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(54) Title: MULTIFUNCTIONAL MOLECULES THAT BIND TO T CELLS AND USES THEREOF TO TREAT
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(57) Abrégé/Abstract:

Multifunctional molecules that include i) an antigen binding domain that binds to a TCR variable beta chain (TCRBV) antigen; and one, two or all of: (ii) an immune cell engager (e.g., chosen from an NK cell engager, a T cell engager, a B cell engager, a dendritic cell engager, or a macrophage cell engager); (iii) a cytokine molecule or cytokine inhibitor molecule; and/or (iv) a death receptor signal enhancer. Additionally, disclosed are nucleic acids encoding the same, methods of producing the aforesaid molecules, and methods of treating autoimmune diseases using the aforesaid molecules.



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(54) Title: MULTIFUNCTIONAL MOLECULES THAT BIND TO T CELLS AND USES THEREOF TO TREAT AUTOIMMUNE DISORDERS

(57) Abstract: Multifunctional molecules that include i) an antigen binding domain that binds to a TCR variable beta chain (TCRBV) antigen; and one, two or all of: (ii) an immune cell engager (e.g., chosen from an NK cell engager, a T cell engager, a B cell engager, a dendritic cell engager, or a macrophage cell engager); (iii) a cytokine molecule or cytokine inhibitor molecule; and/or (iv) a death receptor signal enhancer. Additionally, disclosed are nucleic acids encoding the same, methods of producing the aforesaid molecules, and methods of treating autoimmune diseases using the aforesaid molecules.

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JUMBO APPLICATIONS/PATENTS

THIS SECTION OF THE APPLICATION/PATENT CONTAINS MORE THAN ONE VOLUME

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MULTIFUNCTIONAL MOLECULES THAT BIND TO T CELLS AND USES THEREOF TO TREAT AUTOIMMUNE DISORDERS

RELATED APPLICATIONS

5 This application claims priority to U.S. Provisional Application 62/808,713 filed on February 21, 2019 and U.S. Provisional Application 62/957,045 filed on January 3, 2020, the entire contents of each of which are hereby incorporated by reference.

SEQUENCE LISTING

10 The instant application contains a Sequence Listing which has been submitted electronically in ASCII format and is hereby incorporated by reference in its entirety. Said ASCII copy, created on February 19, 2020, is named E2070-7024WO_SL.txt and is 1,519,578 bytes in size.

BACKGROUND

15 T cell mediated antigen recognition depends on the interaction of the T cell receptor (TCR) with the antigen-major histocompatibility complex (MHC). The heterodimeric TCRs consist of a combination of α and β chains ($\alpha\beta$ TCR) expressed by the majority of T cells, or $\gamma\delta$ chains ($\gamma\delta$ TCR) present only in about 1-5% of the T cells. A highly diverse TCR repertoire is a
20 fundamental property of an effective immune system. However, the immune repertoire can change greatly with the onset and progression of diseases, such as cancer, autoimmune, inflammatory, and infectious diseases.

 Autoimmunity may result from abnormal regulation of the immune system. This may be manifested by autoreactive TCR clones that attack a patient's own cells. There is a need for
25 improved therapies for autoimmune diseases.

SUMMARY OF THE INVENTION

 The disclosure relates, inter alia, to novel multispecific or multifunctional molecules that include (i) an antigen binding domain that binds to a TCR variable beta chain (TCRBV) antigen
30 on a T cell (e.g., a TCRBV antigen corresponding to a biased TCRBV clonotype); and one, two or all of: (ii) an immune cell engager (e.g., chosen from an NK cell engager, a T cell engager, a

B cell engager, a dendritic cell engager, or a macrophage cell engager); (iii) a cytokine molecule; and/or (iv) a stromal modifying moiety. The terms “multispecific” or “multifunctional” are used interchangeably herein.

Without wishing to be bound by theory, a TCR bias may exist in autoimmune diseases.

