMQ LSSLTSEDSAVYFC	ARVTPAS	WGQGTSL TVSS
M25 8	77_8 9	QVQLQSGAEELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY T	NYNEKFKGKATLTADTSSSTAYMQ LSSLTSEDSAVYFC	ARVTPAS	WGQGTSL TVSS
M25 9	77_8 9	QAYLQSGAEELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY T	NYNEKFKGKATLTADTSSSTAYMQ LSSLTSEDSAVYFC	ARVTPAS	WGQGTSL TVSS
M26 0	77_8 9	QVQLQSGAEELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY T	NYNEKFKGKATLTADTSSSTAYMQ LSSLTSEDSAVYFC	ARVTPAS	WGQGTTL TVSS
M26 1	33_6 3	QAYLQSGAEELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY TNVNE	KFKGKATLTADTSSSTAYMQ LSSLTSEDSAVYFC	ARVTPAS	WGQGTSL TVSS
M26 2	33_6 3	QIQLQPGAEELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY TNVNE	KFKGKATLTADTSSSTAYMQ LSSLTSEDSAVYFC	ARVTPAS	WGQGTTL TVSS
M26 3	147_... 157	QVQLQSGAEELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY TNVNE	KFKGKATLTADTSSSTAYMQ LSSLTSEDSAVYFC	ARVTPAS	WGQGTTL TVSS
M26 4	147_... 157	QIQLQSGAEELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY TNVNE	KFKGKATLTADTSSSTAYMQ LSSLTSEDSAVYFC	ARVTPAS	WGQGTSL TVSS

M26 5	147_157	QVQLQQSGAELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY TNINE	KFKGKATLTADTSSSTAYMQLSSL TSEDSAVYFC	ARVTPAS	WGQGTIV TVSS
M26 6	147_157	QVQL*QPGAELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY TNINE	KFKGKATLTADTSSSTAYMQLSSL TSEDSAVYFC	ARVTPAS	WGQGTIV TVSS
M26 7	147_157	QVQLQQSGAELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY TNINE	EFKGAATLTADTSSSTAYMQLSSL TSEDSAVYFC	ARVTPAS	WGQGTIV TVSS
M26 8	147_157	QVQLQQSGAELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY TNINE	KFKGKATLTADTSSSTAYMQLSSL TSEDSAVYFC	ARVTPAS	WGQGTIV TVSS
M26 9	147_157	QVQLQQSGAELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY TNINE	KFKGKATLTADTSSSTAYMQLSSL TSEDSAVYFC	ARVTPAS	WGQGTIV TVSS
M27 0	147_157	QVQLQQSGAELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY TNINE	KFKGKATLTADTSSSTAYMQLSSL TSEDSAVYFC	ARVTPAS	WGQGTIV TVSS
M27 1	147_157	QVQLQQSGAELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY TNINE	KFKGKATLTADTSSSTAYMQLSSL TSEDSAVYFC	ARVTPAS	WGQGTIV TVSS
M27 2	147_157	QVQLQQSGAELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY TNINE	KFKGKATLTADTSSSTAYMQLSSL TSEDSAVYFC	ARVTPAS	WGQGTIV TVSS
M27 3	147_157	QVQLQQSGAELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY TNINE	KFKGKATLTADTSSSTAYMQLSSL TSEDSAVYFC	ARVTPAS	WGQGTIV TVSS
M27 4	147_157	QVQLQQSGAELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY TNINE	KFKGKATLTADTSSSTAYMQLSSL TSEDSAVYFC	ARVTPAS	WGQGTIV TVSS
M27 5	33_6	QVQLQQSGAELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY TNINE	KFKGKATLTADTSSSTAYMQLSSL TSEDSAVYFC	ARVTPAS	WGQGTIV TVSS
M27 6	33_6	QVQLQQSGAELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY TNINE	KFKGKATLTADTSSSTAYMQLSSL TSEDSAVYFC	ARVTPAS	WGQGTIV TVSS
M27 7	33_6	QVQLQQSGAELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY TNINE	KFKGKATLTADTSSSTAYMQLSSL TSEDSAVYFC	ARVTPAS	WGQGTIV TVSS
M27 8	33_6	QVQLQQSGAELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY TNINE	KFKGKATLTADTSSSTAYMQLSSL TSEDSAVYFC	ARVTPAS	WGQGTIV TVSS
M27 9	33_6	QVQLQQSGAELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY TNINE	KFKGKATLTADTSSSTAYMQLSSL TSEDSAVYFC	ARVTPAS	WGQGTIV TVSS
M28 0	33_6	QVQLQQSGAELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY TNINE	KFKGKATLTADTSSSTAYMQLSSL TSEDSAVYFC	ARVTPAS	WGQGTIV TVSS
M28 1	33_6	QVQLQQSGAELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY TNINE	KFKGKATLTADTSSSTAYMQLSSL TSEDSAVYFC	ARVTPAS	WGQGTIV TVSS
M28 2	33_6	QVQLQQSGAELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY TNINE	KFKGKATLTADTSSSTAYMQLSSL TSEDSAVYFC	ARVTPAS	WGQGTIV TVSS
M28 3	33_6	QVQLQQSGAELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY TNINE	KFKGKATLTADTSSSTAYMQLSSL TSEDSAVYFC	ARVTPAS	WGQGTIV TVSS

M28 4	33__ 3	QVQLQQSGAELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY TNVNE	KFKGKATLTADTSSSTAYMQLSSL TSEDSAVYFC	ARVTPAS	WGQGTTL TVSS
M28 5	33__ 3	QVQLQQPGAELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY TNVNE	KFKGKATLTADTSSSTAYMQLSSL TSEDSAVYFC	ARVTPAS	WGQGTTL TVSS
M28 6	33__ 3	QVQLQQSGAELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY TNVNE	KFKGKATLTADTSSSTAYMQLSSL TSEDSAVYFC	ARVTPAS	WGQGTSL TVSS
M28 7	33__ 3	QVQLQQSGAELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY TNVNE	KFKGKATLTADTSSSTAYMQLSSL TSEDSAVYFC	ARVTPAS	WGQGTSL TVSS
M28 8	33__ 3	QVQLQQSGAELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY TNVNE	KFKGKATLTADTSSSTAYMQLSSL TSEDSAVYFC	ARVTPAS	WGQGTSL TVSS
M28 9	33__ 3	QVQLQQSGAELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY TNVNE	KFKGKATLTADTSSSTAYMQLSSL TSEDSAVYFC	ARVTPAS	WGQGTTL TVSS
M29 0	33__ 3	QVQLQQSGAELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY TNVNE	KFKGKATLTADTSSSTAYMQLSSL TSEDSAVYFC	ARVTPAS	WGQGTSL TVSS
M29 1	33__ 3	QVQLQQSGAELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY TNVNE	KFKGKATLTADTSSSTAYMQLSSL TSEDSAVYFC	ARVTPAS	WGQGTSL TVSS
M29 2	33__ 3	QVQLQQSGAELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY TNVNE	KFKGKATLTADTSSSTAYMQLSSL TSEDSAVYFC	ARVTPAS	WGQGTTV TVSS
M29 3	33__ 3	QVQLQQSGAELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY TNVNE	KFKGKATLTADTSSSTAYMQLSSL TSEDSAVYFC	ARVTPAS	WGQGTSL TVSS
M29 4	33__ 3	QVQLQQSGAELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY TNVNE	KFKGKATLTADTSSSTAYMQLSSL TSEDSAVYFC	ARVTPAS	WGQGTTL TVSS
M29 5	33__ 3	QVQLQQSGAELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY TNVNE	KFKGKATLTADTSSSTAYMQLSSL TSEDSAVYFC	ARVTPAS	WGQGTTL TVSS
M29 6	44__ 6	QVQLQQSGAELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY TNVNE	KFKGKATLTADTSSSTAYMQLSSL TSEDSAVYFC	ARVTPAS	WGQGTTV TVSS
M29 7	44__ 6	QVQLQQSGAELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY TNVNE	KFKGKATLTADTSSSTAYMQLSSL TSEDSAVYFC	ARVTPAS	WGQGTTL TVSS
M29 8	44__ 6	QVQLQQSGAELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY TNVNE	KFKGKATLTADTSSSTAYMQLSSL TSEDSAVYFC	ARVTPAS	WGQGTSL TVSS
M29 9	44__ 6	QVQLQQSGAELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY TNVNE	KFKGKATLTADTSSSTAYMQLSSL TSEDSAVYFC	ARVTPAS	WGQGTTV TVSS
M30 0	44__ 6	QVQLQQSGAELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY TNVNE	KFKGKATLTADTSSSTAYMQLSSL TSEDSAVYFC	ARVTPAS	WGQGTTL TVSS
M30 1	44__ 6	QVQLQQSGAELVRPGT SVKISCKAS	GYFTN YW	LGWVKQRPBGHL EWIGD	IYPGGGY TNVNE	KFKGKATLTADTSSSTAYMQLSSL TSEDSAVYFC	ARVTPAS	WGQGTTL TVSS

Table 14B

ID	Epitope	L_FR1_AA	L_CDR1_AA	L_FR2_AA	L_CDR2_AA	L_FR3_AA	L_CDR3_AA	L_FR4_AA
M1	33_63	DVLTQTPLSLPVSLGDQ ASISCRSS	QSIVHSN GNTY	LEWYLQKPGQP PKLLIY	KVS	NRFSGVPDRFSGSGSGTDFTLKIS RVEAEDLGVIYC	FQGSHP T	FGGK LEIK
M2	33_63	DVVTQTPLSLPVSLGDQ ASISCRSS	QSLVHSN GNTY	LEWYLQKPGQS PKLLIY	KVS	NRFSGVPDRFSGSGSGTDFTLKIS RVEAEDLGVIYC	FQGSHP PT	FGGK LEMK
M3	44_56	DVVTQTPLSLPVSLGDQ ASISCRSS	QSLVHSN GNTY	LEWYLQKPGQS PKLLIY	KVS	NRFSGVPDRFSGSGSGTDFTLKIS RVEAEDLGVIYC	FQGSHP PT	FGGK LEMK
M4	44_56	DVLTQTPLSLPVSLGDQ ASISCRSS	QSIVHSN GNTY	LEWYLQKPGQS PKLLIY	KVS	NRFSGVPDRFSGSGSGTDFTLKIS RVEAEDLGVIYC	FQGSHP PT	FGGK LEIK
M5	147_56	DVMTQTPLSLPVSLGDQ ASISCRSS	QSIVHSN GNTY	LEWYLQKPGQS PKLLIY	KVS	NRFSGVPDRFSGSGSGTDFTLKIS RVEAEDLGVIYC	FQGSHP PT	FGGK LEIK
M6	44_56	DVLTQTPLSLPVSLGDQ ASISCRSS	QSIVHSN GNTY	LEWYLQKPGQS PKLLIY	KVS	NRFSGVPDRFSGSGSGTDFTLKIS RVEAEDLGVIYC	FQGSHP PT	FGGK LEMK
M7	6_130	DVLTQTPLSLPVSLGDQ ASISCRSS	QSIVHSN GNTY	LEWYLQKPGQS PKLLIY	KVS	NRFSGVPDRFSGSGSGTDFTLKIS RVEAEDLGVIYC	FQGSHP PT	FGGK LEIK
M8	6_163	DVMTQTPLSLPVSLGDQ ASISCRSS	QSIVHSN GNTY	LEWYLQKPGQS PKLLIY	KVS	NRFSGVPDRFSGSGSGTDFTLKIS RVEAEDLGVIYC	FQGSHP PT	FGGK LEIK
M9	147_57	DVMTQTPLSLPVSLGDQ ASISCRSS	QSIVHSN GNTY	LEWYLQKPGQS PKLLIY	KVS	NRFSGVPDRFSGSGSGTDFTLKIS RVEAEDLGVIYC	FQGSHP PT	FGGK LEMK
M10	147_57	DIQMTQSPASLSASVGEIS VTICRAS	ENIYSY	LEWYQKQKGS PQLIY	NAK	TLAEGVPSRFSGSGSGTDFTLKIS SLQPEDFGTYIC	QHGYGSP YT	FGGK LEIK
M11	147_57	DIQMTQTSSLSASLGDR VTICRAS	QDISNY	LNWYQKQKQDGT VKLLIY	HTS	RLQSGVPSRFSGSGSGTDYSLTIS NLEQEDATYFC	QQNSLP PT	FGGK LEIK
M12	33_63	DVVTQTPLSLPVSLGDQ ASISCRSS	QSLVHSN GNTY	LEWYLQKPGQS PKLLIY	KVS	NRFSGVPDRFSGSGSGTDFTLKIS RVEAEDLGVIYC	FQGSHP PT	FGGK LEMK
M13	33_63	DVLTQTPLSLPVSLGDQ ASISCRSS	QSIVHSN GNTY	LEWYLQKPGQP PKLLIY	KVS	NRFSGVPDRFSGSGSGTDFTLKIS RVEAEDLGVIYC	FQGSHP TF	GGGK LEIK
M14	33_63	DVMTQTPLSLPVSLGDQ ASISCRSS	QSIVHSN GNTY	LEWYLQKPGQS PKLLIY	KVS	NRFSGVPDRFSGSGSGTDFTLKIS RVEAEDLGVIYC	FQGSHP PT	FGGK LEMK
M15	33_63	DVMTQTPLSLPVNLGDQ ASISCRSS	QSIVHSN GNTY	LEWYLQKPGQS PKLLIY	KVS	NRFSGVPDRFSGSGSGTDFTLKIS RVEAEDLGVIYC	FQGSHP PT	FGGK LEIK
M16	33_63	DVLTQTPLSLPVSLGDQ ASISCRSS	QSIVHSN GNTY	LEWYLQKPGQS PKLLIY	KVS	NRFSGVPDRFSGSGSGTDFTLKIS RVEAEDLGVIYC	FQGSHP PT	FGGK LEIK
M17	33_63	DVLTQTPLSLPVSLGDQ ASISCRSS	QSIVHSN GNTY	LEWYLQKPGQS PKLLIY	KVS	NRFSGVPDRFSGSGSGTDFTLKIS RVEAEDLGVIYC	FQGSHP PT	FGGK LEIK

M18	44_56	DVMTQTPLSLPVSIGDQ ASISCRSS	QSIHNSN GNTY	LEWYLOKPGQS PKLLIY	KVS	NRFGVDPDRFSGSGTDFTLKIS RVEAEDLGVIYC	FQGSHP PT	FGGK LEIK
M19	44_56	DVMTQTPLSLPVSIGDQ ASISCRSS	QSIHNSN GNTY	LEWYLOKPGQS PKLLIY	KVS	NRFGVDPDRFSGSGTDFTLKIS RVEAEDLGVIYC	FQGSHP PT	FGGK LEIK
M20	33_63	DIQMTQSKFMSTSVGDR VSVTCAS	QNVGTN	VAWYQKPGQS PKLLIY	SAS	YRSGVDPDRFSGSGTDFTLTIS NVQSEDIAEYFC	QQNSYP LT	FGGK LEIK
M21	33_63	DIQMTQSPKFLDVSAGDR VTITCKAS	QSVNND	VWYQKPGQS PKLLIY	YAS	NRVTGVPDRFSGSGTDFTLTIS TVQAEADIAVYFC	QQAYWSP YT	FGGK LEMK
M22	44_56	EIVMTQSPPTLSLSPGER VTLSCAS	QDVNTA	VAWYQKPGQA PKLLIY	WAS	TRHTGVPSRFRSGSGTDFTLTIS SLQPEDFATYFC	QQHYSSP WT	FGGK VEIK
M23	44_56	EIVMTQSPPTLSLSPGER VTLSCAS	QDVNTA	VAWYQKPGQA PKLLIY	WAS	TRHTGVPSRFRSGSGTDFTLTIS SLQPEDFATYFC	QQHYSSP WT	FGGK VEIK
M24	6_130	DVMTQTSSLSASLGDR VTITCRAS	QDISNY	LNWYQKPDGT VKLLIY	HTS	RLHSGVPSRFRSGSGTDFTLTIS NLEQEDIAFYFC	QQGNTLP PT	FEGK LEIK
M25	33_63	DIQMTQTSSLSASLGDR VTITCRAS	QDISNY	LNWYQKPDGT VKLLIY	YTS	RLHSGVPSRFRSGSGTDFTLTIS NLEQEDIAFYFC	QQGNTLP LT	FGAGK LEMK
M26	6_163	DIQMTQTSSLSASLGDR VTITCRAS	QYISNY	LNWYQKPDGT VKLLIY	YTS	RLHSGVPSRFRSGSGTDFTLTIS NLEQEDIAFYFC	QQGNTLP PT	FGGK LEMK
M27	33_63	DIQMTQTSSLSASLGDR VTITCRAS	QDISNY	LNWYQKPDGT VKLLIY	YTS	RLHSGVPSRFRSGSGTDFTLTIS NLEQEDIAFYFC	QQGNTLP PT	FGGK LEIK
M28	33_63	DIQMTQTSSLSASLGDR VTITCRAS	QDISNY	LNWYQKPDGT VKLLIY	HTS	RLQSGVPSRFRSGSGTDFTLTIS NLEQEDIAFYFC	QQNSLP PT	FGGK LEIK
M29	33_63	DVMTQTSSLSASLGDR VTITCRAS	QDISNY	LNWYQKPDGT VKLLIY	HTS	RLHSGVPSRFRSGSGTDFTLTIS NLEQEDIAFYFC	QQGNTLP PT	FGGK LEIK
M30	33_63	DIQMTQTSSLSASLGDR VTITCRAS	QDISNY	LNWYQKPDGT VKLLIY	HTS	RLHSGVPSRFRSGSGTDFTLTIS NLEQEDIAFYFC	QQGNTLP PT	FGGK LEIK
M31	44_56	DIQMTQTSSLSASLGDR VTITCRAS	QDISNY	LNWYQKPDGT VKLLIY	HTS	RLQSGVPSRFRSGSGTDFTLTIS NLEQEDIAFYFC	QQNSLP PT	FGGK LEIK
M32	44_56	DIQMTQTSSLSASLGDR VTITCRAS	QDISNY	LNWYQKPDGT VKLLIY	HTS	RLQSGVPSRFRSGSGTDFTLTIS NLEQEDIAFYFC	QQNSLP PT	FGGK LEIK
M33	44_56	DIQMTQTSSLSASLGDR VTITCRAS	QDISNY	LNWYQKPDGT VKLLIY	HTS	RLQSGVPSRFRSGSGTDFTLTIS NLEQEDIAFYFC	QQNSLP PT	FGGK LEIK
M34	44_56	DIQMTQTSSLSASLGDR VTITCRAS	QDISNY	LNWYQKPDGT VKLLIY	HTS	RLQSGVPSRFRSGSGTDFTLTIS NLEQEDIAFYFC	QQNSLP PT	FGGK LEIK
M35	44_56	DIQMTQTSSLSASLGDR VTITCRAS	QDISNY	LNWYQKPDGT VKLLIY	HTS	RLQSGVPSRFRSGSGTDFTLTIS NLEQEDIAFYFC	QQNSLP PT	FGGK LEIK
M36	44_56	DIQMTQTSSLSASLGDR VTITCRAS	QDISNY	LNWYQKPDGT VKLLIY	HTS	RLQSGVPSRFRSGSGTDFTLTIS NLEQEDIAFYFC	QQNSLP PT	FGGK LEIK

M37	44_56	DIQMTQTSSLSASLGDR VTISCRAS	QDISNY	LNWYQKPDGT VKLLIY	HTS	RLQSGVPSRFTGSGSGTDYSLTIS NLEQEDIATYFC	QQNSLP PT	FGGTK LEIK
M38	44_56	DIQMTQTSSLSASLGDR VTISCRAS	QDISNY	LNWYQKPDGT VKLLIY	HTS	RLQSGVPSRFTGSGSGTDYSLTIS NLEQEDIATYFC	QQNSLP PT	FGGTK LEIK
M39	44_56	DIQMTQTSSLSASLGDR VTISCRAS	QDISNY	LNWYQKPDGT VKLLIY	HTS	RLQSGVPSRFTGSGSGTDYSLTIS NLEQEDIATYFC	QQNSLP PT	FGGTK LEIK
M40	44_56	DIQMTQTSSLSASLGDR VTISCRAS	QDISNY	LNWYQKPDGT VKLLIY	HTS	RLQSGVPSRFTGSGSGTDYSLTIS NLEQEDIATYFC	QQNSLP PT	FGGTK LEIK
M41	44_56	DIQMTQTSSLSASLGDR VTISCRAS	QDISNY	LNWYQKPDGT VKLLIY	HTS	RLHSGVPSRFTGSGSGTDYSLTIS NLEQEDIATYFC	QQSNTLP PT	FGGTK LEIK
M42	44_56	DIQMTQTSSLSASLGDR VTISCRAS	QDISNY	LNWYQKPDGT VKLLIY	HTS	RLHSGVPSRFTGSGSGTDYSLTIS NLEQEDIATYFC	QQSNTLP PT	FGGTK LEIK
M43	44_56	DVMTQTSSLSASLGDR VTITCRAS	QDISNY	LNWYQKPDGT VKLLIY	HTS	RLHSGVPSRFTGSGSGTDYSLTIS NLEQEDIATYFC	QQGNTLP PT	FGGTK LEIK
M44	44_56	DIQMTQTSSLSASLGDR VTISCRAS	QDISNY	LNWYQKPDGT VKLLIY	YTS	RLHSGVPSRFTGSGSGTDYSLTIS NLEQEDIATYFC	QQGNTLP PT	FGGTK LEIK
M45	44_56	DVMTQTSSLSASLGDR VTITCRAS	QDISNY	LNWYQKPDGT VKLLIY	HTS	RLHSGVPSRFTGSGSGTDYSLTIS NLEQEDIATYFC	QQGNTLP PT	FGGTK LEIK
M46	44_56	DIQMTQTSSLSASLGDR VTITCRAS	QDISNY	LNWYQKPDGT VKLLIY	HTS	RLHSGVPSRFTGSGSGTDYSLTIS NLEQEDIATYFC	QQGNTLP PT	FGGTK LEIK
M47	57_63	DIQMTQTSSLSASLGDR VTISCRAS	QDISNY	LNWYQKPDGT VKLLIY	HTS	RLQSGVPSRFTGSGSGTDYSLTIS NLEQEDIATYFC	QQNSLP PT	FGGTK LEIK
M48	6_130	DIQMTQTSSLSASLGDR VTISCRAS	QDISNY	LNWYQKPDGT VKLLIY	HTS	RLQSGVPSRFTGSGSGTDYSLTIS NLEQEDIATYFC	QQNSLP PT	FGGTK LEIK
M49	6_130	DIQMTQTSSLSASLGDR VTITCRAS	QDISNY	LNWYQKPDGT VKLLIY	HTS	RLQSGVPSRFTGSGSGTDYSLTIS NLEQEDIATYFC	QQNSLP PT	FGGTK LEIK
M50	6_130	DIQMTQTSSLSASLGDR VTITCRAS	QDISNY	LNWYQKPDGT VKLLIY	HTS	RLHSGVPSRFTGSGSGTDYSLTIS NLEQEDIATYFC	QQGNTLP PT	FGGTK LEIK
M51	6_163	DIQMTQTSSLSASLGDR VTITCRAS	QDISNY	LNWYQKPDGT VKLLIY	HTS	RLHSGVPSRFTGSGSGTDYSLTIS NLEQEDIATYFC	QQSNTLP PT	FGGTK LEIK
M52	6_163	DIQMTQTSSLSASLGDR VTITCRAS	QDISNY	LNWYQKPDGT VKLLIY	HTS	RLHSGVPSRFTGSGSGTDYSLTIS NLEQEDIATYFC	QQGNTLP PT	FGGTK LEIK
M53	57_63	DIQMTQTSSLSASLGDR VTISCRAS	QDISNY	LNWYQKPDGT VKLLIY	HTS	RLQSGVPSRFTGSGSGTDYSLTIS NLEQEDIATYFC	QQNSLP PT	FGGTK LEIK
M54	33_63	DIQMTQTSSLSASLGDR VTITCRAS	QDISNY	LNWYQKPDGT VKLLIY	HTS	RLHSGVPSRFTGSGSGTDYSLTIS NLEQEDIATYFC	QQSNTLP PT	FGGTK LEIK
M55	147_57	DIQMTQTSSLSASLGDR VTISCRAS	QDISNY	LNWYQKPDGT VKLLIY	YTS	RLHSGVPSRFTGSGSGTDYSLTIS NLEQEDIATYFC	QQGNTLP PT	FGGTK LEIK

M56	147_1 57	DIQMTQSTSSLSASLGDR VTITCRAS	QDISNY	LNWYQKQPDGT VKLLIY	HTS	RLHSGVPSRFSGSESGTDYSLTIS NLEQEDIATYFC	QQSNTLP PT	FGGGTK LEIK
M57	147_1 57	DIQMTQSTSSLSASLGDR VTISCRAS	QDISNY	LNWYQKQPDGT VKLLIY	YTS	RLHSGVPSRFSGSESGTDYSLTIS NLEQEDIATYFC	QQGNTLP PT	FGGGTK LEIK
M58	33_63	DIQMTQTTSSLSASLGDR VTISCRAS	QDISNY	LNWYQKQPDGT VKLLIY	YTS	RLHSGVPSRFSGSESGTDYSLTIS NLEQEDIATYFC	QQGNTLP PT	FGGGTK LEIK
M59	33_63	DIQMTQSTSSLSASLGDR VTITCRAS	QDISNY	LNWYQKQPDGT VKLLIY	HTS	RLHSGVPSRFSGSESGTDYSLTIS NLEQEDIATYFC	QQSNTLP PT	FGGGTK LEIK
M60	33_63	DVMTQTTSSLSASLGDR VTITCRAS	QDISNY	LNWYQKQPDGT VKLLIY	HTS	RLHSGVPSRFSGSESGTDYSLTIS NLEQEDIATYFC	QQGNTLP PT	FGGGTK LEIK
M61	33_63	DVMTQSPASLSASVGET VTITCRAS	ENSYSY	LEWYQKQKGS PQLLYY	NAK	TLAEGVPSRFSGSESGTQFSLKIN SLQPEDFGTYFC	QHAYGTP YT	FGGGTK LEIK
M62	33_63	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQKQKGS PQLLYY	NAK	TLVEGVPSRFSGSESGTQFSLKIN SLQPEDFGSYFC	QHAYDTP YT	FGGGTK LEIK
M63	33_63	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQKQKGS PQLLYY	NAK	TLVEGVPSRFSGSESGTQFSLKIN SLQPEDFGSYFC	QHAYDTP YT	FGGGTK LEIK
M64	33_63	DIQMTQTTSSLSASLGDR VTISCRAS	QYISNY	LNWYQKQDGT VKLLIY	YTS	RLHSGVPSRFSGSESGTDYSLTIS NLEQEDIATYFC	QQGNTLP PT	FGGGTK LEMK
M65	33_63	DIVMTQTTSSLSASLGDR VTITCGAS	QDISNY	LNWYQKQDGT VKLLIY	HTS	RLHSGVPSRFSGSESGTDYSLTIS NLEQEDIATYFC	QQGNTLP PT	FGGGTK LEIK
M66	33_63	DIQMTQSTSSLSASLGDR VTITCRAS	QDISNY	LNWYQKQDGT VKLLIY	HTS	RLHSGVPSRFSGSESGTDYSLTIS NLEQEDIATYFC	QQGNTLP PT	FGGGTK LEIK
M67	33_63	DIQMTQTTSSLSASLGDR VTISCRAS	QDISNY	LNWYQKQPDGT VKLLIY	HTS	RLQSGVPSRFTGSGSGTDYSLTIS NLEQEDIATYFC	QQNSLP PT	FGGGTK LEIK
M68	33_63	DIVMTQTTSSLSASLGDR VTISCRAS	QDISNY	LNWYQKQPDGT VKLLIY	YTS	RLHSGVPSRFSGSESGTDYSLTIS NLEQEDIATYFC	QQGNTLP PT	FGGGTK LEIK
M69	33_63	DIQMTQTTSSLSASLGDR VTITCRAS	QDISNY	LNWYQKQPDGT VKLLIY	HTS	RLHSGVPSRFSGSESGTDYSLTIS NLEQEDIATYFC	QQGNTLP PT	FGGGTK LEIK
M70	33_63	DIQMTQTTSSLSASLGDR VTITCRAS	QDISNY	LNWYQKQPDGT VKLLIY	HTS	RLHSGVPSRFSGSESGTDYSLTIS NLEQEDIATYFC	QQGNTLP PT	FGGGTK LEIK
M71	33_63	DIQMTQTTSSLSASLGDR VTISCRAS	QDISNY	LNWYQKQPDGT VKLLIY	HTS	RLQSGVPSRFTGSGSGTDYSLTIS NLEQEDIATYFC	QQNSLP PT	FGGGTK LEIK
M72	33_63	DIQMTQTTSSLSASLGDR VTITCRAS	QDISNY	LNWYQKQDGT VKLLIY	HTS	RLHSGVPSRFSGSESGTDYSLTIS NLEQEDIATYFC	QQGNTLP PT	FGGGTK LEIK
M73	44_56	DIQMTQTTSSLSASLGDR VTISCRAS	QDISNY	LNWYQKQPDGT VKLLIY	HTS	RLQSGVPSRFTGSGSGTDYSLTIS NLEQEDIATYFC	QQNSLP PT	FGGGTK LEIK
M74	44_56	DIQMTQTTSSLSASLGDR VTISCRAS	QDISNY	LNWYQKQPDGT VKLLIY	YTS	RLHSGVPSRFSGSESGTDYSLTIS NLEQEDIATYFC	QQGNTLP PT	FGGGTK LEIK

M75	6_163	DIQMTQTSSLSASLGDR VTISCRAS	QDISNY	LNWYQQKPDGT VKLLIY	YTS	RLHSGVPSRFSGSGGADYSLTIS NLEQEDIAFYC	QQGNTLP PT	FGGKTK LEIK
M76	147__1 57	DIQMTQSQKFMTSVGDR VSVTCKAS	QNVSTN	VAWYQQKPGQS PKALIY	SAS	YRYSGVDPDRFTGSGSGDTFTILTIS NVQSEDIAEYFC	QQYNSYP YT	FGGKTK LEMK
M77	44__56	DIQMTQSPASLSASVGET VTITCRAS	ENIHSY	LEWYQQKQKGS PQLLYY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGSYCC	QHHYGTP YT	FGGKTK LEMK
M78	33__63	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQQKQKGS PQLLYY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGSYCC	QHHYDTP YT	FGGKTK LEIK
M79	57__63	DVMTQSPASLSASVGET VTITCRAS	ENSYSY	LEWYQQKQKGS PQLLYY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGTYCC	QHHYGTP YT	FGGKTK LEIK
M80	44__56	DIQMTQSPASLSASVGET VTITCRAS	ENSYSY	LEWYQQKQKGS PQLLYY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGTYCC	QHHYGTP YT	FGGKTK LEIK
M81	147__1 56	DVMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQQKQKGS PQLLYY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGSYCC	QHHYDTP YT	FGGKTK LEIK
M82	33__63	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQQKQKGS PQLLYY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGTYCC	QHHYGTP YT	FGGKTK LEIK
M83	33__63	DIVLTQSPASLSASVGET VTITCRAS	ENSYSY	LEWYQQKQKGS PQLLYY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGTYCC	QHHYGTP YT	FGGKTK LEIK
M84	33__63	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQQKQKGS PQLLYY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGSYCC	QHHYDTP YT	FGGKTK LEIK
M85	33__63	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQQKQKGS PQLLYY	NAK	TLVEGVPSRFSGSGSGTQFSLKIN SLQPEDFGSYCC	QHHYDTP YT	FGGKTK LEIK
M86	33__63	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQQKQKGS PQLLYY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGSYCC	QHHYDTP YT	FGGKTK LEIK
M87	33__63	DVMTQSPASLSASVGET VTITCRAS	ENSYSY	LEWYQQKQKGS PQLLYY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGTYCC	QHHYGTP YT	FGGKTK LEIK
M88	33__63	DVMTQSPASLSASVGET VTITCRAS	ENSYSY	LEWYQQKQKGS PQLLYY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGTYCC	QHHYGTP YT	FGGKTK LEIK
M89	33__63	DVMTQSPASLSASVGET VTITCRAS	ENSYSY	LEWYQQKQKGS PQLLYY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGTYCC	QHHYGTP YT	FGGKTK LEMK
M90	33__63	DIQMTQSPASLSASVGET VTITCRAS	ENSYSY	LEWYQQKQKGS PQLLYY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGTYCC	QHHYGTP YT	FGGKTK LEIK
M91	33__63	DIQMTQSPASLSASVGET VTITCRAS	ENSYSY	LEWYQQKQKGS PQLLYY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGTYCC	QHHYGTP YT	FGGKTK LEIK
M92	33__63	DIQMTQSPASLSASVGET VTITCRAS	ENSYSY	LEWYQQKQKGS PQLLYY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGTYCC	QHHYGTP YT	FGGKTK LEIK
M93	33__63	DVMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQQKQKGS PQLLYY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGSYCC	QHHYDTP YT	FGGKTK LEIK

M94	33__63	DIQMTQSPASLSASVGET VTITCRAS	ENSYSY	LEWYQQKQKGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGTYYC	QHHYGTP YT	FGGGTK LEIK
M95	44__56	DIQMTQSPASLSASVGET VTITCRAS	ENSYSY	LEWYQQKQKGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGTYYC	QHHYGTP YT	FGGGTK LEIK
M96	44__56	DIQMTQSPASLSASVGET VTITCRAS	ENSYSY	LEWYQQKQKGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGTYYC	QHHYGTP YT	FGGGTK LEIK
M97	44__56	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQQKQKGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGTYYC	QHHYDTP YT	FGGGTK LEIK
M98	147__1 56	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQQKQKGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGTYYC	QHHYDTP YT	FGGGTK LEIK
M99	147__1 56	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQQKQKGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGTYYC	QHHYDTP YT	FGGGTK LEIK
M10 0	147__1 56	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQQKQKGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGTYYC	QHHYGSP YT	FGGGTK LEIK
M10 1	44__56	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQQKQKGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIS SLQPEDFGTYYC	QHHYGIP YT	FGGGTK LEIK
M10 2	57__63	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQQKQKGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGTYYC	QHHYDTP YT	FGGGTK LEIK
M10 3	57__63	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQQKQKGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGTYYC	QHHYDTP YT	FGGGTK LEIK
M10 4	6__130	DIQMTQSPASLSASVGET VTITCRAS	ENIHSY	LEWYQQKQKGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGTYYC	QHHYGTP YT	FGGGTK LEMK
M10 5	6__130	DIQMTQSPASLSASVGET VTITCRAS	ENSYSY	LEWYQQKQKGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGTYYC	QHHYGTP YT	FGGGTK LEIK
M10 6	6__130	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQQKQKGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGTYYC	QHHYGTP YT	FGGGTK LEIK
M10 7	6__130	DIQMTQSPASLSASVGET VTITCRAS	QDISNY	LNWYQQKPDGT VKLLIY	YTS	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGTYYC	QHHYGTP YT	FGGGTK LEIK
M10 8	6__163	DVMTQSPASLSASVGET VTITCRAS	ENSYSY	LEWYQQKQKGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGTYYC	QHHYGTP YT	FGGGTK LEIK
M10 9	77__89	DVMTQSPASLSASVGET VTITCRAS	ENSYSY	LEWYQQKQKGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGTYYC	QHHYGTP YT	FGGGTK LEIK
M11 0	77__89	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQQKQKGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGTYYC	QHHYDTP YT	FGGGTK LEIK
M11 1	77__89	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQQKQKGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGTYYC	QHHYGSP YT	FGGGTK LEIK
M11 2	77__89	DVMTQSPSSMYASLGER VTITCKAS	QDISNY	LSWFQKQPGKS PKLLIY	RAN	RLVDGAPSRFSGSGSGTQFSLKIN SLQPEDFGTYYC	LQYDEFP YT	FGGGTK LEIK

M11 3	77__89	DVQMTQSPSSMYASLGER VTFTCKAS	QDINRY	LSWFQKQPKGS PKLLIY	RAN	RLVDGVPSRFRSGSGSQNYSLTIS SLEYEDMGIYYC	LQYDEFP YT	FGGKTK LEIK
M11 4	57__63	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQKQKGS PQLLVY	NAK	TLAEGVPSRFRSGSGGTQFSLKIN SLOPEDFGSIYYC	QHHYDTP YT	FGGKTK LEIK
M11 5	44__56	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQKQKGS PQLLVY	NAK	TLAEGVPSRFRSGSGGTQFSLKIN SLOPEDFGSIYYC	QHHYDTP YT	FGGKTK LEIK
M11 6	57__63	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQKQKGS PQLLVY	NAK	TLAEGVPSRFRSGSGGTQFSLKIN SLOPEDFGSIYYC	QHHYDTP YT	FGGKTK LEIK
M11 7	147__1 57	DVMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQKQKGS PQLLVY	NAK	TLAEGVPSRFRSGSGGTQFSLKIN SLOPEDFGSIYYC	QHHYDTP YT	FGGKTK LEIK
M11 8	147__1 57	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQKQKGS PQLLVY	NAK	TLAEGVPSRFRSGSGGTQFSLKIN SLOPEDFGSIYYC	QHHYDTP YT	FGGKTK LEIK
M11 9	147__1 57	DVMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQKQKGS PQLLVY	NAK	TLAEGVPSRFRSGSGGTQFSLKIN SLOPEDFGSIYYC	QHHYDTP YT	FGGKTK LEIK
M12 0	147__1 57	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQKQKGS PQLLVY	NAK	TLAEGVPSRFRSGSGGTQFSLKIN SLOPEDFGSIYYC	QHHYDTP YT	FGGKTK LEIK
M12 1	147__1 57	DVMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQKQKGS PQLLVY	NAK	TLAEGVPSRFRSGSGGTQFSLKIN SLOPEDFGSIYYC	QHHYDTP YT	FGGKTK LEIK
M12 2	147__1 57	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQKQKGS PQLLVY	NAK	TLAEGVPSRFRSGSGGTQFSLKIN SLOPEDFGSIYYC	QHHYDTP YT	FGGKTK LEIK
M12 3	147__1 57	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQKQKGS PQLLVY	NAK	TLAEGVPSRFRSGSGGTQFSLKIN SLOPEDFGSIYYC	QHHYDTP YT	FGGKTK LEIK
M12 4	147__1 57	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQKQKGS PQLLVY	NAK	TLAEGVPSRFRSGSGGTQFSLKIN SLOPEDFGSIYYC	QHHYDTP YT	FGGKTK LEIK
M12 5	147__1 57	DVMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQKQKGS PQLLVY	NAK	TLAEGVPSRFRSGSGGTQFSLKIN SLOPEDFGSIYYC	QHHYDTP YT	FGGKTK LEIK
M12 6	147__1 57	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQKQKGS PQLLVY	NAK	TLAEGVPSRFRSGSGGTQFSLKIN SLOPEDFGSIYYC	QHHYDTP YT	FGGKTK LEIK
M12 7	147__1 57	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQKQKGS PQLLVY	NAK	TLAEGVPSRFRSGSGGTQFSLKIN SLOPEDFGSIYYC	QHHYDTP YT	FGGKTK LEIK
M12 8	147__1 57	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQKQKGS PQLLVY	NAK	TLAEGVPSRFRSGSGGTQFSLKIN SLOPEDFGSIYYC	QHHYDTP YT	FGGKTK LEIK
M12 9	147__1 57	DVMTQSPASLSASVGET VTITCRAS	QDISNY	LNWYQKQKDG VKLLIY	HTS	RLHSGVPSRFRSGSEPGTDYSLTIS NLEQEDATYFC	QOQNTLP PT	FGGKTK LEIK
M13 0	147__1 57	DIQMTQSPASLSASVGET VTITCRAS	QDISNY	LNWYQKQKDG VKLLIY	HTS	RLQSGVPSRFRSGSGGTQFSLKIN NLEQEDATYFC	QOQNSLP PT	FGGKTK LEIK
M13 1	33__63	DVMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQKQKGS PQLLVY	NAK	TLAEGVPSRFRSGSGGTQFSLKIN SLOPEDFGSIYYC	QHHYDTP YT	FGGKTK LEIK

M13 2	33__63	DVMTQSPASLSASVGET VTITCRAS	ENSYSY	LEWYQKQKGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGTYYC	QHHYGTP YT	FGGGTK LEIK
M13 3	33__63	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQKQKGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGTYYC	QHHYDTP YT	FGGGTK LEIK
M13 4	33__63	DVMTQSPASLSASVGET VTITCRAS	ENSYSY	LEWYQKQKGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGTYYC	QHHYGTP YT	FGGGTK LEIK
M13 5	33__63	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQKQKGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIS SLQPEDFGTYYC	QHHYGTP YT	FGGGTK LEIK
M13 6	33__63	DVMTQSPASLSASVGET VTITCRAS	ENSYSY	LEWYQKQKGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGTYYC	QHHYGTP YT	FGGGTK LEIK
M13 7	33__63	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQKQKGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGTYYC	QHHYDTP YT	FGGGTK LEIK
M13 8	33__63	DVMTQSPASLSASVGET VTITCRAS	ENSYSY	LEWYQKQKGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGTYYC	QHHYGTP YT	FGGGTK LEIK
M13 9	33__63	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQKQKGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGTYYC	QHHYGSP YT	FGGGTK LEMK
M14 0	33__63	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQKQKGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLRIN SLQPEDFGTYYC	QHHYGTP YT	FGGGTK LEIK
M14 1	33__63	DVMTQSPASLSASVGET VTITCRAS	QDINSY	LSWFQKPKGS PKTLIY	RAN	RLVDGVPFRFSGSGSGTQFSLTIS SLEYEDMGIIYYC	LQYDEFP YT	FGGGTK LEIK
M14 2	33__63	DIQMTQSPASLSASVGET VTITCRAS	ENSYSY	LEWYQKQKGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGTYYC	QHHYGTP YT	FGGGTK LEIK
M14 3	33__63	DVMTQSPASLSASVGET VTITCRAS	ENSYSY	LEWYQKQKGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGTYYC	QHHYGTP YT	FGGGTK LEIK
M14 4	33__63	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQKQKGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGTYYC	QHHYDTP YT	FGGGTK LEIK
M14 5	33__63	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQKQKGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGTYYC	QHHYDTP YT	FGGGTK LEIK
M14 6	33__63	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQKQKGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGTYYC	QHHYDTP YT	FGGGTK LEIK
M14 7	33__63	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQKQKGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGTYYC	QHHYGSP YT	FGGGTK LEIK
M14 8	33__63	DTVTQSPSSMYASLGER VTITCRAS	QDINN	LSWFQKPKGS PQTLIY	RAN	RLVDGVPFRFSGSGSGTQFSLTIS SLEYEDLGIYYC	LQYDEFP WT	FGGGTK LEIK
M14 9	33__63	DIQMTQSPASLSASVGET VTITCRAS	ENSYSY	LEWYQKQKGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGTYYC	QHHYGTP YT	FGGGTK LEIK
M15 0	33__63	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQKQKGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGTYYC	QHHYDTP YT	FGGGTK LEIK

M15 1	33__63	DIQMTQSPASLSASVGET VTITCRAS	ENSYSY	LEWYQQKQGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGYYC	QHYYGTP YT	FGGKTK LEIK
M15 2	33__63	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQQKQGS PQLLVY	NAK	TLVEGVPSRFSGSGSGTQFSLKIN SLQPEDFGYYC	QHYYDTP YT	FGGKTK LEIK
M15 3	33__63	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQQKQGS PQLLVY	NAK	TLVEGVPSRFSGSGSGTQFSLKIN SLQPEDFGYYC	QHYYDTP YT	FGGKTK LEIK
M15 4	33__63	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQQKQGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGYYC	QHYYDTP YT	FGGKTK LEIK
M15 5	44__56	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQQKQGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGYYC	QHYYGSP YT	FGGKTK LEIK
M15 6	44__56	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQQKQGS PQLLVY	NAK	TLVEGVPSRFSGSGSGTQFSLKIN SLQPEDFGYYC	QHYYDTP YT	FGGKTK LEIK
M15 7	44__56	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQQKQGS PQLLVY	NAK	TLVEGVPSRFSGSGSGTQFSLKIN SLQPEDFGYYC	QHYYDTP YT	FGGKTK LEIK
M15 8	44__56	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQQKQGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGYYC	QHYYGSP YT	FGGKTK LEIK
M15 9	44__56	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQQKQGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGYYC	QHYYGSP YT	FGGKTK LEIK
M16 0	44__56	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQQKQGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGYYC	QHYYGSP YT	FGGKTK LEIK
M16 1	44__56	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQQKQGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGYYC	QHYYDTP YT	FGGKTK LEIK
M16 2	44__56	DIQMTQSPASLSASVGET VTITCRAS	ENSYSY	LEWYQQKQGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGYYC	QHYYGTP YT	FGGKTK LEIK
M16 3	44__56	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQQKQGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGYYC	QHYYDTP YT	FGGKTK LEIK
M16 4	44__56	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQQKQGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGYYC	QHYYDTP YT	FGGKTK LEIK
M16 5	44__56	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQQKQGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGYYC	QHYYDTP YT	FGGKTK LEIK
M16 6	44__56	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQQKQGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGYYC	QHYYDTP YT	FGGKTK LEIK
M16 7	44__56	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQQKQGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGYYC	QHYYDTP YT	FGGKTK LEIK
M16 8	44__56	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQQKQGS PQLLVY	NAK	TLVEGVPSRFSGSGSGTQFSLKIN SLQPEDFGYYC	QHYYDTP YT	FGGKTK LEIK
M16 9	44__56	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQQKQGS PQLLVY	NAK	TLVEGVPSRFSGSGSGTQFSLKIN SLQPEDFGYYC	QHYYDTP YT	FGGKTK LEIK

M17 0	44_56	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQKQKGS PQLLYV	NAK	TLVEGVPSRFSGSGSGTQFSLKIN SLQPEDFGSYIC	QHHYDTP YT	FGGKTK LEIK
M17 1	44_56	DIQMTQTTSSLASLGD VTISCRAS	QDISNY	LNWYQKQDGT VKLLIY	HTS	RLQSGVPSRFTGSGSGTDYSLTIS NLEQEDIAFYC	QQNSLP PT	FGGKTK LEIK
M17 2	44_56	EIVMTQSPPTLSLSPGER VTLSCKAS	QDVNTA	VAWYQKQKQA PRLLIY	WAS	TRHTGVPSRFSGSGSGTDFLTIS SLQPEDFATYIC	QQHYSSP WT	FGGKTK VEIK
M17 3	33_63	DIQMTQSPASLSASVGET VTITCRAS	ENSYSY	LEWYQKQKGS PQLLYV	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGTYIC	QHHYCTP YT	FGGKTK LEIK
M17 4	33_63	DIQMTQSPASLSASVGET VTITCRAS	ENSYSY	LEWYQKQKGS PQLLYV	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGTYIC	QHHYCTP YT	FGGKTK LEIK
M17 5	33_63	DIQMTQSPASLSASVGET VTITCRAS	ENSYSY	LEWYQKQKGS PQLLYV	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGTYIC	QHHYCTP YT	FGGKTK LEIK
M17 6	44_56	DIQMTQSPASLSASVGET VTITCRAS	ENSYSY	LEWYQKQKGS PQLLYV	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGTYIC	QHHYCTP YT	FGGKTK LEIK
M17 7	44_56	DIQMTQSPASLSASVGET VTITCRAS	ENSYSY	LEWYQKQKGS PQLLYV	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGTYIC	QHHYCTP YT	FGGKTK LEIK
M17 8	44_56	DVQMNQSPSSMYASLGER VTITCKAS	QDINN	LSWFQKQKGS PQTLIY	RAN	RLVDGVPSRFSGSGSGQHYSLTIS GLEVEDLGIYIC	LQYDEFP WT	FGGKTK LEIK
M17 9	44_56	DVQMNQSPSSMYASLGER VTITCKAS	QDINN	LSWFQKQKGS PQTLIY	RAN	RLVDGVPSRFSGSGSGQHYSLTIS GLEVEDLGIYIC	LQYDEFP WT	FGGKTK LEIK
M18 0	44_56	DVQMTQSPPLSASVGET VTITCRAS	ENIYSY	LEWYQKQKGS PQLLYV	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGTYIC	QHHYCTP YT	FGGKTK LEIK
M18 1	33_63	DIVMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQKQKGS PQLLYV	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQSEDFGSYIC	QHHYSTP YT	FGGKTK LEIK
M18 2	33_63	DIVMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQKQKGS PQLLYV	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGSYIC	QHHYDTP YT	FGGKTK LEIK
M18 3	33_63	DIQMTQSPASLSASVGET VTITCRAS	ENSYSY	LEWYQKQKGS PQLLYV	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGTYIC	QHHYCTP YT	FGGKTK LEMK
M18 4	33_63	DIQMTQSTSSLASLGD VTISCRAS	QDISNY	LNWYQKQKPDGT VKLLIY	YTS	RLHSGVPSRFSGSGSGTDYSLTIS NLEQEDIAFYC	QQGNTLP PT	FGGKTK LEMK
M18 5	44_56	DIQMTQSPASLSASVGET VTITCRAS	ENSYSY	LEWYQKQKGS PQLLYV	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGTYIC	QHHYCTP YT	FGGKTK LEIK
M18 6	6_130	DVMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQKQKGS PQLLYV	NAK	TLAEGVPSRFSGSGSGTQFSLRIN SLQPEDFGTYIC	QHHYGSP YT	FGGKTK LEIK
M18 7	6_130	DIQMTQTTSSLASLGD VTISCRAS	QDISNY	LNWYQKQKPDGT VKLLIY	YTS	RLHIGIPSRFSGSGSGTDYSLTIS NLEQEDIAFYC	QQGNTLP ST	FGGKTK LEIK
M18 8	6_163	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQKQKGS PQLLYV	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGSYIC	QHHYCTP YT	FGGKTK LEIK

M18 9	6__163	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQQKQKGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGSYIC	QHYYDTP YT	FGGGTK LEIK
M19 0	77__89	DIQMTQSPASLSASVGES VTITCRAS	ENIYSY	LEWYQQKQKGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLRIN SLQPEDFGTYIC	QHYYGSP YT	FGGGTK LEMK
M19 1	77__89	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQQKQKGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGSYIC	QHYYGTP YT	FGGGTK LEIK
M19 2	57__63	DIVMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQQKQKGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGSYIC	QHYYDTP YT	FGGGTK LEMK
M19 3	147__1 57	DIQMTQSPASLSASVGES VTITCRAS	ENIYSY	LEWYQQKQKGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGSYIC	QHYYGSP YT	FGGGTK LEMK
M19 4	33__63	DIQMTQSPASLSASVGES VTITCRAS	ENIYSY	LEWYQQKQKGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGSYIC	QHYYGSP YT	FGGGTK LEMK
M19 5	44__56	DIQMTQSPASLSASVGES VTITCRAS	ENIYSY	LEWYQQKQKGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGSYIC	QHYYGSP YT	FGGGTK LEMK
M19 6	44__56	DIQMTQSPASLSASVGES VTITCRAS	ENIYSY	LEWYQQKQKGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGSYIC	QHYYGSP YT	FGGGTK LEMK
M19 7	44__56	DIQMTQSPASLSASVGES VTITCRAS	ENIYSY	LEWYQQKQKGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGSYIC	QHYYGSP YT	FGGGTK LEMK
M19 8	147__1 57	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQQKQKGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGTYIC	QHYYGTP YT	FGGGTK LEMK
M19 9	147__1 57	DIQMTQSPASLSASVGES VTITCRAS	ENIYSY	LEWYQQKQKGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGSYIC	QHYYGSP YT	FGGGTK LEIK
M20 0	33__63	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQQKQKGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGSYIC	QHYYDTP YT	FGGGTK LEIK
M20 1	33__63	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQQKQKGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGTYIC	QHYYGTP YT	FGGGTK LEIK
M20 2	33__63	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQQKQKGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGTYIC	QHYYGTP YT	FGGGTK LEIK
M20 3	33__63	DIQMTQSPASLSASVGES VTITCRAS	ENIYSY	LEWYQQKQKGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLRIN SLQPEDFGTYIC	QHYYGSP YT	FGGGTK LEIK
M20 4	33__63	DIVMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQQKQKGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGSYIC	QHYYDTP YT	FGGGTK LEIK
M20 5	33__63	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQQKQKGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGTYIC	QHYYGTP YT	FGGGTK LEIK
M20 6	33__63	DIQMTQSPASLSASVGES VTITCRAS	ENIYSY	LEWYQQKQKGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGSYIC	QHYYGSP YT	FGGGTK LEIK
M20 7	33__63	DIQMTQSPASLSASVGES VTITCRAS	ENIYSY	LEWYQQKQKGS PQLLVY	NAK	TLAEGVPSRFSGSGSGTQFSLKIN SLQPEDFGSYIC	QHYYGSP YT	FGGGTK LEMK

M20 8	33__63	DVMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQKQKGS PQLLY	NAK	TLAEGVPSRFSGSGGTQFSLKIN SLQPEDFGSYIC	QHYYDTP YT	FGGKTK LEIK
M20 9	33__63	DIQMTQSPASLSASVGES VTITCRAS	ENIYSY	LEWYQKQKGS PQLLY	NAK	TLAEGVPSRFSGSGGTQFSLKIN SLQPEDFGSYIC	QHYYGSP YT	FGGKTK LEIK
M21 0	33__63	DVMTQSPASLSASVGES VTITCRAS	ENIYSY	LEWYQKQKGS PQLLY	NAK	TLAEGVPSRFSGSGGTQFSLKIN SLQPEDFGSYIC	QHYYGSP YT	FGGKTK LEIK
M21 1	33__63	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQKQKGS PQLLY	NAK	TLAEGVPSRFSGSGGTQFSLKIN SLQPEDFGSYIC	QHYYGTP YT	FGGKTK LEIK
M21 2	33__63	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQKQKGS PQLLY	NAK	TLAEGVPSRFSGSGGTQFSLKIN SLQPEDFGSYIC	QHYYGTP YT	FGGKTK LEIK
M21 3	44__56	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQKQKGS PQLLY	NAK	TLAEGVPSRFSGSGGTQFSLKIN SLQPEDFGSYIC	QHYYGTP YT	FGGKTK LEIK
M21 4	44__56	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQKQKGS PQLLY	NAK	TLAEGVPSRFSGSGGTQFSLKIN SLQPEDFGSYIC	QHYYGTP YT	FGGKTK LEIK
M21 5	44__56	DIQMTQSPASLSASVGES VTITCRAS	ENIYSY	LEWYQKQKGS PQLLY	NAK	TLAEGVPSRFSGSGGTQFSLKIN SLQPEDFGSYIC	QHYYGSP YT	FGGKTK LEIK
M21 6	44__56	DIQMTQSPASLSASVGES VTITCRAS	ENIYSY	LEWYQKQKGS PQLLY	NAK	TLAEGVPSRFSGSGGTQFSLKIN SLQPEDFGSYIC	QHYYGSP YT	FGGKTK LEIK
M21 7	44__56	DIVMTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQKQKGS PKALIY	SAS	YRYSVGPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNSYP YT	FGGKTK LEIK
M21 8	33__63	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQKQKGS PQLLY	NAK	TLAEGVPSRFSGSGGTQFSLKIN SLQPEDFGSYIC	QHYYGTP YT	FGGKTK LEIK
M21 9	6__163	DIQMTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQKQKGS PKALIY	SAS	YRYSVGPDRFTGSGSGTDFTLTIS SVKSEDLAEYFC	HQYNNYP YT	FGGKTK LEIK
M22 0	33__63	DIQMTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQKQKGS PKALIY	SAS	YRYSVGPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	HQYNNYP YT	FGGKTK LEIK
M22 1	33__63	DIQMTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQKQKGS PKALIY	SAS	YRYSVGPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	HQYNNYP YT	FGGKTK LEIK
M22 2	33__63	DVMTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQKQKGS PKALIY	SAS	YRYSVGPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNSYP YT	FGGKTK LEIK
M22 3	44__56	DTVTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQKQKGS PKALIY	SAS	YRYSVGPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNSYP YT	FGGKTK LEIK
M22 4	147__1 57	DIVLTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQKQKGS PKALIY	SAS	YRYSVGPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNSYP YT	FGGKTK LEIK
M22 5	147__1 57	DVMTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQKQKGS PKALIY	SAS	YRYSVGPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNSYP YT	FGGKTK LEIK
M22 6	33__63	DIQMTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQKQKGS PKALIY	SAS	YRYSVGPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	HQYNNYP YT	FGGKTK LEIK

M22 7	33__63	DVMTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQQKPGQS PKALIY	SAS	YRYSVDPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNSYP YT	FGGGTK LEIK
M22 8	44__56	DIQMTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQQKPGQS PKALIY	SAS	YRYSVDPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	HQYNNYP YT	FGGGTK LEIK
M22 9	33__63	DIVMTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQQKPGQS PKALIY	SAS	YRYSVDPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNSYP YT	FGGGTK LEIK
M23 0	147__1 57	DIQMTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQQKPGQS PKALIY	SAS	YRYSVDPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNSYP YT	FGGGTK LEIK
M23 1	147__1 57	DIQMTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQQKPGQS PKALIY	SAS	YRYSVDPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNSYP YT	FGGGTK LEIK
M23 2	33__63	DIVMTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQQKPGQS PKALIY	SAS	YRYSVDPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNSYP YT	FGGGTK LEIK
M23 3	33__63	DIQMTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQQKPGQS PKALIY	SAS	YRYSVDPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNSYP YT	FGGGTK LEIK
M23 4	33__63	DIVLTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQQKPGQS PKALIY	SAS	YRYSVDPDRITGRSGTDFTLTIS NVQSEDIAEYFC	QQYNTYP YT	FGGGTK LEIK
M23 5	33__63	DTVTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQQKPGQS PKALIY	SAS	YRYSVDPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNSYP YT	FGGGTK LEIK
M23 6	33__63	DIQMTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQQKPGQS PKALIY	SAS	YRYSVDPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNSYP YT	FGGGTK LEMK
M23 7	33__63	DVMTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQQKPGQS PKALIY	SAS	YRYSVDPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNSYP YT	FGGGTK LEMK
M23 8	33__63	DTVTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQQKPGQS PKALIY	SAS	YRYSVDPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNSYP YT	FGGGTK LEIK
M23 9	33__63	DTVTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQQKPGQS PKALIY	SAS	YRYSVDPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNSYP YT	FGGGTK LEMK
M24 0	33__63	DTVTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQQKPGQS PKALIY	SAS	YRYSVDPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNSYP YT	FGGGTK LEMK
M24 1	33__63	HIQMTSPPLSASVGET VTLTCKAS	ENIYNY	LEWYQQKQKGS PHLLVY	NAK	TLAEGVPSRFTGSGSGTQFSLKIN SLQPEDFGTYC	QHNYGTP YT	FGGGTK LEIK
M24 2	44__56	DIQMTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQQKPGQS PKALIY	SAS	YRYSVDPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNSYP YT	FGGGTK LEIK
M24 3	44__56	DIQMTQSPASLSASVGET VTITCKAS	ENIYSY	LEWYQQKQKGS PQLLVY	NAK	TLVEGVPSRFTGSGSGTQFSLKIN SLQPEDFGSYC	QHNYDTP YT	FGGGTK LEIK
M24 4	6__130	DIVLTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQQKPGQS PKALIY	SAS	YRYSVDPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	HQYNNYP YT	FGGGTK LEMK
M24 5	6__130	DIVLTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQQKPGQS PKALIY	SAS	YRYSVDPDRITGRSGTDFTLTIS NVQSEDIAEYFC	QQYNTYP YT	FGGGTK LEIK