5 This bias may be associated with dominant autoreactive TCR clones responsible for disease or associated with symptoms. Re-balancing the TCR repertoire, e.g., by eliminating or depleting T cells comprising an autoreactive clonotype, may treat the associated autoimmune disease and/or reduce symptoms of the autoimmune disease. Accordingly, the multispecific or multifunctional molecules disclosed herein are expected to target (e.g., localize, bridge and/or activate) an
10 immune cell (e.g., an immune effector cell chosen from an NK cell, a T cell, a B cell, a dendritic cell or a macrophage), at a target cell (e.g., a T cell comprising a biased TCRBV clonotype or comprising a TCRBV antigen corresponding to a biased TCRBV clonotype). Increasing the proximity and/or activity of the immune cell using the multispecific molecules described herein is expected to enhance an immune response against the target cell (e.g., the T cell comprising a
15 TCRBV, e.g., TCRBV antigen (e.g., a TCRBV antigen corresponding to a biased TCRBV clonotype), thereby providing a more effective therapy (e.g., a more effective autoimmune disease therapy). Without being bound by theory, a targeted, localized immune response against the target cell (e.g., a T cell comprising a biased TCRBV clonotype, e.g., and not T cells not comprising the biased TCRBV clonotype) is believed to reduce the effects of systemic toxicity of
20 the multispecific molecules described herein. A targeted immune response against the autoreactive T cell population that targets non-autoreactive T cells to a lesser degree (e.g., does not target non-autoreactive T cells) is believed to have fewer deleterious effects than systemic ablation of all T cells.

Accordingly, provided herein are, *inter alia*, multispecific molecules (e.g., multispecific
25 or multifunctional antibody molecules) that include the aforesaid moieties, nucleic acids encoding the same, methods of producing the aforesaid molecules, and methods of treating autoimmune disease using the aforesaid molecules. Also provided herein are anti-TCR β V antibody molecules, nucleic acids encoding the same, methods of producing the aforesaid molecules, and methods of treating autoimmune disease using the anti-TCR β V antibody
30 molecules.

Further provided are methods for depletion (e.g., in vivo depletion) of biased TCRBV clonotypes, e.g., in the context of autoimmune disease with a multispecific molecule or an anti-TCR β V antibody molecule. In some embodiments, the method involves identifying in a patient a clonal bias in TCRBV usage, e.g., associated with the autoreactive subpopulation, and responsive to this analysis administering a multifunctional molecule targeted to the TCRBV antigen corresponding to the biased TCRBV clonotype to decrease, e.g., eliminate, the clonal bias and promote, e.g., establish, a normal TCRBV distribution.

Accordingly, in one aspect, the disclosure features a multifunctional molecule, comprising:

- (i) a first antigen binding domain that binds to, e.g., selectively binds to, T cell receptor variable beta (TCRBV), e.g., a TCRBV antigen,
and
- (ii) one, two, or all of:
 - (a) an immune cell engager chosen from an NK cell engager, a T cell engager, a B cell engager, a dendritic cell engager, or a macrophage cell engager;
 - (b) a cytokine molecule or cytokine inhibitor molecule; and
 - (c) a death receptor signal engager.

In some embodiments, first antigen binding domain comprises an anti-TCR β V antibody molecule, e.g., as described herein.

In another aspect, the disclosure features a nucleic acid molecule encoding a multifunctional molecule disclosed herein.

In another aspect, the disclosure features a vector, e.g., an expression vector, comprising the nucleic acid molecules disclosed herein.

In another aspect, the disclosure features a host cell comprising a nucleic acid molecule or vector disclosed herein.

In another aspect, the disclosure features a method of making, e.g., producing, a multifunctional molecule disclosed herein, comprising culturing a host cell disclosed herein under suitable conditions, e.g., conditions suitable for gene expression and/or homo- or heterodimerization.

In another aspect, the disclosure features a pharmaceutical composition comprising a multifunctional molecule disclosed herein.

In another aspect, the disclosure features a method of treating a TCR bias, comprising administering to a subject in need thereof a multifunctional molecule disclosed herein, wherein the multifunctional molecule is administered in an amount effective to treat the TCR bias.

5 In another aspect, the disclosure features a method of treating an autoimmune disease (e.g., an autoimmune disease associated with a TCR bias), comprising administering to a subject in need thereof a multifunctional molecule disclosed herein, wherein the multifunctional molecule is administered in an amount effective to treat the autoimmune disease.