M24 6	6__163	DIVITQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQKPGQS PKALIY	SAS	YRYSVDPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNSYP YT	FGGGTK LEIK
M24 7	6__163	DIVMTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQKPGQS PKALIY	SAS	YRYSVDPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNSYP YT	FGGGTK LEIK
M24 8	6__163	DIQMTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQKPGQS PKALIY	SAS	YRYSVDPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNSYP YT	FGGGTK LEIK
M24 9	6__163	DIVLTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQKPGQS PKALIY	SAS	YRYSVDPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNTYP YT	FGGGTK LEMK
M25 0	6__163	DVQMNQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQKPGQS PKALIY	SAS	YRYSVDPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNTYP YT	FGGGTK LEIK
M25 1	77__89	DIVMTQSQKFMSTSVGDR VSVTCKAS	QNVGIN	VAWYQKPGQS PKALIY	SAS	YRYSVDPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNNYP YT	FGGGTK LEIK
M25 2	77__89	DIVMTQSQKFMSTSVGDR VSVTCKAS	QNVGIN	VAWYQKPGQS PKALIY	SAS	YRYSVDPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNNYP YT	FGGGTK LEIK
M25 3	77__89	DVQMTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQKPGQS PKALIY	SAS	YRYSVDPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNSYP YT	FGGGTK LEIK
M25 4	77__89	DVQMTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQKPGQS PKALIY	SAS	YRYSVDPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNSYP YT	FGGGTK LEIK
M25 5	77__89	DIVMTQTQKFMSTSVGGR VSVTCKAS	QNVGTN	VAWYQKPGQS PKALIY	SAS	YRYSVDPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNSYP YT	FGGGTK LEIK
M25 6	77__89	DIVMTQSQKFMSTSVGDR VSVTCKAS	QNVGIN	VAWYQKPGQS PKALIY	SAS	YRYSVDPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNSYP YT	FGGGTK LEIK
M25 7	77__89	DIQMTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQKPGQS PKALIY	SAS	YRYSVDPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNSYP YT	FGGGTK LEMK
M25 8	77__89	DIQMTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQKPGQS PKALIY	SAS	YRYSVDPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNSYP YT	FGGGTK LEIK
M25 9	77__89	DIVITQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQKPGQS PKALIY	SAS	YRYSVDPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNSYP YT	FGGGTK LEIK
M26 0	77__89	DVQMTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQKPGQS PKALIY	SAS	YRYSVDPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNSYP YT	FGGGTK LEIK
M26 1	33__63	DIQMTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQKPGQS PKALIY	SAS	YRYSVDPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNSYP YT	FGGGTK LEIK
M26 2	33__63	DVMTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQKPGQS PKALIY	SAS	YRYSVDPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNSYP YT	FGGGTK LEIK
M26 3	147__1 57	DIVLTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQKPGQS PKALIY	SAS	YRYSVDPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNSYP YT	FGGGTK LEIK
M26 4	147__1 57	DIQMTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQKPGQS PKALIY	SAS	YRYSVDPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNSYP YT	FGGGTK LEMK

M26 5	147__1 57	RHCESQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQKQPGQS PKALIY	SAS	YRYSVGPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNSYP LT	FGGGTK LEIK
M26 6	147__1 57	DIQMTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQKQPGQS PKALIY	SAS	YRYSVGPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNSYP YT	FGGGTK LEIK
M26 7	147__1 57	DIVMTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQKQPGQS PKALIY	SAS	YRYSVGPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNSYP LT	FGGGTK LEIK
M26 8	147__1 57	DIVLTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQKQPGQS PKALIY	SAS	YRYSVGPDRITGRSGSGTDFTLTIS NVQSEDIAEYFC	QQYNTYP YT	FGGGTK LEIK
M26 9	147__1 57	DIQMTQTTSLSASLGDR VTISCRAS	QDISNY	LNWYQKQPGQT VKLIY	HTS	RIQSGVPSRFTGSGSGTDYSLTIS NLEQEDIAEYFC	QQSNSLP PT	FGGGTK LEIK
M27 0	147__1 57	DIQMTQSPASLSASVGET VTITCRAS	ENSYSY	LEWYQKQKQGS PQLIY	NAK	TLAEGVPSRFTGSGSGTQFSLKIN SLQPEDFGTYFC	QHGYGTP YT	FGGGTK LEMK
M27 1	147__1 57	DVMTQTPASLSASVGET VTITCRAS	ENSYSY	LEWYQKQKQGS PQLIY	NAK	TLAEGVPSRFTGSGSGTQFSLKIN SLQPEDFGTYFC	QHGYGTP YT	FGGGTK LEIK
M27 2	147__1 57	DVQMTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQKQKQGS PKALIY	SAS	YRYSVGPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNSYP YT	FGGGTK LEIK
M27 3	147__1 57	DIVMTQSPPTLSLSPGEIR VTLSCGAS	RDVNTA	VAWYQKQKQQA PRLIY	WAS	TRHTGVPSRFTGSGSGTDFTLTIS RLQPFATYFC	QHYSYSP WT	FGGGTK LEMK
M27 4	147__1 57	DIVMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQKQKQGS PQLIY	NAK	TLAEGVPSRFTGSGSGTQFSLKIN SLQPEDFGTYFC	QHGYDTP YT	FGGGTK LEIK
M27 5	33__63	DIVMTQSPASLSASVGET VTITCRAS	ENSYSY	LEWYQKQKQGS PQLIY	NAK	TLAEGVPSRFTGSGSGTQFSLKIN SLQPEDFGTYFC	QHGYGTP YT	FGGGTK LEIK
M27 6	33__63	DIQMTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQKQPGQS PKALIY	SAS	YRYSVGPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNSYP YT	FGGGTK LEIK
M27 7	33__63	DIQMTQSPASLSASVGET VTITCRAS	ENIYSY	LEWYQKQKQGS PQLIY	NAK	TLVEGVPSRFTGSGSGTQFSLKIN SLQPEDFGTYFC	QHGYDTP YT	FGGGTK LEIK
M27 8	33__63	DIVMTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQKQPGQS PKALIY	SAS	YRYSVGPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNSYP YT	FGGGTK LEIK
M27 9	33__63	MLVMTQTPLSLPVSIGDQ ASISCRSS	QSLVHSN GNTY	LHWYQKQPGQS PKALIY	KVS	NRFSGVPSRFTSVSGSGTDFTLKIS RVEAEDLGVYFC	SQSTHVP PT	FGGGTK LEIK
M28 0	33__63	DVMTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQKQPGQS PKALIY	SAS	YRYSVGPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNSYP YT	FGGGTK LEIK
M28 1	33__63	DIQMTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQKQPGQS PKALIY	SAS	YRYSVGPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNSYP YT	FGGGTK LEIK
M28 2	33__63	DVQMTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQKQKQGS PKALIY	SAS	YRYSVGPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNSYP YT	FGGGTK LEIK
M28 3	33__63	DIVMTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQKQKQGS PKALIY	SAS	YRYSVGPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNSYP YT	FGGGTK LEIK

M28 4	33__63	DIQMTQSPASLSASVGET VTITCRAS	ENSYSY	LEWYQKQKGS PQLLY	NAK	TLAEGVPSRFGSGSGTQFSLKIN SLQPEDFGTYC	QHGYGTP YT	FGGKTK LEIK
M28 5	33__63	DIQMTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQKQKGS PKALIY	SAS	YRYSGVDPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNSYP YT	FGGKTK LEIK
M28 6	33__63	DIVLTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQKQKGS PKALIY	SAS	YRYSGVDPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNSYP YT	FGGKTK LEIK
M28 7	33__63	DIQMTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQKQKGS PKALIY	SAS	YRYSGVDPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNSYP YT	FGGKTK LEMK
M28 8	33__63	DIVLTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQKQKGS PKALIY	SAS	YRYSGVDPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNSYP YT	FGGKTK LEIK
M28 9	33__63	DIQMTQSPASLSASVGET VTITCQAS	DNIYSY	LEWYQKQKGS PQLLY	NAK	TLAXGVPSRFXGSGSGTQFSLKIN SLQPEDFGSYC	QHGYGTP YT	FGGKTK XEMK
M29 0	33__63	DIQMTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQKQKGS PKALIY	SAS	YRYSGVDPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNSYP YT	FGGKTK LEIK
M29 1	33__63	DIQMTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQKQKGS PKALIY	SAS	YRYSGVDPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNSYP YT	FGGKTK LEIK
M29 2	33__63	DTVTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQKQKGS PKALIY	SAS	YRYSGVDPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNSYP YT	FGGKTK LEIK
M29 3	33__63	DIQMTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQKQKGS PKALIY	SAS	YRYSGVDPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNSYP YT	FGGKTK LEIK
M29 4	33__63	DVQMTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQKQKGS PKALIY	SAS	YRYSGVDPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNSYP YT	FGGKTK LEIK
M29 5	33__63	DVMTQSPPSLSASVGET VTISCRAS	GNVHNF	LTWYQKQKGS PQLLY	NAE	TLADGVPSRFXGSGSGTQFSLKIN SLQPEDFGTYC	QHFNTPT PT	FGGKTK LEIK
M29 6	44__56	DTVTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQKQKGS PKALIY	SAS	YRYSGVDPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNSYP YT	FGGKTK LEIK
M29 7	44__56	DVQMTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQKQKGS PKALIY	SAS	YRYSGVDPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNSYP YT	FGGKTK LEIK
M29 8	44__56	DVMTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQKQKGS PKALIY	SAS	YRYSGVDPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNSYP YT	FGGKTK LEMK
M29 9	44__56	DTVTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQKQKGS PKALIY	SAS	YRYSGVDPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNSYP YT	FGGKTK LEMK
M30 0	44__56	DWLTQTPSLPVSIGDQ ASISCRSS	QSIVHSN GNTY	LEWYQKQKGS PKALIY	KVS	NRFSGVDPDRFTGSGSGTDFTLKIS RVEAEDLGVYFC	FQGSHPV PT	FGGKTK LEIK
M30 1	44__56	DIVMTQSQKFMSTSVGDR VSVTCKAS	QNVGTN	VAWYQKQKGS PKALIY	SAS	YRYSGVDPDRFTGSGSGTDFTLTIS NVQSEDIAEYFC	QQYNSYP YT	FGGKTK LEIK

[0307] Sequence analysis suggests that these antibodies derive from clonal lineages that may be grouped as indicated in **Table 15A** and **Table 15B**.

Table 15A

#	Baits	CDRH1	CDRH2	CDRH3
1	147_156 147_157_J2 33_63_J1 33_63_J2 33_63_J3 44_56 44_56_J1 44_56_J2 6_130 6_163	GFNIKDY Y	IDPDNGET	TVFWYGNNYAGFAY
2	147_156 147_157_J2 33_63_J1 33_63_J2 33_63_J3 44_56 44_56_J1 44_56_J2 57_63 6_130 6_163 77_89	GYTFTDYA GYTFTRYW GYSFTSYW GYTFSNYW GYTFTKYW GYTFNRFW GYTFTRFW	ISTYSGDA INPRTDYTEYNQ ISTYSGDAIYNQ ISTYSGDVNYNQ ISTYSGDVSYNQ IHPSDSETRLNQ ILPGSGFTNYNE ISTYSGDALYNQ INPRTDYT ISTYSGDV INPNSDYI INTYSGDA INPSTDYI INPGSDYT INPSTGYI	ARGVTFDI ARGVTFDY ARHGYFDY ARGVTFDS ARSRGIPFAY ARGGTSVVHFDY AIHGYFDY ARGVTSDS ARGTIIDY ARGVSFDY ARGVPFDY ATGVTFDY SRGGTSFVHFDY AXGVTFDY ARHXYFDY ARXVTFDY ATXVTFDS ARXGYFDY ARGTVVDY
3	6_163 33_63_J3 44_56_J2 147_157_J2 33_63_J1 33_63_J2	GYTFTKYW GYTFTNYW	IYPGGDYT IYPGGDYTNYNE IYPGGGYA	ARVTPAS ARVTPSS ARITPAS ARVSPAS

#	Baits	CDRH1	CDRH2	CDRH3
	147_157_J1 44_56_J1 6_130 77_89		IYPGGGYT IYPGGGYTNYNE	

Table 15B

#	Baits	CDRL1	CDRL2	CDRL3
1	147_156 147_157_J2 33_63_J1 33_63_J2 33_63_J3 44_56 44_56_J1 44_56_J2 6_130 6_163	QSIVHSNGNTY ENIYSY QDISNY	KVS NAK HTS	FQGSHPVPT FQGSHPVPT QHGYGSPYT QQSNSLPPT
2	147_156 147_157_J2 33_63_J1 33_63_J2 33_63_J3 44_56 44_56_J1 44_56_J2 57_63 6_130 6_163 77_89	ENIYSY QDISNY ENSYSY QNVGTN QSVNND QYISNY QDINSY QDINNF ENSYNY ENIHSY QDVNTA QDINRY	NAK YTS HTS SAS YAS RAN WAS	QHGYDTPYT QHGYGSPYT QQGNTLPPT QQSNTLPPT QHGYGTPYT QQHYGTPYT QQSNSLPPT QQYNSYPLT QQAYWSPYT QHGYGIPYT LQYDEFPYT LQYDEFPWT QHGYSTPYT QQGNTLPLT QQHYSSPWT QQYNSYPYT QQGNTLPWT QQGNTLPST
3	6_163 33_63_J3	QNVGTN ENIYNY	SAS NAK	HQYNNYPYT QQYNSYPYT

#	Baits	CDRL1	CDRL2	CDRL3
	44_56_J2	ENIYSY	HTS	QQYNTYPYT
	147_157_J2	QNVGIN	WAS	QHHYGTPYT
	33_63_J1	QDISNY	KVS	QHHYDTPYT
	33_63_J2	ENSYSY	NAE	QQYNNYPYT
	147_157_J1	RDVNTA		QQYNSYPLT
	44_56_J1	QSLVHSNGNTY		QQSNSLPPT
	6_130	DNIYSY		QHHYSSPWT
	77_89	GNVHNF		SQSTHVPPT
		QSIVHSNGNTY		QHFWNTPPT
				FQGSHVPPT

CLAIMS

What is claimed is:

1. An engineered polypeptide, wherein the engineered polypeptide shares at least 46% structural and/or dynamic identity to a CD25 reference target, wherein the CD25 reference target is a portion of a CD25 selected from:

Reference Target No.	CD25 Residues	Sequence
1	55-63	SWDNQCQCT
2	13-20:127-132	ATFKAMA:MVYYQC
3	5-17	DDPPEIPHATFKA
4	5-11:156-163	DDPPEIP:RWTQPQLI
5	77-89	QPEEQKERKTTEM
6	147-157	VCKMTHGKTRW
7	11-14	IPHA
8	44-56	YMLCTGSSSHSSW

2. The engineered polypeptide of claim 1, wherein the engineered polypeptide shares at least 60% structural and/or dynamic identity to the CD25 reference target.
3. The engineered polypeptide of claim 1, wherein the engineered polypeptide shares at least 80% structural and/or dynamic identity to the CD25 reference target.
4. The engineered polypeptide of claim 1, wherein the engineered polypeptide shares at least 80% sequence identity to an amino-acid sequence selected from:

CD <u>C</u> <u>Q</u> A <u>Q</u> WT PGMRAPGYDPYCLNC
MVY <u>C</u> <u>Q</u> PDCT <u>A</u> <u>K</u> <u>M</u> HGCDRDTMKECCDRLK
DD <u>C</u> <u>P</u> <u>E</u> V <u>P</u> HAT <u>F</u> KGPGQKWEGPGGGDCSK
DD <u>C</u> <u>I</u> <u>E</u> V <u>P</u> GPAECAERACRAQEER <u>R</u> <u>Q</u> <u>R</u> <u>Q</u> <u>P</u> <u>Q</u> <u>C</u> <u>I</u>
AE <u>E</u> <u>E</u> KI <u>K</u> IE <u>Q</u> <u>K</u> <u>E</u> <u>R</u> <u>K</u> <u>T</u> <u>T</u> IKLAKEAK
CHLQI <u>M</u> <u>T</u> <u>H</u> <u>G</u> <u>K</u> IIYVPC
DDGDRCAKEH <u>E</u> <u>I</u> <u>P</u> <u>H</u> <u>A</u> <u>T</u> GEECQKRDKS
CKQLVIYF <u>T</u> <u>G</u> <u>N</u> <u>S</u> <u>S</u> HSSVFYIIYYDC
GSGDEDCKKFQSD <u>D</u> <u>N</u> <u>W</u> <u>E</u> NYTSTR <u>H</u> <u>L</u> <u>T</u> <u>F</u> CDEKRS
GSGNEEIEKKIKDC <u>T</u> <u>G</u> <u>N</u> <u>S</u> <u>S</u> <u>H</u> <u>S</u> <u>S</u> <u>W</u> <u>E</u> <u>E</u> <u>A</u> <u>L</u> <u>E</u> <u>C</u> <u>A</u> <u>L</u> <u>K</u> <u>K</u>
GSGDERIERLIKEC <u>T</u> <u>G</u> <u>N</u> <u>S</u> <u>S</u> <u>H</u> <u>S</u> <u>S</u> <u>W</u> <u>E</u> <u>E</u> <u>A</u> <u>L</u> <u>E</u> <u>C</u> <u>A</u> <u>L</u> <u>R</u> <u>R</u>
GSGSHPCAYWRWVI <u>K</u> <u>M</u> <u>T</u> <u>H</u> <u>G</u> <u>K</u> <u>T</u> <u>R</u> <u>W</u> VLELVFCYRD
GSGKCEEEAKKIAS <u>K</u> <u>M</u> <u>T</u> <u>H</u> <u>G</u> <u>K</u> <u>T</u> <u>R</u> <u>E</u> <u>E</u> <u>E</u> <u>A</u> <u>E</u> <u>E</u> <u>Y</u> <u>L</u> <u>K</u> <u>K</u> <u>C</u>
GSGDDESEKRTTERDTRKCTKAKAN <u>D</u> <u>N</u> <u>Q</u> <u>C</u> <u>Q</u> <u>P</u> <u>T</u> <u>E</u>
GSGSSEWDKWVEEWYKKMCTEAKKN <u>D</u> <u>N</u> <u>Q</u> <u>C</u> <u>Q</u> <u>P</u> <u>T</u> <u>K</u>
GSGQCRVWVFRNGDKILYIYEDCDN <u>D</u> <u>N</u> <u>Q</u> <u>H</u> <u>Q</u> <u>Q</u> <u>T</u> <u>L</u>

5. An engineered polypeptide designed to mimic a selected CD25 epitope, wherein the engineered polypeptide shares at least 80% sequence identity to an amino-acid sequence selected from:

CD <u>CQAQWT</u> PGMRAPGYDPYCLNC
<u>MVYCQ</u> PDC <u>TAKCM</u> HGCDRDTMKECCDRLK
<u>DDCPEVPHATFK</u> GPGQKWEGPGGGDCSK
<u>DDCI</u> <u>EVP</u> GPAECAERACRAQEE <u>RQRQPQC</u> <u>I</u>
AE <u>EEKIKIEQKERKTT</u> IKLAKEAK
CHLQI <u>MTHGK</u> IIYVPC
DDGDRCAKEH <u>EIPHAT</u> GEECQKRDKS
CKQLVIYF <u>TGNSS</u> HSSVFYIYYDC
GSGDEDCKKFQSD <u>DNW</u> <u>ENY</u> TSTR <u>HLTF</u> CDEKRS
GSGNEEIEKKIKDC <u>TGNSSHSSW</u> EAEALCKK
GSGDERIERLIKEC <u>TGNSSHSSW</u> EAEALCALRR
GSGSHPCAYWRWVI <u>KMTHGKTRW</u> VLELVFCYRD
GSGKCEEEAKKIAS <u>KMTHGKTR</u> EEEAEEYLKKC
GSGDDESEKRTTERDTRKCTKAKAN <u>DNQCQPT</u> E
GSGSSEWDKWVEEWYKKMCTEAKKN <u>DNQCQPT</u> TK

GSGQCRVWVFRNGDKILYIYEDCDNDNQHQQTL

6. The engineered polypeptide of claim 5, wherein the engineered polypeptide shares at least 46% structural and/or dynamic identity to a CD25 reference target, wherein the CD25 reference target is a portion of CD25 selected from:

Reference Target No.	CD25 Residues	Sequence
1	55-63	SWDNQCQCT
2	13-20:127-132	ATFKAMA . . . MVYYQC
3	5-17	DDPPEIPHATFKA
4	5-11:156-163	DDPPEIP . . . RWTQPQLI
5	77-89	QPEEQKERKTTEM
6	147-157	VCKMTHGKTRW
7	11-14	IPHA
8	44-56	YMLCTGSSSHSSW

7. The engineered polypeptide of claim 6, wherein the engineered polypeptide shares at least 80% structural and/or dynamic identity to the CD25 reference target.

8. The engineered polypeptide of any one of claims 1-7, wherein the structural and/or dynamic identity to the CD25 reference target is determined using the structure of CD25 deposited at PDB ID NO: 2ERJ, chain A.

9. The engineered polypeptide of any one of claims 1-8, wherein the engineered polypeptide comprises an N-terminal modification or a C-terminal modification, optionally an N-terminal Biotin-PEG₂- or a C-terminal -GSGSGK-Biotin.

10. The engineered polypeptide of any one of claims 1-9, wherein between 10% to 98% of the amino acids of the engineered polypeptide meet one or more CD25 reference target-derived constraints, wherein optionally the amino acids of the polypeptide that meet the one or more reference target-derived constraints are the underlined residues in claim 5.

11. The engineered polypeptide of claim 10, wherein the amino acids that meet the one or more CD25 reference target-derived constraints have less than 8.0 Å backbone root-mean-square deviation (RMSD) structural homology with the CD25 reference target,

12. The engineered polypeptide of claim 10 or claim 11, wherein the amino acids that meet the one or more CD25 reference target-derived constraints have a van der Waals surface area overlap with the reference of between 30 Å² to 3000 Å².

13. The engineered polypeptide of any one of claims 1-12, wherein the CD25 reference target-derived constraints are independently selected from the group consisting of: atomic distances; atomic fluctuations; atomic energies; chemical descriptors; solvent exposures; amino acid sequence similarity; bioinformatic descriptors; non-covalent bonding propensity; phi angles; psi angles; van der Waals radii; secondary structure propensity; amino acid adjacency; and amino acid contact.

14. The engineered polypeptide of any one of claims 1-13, wherein the engineered polypeptide shares 46%-96% RMSIP or more structural similarity to the reference target across the amino acids of the polypeptide that meet the one or more reference target-derived constraints.

15. A CD25-specific antibody, comprising an antigen-binding domain that specifically binds a CD25 epitope selected from:

1	55-63	SWDNQCQCT
2	13-20:127-132	ATFKAMA . . . MVYYQC

3	5-17	DDPPEIPHATFKA
4	5-11:156-163	DDPPEIP . . . RWTQPQLI
5	77-89	QPPEQKERKTTEM
6	147-157	VCKMTHGKTRW
7	11-14	IPHA
8	44-56	YMLCTGSSSSHSSW

16. The antibody of claim 15, wherein the CD25 epitope is 55-63, and wherein the antibody comprises six complementarity determining regions (CDRs) each independently selected from:

CDR-H1	CDR-H2	CDR-H3	CDR-L1	CDR-L2	CDR-L3
GFTFSSYG	ISYDGSNK	AKGDVNYGMDV	NIGSKS	DDT	QVWDSSSDLWV
			NIGSKT	DGR	QVWDTSGDLHWA
	ISYDGNNK	AKGYSSSPGDY	SSDVGAYNY	DVS	SSYTSSSTLWV
GGTFSSYA	IIPIFGTA	ARDFNPFSITIFEMDV	SSNIGNNY	DNN	GTWDSLSALV
GGSISSSNW	IYHSGST	ARDFYGGSGSYPNGYYYGMDV	QSINSY	TAS	QQSYTTPLT
GYSFNITYW	IYPSDSST	ARDGGYYFDD	QSVSSTY	GTS	QQYNSSPLMYT
GGTFSSYA	IIPIFGTA	ARDYYYYGMDV	QSISSY	GAS	QQTYNDPPT
		AREMYYYYGMDV	QSISSY	AAS	QQSYSTPPT
			QSISSY		
			QSIITY		
			QSISSY		
GGSISRSNW	IYHTGST	ARGKGSYAFDI	GGNIARNY	EDD	QSYDGNNHMV

17. The antibody of claim 15, wherein the CD25 epitope is 13-20:127-132, and wherein the antibody comprises six CDRs each independently selected from:

CDR-H1	CDR-H2	CDR-H3	CDR-L1	CDR-L2	CDR-L3
GFTFSSYG	ISYDGSNK	ANLAMGQYFDY	SSNIGSNT	SNN	AAWDDSLNGPV
GFTFSSYA		ARDLGEAKSSSPHEPDY	QSLHSDGKTY	EVS	MQTKQLPLT
GDSISSSSYY	INHSGST	ARDQEMYYFDY	QGISSW	AAS	QQANSFPPT
GGTFSSYA	IIPIFGTA	AREMYYYYGMDV	QSISSY	AAS	QQSYSTPPT

18. The antibody of claim 15, wherein the CD25 epitope is 5-17, and wherein the antibody comprises six CDRs each independently selected from:

CDR-H1	CDR-H2	CDR-H3	CDR-L1	CDR-L2	CDR-L3
GFTFSSYG	ISYDGSNK	AKAITSIEPY	SGSVSTSY	NTD	VLYMGSGIWV
GFTFSSYG	ISYDGSNK	AKELLEGAFDI	NIETKS	DDD	QVWDSSSGHREV
GGTFSSYA	IIPIFGTA	AREMYYYYGMDV	QSISSY	AAS	QQSYSTPPT
			QSISSY		

19. The antibody of claim 15, wherein the CD25 epitope is 5-11:156-163, and wherein the antibody comprises six CDRs each independently selected from:

CDR-H1	CDR-H2	CDR-H3	CDR-L1	CDR-L2	CDR-L3
GGTFSSYA	IIPIFGTA	AREMYYYYGMDV	QSISSY	AAS	QQSYSTPPT
GYTFSSYG	ISAYNGNT	ARERSYYGMDV	QSVSNY	GAS	QQYNHWPL

20. The antibody of claim 15, wherein the CD25 epitope is 77-89, and wherein the antibody comprises six CDRs each independently selected from:

CDR-H1	CDR-H2	CDR-H3	CDR-L1	CDR-L2	CDR-L3
GFTFSSYG	ISYDGSNK	AKELLEGAFDI	NIETKS	DDD	QVWDSSSGHREV
GYTFSSY	INPSGGST	ARDRTMVRGALAY	KLGDY	KDN	QAWDSSTYV

21. The antibody of claim 15, wherein the CD25 epitope is 147-157, and wherein the antibody comprises six CDRs each independently selected from:

CDR-H1	CDR-H2	CDR-H3	CDR-L1	CDR-L2	CDR-L3
GFTFSSYG	ISYDGSNK	AKQGGDGMV	SSNVGSRT	SNN	AAWDDSLIGHV
GGSISSGGYS	IYHSGST	ARAGYYYGMDV	RNIWSY	GAS	QQSHSTPIT
GYTFSSY	ISAYNGNT	ARDIGYYYGMDV	SLRSY	GKN	NSRDSSGNHVV
GYTFSSY	INPSGGST	ARDILGLDY	SSNIGSNY	RNN	AAWDDSLSGVV
GGTFSSYA	IIPIFGTA	AREMYYYYGMDV	QSISSY	AAS	QQSYSTPPT
			QSISSY		
GFTFSSYW	IKQDGSEK	AREYDYG DYVFDY	NSNVGNYY	DND	GSWEARES VEV

GYSFTSYW	IYPGDSDT	ARLENNWDYGGWFDP	NIGSKS	DDS	QVWDSSSDHWV
	IYPGDSDT				
GYTFTDYY	VDPEDGET	ATEDTAMGGIDY	SSNIGSNY	SNN	AAWDDSLNGVV
		ATEGRYGMDV	NFNIGNNL	AND	ATWDDSLSGVV
		AVEGGRAPGTYYYDSSGLAY	SSNIGSNY	SNN	

22. The antibody of claim 15, wherein the CD25 epitope is 11-14, and wherein the antibody comprises six CDRs each independently selected from:

CDR-H1	CDR-H2	CDR-H3	CDR-L1	CDR-L2	CDR-L3
GGTFSSYA	IIPIFGTA	AREMYYYYGMDV	QSISSY	AAS	QQSYSTPPT

23. The antibody of claim 15, wherein the CD25 epitope is 44-56, and wherein the antibody comprises six CDRs each independently selected from:

CDR-H1	CDR-H2	CDR-H3	CDR-L1	CDR-L2	CDR-L3
GYSFTSYW	IYPGDSDT	AIPWDAELGNYGMDV	QSISSY	AAS	LQDYNYPPE
GFAFSSYG	ISYDGSNK	AKGQGDGMDV	SSDVGGYNY	GVS	SSYTSSSTLVV
GGSISSSNW	IYHSGST	ARARGGRYFDY	QGISTY	AAS	QQLNGYPTT
GGTFSSYA	IIPIFGTA	AREMYYYYGMDV	QSISSY	AAS	QQSYSTPPT
			QSISSY		
		ARGRWGLGDY	EDIRMY	EGS	QQYYDDPQ
GYKFANYW	IYPGDSDT	ARLWGMDV	QSISSY	AAS	QQSYSTPWT
GFTFSSYE	ISSSGSTI	ARRRGGGFDY	SSDVGGYNY	DVS	SSYTSSSTWV
GYSFSTYW	IYPGDSDT	ARVGDGYSLDY	SSNIGRNY	RNH	ATWDDALSGWV
			KLGERF	QYI	QTWDGSIVV
GYTFKNFG	ISGRKGNT	ARVWGDITLGYGMDV	QDISNY	DAS	QQYDNLPLT
GFTFSSYG	ISYDGSNK	AKDLLGELSFFDY	DIESEM	DDS	QVWHTTNDHVL
GFTFSNYG	ISHDGHVK	AKEISPRSSVGWPLDY	QSVSSTY	GAS	QQFDISGGLI
GFTFRRYW	IKQDGSEK	ARDAYAYGLDV	SGSIASSY	EDN	QSYDGSSVV
GYTFTSYG	ISAYNGNT	ARDFRMDV	QDIKRR	DAS	QQANTFPQT
GFTFSSSA	ISYDGSNK	ARDFWGSYNELGGMDV	QDISNY		QQYDNLPLT
GYTFNNYG	ISVYNGDI	ARDILRGESSILDH	QGISNS	AAS	QQYYSTPPH
GGTFSSYA	IIPIFGTA	ARDKGYGMDV	QSIKNY		QQTYSTPLT
			QGINSY		QQVHSFPFT
			QGISSW	AVS	QQSYSLPLT
		ARDLGTMRGVIEPYFDY	QSISSW	DAF	QQYNSYSRT
GFTFSSYA	ISYDGSNK	ARDLLGSGYDIIDY	NIGSKS	DDS	QVWDSSSDHWV

CDR-H1	CDR-H2	CDR-H3	CDR-L1	CDR-L2	CDR-L3
GGSISSSNW	IYHSGST	ARDLMNYGMDV	QSISSY	AAS	QQSYSTPPT
GFTFSSYS	ISSSSSYI	ARDQLAARRGYYYGMDV	NIGTKS	DDS	QVWDSSTDHVV
GYTFTTYA	INTNTGDP	ARDRFHYGMDV	EGIRTS	GAS	QQTHTWPWT
GFTFSSYG	ISSRGSTI	ARDRGDRVGGLVFDY	NIGSKS	DDS	QVWDSSTDHVV
GYTFTSYG	ISAYNGNT	ARDRGDY	QGTSSW	AAS	QQANSFPLT
		ARDRGYYGMDV	QSISSY		QQSHSTPLT
		ARDRNGYFQH	QTISGL	GAS	LQYDRYSGA
GGTFSSYA	IIPIFGTA	ARDSYYGMDV	QSIGNY	AAT	QQSKQIPYT
		ARDRIYYGMDV	QSISSY	AAS	QQSYSTPLT
GFTFSSYW	IKQDGSEK	AREKGSWFDP	QSVSNY	GAS	QRYGSSPR
GFIFSRHA	ISYDGSNK	ARGRLAYGDTEGFDY	QDINNY	DAS	QQYDNLPLY
GGSISSSNW	IYHSGST	ARGVRGTGFDP	QSVSSR	GAS	QQYTNPQT
GYSFTTYW	IYPGSDT	ARQVAGGLDY	SSNVGSNY	RNN	AAWDDSLSGVV
			QAVRID	GAS	LQHNTFPYT
GFTFSSYE	ISSSGSTI	ARRRGGGFDY	SSDVGGYNY	DVS	SSYTSSSTYV
GFTFSSYW	IKQDGSEK	ARTWFGEFFDY	NIESES	DDS	QVWDSSTDHTVA
GYTFTSYG	ISAYNGNT	ARVIGGWFPD	SSDVGAYNY	GVS	SSYTSTDFTV
		ARVWGKNGDFDY	SSNIGNNY	DNN	GTWDSLSAYV
GYSFTSYW	IYPGSDT	FRFGEFFDY	QSIGYW	RAS	QQYNSYPFT
GFTFNNAW	IKSKTDGGTT	TTEGVLLSFSGAPFDY	QSISSY	AAS	QQSYSTPYT

24. The antibody of claim 15, wherein the antibody comprises

a) a CDR-H1 selected from: Table 3A, GGTFSSYA, GGSISSGGYY, GFTFSSYG, GYTFTSY, GYTFTSYG, GYTFTDYY, GGSISSGGYS, GGSISSSNW, GYSFTSYW, GFTFSNYG, GFTFSSA, GFTFSSYW, GFIFSRHA, GYTFNNYG, GFTFSSYA, GYTFTTYA, GFTFNNAW, GFTFSSYE, GYSFTTYW, GYSFNTYW, GFTFRRYW, GYSFSTYW, GFAFSSYG, GYKFANYW, GYTFKNFG, GFTFSSYS, GDSISSSSYY, and GGSISRSNW;

b) a CDR-H2 selected from: Table 3A, IIPIFGTA, IIPIFGTA, IYHSGST, ISYDGSNK, INPSGGST, ISAYNGNT, IMPIFDTA, VDPEDGET, IYHSGST, IYPGSDT, ISHDGHVK, IKQDGSEK, ISVYNGDI, INTNTGDP, IKSKTDGGTT, ISSSGSTI, ISSRGSTI, IYPSDSDT, ISGRKGNT, ISSSSSYI, INHSGST, IYHTGST, and ISYDGNNK;

c) a CDR-H3 selected from: Table 3A, AREMYYYYGMDV, AREMYYYYGMDV, ARGNLWSGYF, AKELLEGAFDI, ARDRVMTMVRGALAY, ARERSYYGMDV, ASWSERIGYQYGLDV, ARDILGLDY, ATEDTAMGGIDY, ATEGRYGMVDV, AVEGGRAPGTYYYDSSGLAY, ARAGYYYGMDV, ARDLGTMVRGVIEPYFDY, ARGVRGTGFDP, ARDRNGYFQH, AKDLLGELSFFDY, ARLENNWDYGGWFDP, ARDRSYYGMDV, ARDKGYYGMDV, AKEISPRSSVGWPLDY, ARDFWSGYNELGGMDV, ARTWFGEFFDY, ARVIGGWFP, ARGRLAYGDTEGFDY, ARDILRGESSILDH, ARDRYYYGMDV, ARDLLGSGYDIIDY, ARVWGKNGDFDY, ARDRFHYGMDV, ARDRGDY, TTEGVLLSFGGAPFDY, ARRRGGGFDY, AREKGSWFDP, ARDRGDRVGGLVFDY, ARQVAGGLDY, ARDRGYYGMDV, FRFGEGFDY, ARDGGYYFDD, ARDFRMDV, ARDAYAYGLDV, ARDLMNYGMDV, AREYDYGDYVFDY, ARLENNWNYGGWFDP, ARDYYYYGMDV, ARDIGYYYGMDV, ARVGDGYSLDY, AKAITSIPEY, AKGQGDGMDV, ARLGWGMDV, ARVWGDTTLGYGMDV, AIPWDAELGNYGMDV, ARGRWSGLGDY, ARARGGRYFDY, ARDQLAARRGYYYGMDV, AKGDVNYGMDV, ARDFYYGSGSYPNGYYYGMDV, ARDFNPFSITIFEMDV, ANLAMGQYFDY, ARDLGEAKSSSPHEPDY, ARDQEMYFDY, ARGKGSYAFDI, and AKGYSSSPGDY;

d) a CDR-L1 selected from: Table 3B, QSISSY, QSISSY, SSNIGNNF, QSISSY, NIETKS, KLGDY, QSVSNY, QTISQW, SSNIGSNY, NFNIGNNL, RNIWSY, QSISSW, QSVSSR, QTISGL, DIESEM, NIGSKS, QSIGNY, QGISSW, QSVSSTY, QDISNY, NIESES, SSDVGAYNY, QDINNY, QGISNS, SSNIGNNY, EGIRTS, QGTSSW, SSDVGGYNY, QSVSNY, QGINSY, QAVRID, QSISSY, QSIGYW, SSNVGSNY, QSIKNY, QDIKRR, SGSIASSY, NSNVGNYY, SLRSYY, KLGERF, SGSVSTSY, SSNIGRNY, EDIRMY, QGISTY, SSNVGSRT, NIGTKS, NIGSKT, QSINSY, SSNIGSNT, QSIITY, QSLHSDGKTY, and GGNIARNY;

e) a CDR-L2 selected from: Table 3B, AAS, AAS, DST, DDD, KDN, GAS, KAS, RNN, SNN, AND, DAF, DDS, AAT, AVS, DAS, GVS, DNN, DVS, RAS, GTS, EDN, DND, GKN, QYI, NTD, RNH, EGS, DGR, TAS, DDT, EVS, and EDD; and/or

f) a CDR-L3 selected from: Table 3B, QQSYSTPPT, QQSYSTPPT, GSWDTNLSGYV, QVWDSSSGHREV, QAWDSSTYV, QQYNHWPPL, QQYSGDSMYT, AAWDDSLSGVV, AAWDDSLNGVV, ATWDDSLSGVV, QQSHSTPIT, QQYNSYSRT, QQYTNWPQT, LQYDRYSGA, QVWHTTNDHVL, QVWDSSSDHWV, QQSKQIPYT, QQSYSLPLT, QQFDISGGLI, QQYDNLPLT, QVWDSSSDHTVA, SSYTTTDTFV, QQYDNLPLYT, QQYYSTPPH, QQSYSTPLT, QVWDSSSDHVV, GTWDSSLSAYV, QQTHTWPWT, QQANSFPLT, QQSYSTPYT, SSYTSSSTYV, QRYGSSPR, QQVHSFPFT, LQHNTFPYT, QQSHSTPLT, QQYNSYPFT, QQYNSSPLMYT, QQTYSTPLT, QQANTFPQT, QSYDGSSVV, GSWEARESVFV, QQTYNDPPT, NSRDSSGNHVV, QTWGDSIVV, VLYMGSGI WV, ATWDDALSGWV, SSYTSSSTLVV, QQSYSTPWT, SSYTSSSTWV, LQDYNYP PA, QQYYDDPQ, QQLNGYPTT, AAWDDSLIGHV, QVWDTSGDLHWA, QQSYTTPLT, QVWDSSSDLLWV, GTWDSSLSALV, AAWDDSLNGPV, MQTKQLPLT, QQANSFPPT, QSYDGNNH MV, and SSYTSSSTLWV.

25. The antibody of any one of claims 15-24, wherein the antibody competes for binding of CD25 with an epitope-specific reference binding agent, wherein the epitope-specific binding agent is IL-2, daclizumab, basioliximab, and/or 7G7B6.

26. The antibody of any one of claims 15-25, wherein the antibody does not compete with an off-target reference binding agent, wherein the off-target binding agent is IL-2, daclizumab, basioliximab, and/or 7G7B6.

27. The antibody of any one of claims 15-26, wherein binding of the antibody to IL-2 is disrupted by mutations to IL-2 selected from:

- a) D77A and Q79A;
- b) Q81A and T83A;
- c) D77A and N78A;
- d) T35A and Q151A;

- e) M39A and M147A;
- f) H33A and T35A;
- g) K37A and Y149A;
- h) E30A and H33A;
- i) D27A and E30A;
- j) R176A and Q179A;
- k) Q181A and I183A;
- l) E100A and R104A;
- m) Q101A and K105A;
- n) K102A and K105A;
- o) K169A and T171A;
- p) K174A and R176A;
- q) T175A and R176A;
- r) M170A and H172A;
- s) N70A and S71A;
- t) S72A and H73A;
- u) S74A and S75A; and
- v) L23A and D25A.

28. The antibody any one of claims 15-27, wherein the antibody has a k_{off} of less than $10^{-2}/\text{s}$, less than $10^{-3}/\text{s}$, or less than $10^{-4}/\text{s}$, wherein the k_{off} is measured using biolayer interferometry with soluble human CD25.
29. The antibody of any one of claims 15-28, wherein the antibody has a k_{off} of between $10^{-2}/\text{s}$ and $10^{-5}/\text{s}$, wherein the k_{off} is measured using biolayer interferometry with soluble human CD25.
30. The antibody of any one of claims 15-29, wherein the antibody has a K_D less than 100 nM, less than 25 nM, or less than 5 nM, wherein the K_D is measured using biolayer interferometry with soluble human CD25.
31. The antibody of any one of claims 15-30, wherein the antibody has a K_D between 100 nM and 1 nM, wherein the K_D is measured using biolayer interferometry with soluble human CD25.
32. The antibody of any one of claims 15-31, wherein the antibody specifically binds cells expressing CD25.
33. The antibody of any one of claims 15-32, wherein the antibody binds cells expressing CD25 with a mean fluorescence intensity (MFI) of at least 10^4 or at least 10^5 .
34. The antibody of any one of claims 15-33, wherein the antibody binds cells expressing CD25 with a mean fluorescence intensity (MFI) of between 10^4 and 10^6 .
35. The antibody of any one of claims 15-34, wherein the antibody does not bind CD25(-) cells.
36. The antibody of any one of claims 15-35, wherein the antibody binds CD25(-) cells with a mean fluorescence intensity (MFI) of less than 10^3 .
37. The antibody of claim 15, wherein the antibody comprises the six CDRs of any one of Combinations 1-126 of Table 7D.
38. A pharmaceutical composition comprising any one of the antibodies of claims 15-37, and optionally a pharmaceutically acceptable excipient.

39. A method of treating a subject in need of treatment comprising administering to the subject a therapeutically effective amount of any one of the antibodies of claims 15-37, or the pharmaceutical composition of claim 38.
40. The method of claim 39, wherein the subject suffers from a cancer.
41. The method of claim 39, wherein the subject suffers from an autoimmune disease or disorder.
42. An engineered immunogen, having at least 60% sequence similarity to a sequence selected from the group consisting of SEQ ID NOS: 2-5, SEQ ID NOS: 7-8 and SEQ ID NOS: 17-21.
43. The engineered immunogen of claim 42, having at least 80% similarity to the sequence.
44. The engineered immunogen of claim 42 or 43, having at least 90% similarity to the sequence.
45. The engineered immunogen of any one of claims 42 to 44, wherein the engineered immunogen shares at least one characteristic with CD25.
46. The engineered immunogen of any one of claims 42 to 45, wherein the engineered immunogen binds to an antibody of CD25.
47. The engineered immunogen of any one of claims 42 to 46, wherein the engineered immunogen has higher binding affinity to an antibody of CD25 at pH below 7.0, compared to binding affinity at pH between about 7.3 and about 7.5.
48. The engineered immunogen of claim 47, wherein the engineered immunogen has higher binding affinity to an antibody of CD25 at pH between about 6.4 and about 6.6, compared to binding affinity at pH between about 7.3 and about 7.5.
49. A method of producing an antibody, comprising immunizing an animal with the engineered immunogen of any one of claims 42 to 48, and producing an antibody.
50. The method of claim 49, wherein the antibody is an antibody to CD25.

51. The method of claim 49 or 50, wherein the antibody exhibits higher binding affinity for CD25 at pH below 7.0, compared to binding affinity at pH between about 7.3 and about 7.5.

52. The method of any one of claims 49 to 51, wherein the antibody exhibits higher binding affinity for CD25 at pH between about 6.4 and about 6.6, compared to binding affinity at pH between about 7.3 and about 7.5.

53. The method of any one of claims 49 to 52, wherein the antibody does not block binding of CD25 to IL-2.

54. The method of any one of claims 49 to 52, wherein the antibody does block binding of CD25 to IL-2.

55. The method of any one of claims 49 to 53, wherein the antibody prevents heterotrimerization of IL-2R-alpha, IL-2R-beta, and IL-2R-gamma.

56. The method of any one of claims 49 to 55, wherein the antibody is capable of binding to both the cis orientation and the trans orientation of CD25.

57. The antibody of any one of claims 15-37, wherein the antibody comprises six complementarity determining regions (CDRs) each independently selected from:

CDR-H1	CDR-H2	CDR-H3	CDR-L1	CDR-L2	CDR-L3
GFNIKDY	IYPGGDY	TVFWYGN	QSI	KVS	FQGS
YDY	YT	NYAGFAY	VHSNGNTY	NAK	SHVPT
GYTFTDYA	IYPGGDY	ARGVTFDI	ENIYSY	HTS	FQGS
GYTFTTRYW	TYNYNE	ARGVTFDY	QDISNY	NAK	SHVPT
GYSFTSYW	IYPGGGYA	ARHGYFDY	ENIYSY	YTS	QHHY
GYTFSNYW	IYPGGGYT	ARGVTFDS	QDISNY	HTS	GSPYT
GYTFNRFW	IYPGGGY	ARSGIPFAY	ENIYSY	SAS	QNSL
GYTFTTRFW	TYNYNE	ARGGTSV	QDISNY	YAS	PPT
GYTFTTKYW		VFHFDY	QSVNND	RAN	QHHY
GYTFTNYW		AIHGYFDY	QYISNY	WAS	DT
		ARGVTS	QDINSY	NAE	TPYT
		ARGTI	QDINNF		QHHY
		ARGVS	ENSYNY		DT
		ARGVP	ENIHSY		TPYT
		ATGV	QDVNTA		QHHY
		SRGGTS	QDINRY		GIPYT
		FVHFDY	QNVGTN		LQY
		AXGV	ENIYNY		DEFPYT
		TFDY	ENIYSY		LQY
		ARHX	QNVGIN		DEFPWT
		YFDY			QHHY
		ATXV			STPYT
		TFDS			QNGT
		ARXG			TLPLT
		YFDY			QHYSSPW

CDR-H1	CDR-H2	CDR-H3	CDR-L1	CDR-L2	CDR-L3
		ARGTVVDY ARVTPAS ARVTPSS ARITPAS ARVSPAS	QDISNY ENSYSY RDVNTA QSLVHSNGNTY DNIYSY GNVHNF QSIVHSNGNTY		QQYNSYPYT QQGNTLPWT QQGNTLPST HQYNNYPYT QQYNSYPYT QQYNTYPYT QHHYGTPYT QHHYDTPYT QQYNNYPYT QQYNSYPLT QQSNSLPPT QHHYSSPWT SQSTHVPPT QHFWNTPPT FQGSHVPPT

58. The antibody of any one of claims 15-37, wherein the antibody comprises six complementarity determining regions (CDRs) each independently selected from:

CDR-H1	CDR-H2	CDR-H3	CDR-L1	CDR-L2	CDR-L3
GFIKDY	IDPDNGET	TVFWYGNNYAGFAY	QSIVHSNGNTY ENIYSY QDISNY	KVS NAK HTS	FQGSHVPPT FQGSHVPT QHHYGSPYT QQSNSLPPT

59. The antibody of any one of claims 15-37, wherein the antibody comprises six complementarity determining regions (CDRs) each independently selected from:

CDR-H1	CDR-H2	CDR-H3	CDR-L1	CDR-L2	CDR-L3
GYTFTDYA GYTFTRYW GYSFTSYW GYTFSNYW GYTFTKYW GYTFNRFW GYTFTFRW	ISTYSGDA INPRTDYTEYNQ ISTYSGDAIYNQ ISTYSGDVNYNQ ISTYSGDVSYNQ IHPSDSETRLNQ ILPGSGFTNYNE ISTYSGDALYNQ INPRTDYT ISTYSGDV INPNSDYI INTYSGDA INPSTDYI INPGSDYT	ARGVTFDI ARGVTFDY ARHGYFDY ARGVTFDS ARSRGIPFAY ARGGTSVVHFDY AIHGYFDY ARGVTSDS ARGTHIDY ARGVSFDY ARGVPFDY ATGVTFDY SRGGTSFVHFDY AXGVTFDY	ENIYSY QDISNY ENSYSY QNVGTN QSVNND QYISNY QDINSY QDINNF ENSYNY ENIHSY QDVNTA QDINRY	NAK YTS HTS SAS YAS RAN WAS	QHHYDTPYT QHHYGSPYT QQGNTLPPT QQSNTLPPT QHHYGTPYT QHHYDTPYT QQSNSLPPT QQYNSYPLT QQAYWSPYT QHHYGIPYT LQYDEFPYT LQYDEFPWT QHHYSTPYT QQGNTLPLT

CDR-H1	CDR-H2	CDR-H3	CDR-L1	CDR-L2	CDR-L3
	INPSTGYI	ARHXYFDY ARXVTFDY ATXVTFDS ARXGYFDY ARGTVVDY			QQHYSSPWT QQYNSYPYT QQGNTLPWT QQGNTLPST

60. The antibody of any one of claims 15-37, wherein the antibody comprises six complementarity determining regions (CDRs) each independently selected from:

CDR-H1	CDR-H2	CDR-H3	CDR-L1	CDR-L2	CDR-L3
GYTFTKYW GYTFTNYW	IYPGGDYT IYPGGDYTNINE IYPGGGYA IYPGGGYT IYPGGGYTNINE	ARVTPAS ARVTPSS ARITPAS ARVSPAS	QNVGTN ENIYNY ENIYSY QNVGIN QDISNY ENSYSY RDVNTA QSLVHSNGNTY DNIYSY GNVHNF QSIVHSNGNTY	SAS NAK HTS WAS KVS NAE	HQYNNYPYT QQYNSYPYT QQYNTYPYT QHHYGTPTY QHHYDTPYT QQYNNYPYT QQYNSYPLT QQSNSLPPT QHHYSSPWT SQSTHVPPT QHFWNTPT FQGSHPPT

61. The antibody of any one of claims 15-37, wherein the antibody comprises six complementarity determining regions (CDRs) selected from any one of the combinations provided in Table 4.

62. The antibody of any one of claims 15-37, wherein the antibody comprising six complementarity determining regions (CDRs) for any one of YU390-B12, YU397-F01, YU397-D01, YU398-A11, YU404-H01, YU400-B07, YU400-D09, YU401-B01, YU401-G07, YU404-C02, YU403-G07, YU403-G05, YU391-B12, YU400-A03, YU400-D02, YU392-A09, YU392-B11, YU392-B12, YU392-E05, YU392-E06, YU392-G08, YU389-A03, YU392-G09, YU392-G12, YU392-H02, YU392-H04, YU402-F01, YU389-B11, YU394-D08, or YU390-A11, as provided in Table 3A and Table 3B.

63. The antibody of any one of claims 15-37, wherein the antibody comprises a heavy chain variable region and a light chain variable region that each share at least 90%, 95%, 99%, or 100%

sequence identity with the heavy chain variable region and the light chain variable region of YU390-B12, YU397-F01, YU397-D01, YU398-A11, YU404-H01, YU400-B07, YU400-D09, YU401-B01, YU401-G07, YU404-C02, YU403-G07, YU403-G05, YU391-B12, YU400-A03, YU400-D02, YU392-A09, YU392-B11, YU392-B12, YU392-E05, YU392-E06, YU392-G08, YU389-A03, YU392-G09, YU392-G12, YU392-H02, YU392-H04, YU402-F01, YU389-B11, YU394-D08, or YU390-A11, as provided in Table 5.

64. The antibody of claim 63, wherein the antibody is a full-length immunoglobulin G monoclonal antibody.

65. The antibody of any one of claims 15-37, wherein the antibody comprises single chain variable fragment (scFv) that share at least 90%, 95%, 99%, or 100% sequence identity with the scFv sequence of YU390-B12, YU397-F01, YU397-D01, YU398-A11, YU404-H01, YU400-B07, YU400-D09, YU401-B01, YU401-G07, YU404-C02, YU403-G07, YU403-G05, YU391-B12, YU400-A03, YU400-D02, YU392-A09, YU392-B11, YU392-B12, YU392-E05, YU392-E06, YU392-G08, YU389-A03, YU392-G09, YU392-G12, YU392-H02, YU392-H04, YU402-F01, YU389-B11, YU394-D08, or YU390-A11, as provided in Table 5.

66. The antibody of any one of claims 15-37 or 61-65, wherein the antibody is a human antibody.

67. The antibody of any one of claims 15-37 or 61-65, wherein the antibody is a humanized antibody.

68. The antibody of any one of claims 15-37 or 61-65, wherein the antibody is a chimeric antibody.

69. The antibody of any one of claims 15-37 or 61-65, wherein the antibody comprises a mouse variable domain and a human constant domain.

70. The antibody of any one of claims 15-37 or 61-69, wherein the antibody also binds cynomolgous monkey CD25.

71. A pharmaceutical composition comprising the antibody of any one of claims 15-37 or 61-70, and optionally a pharmaceutically acceptable excipient.

72. A method of treating a subject in need of treatment comprising administering to the subject a therapeutically effective amount of the antibody of any one of claims 15-37 or 61-70, or the pharmaceutical composition of claim 71.

73. The method of claim 72, wherein the subject suffers from a cancer.

74. The method of claim 72, wherein the subject suffers from an autoimmune disease or disorder.

75. A method of depleting the number of regulatory T cells in a subject comprising administering to the subject a therapeutically effective amount of the antibody of any one of claims 15-37 or 61-70, or the pharmaceutical composition of claim 71.