10 In another aspect, the disclosure features a method of identifying a subject in need of treatment for TCR bias or an autoimmune disease (e.g., associated with a TCR bias) using a multifunctional molecule disclosed herein, comprising determining (e.g., directly determining or indirectly determining, e.g., obtaining information regarding) whether a subject has a TCR bias (e.g., a biased TCRBV clonotype) and/or an autoimmune disease associated with said bias, wherein:

15 responsive to determining that the subject has a TCR bias (e.g., a biased TCRBV clonotype) and/or an autoimmune disease associated with said bias, identifying the subject as a candidate for treatment using a multifunctional molecule comprising an antigen binding domain that binds to the TCRBV antigen.

20 In another aspect, the disclosure features a method of evaluating a subject in need of treatment for a TCR bias (e.g., a biased TCRBV clonotype) and/or an autoimmune disease associated with said bias, comprising determining (e.g., directly determining or indirectly determining, e.g., obtaining information regarding) whether a subject has a TCR bias (e.g., a biased TCRBV clonotype).

25 In yet another aspect, disclosed herein is a method of treating an autoimmune disease (e.g., an autoimmune disease associated with a TCR bias), in a subject in need thereof, comprising administering to said subject an effective amount, *e.g.*, a therapeutically effective amount, of an antibody molecule which binds (e.g., specifically binds) to a T cell receptor beta variable region (TCR β V) (“anti-TCR β V antibody molecule”), thereby treating the disorder.

30 In another aspect, the disclosure provides a method of depleting a population of T cells in a subject having an autoimmune disorder (e.g., an autoimmune disease associated with a TCR

bias), comprising, contacting the T cell population with an effective amount of an antibody molecule which binds (e.g., specifically binds) to a T cell receptor beta variable region (TCR β V) (“anti-TCR β V antibody molecule”).

In some embodiments, the contacting occurs in vivo or in vitro.

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In some embodiments, the anti-TCR β V antibody molecule is not an antibody molecule disclosed in US Patent 5,861,155.

In some embodiments, the anti-TCR β V antibody molecule binds to TCR β V12 with an affinity and/or binding specificity that is less than (e.g., less than about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90% or about 2-, 5-, or 10- fold) the affinity and/or binding specificity of the 16G8 murine antibody or a humanized version thereof as described in US Patent 5,861,155.

In some embodiments, the anti-TCR β V antibody molecule binds to TCR β V12 with an affinity and/or binding specificity that is greater than (e.g., greater than about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90% or about 2-, 5-, or 10- fold) the affinity and/or binding specificity of the 16G8 murine antibody or a humanized version thereof as described in US Patent 5,861,155.

In some embodiments, the anti-TCR β V antibody molecule binds to TCR β V5-5*01 or TCR β V5-1*01 with an affinity and/or binding specificity that is greater than (e.g., greater than about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90% or about 2-, 5-, or 10- fold) the affinity and/or binding specificity of the TM23 murine antibody or a humanized version thereof as described in US Patent 5,861,155.

In some embodiments, the anti-TCR β V antibody molecule binds to TCR β V5-5*01 or TCR β V5-1*01 with an affinity and/or binding specificity that is greater than (e.g., greater than about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90% or about 2-, 5-, or 10- fold) the affinity and/or binding specificity of the TM23 murine antibody or a humanized version thereof as described in US Patent 5,861,155.

In some embodiments, the anti-TCR β V antibody molecule comprises an Fc region, e.g., an Fc region having effector function, e.g., antibody dependent cell-mediated cytotoxicity (ADCC), Antibody-dependent cellular phagocytosis (ADCP) and/or complement dependent cytotoxicity (CDC).

In some embodiments, the anti-TCR β V antibody molecule, the anti-TCR β V antibody molecule comprises an Fc region with enhanced effector function, e.g., as compared to a wildtype Fc region.

5 In some embodiments, the anti-TCR β V antibody molecule, the anti-TCR β V antibody molecule comprises a human IgG1 region or a human IgG4 region.

In another aspect, the disclosure features a nucleic acid molecule encoding an anti-TCR β V antibody molecule disclosed herein.

10 In another aspect, the disclosure features a vector, e.g., an expression vector, comprising the nucleic acid molecules disclosed herein.

In another aspect, the disclosure features a host cell comprising a nucleic acid molecule or vector disclosed herein.

15 In another aspect, the disclosure features a method of making, e.g., producing, an anti-TCR β V antibody molecule disclosed herein, comprising culturing a host cell disclosed herein under suitable conditions, e.g., conditions suitable for gene expression and/or homo- or heterodimerization.

In another aspect, the disclosure features a pharmaceutical composition comprising an anti-TCR β V antibody molecule disclosed herein.

20 Additional features of any of the aforesaid multifunctional molecules, nucleic acids, vectors, host cells, or methods include one or more of the following enumerated embodiments.

Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, many equivalents to the specific embodiments of the invention described herein. Such equivalents are intended to be encompassed by the following enumerated
25 embodiments.

Enumerated Embodiments

1. A multifunctional molecule, comprising:

30 (i) a first antigen binding domain that binds to, e.g., selectively binds to, T cell receptor variable beta (TCRBV), e.g., a TCRBV antigen,

and

(ii) one, two, or all of:

(a) an immune cell engager chosen from an NK cell engager, a T cell engager, a B cell engager, a dendritic cell engager, or a macrophage cell engager;

5 (b) a cytokine molecule or cytokine inhibitor molecule; and

(c) a death receptor signal engager.

2. The multifunctional molecule of embodiment 1, wherein the TCRBV antigen corresponds to a biased TCRBV clonotype, e.g., present in a subject, e.g., a patient, e.g., a subject or a patient with an autoimmune disease.

10

3. The multifunctional molecule of any preceding embodiment, wherein the multifunctional molecule:

(i) binds specifically to a TCRBV antigen, e.g., the same or similar epitope as the epitope recognized by an anti-TCRBV antibody molecule as described herein;

15

(ii) shows the same or similar binding affinity or specificity, or both, as an anti-TCRBV antibody molecule as described herein;

(iii) inhibits, e.g., competitively inhibits, the binding of an anti-TCRBV antibody molecule as described herein;

(iv) binds the same or an overlapping epitope with an anti-TCRBV antibody molecule as described herein; or

20

(v) competes for binding, and/or binds the same epitope, with an anti-TCRBV antibody molecule as described herein.

25 4. The multifunctional molecule of embodiment 3, wherein the antigen binding domain comprises one or more CDRs, framework regions, variable domains, heavy or light chains, or an antigen binding domain chosen from Tables 13 or 14, or a sequence substantially identical thereto.

30 5. The multifunctional molecule of any of embodiments 1-4, wherein the antigen binding domain specifically binds to TCR β V6 (e.g., TCR β V6-5*01).

6. The multifunctional molecule of embodiment 5, wherein the antigen binding domain comprises at least one (e.g., one, two, three, or four) variable region or an antigen-binding fragment thereof, from Antibody A-H.1 or Antibody A-H.2, or as described in **Table 1A**, or encoded by the nucleotide sequence in **Table 1A**, or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences.

7. The multifunctional molecule of either of embodiments 5 or 6, wherein the antigen binding domain comprises at least one, two, or three CDRs (or collectively all of the CDRs) from a heavy chain variable region comprising an amino acid sequence shown in **Table 1A**, or encoded by a nucleotide sequence shown in **Table 1A** (or a sequence with one, two, three, four, five, six or more changes, *e.g.*, amino acid substitutions or deletions, relative to the amino acid sequence shown in **Table 1A**, or encoded by a nucleotide sequence shown in **Table 1A**).

8. The multifunctional molecule of any of embodiments 5-7, wherein the antigen binding domain comprises at least one, two, or three CDRs (or collectively all of the CDRs) from a light chain variable region comprising an amino acid sequence shown in **Table 1A**, or encoded by a nucleotide sequence shown in **Table 1A** (or a sequence with one, two, three, four, five, six or more changes, *e.g.*, amino acid substitutions or deletions, relative to the amino acid sequence shown in **Table 1A**, or encoded by a nucleotide sequence shown in **Table 1A**).

9. The multifunctional molecule of any of embodiments 5-8, wherein the antigen binding domain comprises:

(i) one, two or all of a light chain complementarity determining region 1 (LC CDR1), a light chain complementarity determining region 2 (LC CDR2), and a light chain complementarity determining region 3 (LC CDR3) of SEQ ID NO: 2, SEQ ID NO: 10 or SEQ ID NO: 11, and/or

(ii) one, two or all of a heavy chain complementarity determining region 1 (HC CDR1), heavy chain complementarity determining region 2 (HC CDR2), and a heavy chain complementarity determining region 3 (HC CDR3) of SEQ ID NO: 1 or SEQ ID NO: 9.