76. The method of claim 75, wherein the subject suffers from a cancer.

77. The method of claim 75, wherein the subject suffers from an autoimmune disease or disorder.

78. A kit comprising the antibody of any one of claims 15-37 or 61-70, or the pharmaceutical composition of claim 71.

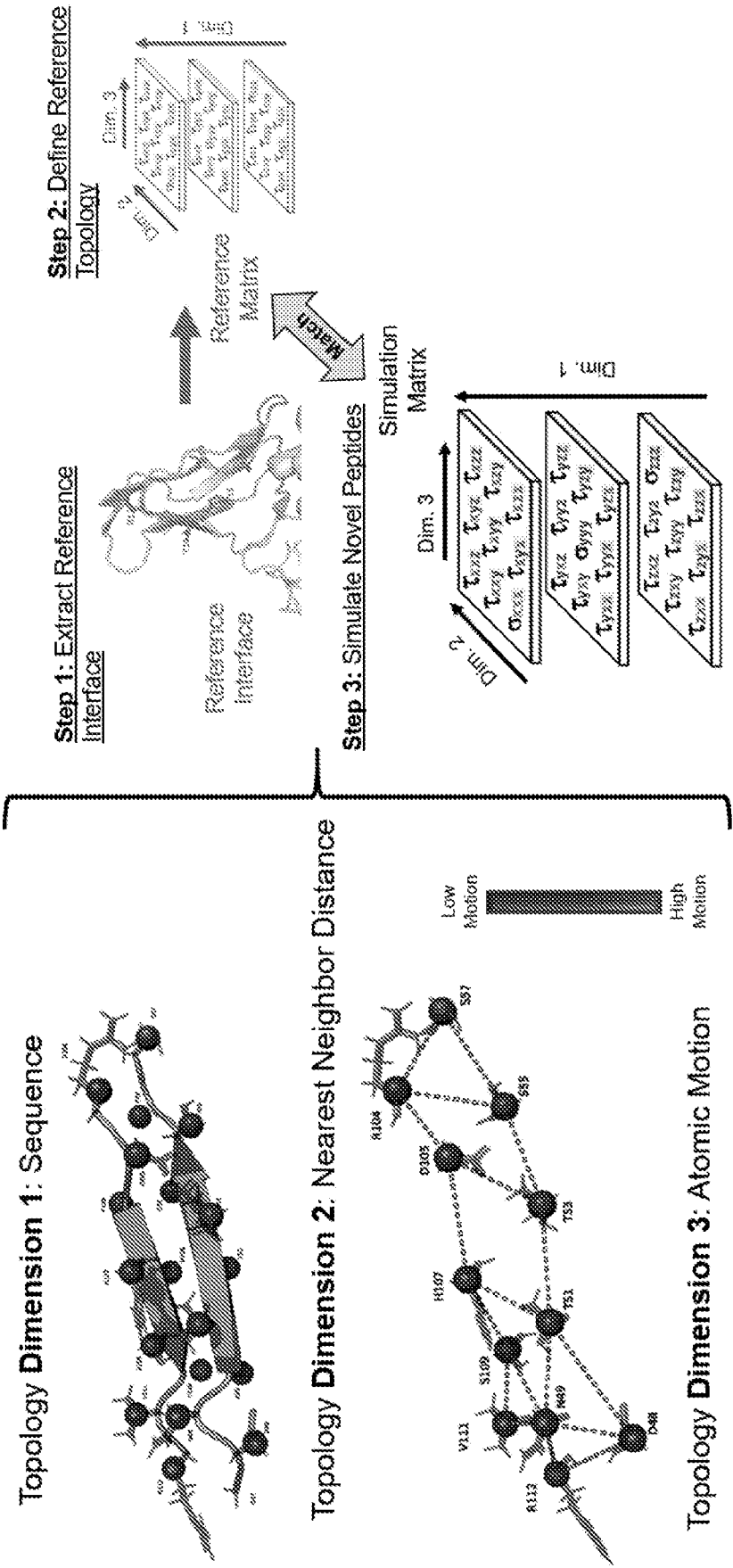


FIG. 1

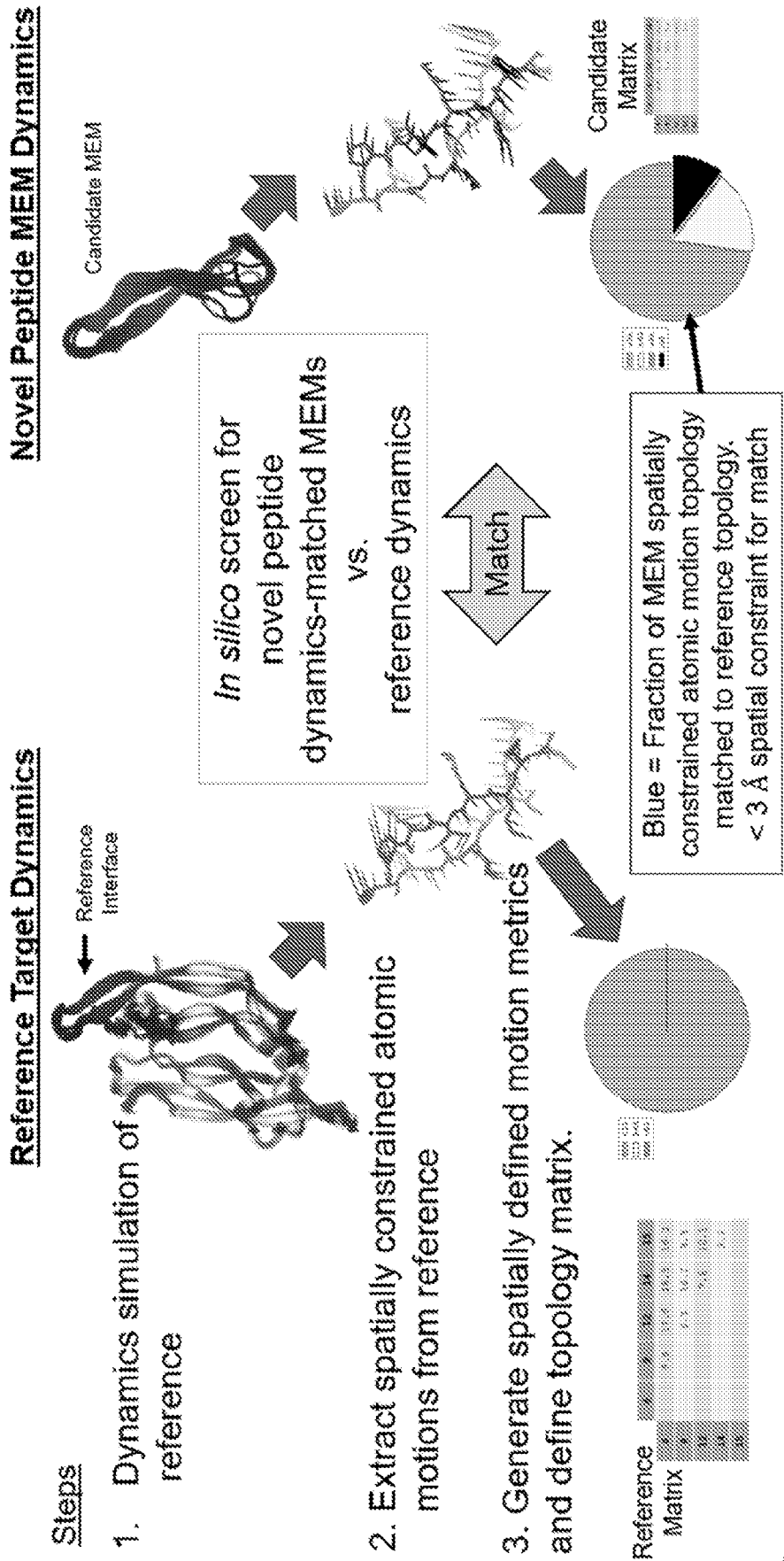


FIG. 2

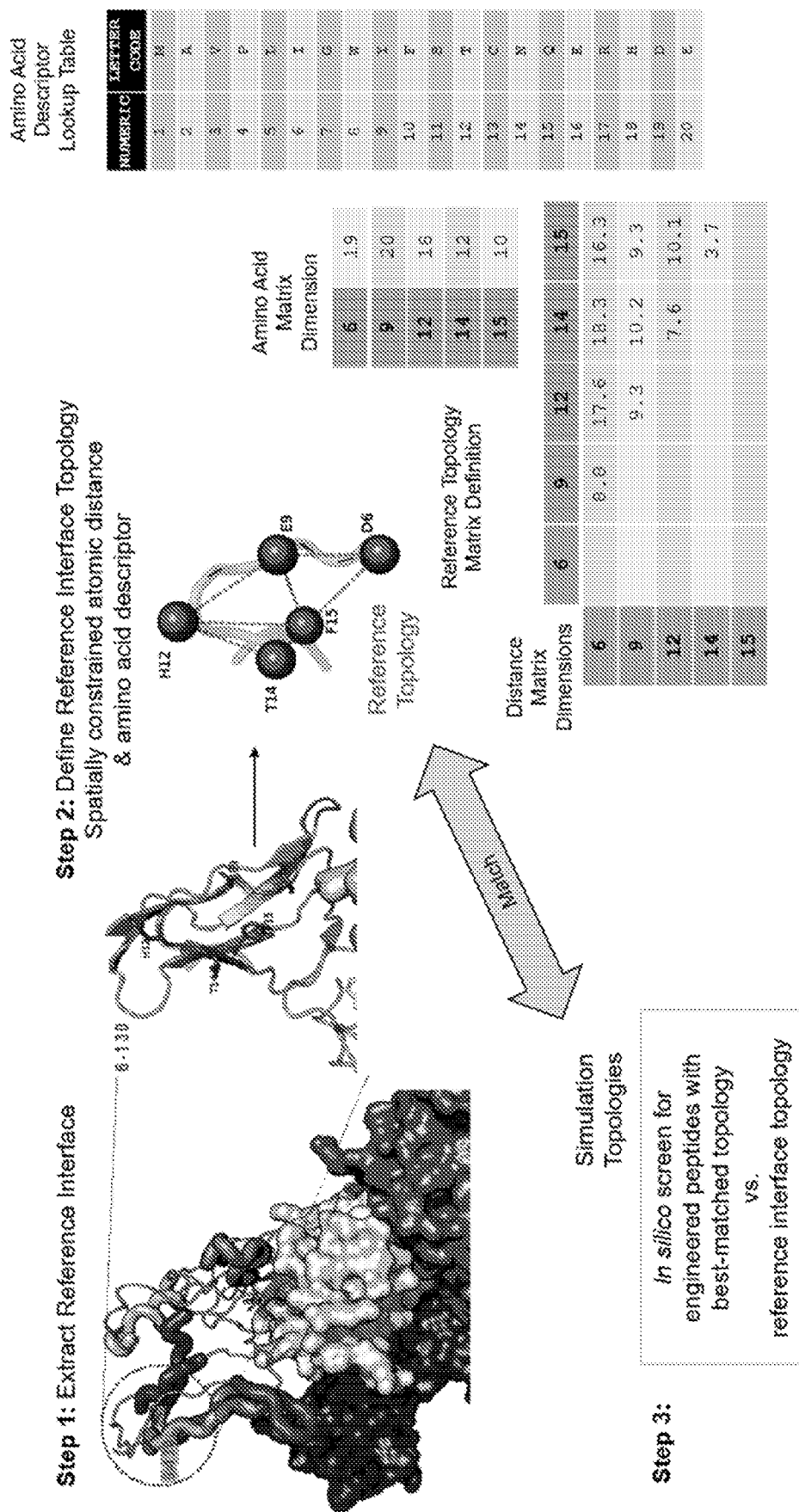
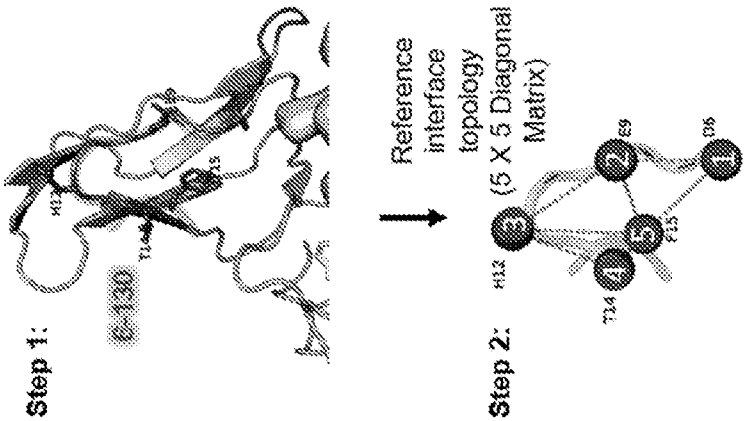


FIG. 3A

**Steps 1 & 2:
Reference**



Step 3: *In Silico* Screen Topologies for Matched Novel Peptides

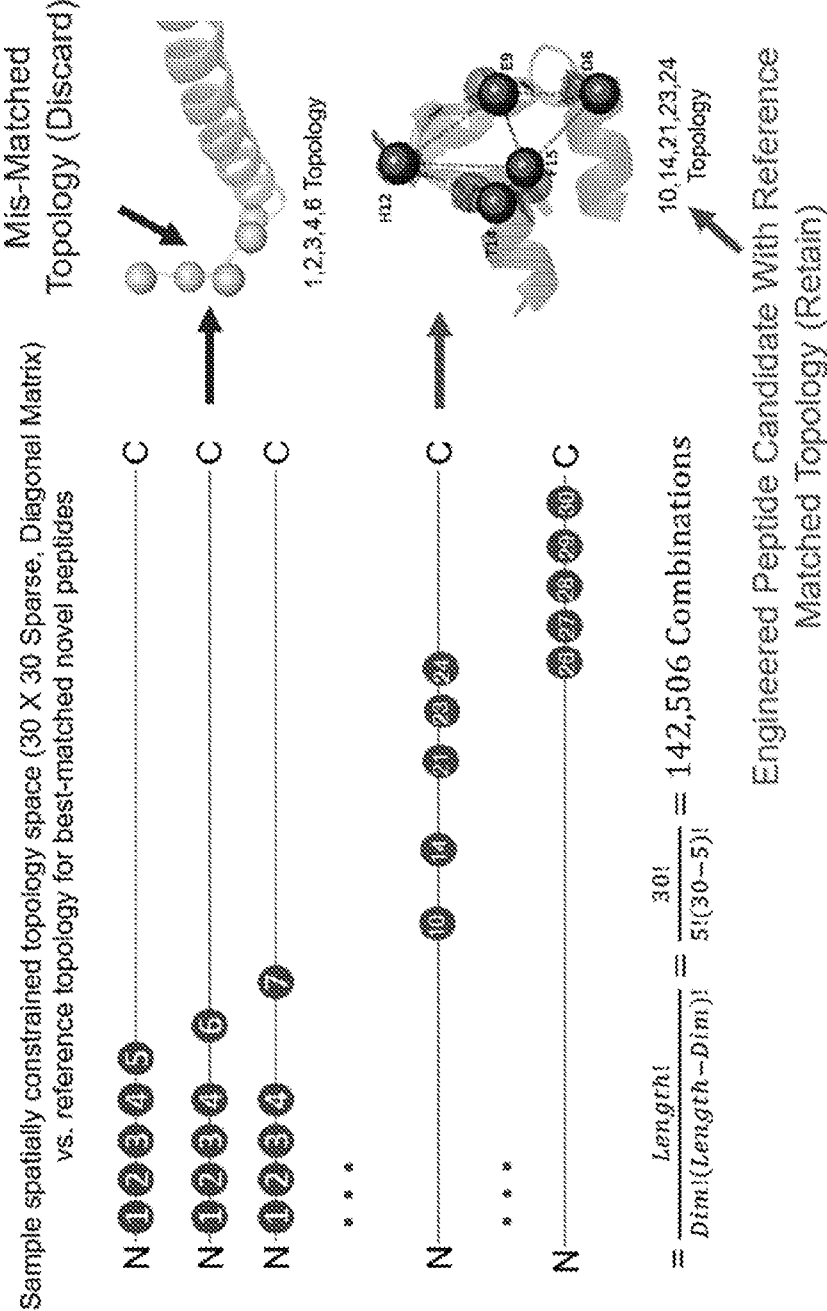
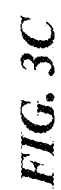


FIG. 3B



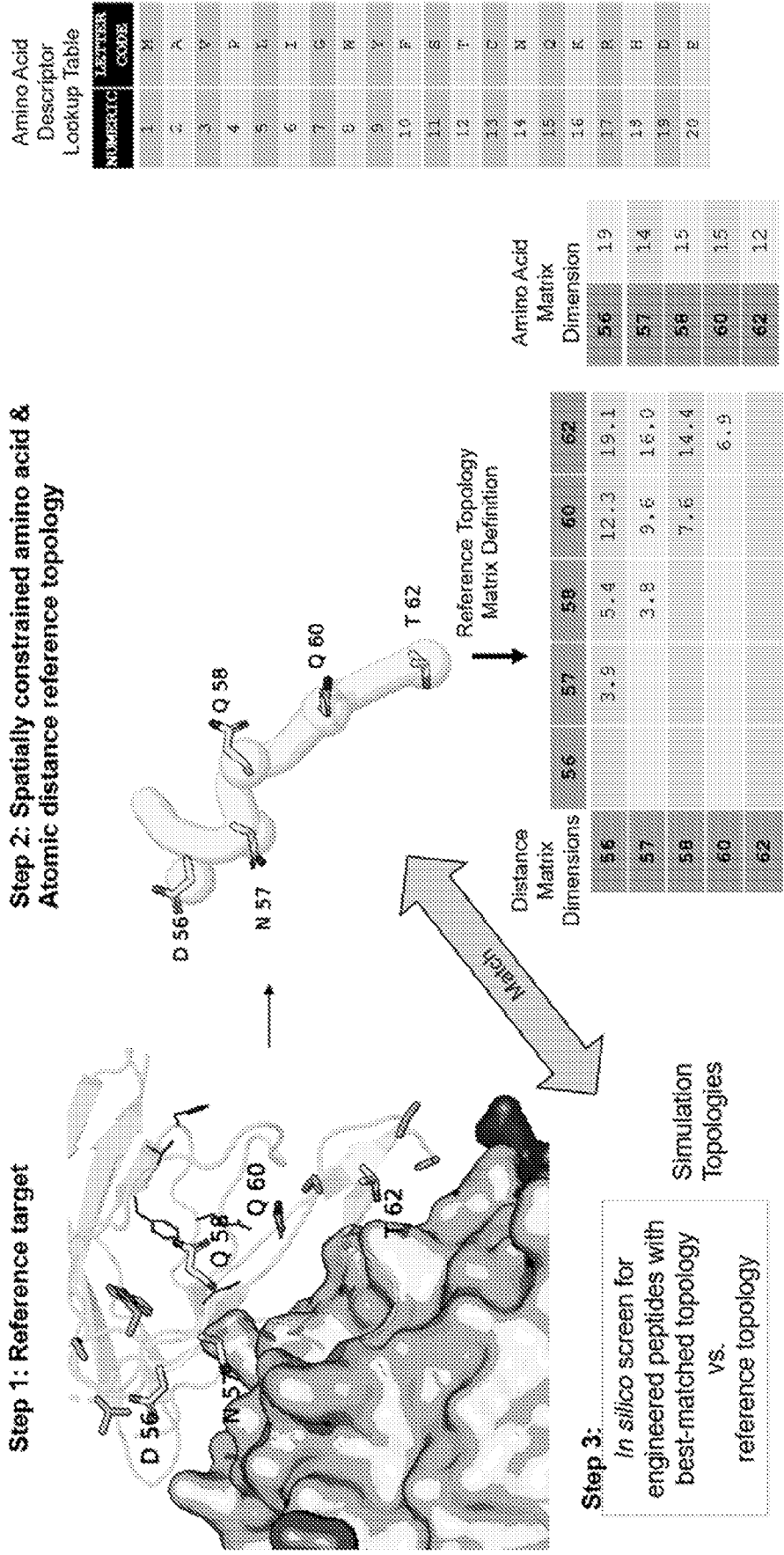


FIG. 4A

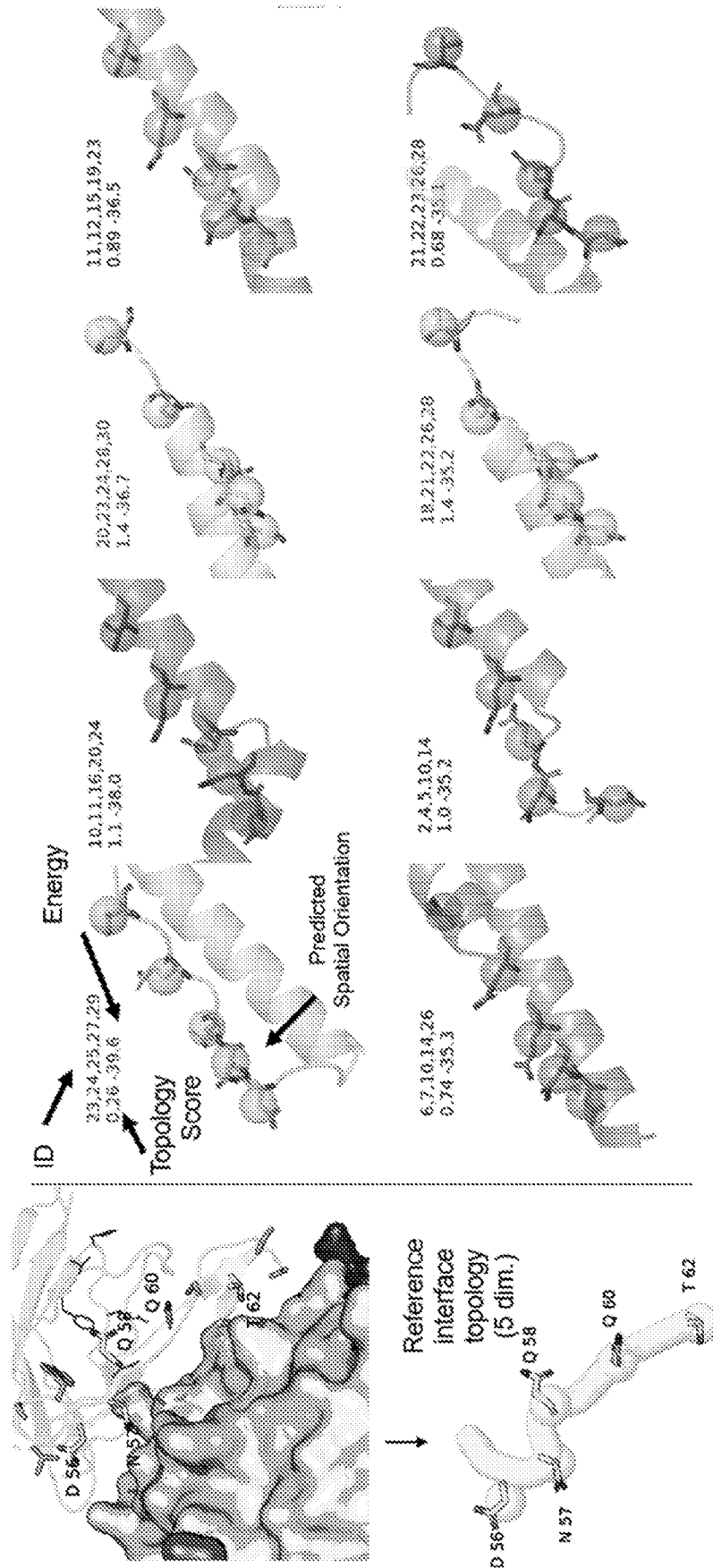


FIG. 4B

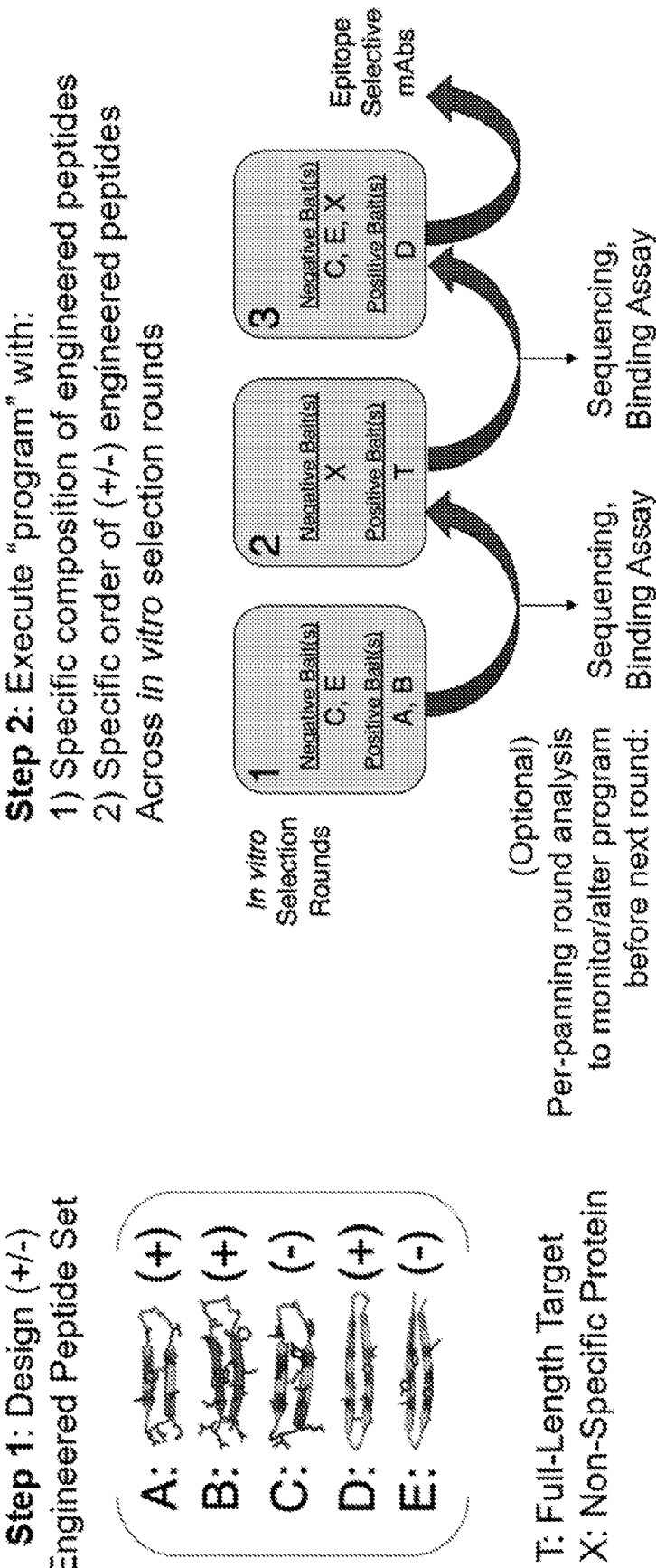
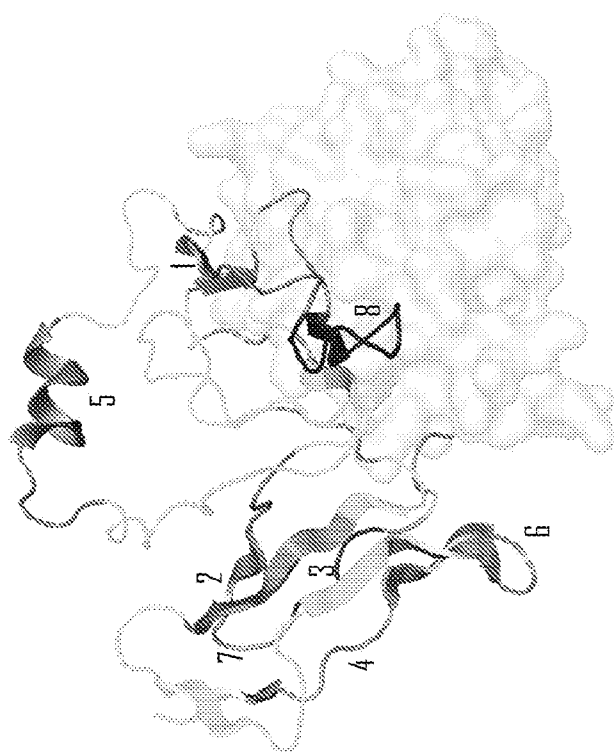