10. The multifunctional molecule of any of embodiments 5-8, wherein the antigen binding domain comprises a LC CDR1, LC CDR2, and LC CDR3 of SEQ ID NO: 2, and a HC CDR1, HC CDR2, and HC CDR3 of SEQ ID NO: 1.

5 11. The multifunctional molecule of any of embodiments 5-8, wherein the antigen binding domain comprises a LC CDR1, LC CDR2, and LC CDR3 of SEQ ID NO: 10, and a HC CDR1, HC CDR2, and HC CDR3 of SEQ ID NO: 9.

12. The multifunctional molecule of any of embodiments 5-8, wherein the antigen binding domain comprises a LC CDR1, LC CDR2, and LC CDR3 of SEQ ID NO: 11, and a HC CDR1, HC CDR2, and HC CDR3 of SEQ ID NO: 9.

10 13. The multifunctional molecule of any of embodiments 5-8, wherein the antigen binding domain comprises:

(i) a LC CDR1 amino acid sequence of SEQ ID NO: 6, a LC CDR2 amino acid sequence of SEQ ID NO: 7, or a LC CDR3 amino acid sequence of SEQ ID NO: 8; and/or

15 (ii) a HC CDR1 amino acid sequence of SEQ ID NO: 3, a HC CDR2 amino acid sequence of SEQ ID NO: 4, or a HC CDR3 amino acid sequence of SEQ ID NO: 5.

14. The multifunctional molecule of any of embodiments 5-8, wherein the antigen binding domain comprises:

20 (i) a light chain variable region (VL) comprising a LC CDR1 amino acid sequence of SEQ ID NO: 6, a LC CDR2 amino acid sequence of SEQ ID NO: 7, or a LC CDR3 amino acid sequence of SEQ ID NO: 8; and/or

(ii) a heavy chain variable region (VH) comprising a HC CDR1 amino acid sequence of SEQ ID NO: 3, a HC CDR2 amino acid sequence of SEQ ID NO: 4, or a HC CDR3 amino acid sequence of SEQ ID NO: 5.

25 15. The multifunctional molecule of any of embodiments 5-8, wherein the antigen binding domain comprises:

(i) a LC CDR1 amino acid sequence of SEQ ID NO: 51, a LC CDR2 amino acid sequence of SEQ ID NO: 52, or a LC CDR3 amino acid sequence of SEQ ID NO: 53; and/or

(ii) a HC CDR1 amino acid sequence of SEQ ID NO: 45, a HC CDR2 amino acid sequence of SEQ ID NO: 46, or a HC CDR3 amino acid sequence of SEQ ID NO: 47.

30 16. The multifunctional molecule of any of embodiments 5-8, wherein the antigen binding domain comprises:

(i) a light chain variable region (VL) comprising a LC CDR1 amino acid sequence of SEQ ID NO: 51, a LC CDR2 amino acid sequence of SEQ ID NO: 52, or a LC CDR3 amino acid sequence of SEQ ID NO: 53; and/or

(ii) a heavy chain variable region (VH) comprising a HC CDR1 amino acid sequence of SEQ ID NO: 45, a HC CDR2 amino acid sequence of SEQ ID NO: 46, or a HC CDR3 amino acid sequence of SEQ ID NO: 47.

17. The multifunctional molecule of any of embodiments 5-8, wherein the antigen binding domain comprises:

(i) a LC CDR1 amino acid sequence of SEQ ID NO: 54, a LC CDR2 amino acid sequence of SEQ ID NO: 55, or a LC CDR3 amino acid sequence of SEQ ID NO: 56; and/or

(ii) a HC CDR1 amino acid sequence of SEQ ID NO: 48, a HC CDR2 amino acid sequence of SEQ ID NO: 49, or a HC CDR3 amino acid sequence of SEQ ID NO: 50.

18. The multifunctional molecule of any of embodiments 5-8, wherein the antigen binding domain comprises:

(i) a light chain variable region (VL) comprising a LC CDR1 amino acid sequence of SEQ ID NO: 54, a LC CDR2 amino acid sequence of SEQ ID NO: 55, or a LC CDR3 amino acid sequence of SEQ ID NO: 56; and/or

(ii) a heavy chain variable region (VH) comprising a HC CDR1 amino acid sequence of SEQ ID NO: 48, a HC CDR2 amino acid sequence of SEQ ID NO: 49, or a HC CDR3 amino acid sequence of SEQ ID NO: 50.

19. The multifunctional molecule of any of embodiments 5-18, wherein the antigen binding domain comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) of Antibody A-H.1 or Antibody A-H.2, *e.g.*, as shown in **FIG. 1B, e.g., of SEQ ID NOs: 2, 10, or 11.**

20. The multifunctional molecule of any of embodiments 5-19, wherein the antigen binding domain comprises a light chain variable region (VL) comprising a light chain framework region 2 (VLFWR2) of Antibody A-H.1 or Antibody A-H.2, *e.g.*, as shown in **FIG. 1B, e.g., of SEQ ID NOs: 2, 10, or 11.**

21. The multifunctional molecule of any of embodiments 5-20, wherein the antigen binding domain comprises a light chain variable region (VL) comprising a light chain framework

region 3 (VLFWR3) of Antibody A-H.1 or Antibody A-H.2, *e.g.*, as shown in **FIG. 1B, e.g., of SEQ ID NOs: 2, 10, or 11.**

22. The multifunctional molecule of any of embodiments 5-21, wherein the antigen binding domain comprises a light chain variable region (VL) comprising a light chain framework region 4 (VLFWR4) of Antibody A-H.1 or Antibody A-H.2, *e.g.*, as shown in **FIG. 1B, e.g., of SEQ ID NOs: 2, 10, or 11.**

23. The multifunctional molecule of any of embodiments 5-22, wherein the antigen binding domain comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1), a light chain framework region 2 (VLFWR2), a light chain framework region 3 (VLFWR3), and a light chain framework region 4 (VLFWR4) **of SEQ ID NO: 2.**

24. The multifunctional molecule of any of embodiments 5-22, wherein the antigen binding domain comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1), a light chain framework region 2 (VLFWR2), a light chain framework region 3 (VLFWR3), and a light chain framework region 4 (VLFWR4) **of SEQ ID NO: 10.**

25. The multifunctional molecule of any of embodiments 5-22, wherein the antigen binding domain comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1), a light chain framework region 2 (VLFWR2), a light chain framework region 3 (VLFWR3), and a light chain framework region 4 (VLFWR4) **of SEQ ID NO: 11.**

26. The multifunctional molecule of any of embodiments 5-25, wherein the antigen binding domain comprises a light chain variable domain comprising a framework region, *e.g.*, framework region 1 (VLFWR1), comprising a change, *e.g.*, a substitution (*e.g.*, a conservative substitution) at position 10 according to Kabat numbering, wherein the change at position 10 is to Phenylalanine, *e.g.*, a Serine to Phenylalanine substitution.

27. The multifunctional molecule of any of embodiments 5-26, wherein the antigen binding domain comprises a light chain variable domain comprising a framework region, *e.g.*, framework region 2 (VLFWR2), comprising one or more (*e.g.*, one or two) changes, *e.g.*, substitutions (*e.g.*, a conservative substitution), at positions selected from 36 and 46 according to Kabat numbering, wherein the change at position 36 is to Histidine, *e.g.*, a Tyrosine to Histidine substitution, and the change at position 46 is to Alanine, *e.g.*, an Arginine to Alanine substitution.

28. The multifunctional molecule of any of embodiments 5-27, wherein the antigen binding domain comprises a light chain variable domain comprising a framework region, *e.g.*, framework region 3 (VLFWR3), comprising a change, *e.g.*, substitution (*e.g.*, a conservative substitution), at position 87 according to Kabat numbering, wherein the change at position 87 is to Phenylalanine, *e.g.*, a Tyrosine to Phenylalanine substitution.

29. The multifunctional molecule of any of embodiments 5-28, wherein the antigen binding domain comprises a light chain variable domain comprising (a) a framework region 1 (VLFWR1) comprising a Phenylalanine at position 10, *e.g.*, a substitution at position 10 according to Kabat numbering, *e.g.*, a Serine to Phenylalanine substitution; (b) a framework region 2 (VLFWR2) comprising a Histidine at position 36, *e.g.*, a substitution at position 36 according to Kabat numbering, *e.g.*, a Tyrosine to Histidine substitution, and a Alanine at position 46, *e.g.*, a substitution at position 46 according to Kabat numbering, *e.g.*, a Arginine to Alanine substitution; and (c) a framework region 3 (VLFWR3) comprising a Phenylalanine at position 87, *e.g.*, a substitution at position 87 according to Kabat numbering, *e.g.*, a Tyrosine to Phenylalanine substitution, *e.g.*, as shown in the amino acid sequence of SEQ ID NO: 10.