FIG. 5

**FIG. 6**

MEM Residue
Color Key
Scaffold
Epitope

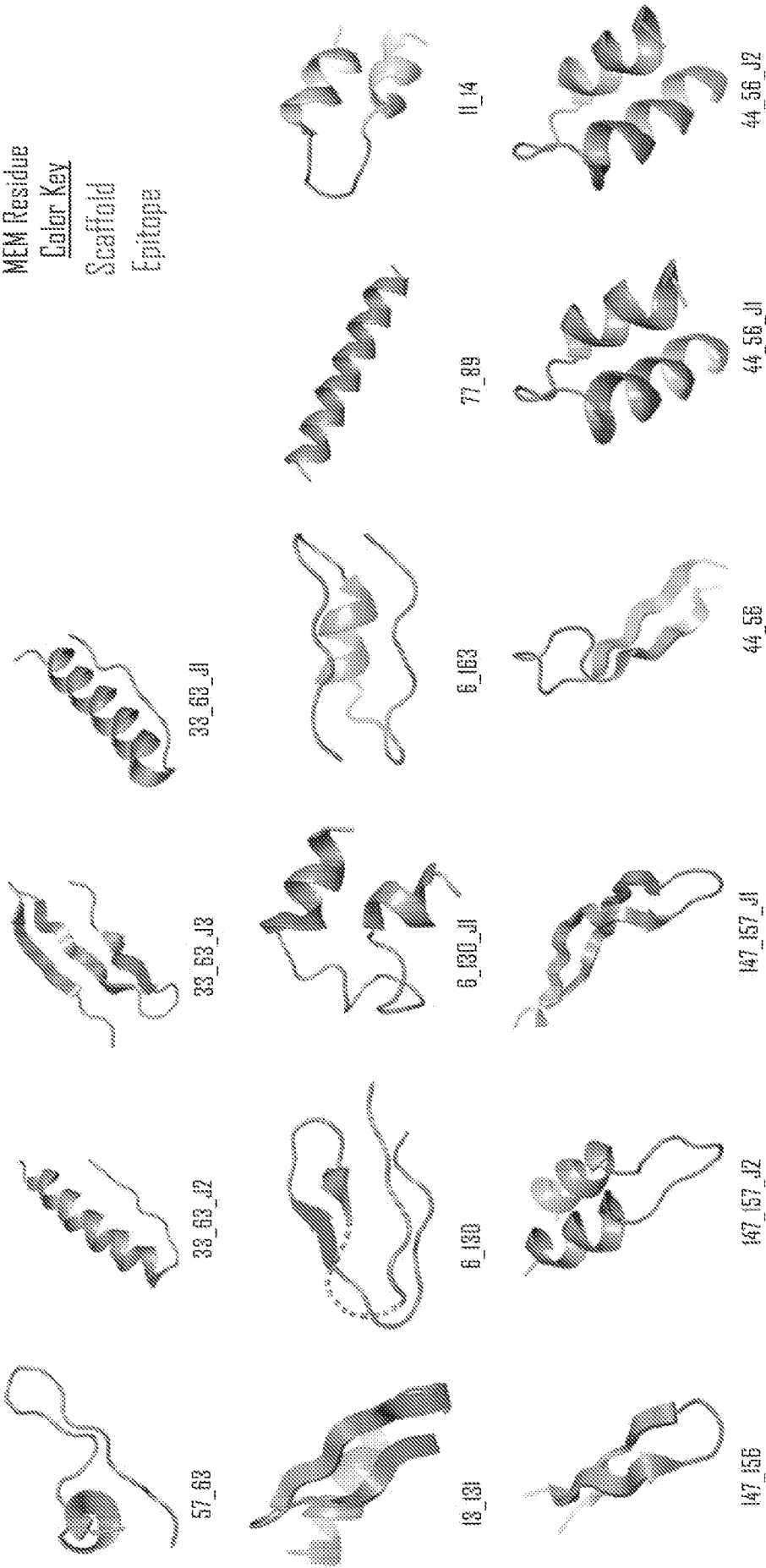


FIG. 7

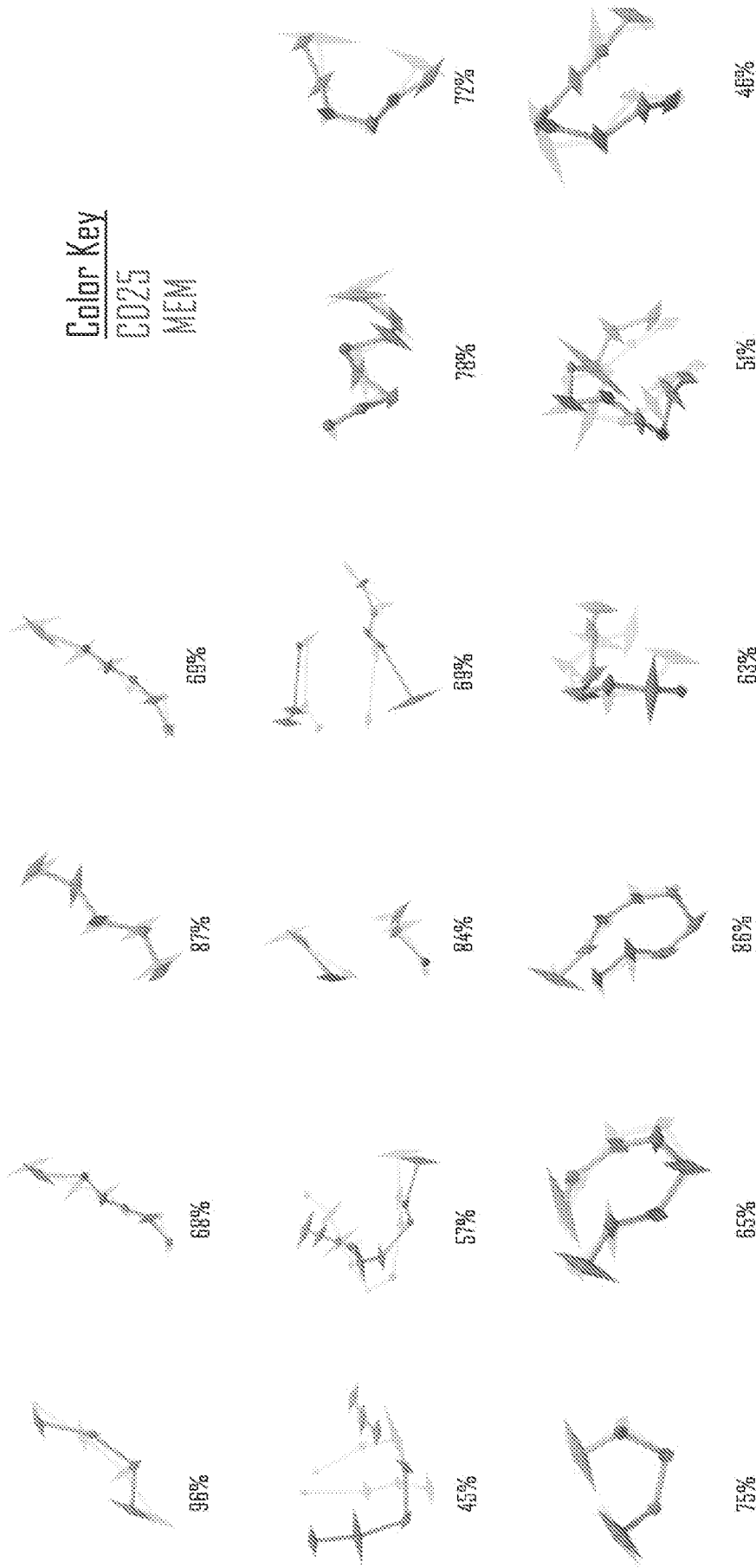


FIG. 8

CD25 ELISA: 384 Clones Per Selection Strategy

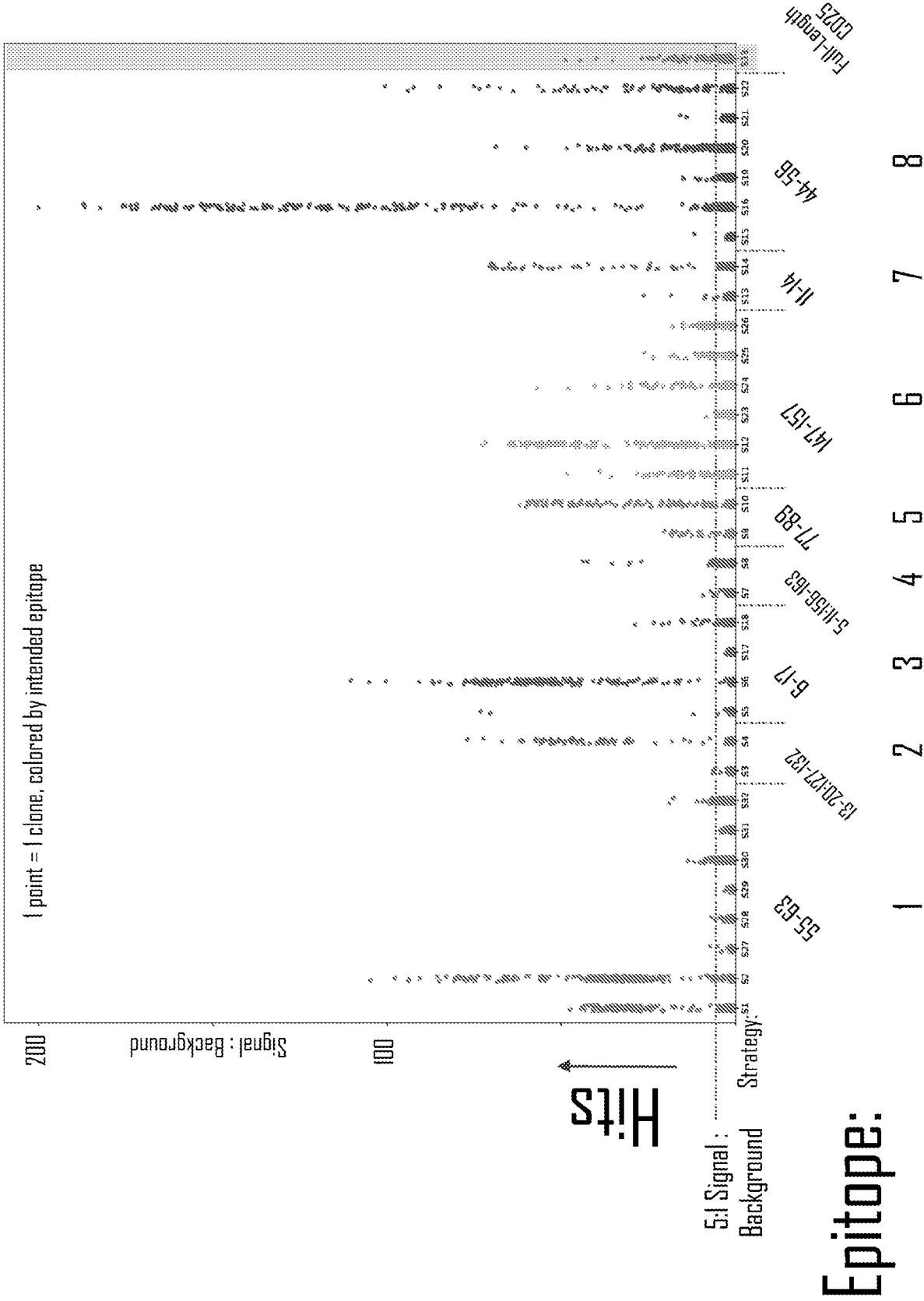


FIG. 9

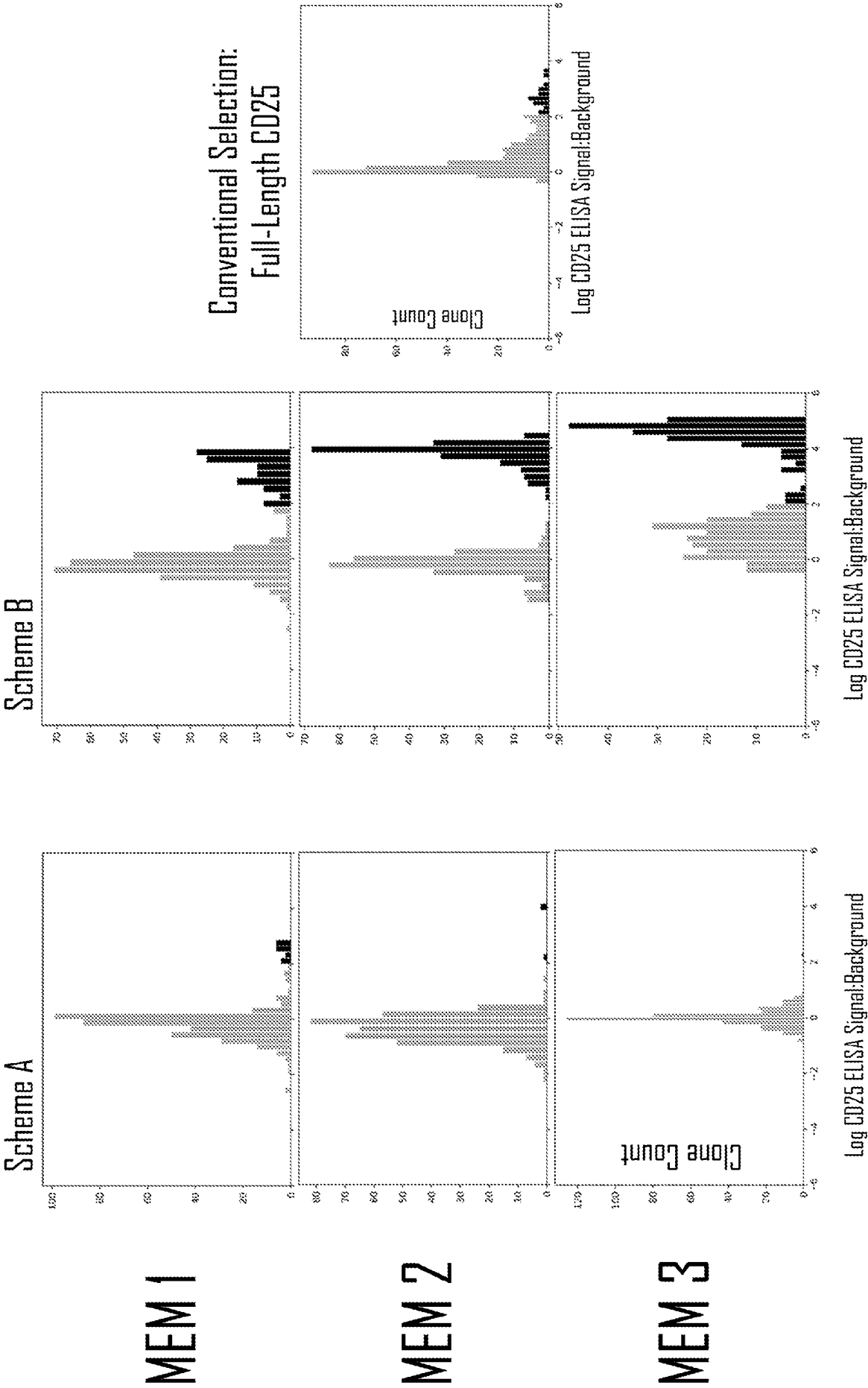
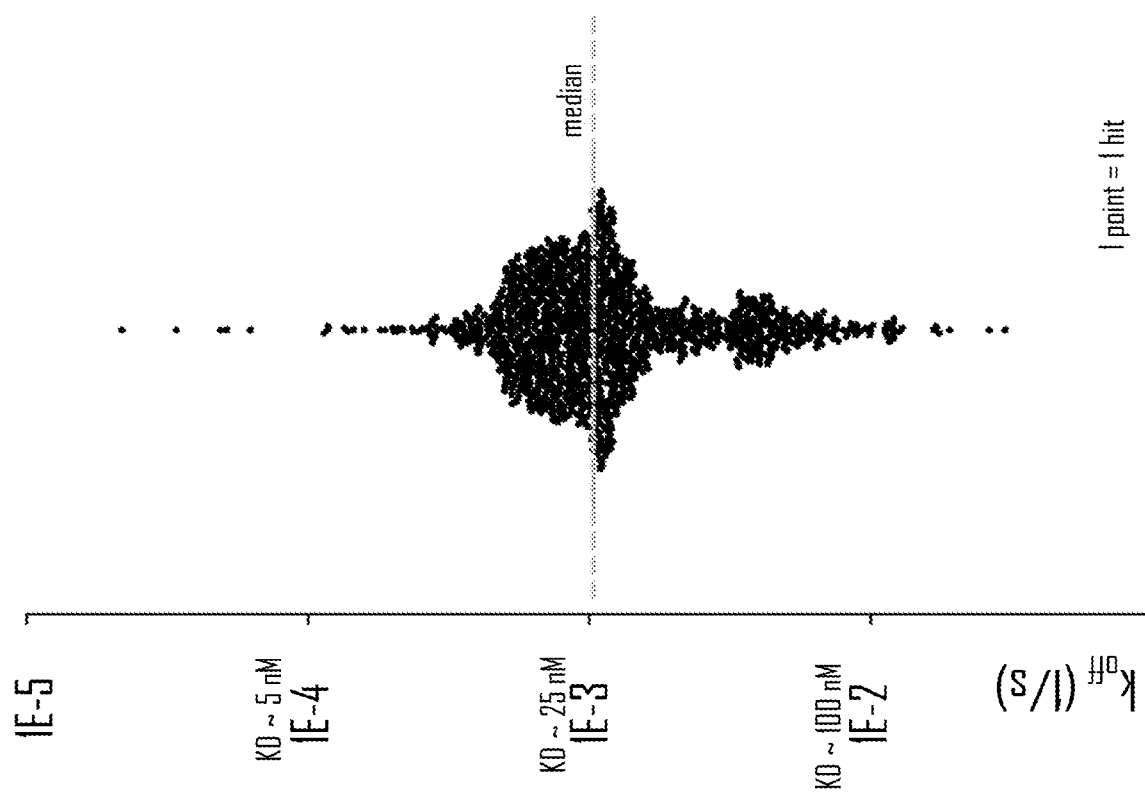


FIG. 10

**FIG. 11**

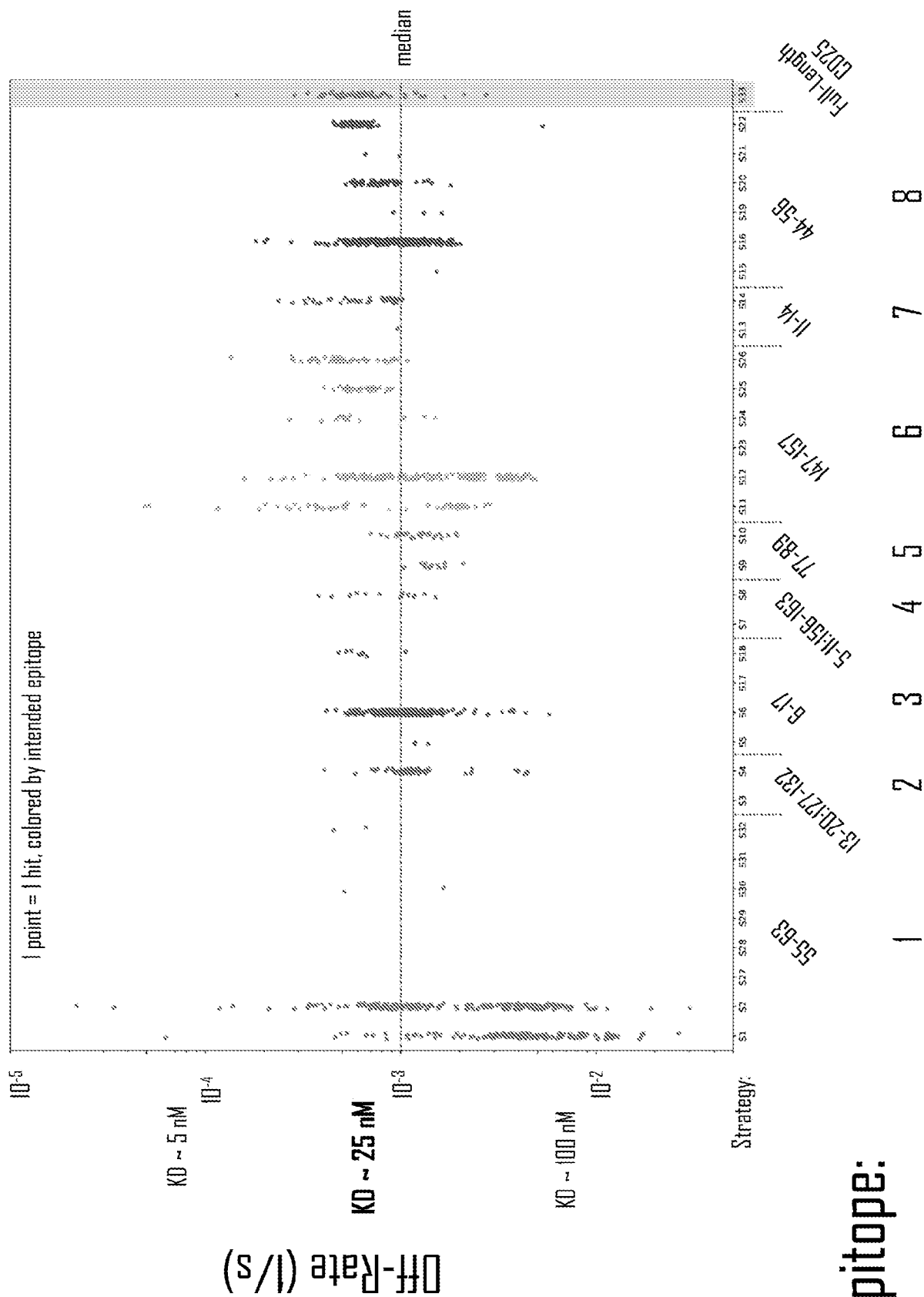


FIG. 12

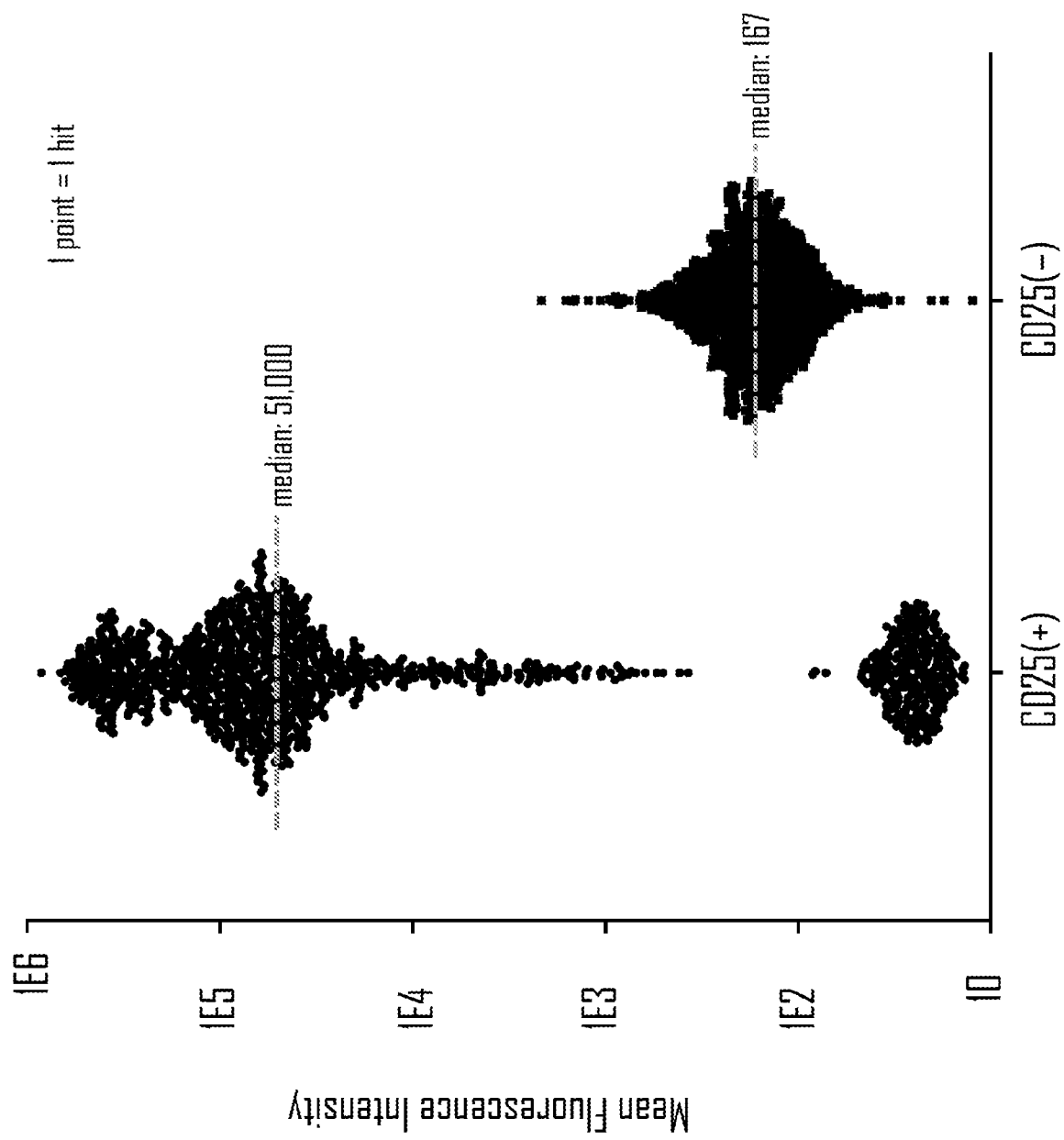


FIG. 13

Cell Binding By Panning Strategy & Epitope

CD25(+)

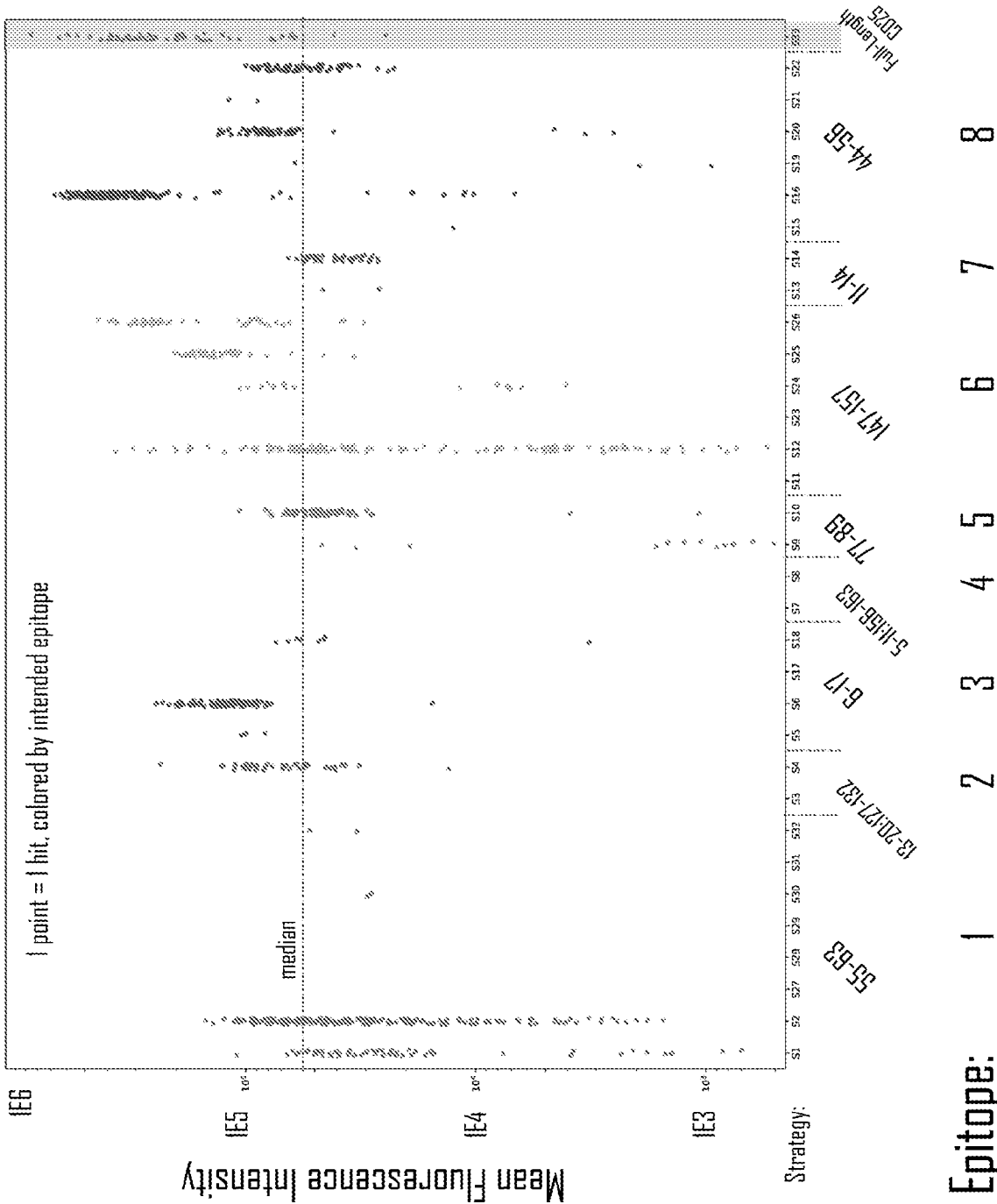


FIG. 14A

CD25(-)

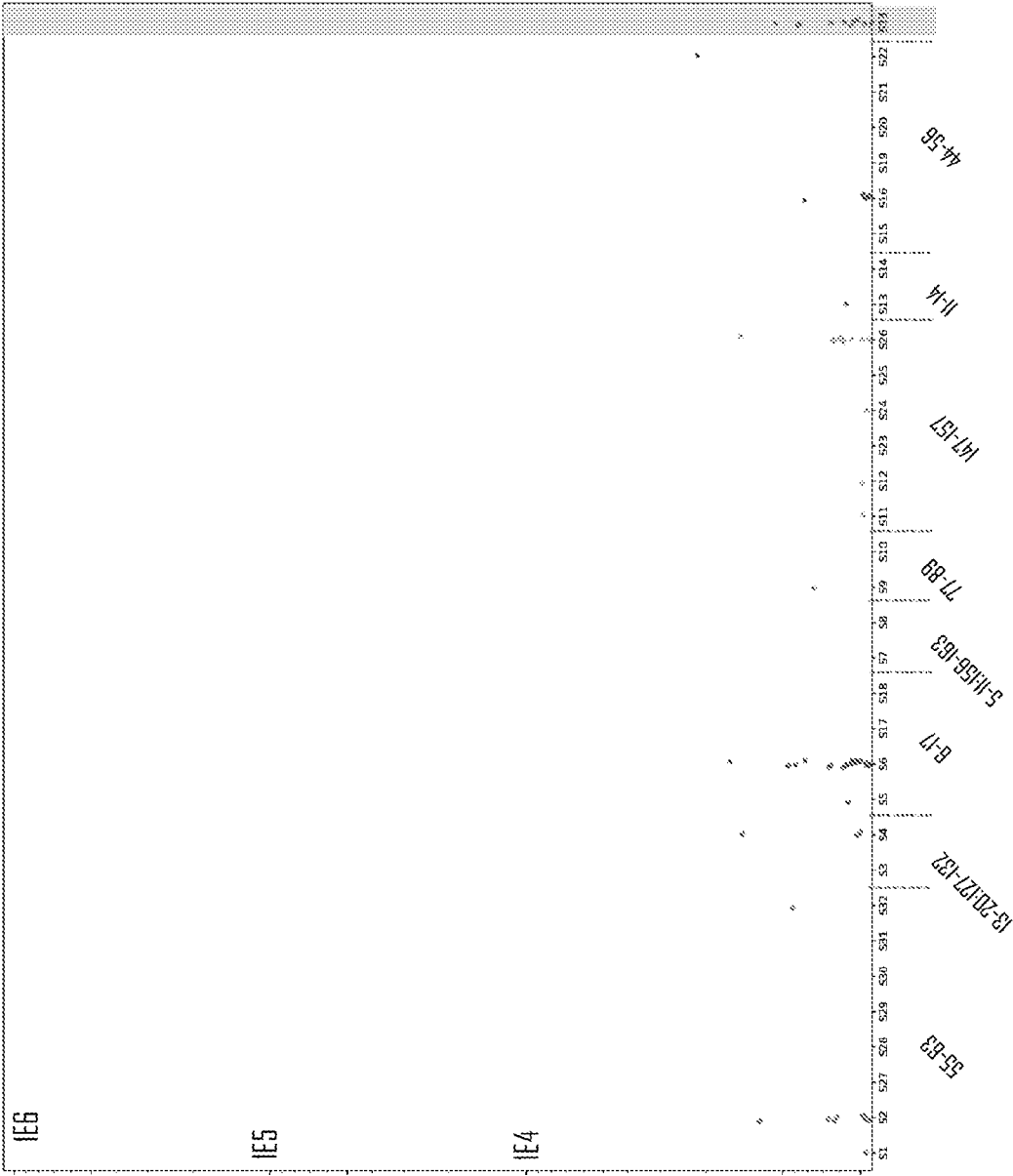


FIG. 14B

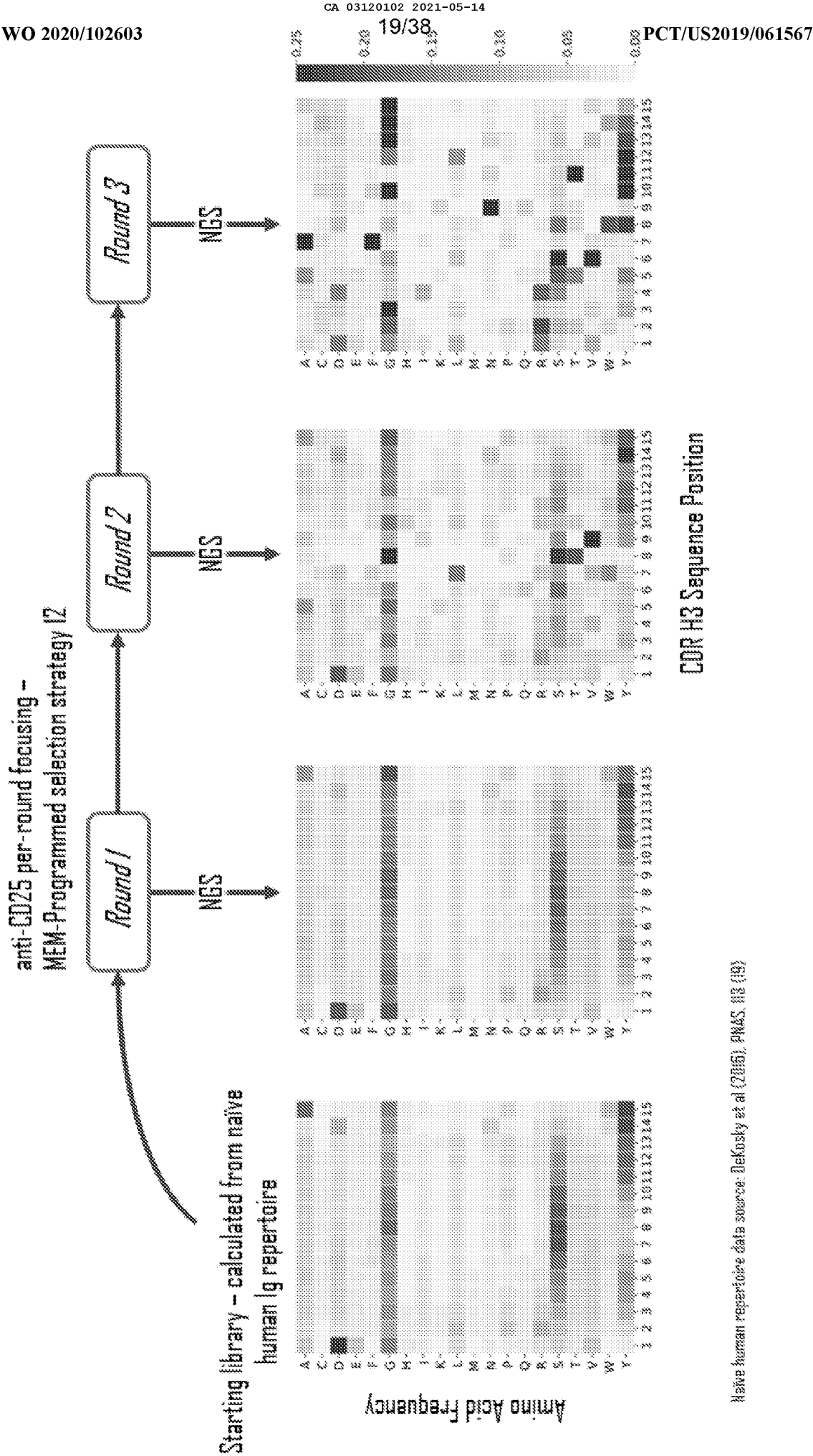
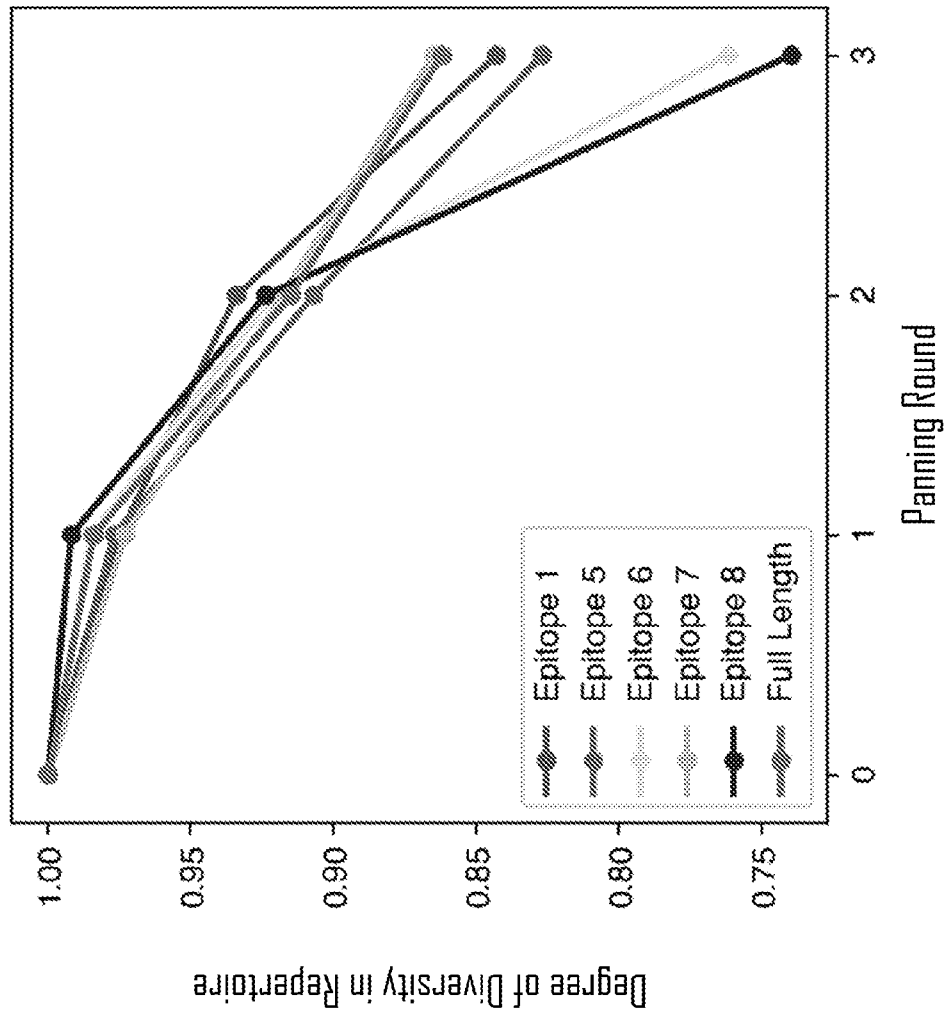
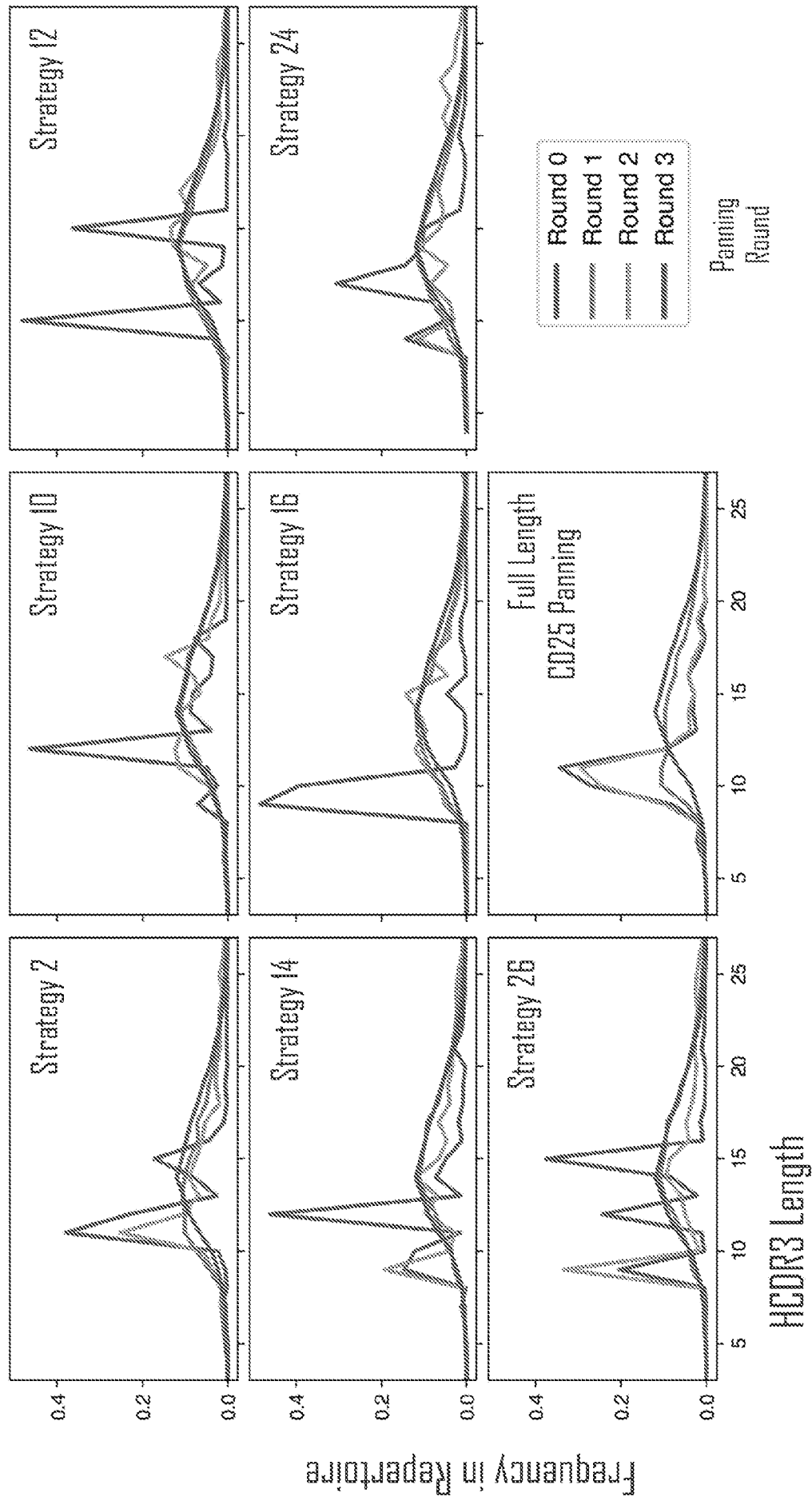
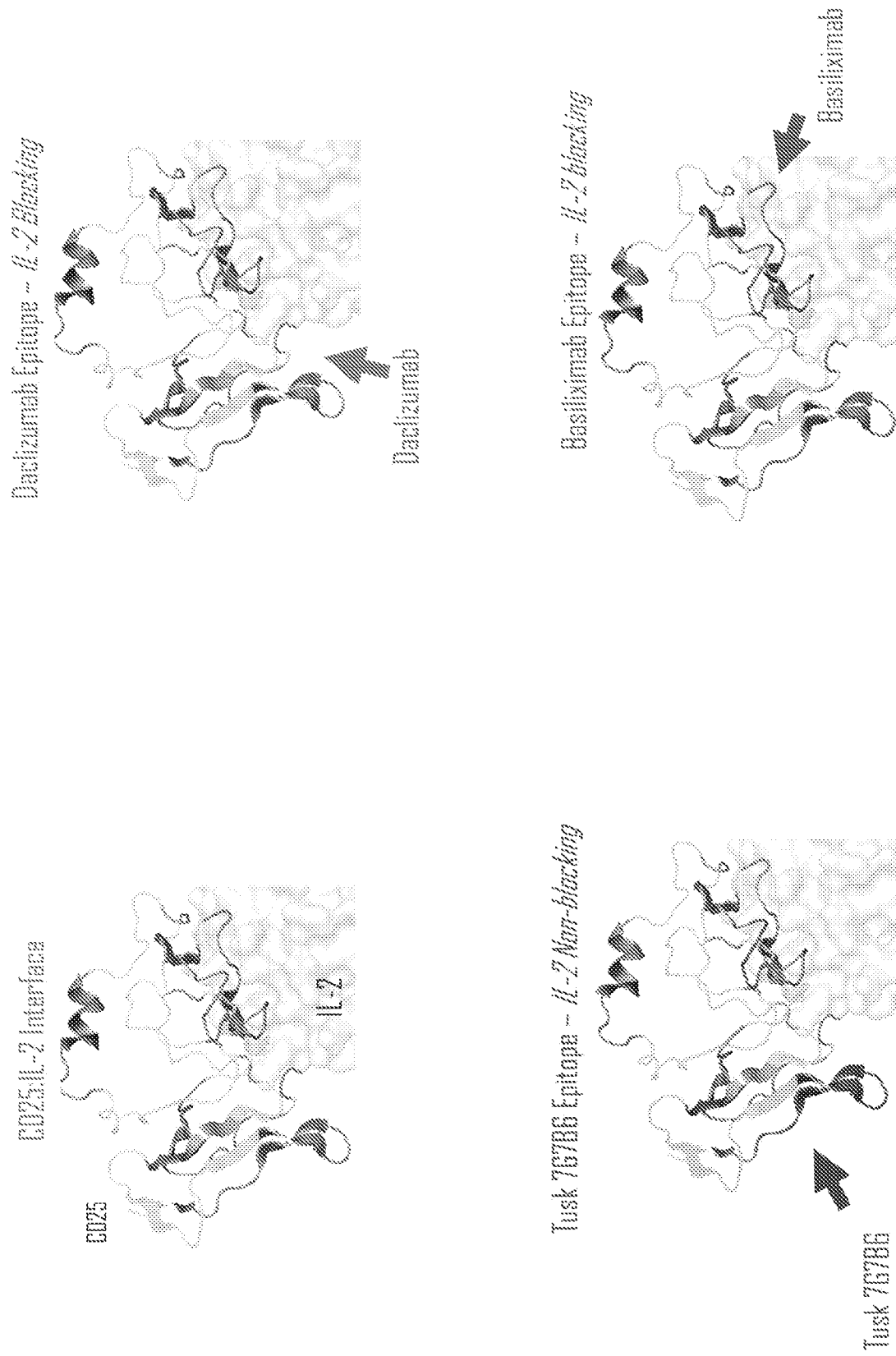


FIG. 15

**FIG. 16**

**FIG. 17**

**FIG. 18**

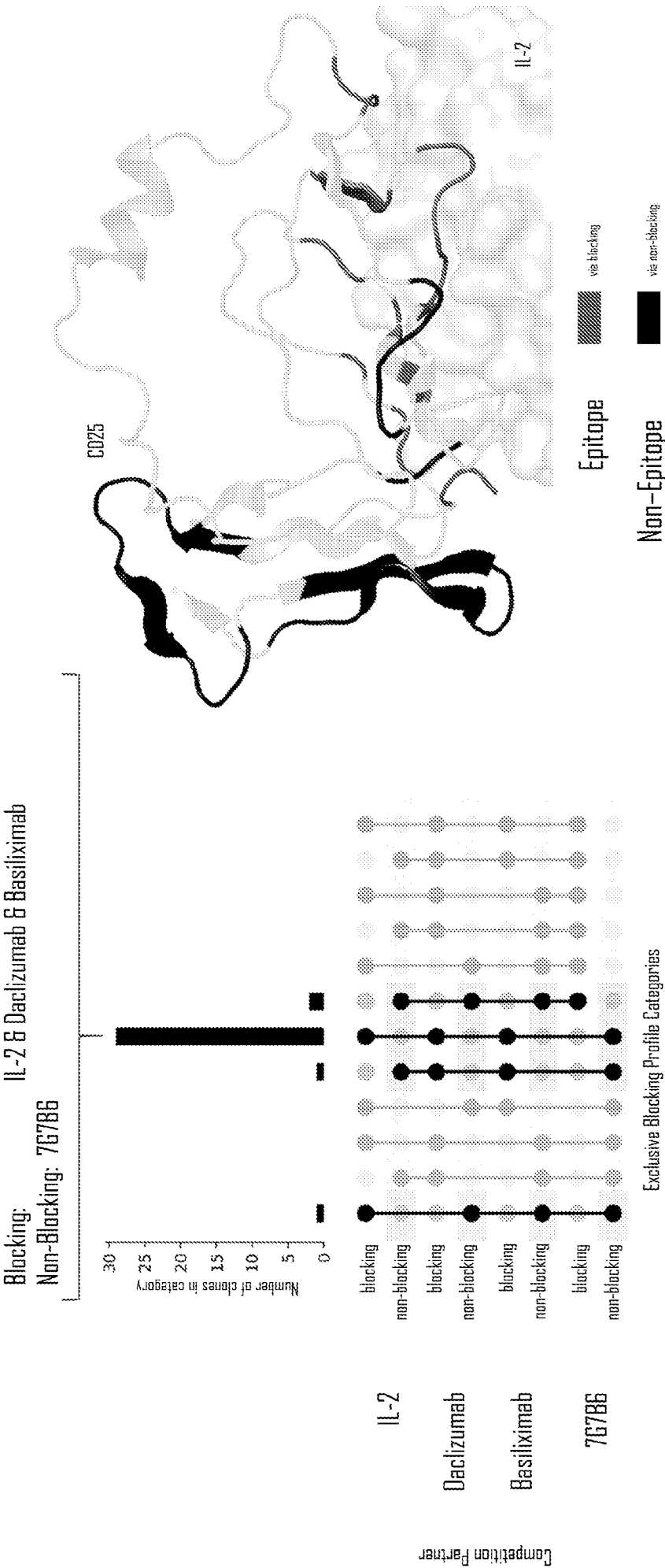


FIG. 19

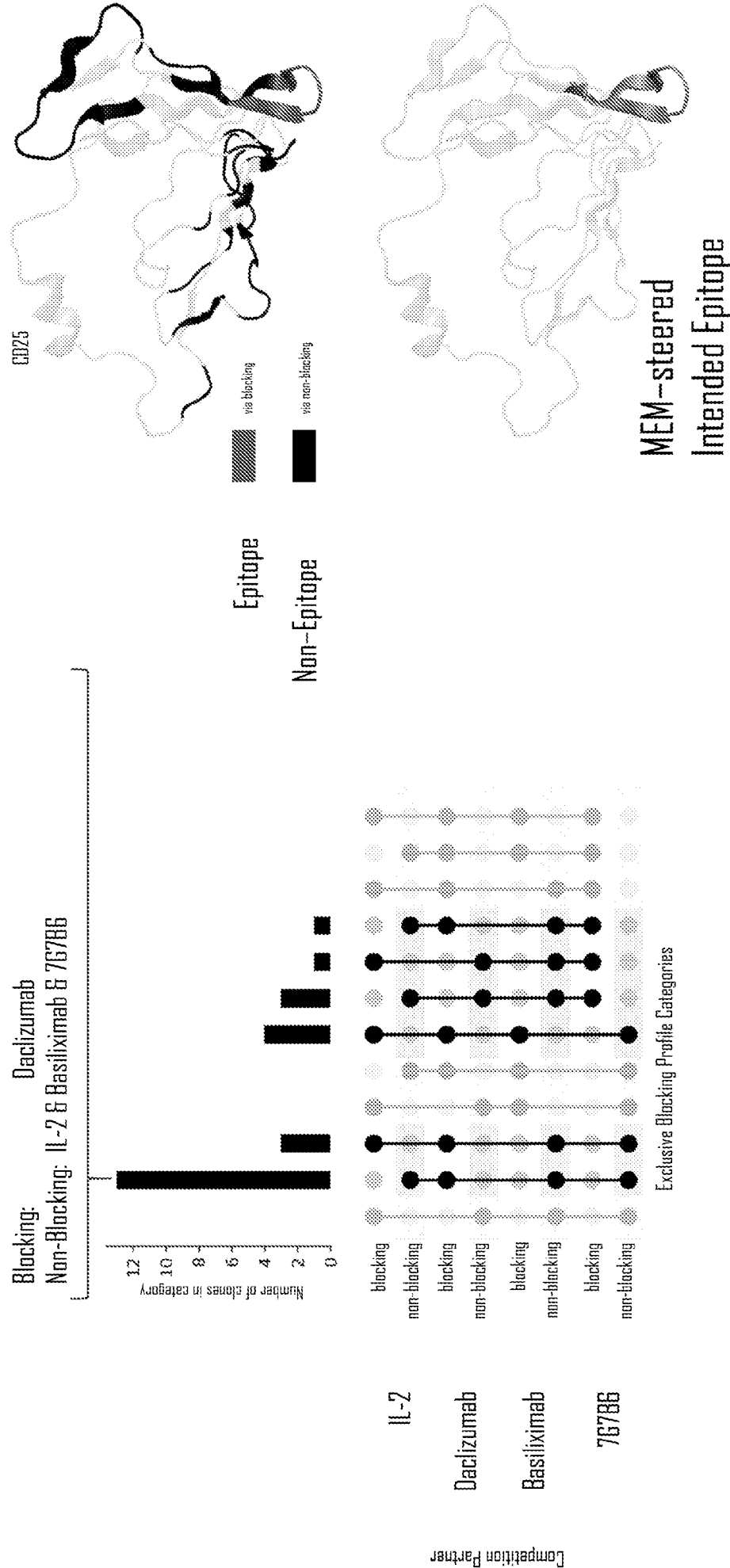


FIG. 20

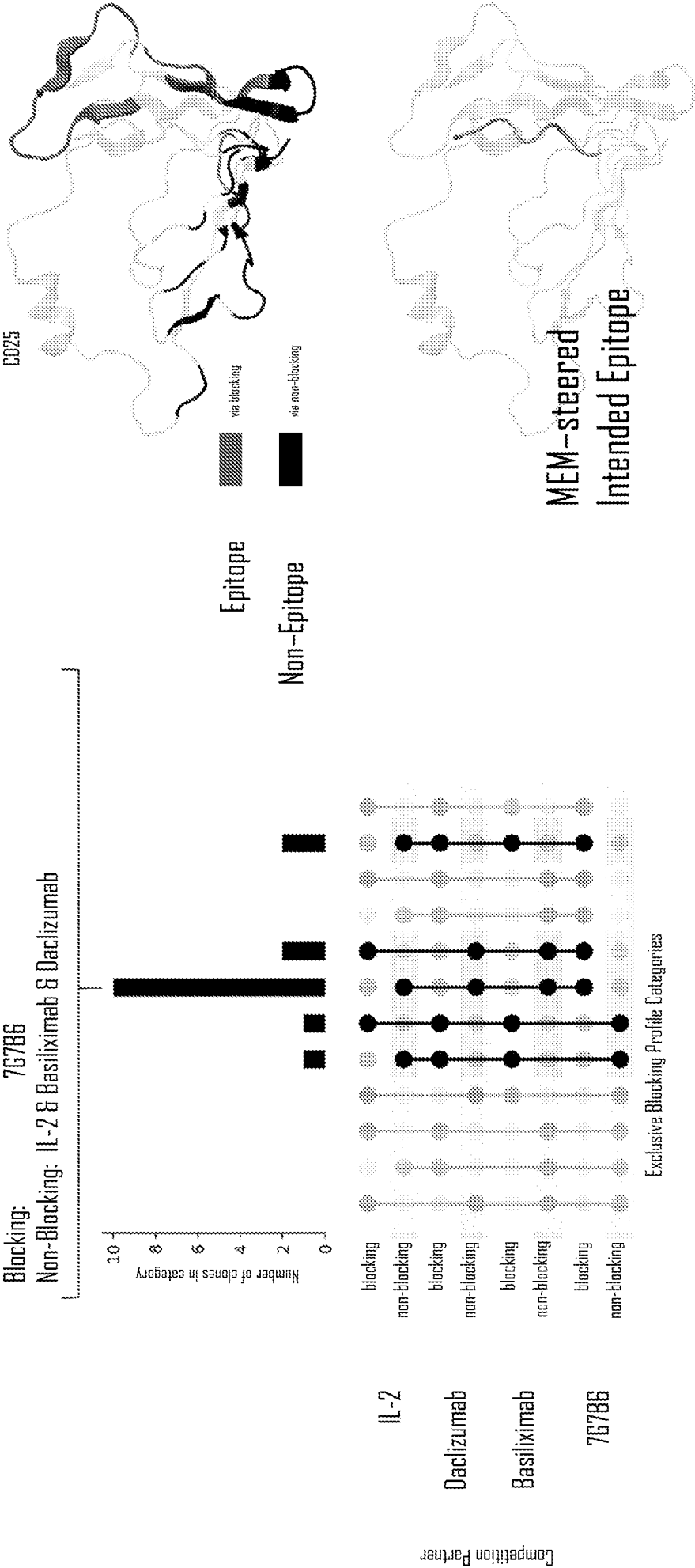


FIG. 21

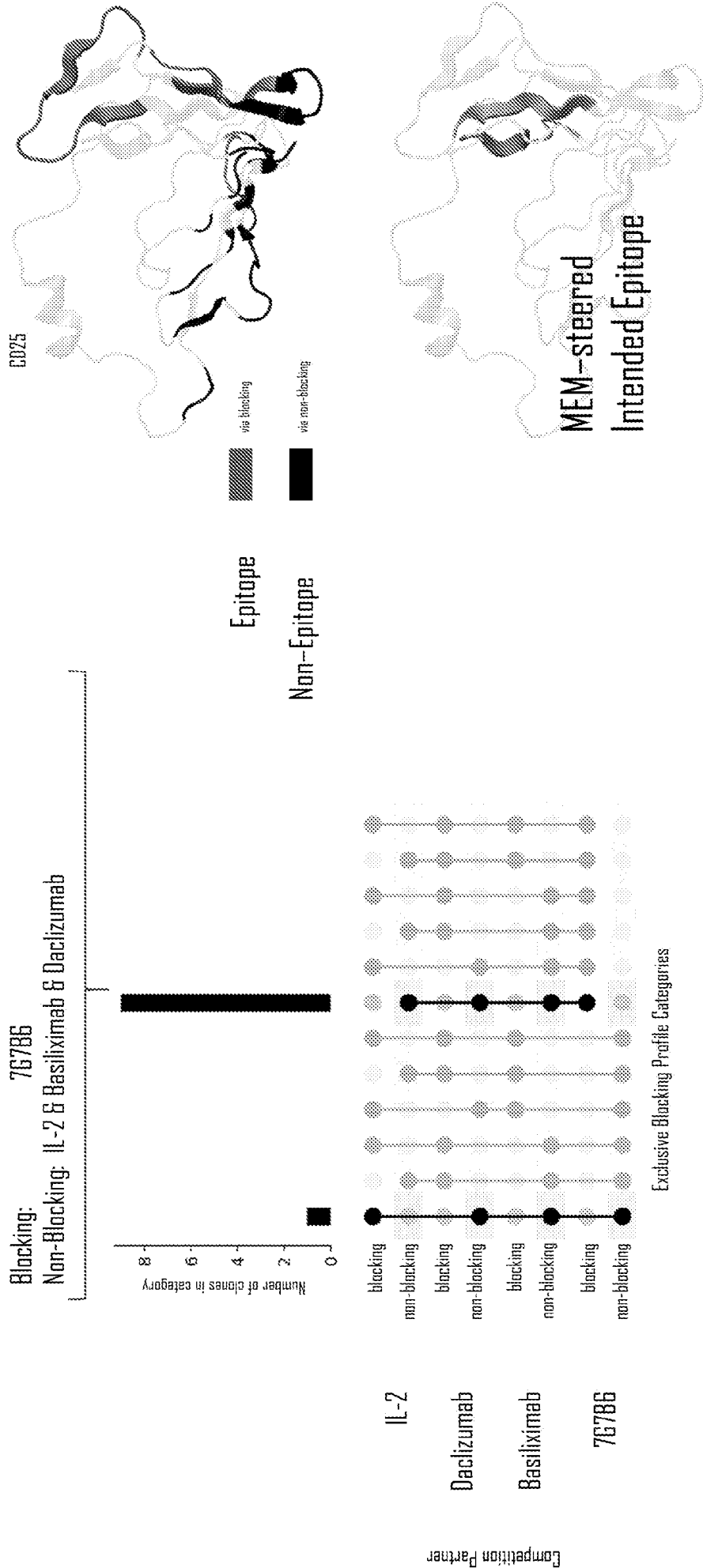


FIG. 22

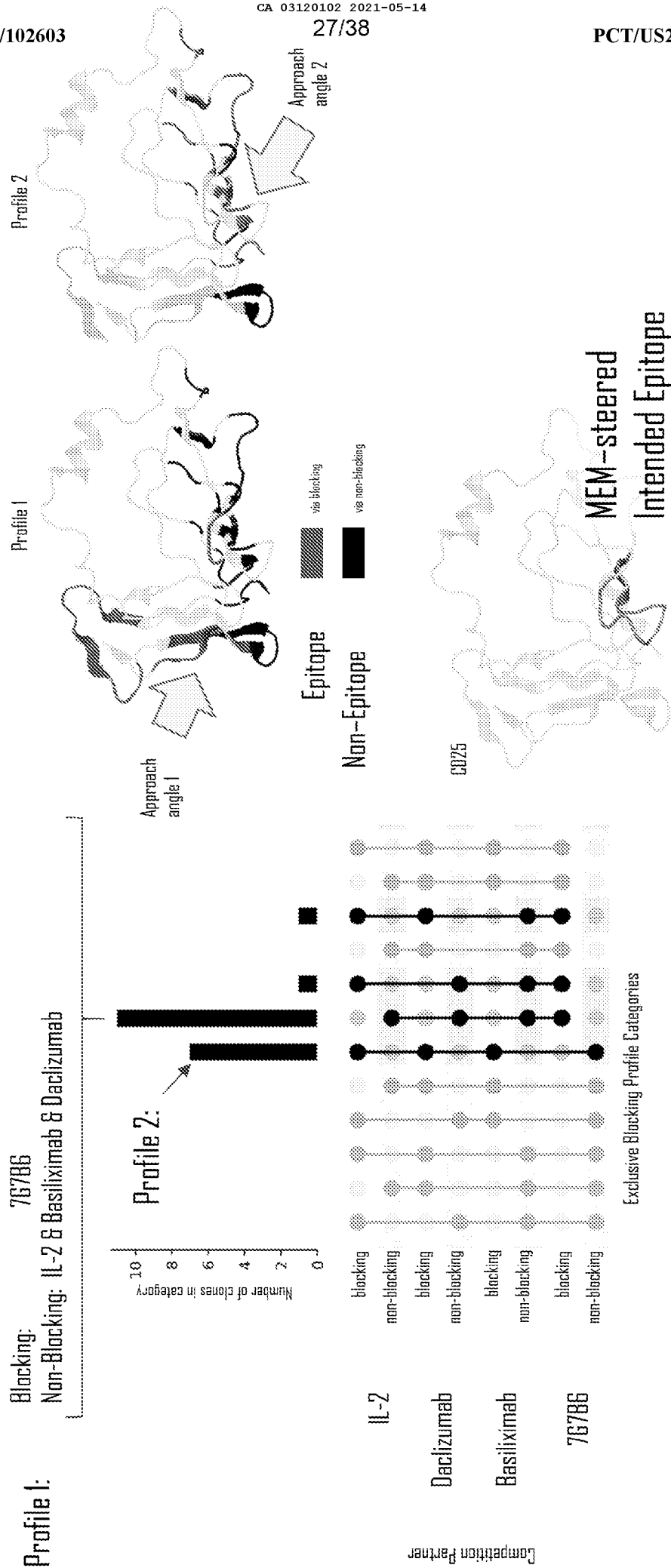


FIG. 23

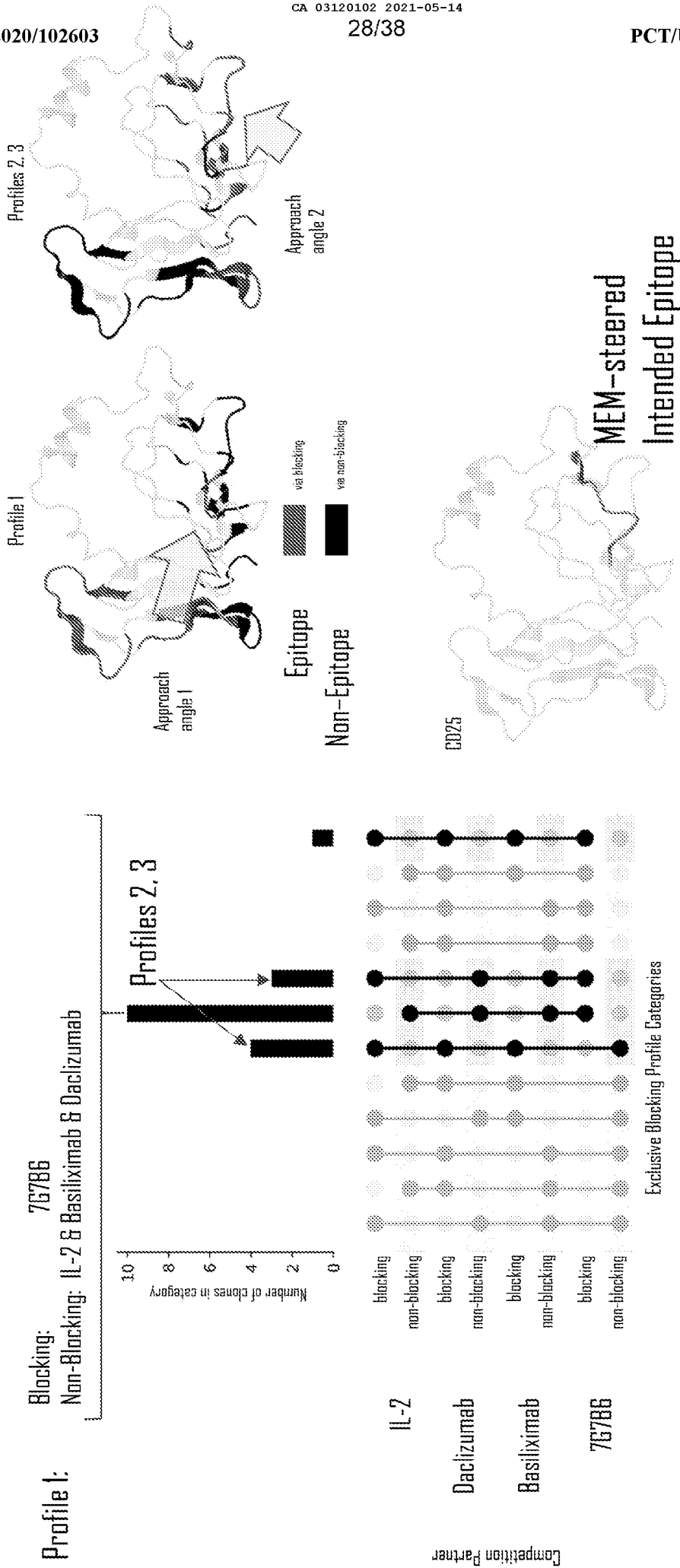


FIG. 24

Epitope(s) Covered	Double Alanine Mutation
1	D77A, Q79A
1	Q81A, T83A
1	D77A, N78A
2	T35A, Q151A
2	M39A, M147A
2, 3, 7	H33A, T35A
2, 3	K37A, Y149A
3, 4, 7	E30A, H33A
3, 4	D27A, E30A
4	R176A, Q179A
4	Q181A, I183A
5	E100A, R104A
5	Q101A, K105A
5	K102A, K105A
6	K169A, T171A
6	K174A, R176A
6	T175A, R176A
6	M170A, H172A
8	N70A, S71A
8	S72A, H73A
8	S74A, S75A
Basiximab, Daclizumab	L23A, D25A

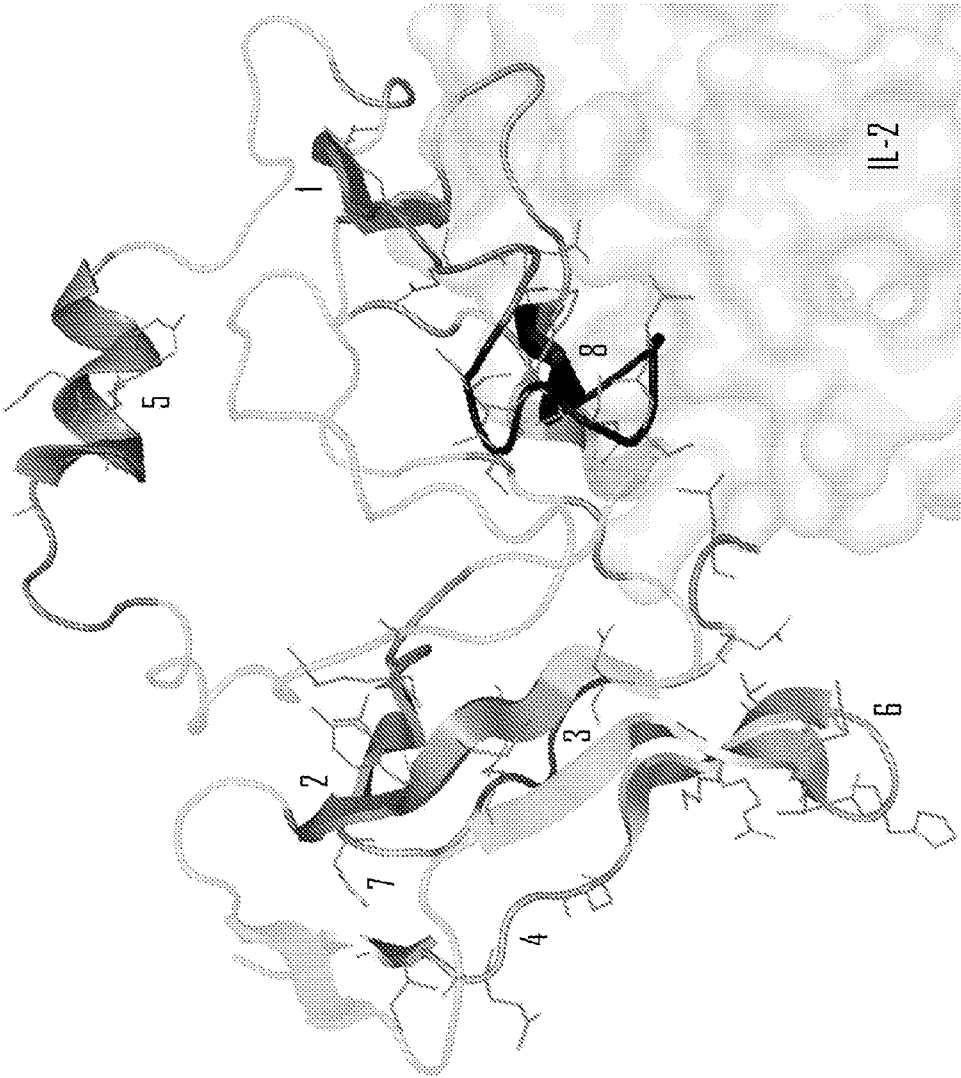


FIG. 25

CD25 Global Stability

Epitope Local Stability

Mutations	Mutant Global RMSD (Å)
K174A, R176A	2.3 ± 0.4
T175A, R176A	2.5 ± 0.8
M170A, H172A	2.1 ± 0.5
K169A, T171A	2.3 ± 0.6

Wild-Type Global RMSD
2.4 ± 0.6

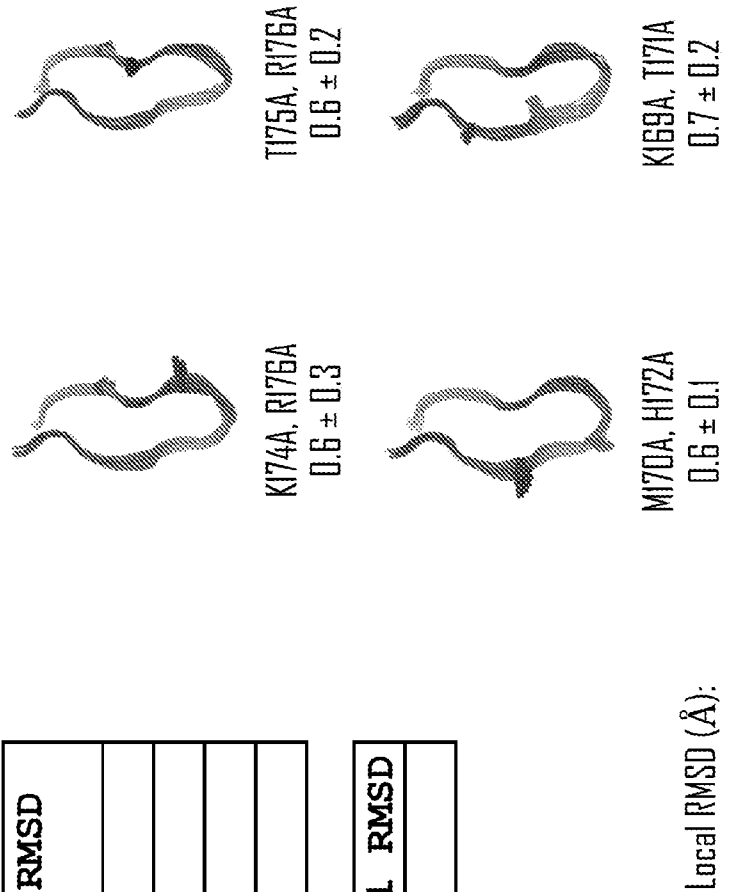


FIG. 26

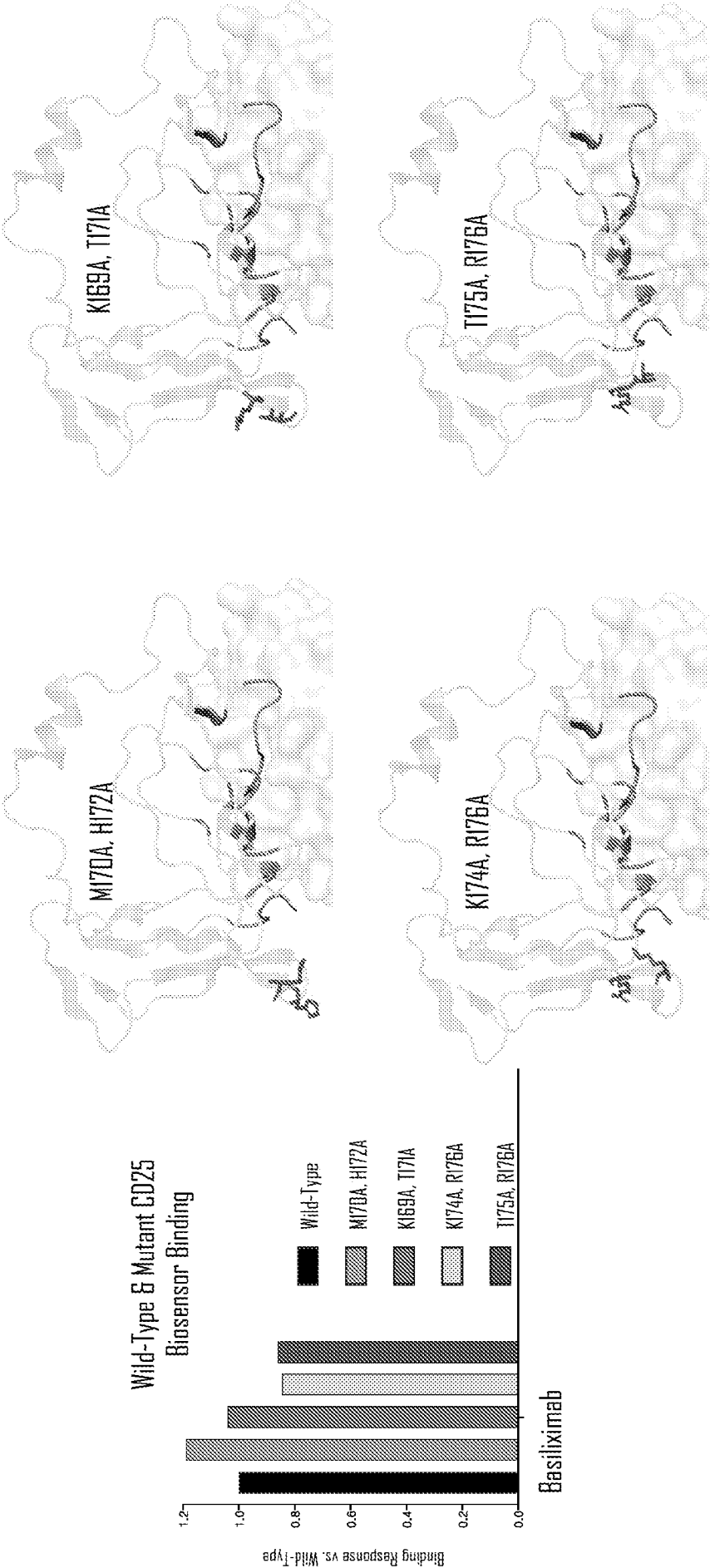


FIG. 27

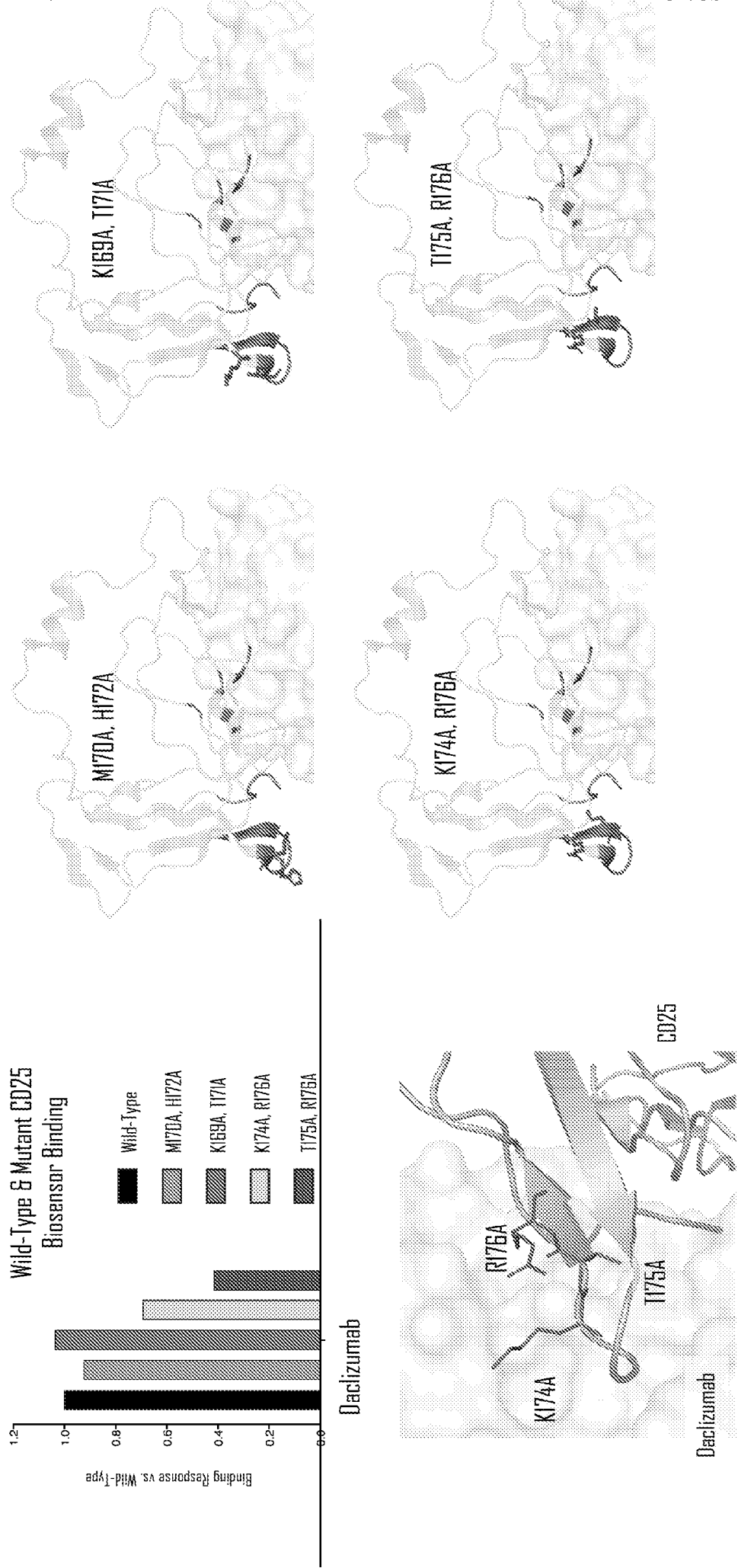


FIG. 28

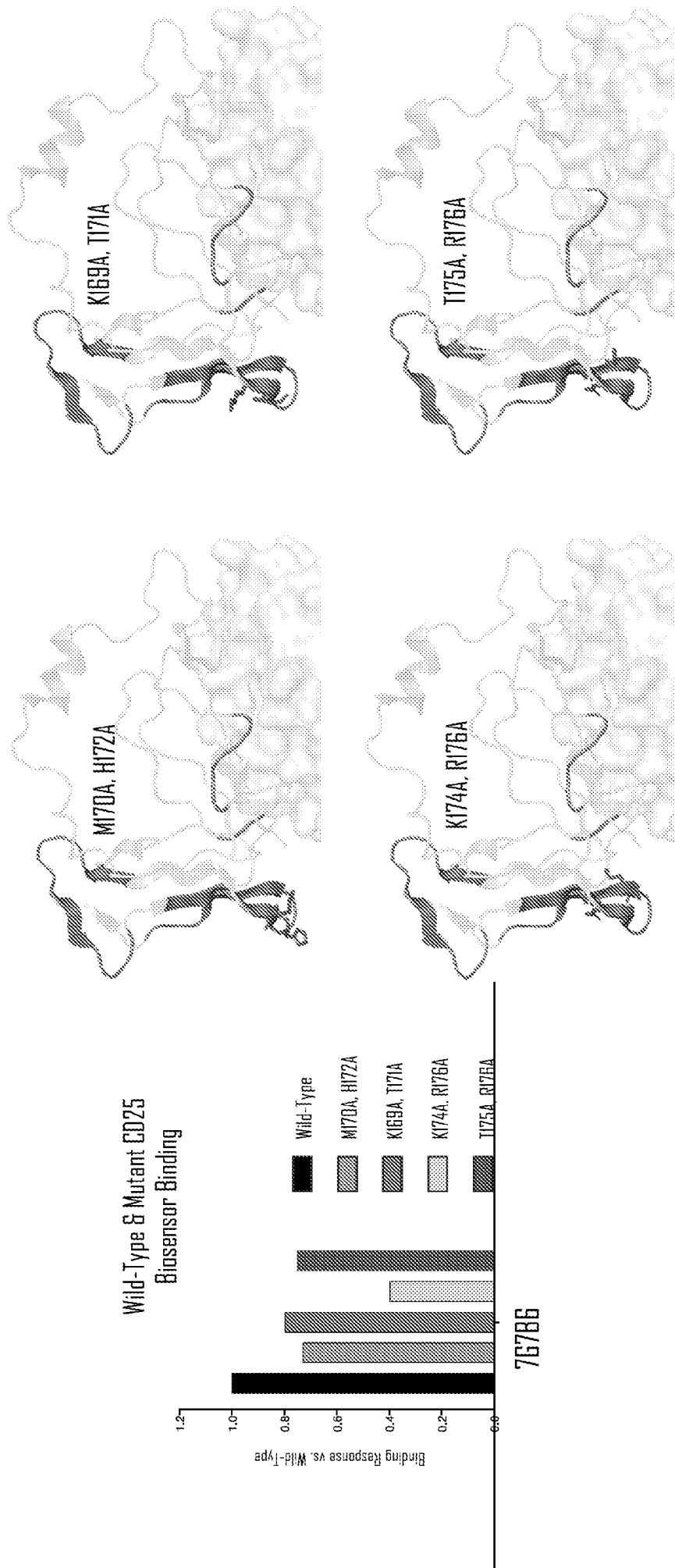


FIG. 29



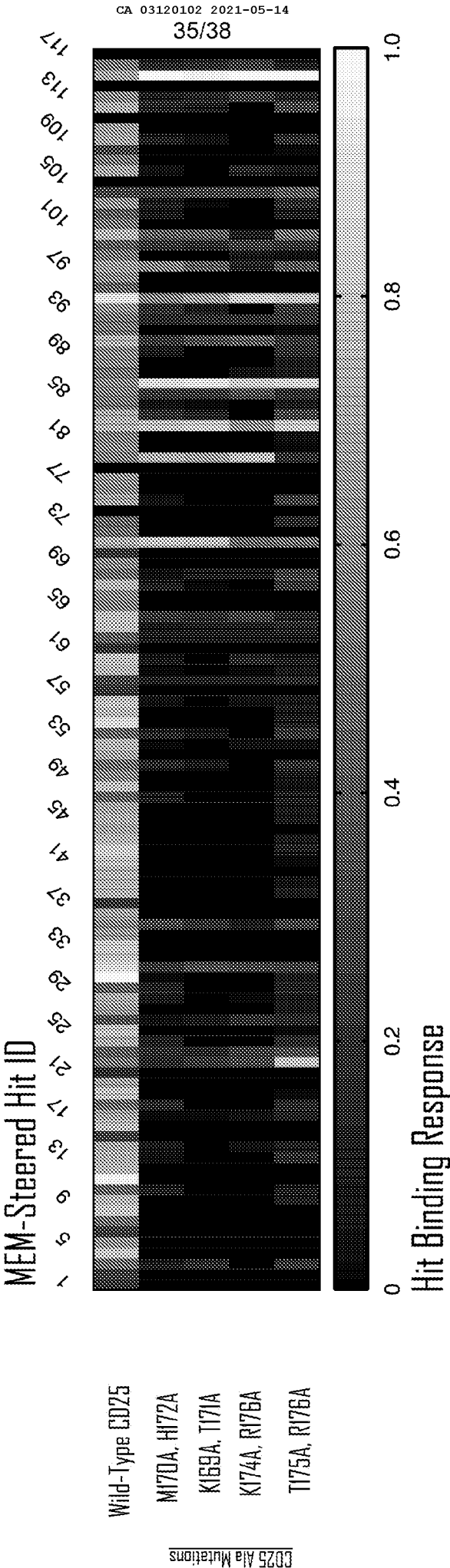


FIG. 31

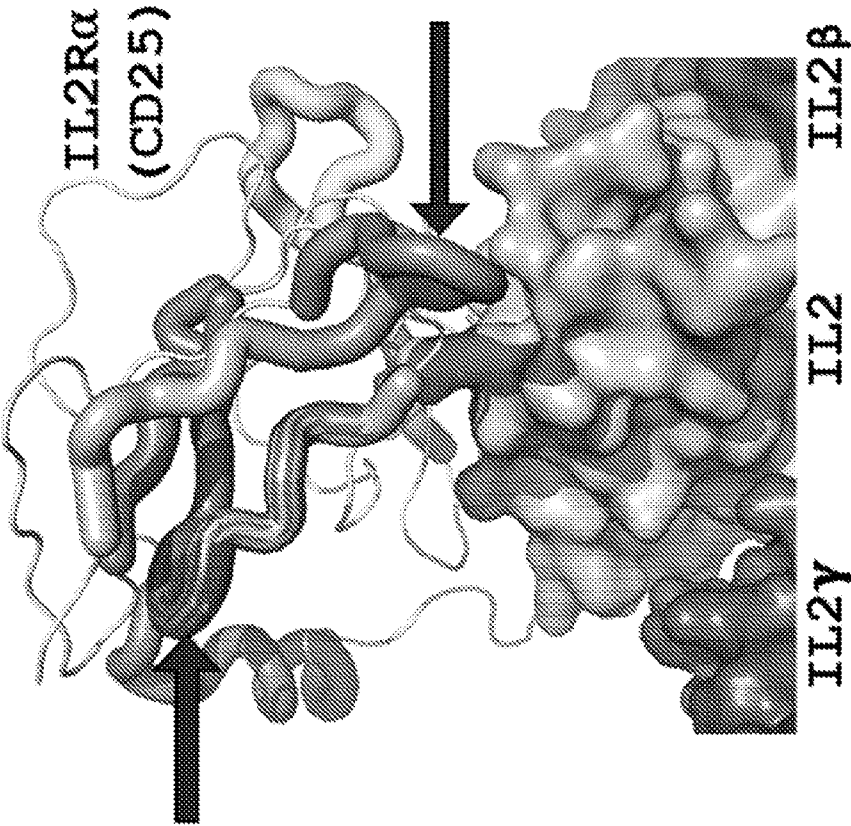


FIG. 32

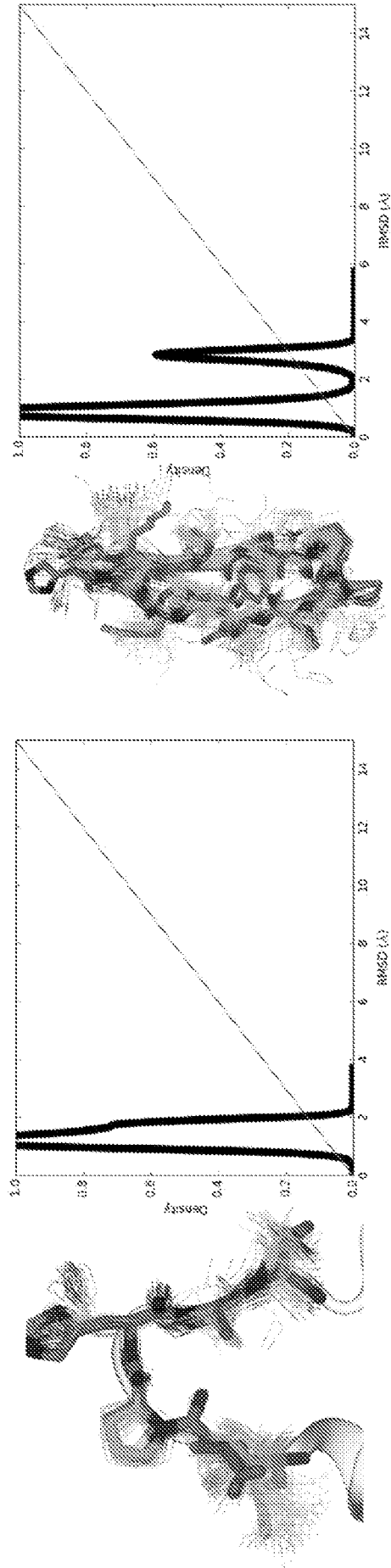


FIG. 33A

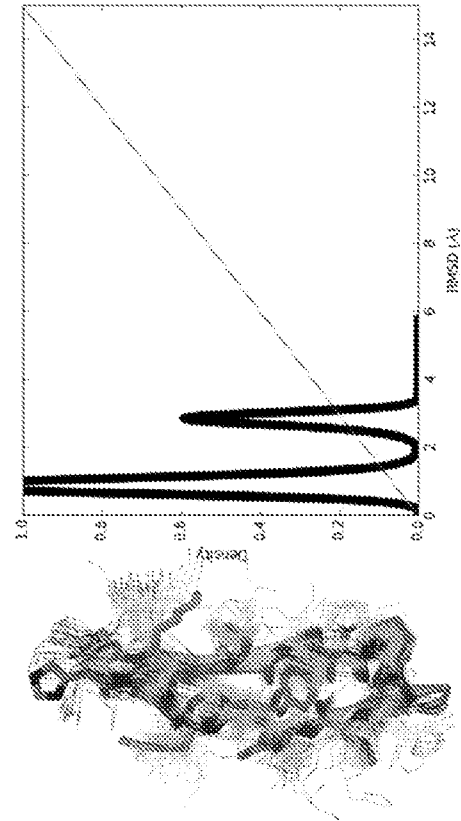


FIG. 33B

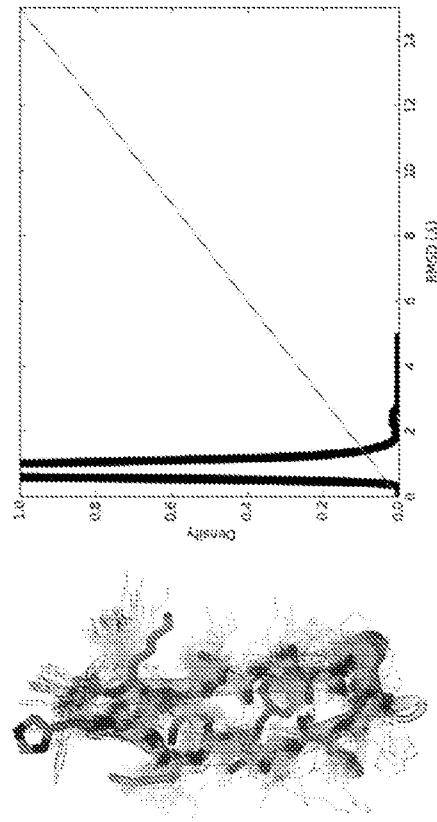


FIG. 33C

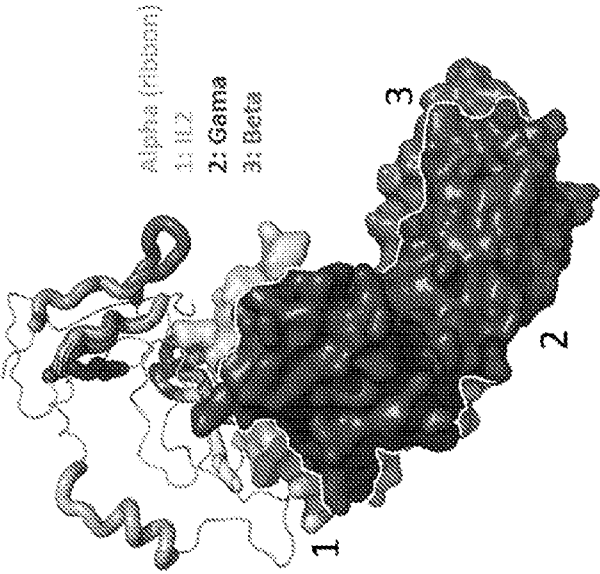


FIG. 34A

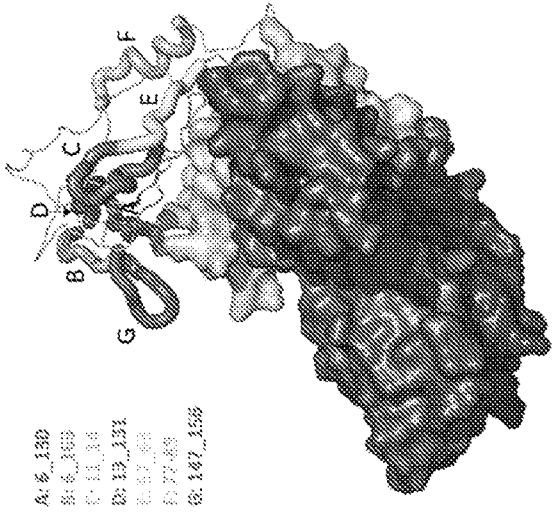


FIG. 34B

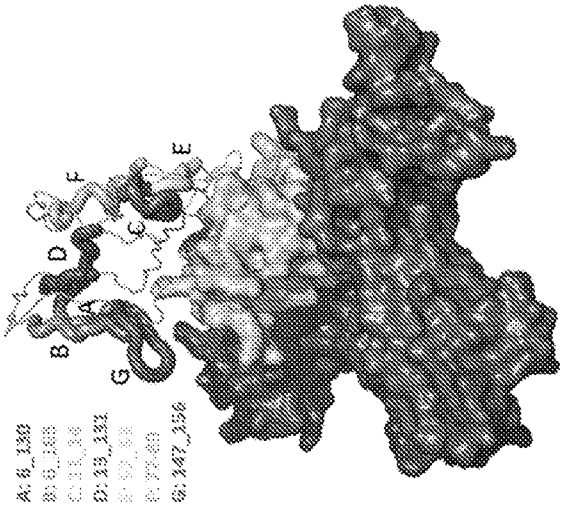


FIG. 34C

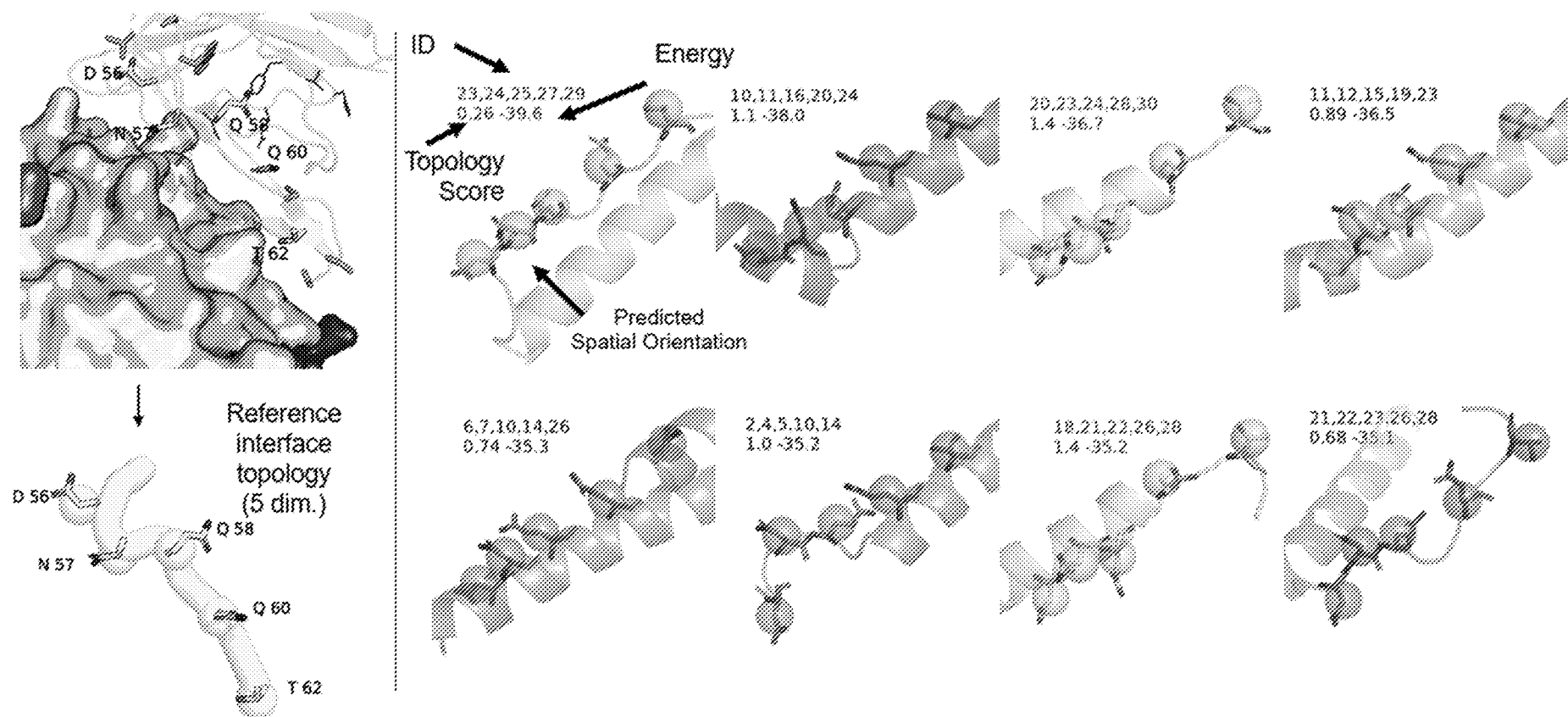


FIG. 4B