30. The multifunctional molecule of any of embodiments 5-28, wherein the antigen binding domain comprises a light chain variable domain comprising (a) a framework region 2 (FR2) comprising a Histidine at position 36, *e.g.*, a substitution at position 36 according to Kabat numbering, *e.g.*, a Tyrosine to Histidine substitution, and a Alanine at position 46, *e.g.*, a substitution at position 46 according to Kabat numbering, *e.g.*, a Arginine to Alanine substitution; and (b) a framework region 3 (FR3) comprising a Phenylalanine at position 87, *e.g.*, a substitution at position 87 according to Kabat numbering, *e.g.*, a Tyrosine to Phenylalanine substitution, *e.g.*, as shown in the amino acid sequence of SEQ ID NO: 11.

31. The multifunctional molecule of any of embodiments 5-30, wherein the antigen binding domain comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) of Antibody A-H.1 or Antibody A-H.2, *e.g.*, as shown in **FIG. 1A, e.g., of SEQ ID NOs: 1 or 9.**

32. The multifunctional molecule of any of embodiments 5-31, wherein the antigen binding domain comprises a heavy chain variable region (VH) comprising a heavy chain framework region 2 (VHFWR2) of Antibody A-H.1 or Antibody A-H.2, *e.g.*, as shown in **FIG. 1A, e.g., of SEQ ID NOs: 1 or 9.**

5 33. The multifunctional molecule of any of embodiments 5-32, wherein the antigen binding domain comprises a heavy chain variable region (VH) comprising a heavy chain framework region 3 (VHFWR3) of Antibody A-H.1 or Antibody A-H.2, *e.g.*, as shown in **FIG. 1A, e.g., of SEQ ID NOs: 1 or 9.**

10 34. The multifunctional molecule of any of embodiments 5-33, wherein the antigen binding domain comprises a heavy chain variable region (VH) comprising a heavy chain framework region 4 (VHFWR4) of Antibody A-H.1 or Antibody A-H.2, *e.g.*, as shown in **FIG. 1A, e.g., of SEQ ID NOs: 1 or 9.**

15 35. The multifunctional molecule of any of embodiments 5-34, wherein the antigen binding domain comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1), a heavy chain framework region 2 (VHFWR2), a heavy chain framework region 3 (VHFWR3), and a heavy chain framework region 4 (VHFWR4) **of SEQ ID NO: 1.**

20 36. The multifunctional molecule of any of embodiments 5-34, wherein the antigen binding domain comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1), a heavy chain framework region 2 (VHFWR2), a heavy chain framework region 3 (VHFWR3), and a heavy chain framework region 4 (VHFWR4) **of SEQ ID NO: 9.**

25 37. The multifunctional molecule of any of embodiments 5-36, wherein the antigen binding domain comprises a heavy chain variable domain comprising a framework region, *e.g.*, framework region 3 (VHFWR3), comprising one or more (*e.g.*, one or two) changes, *e.g.*, substitutions (*e.g.*, a conservative substitution), at positions selected from 73 and 94 according to Kabat numbering, wherein the change at position 73 is to Threonine, *e.g.*, a Glutamic Acid to Threonine substitution, and the change at position 94 is to Glycine, *e.g.*, an Arginine to Glycine substitution.

30 38. The multifunctional molecule of any of embodiments 5-37, wherein the antigen binding domain comprises a heavy chain variable domain comprising a framework region 3

(FR3) comprising a Threonine at position 73, *e.g.*, a substitution at position 73 according to Kabat numbering, *e.g.*, a Glutamic Acid to Threonine substitution, and a Glycine at position 94, *e.g.*, a substitution at position 94 according to Kabat numbering, *e.g.*, a Arginine to Glycine substitution, *e.g.*, as shown in the amino acid sequence of SEQ ID NO: 10.

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39. The multifunctional molecule of any of embodiments 5-18, wherein the antigen binding domain comprises the heavy chain framework regions 1-4 of Antibody A-H.1, *e.g.*, SEQ ID NO: 9; and the light chain framework regions 1-4 of Antibody A-H.1, *e.g.*, SEQ ID NO: 10, or as shown in **FIGs. 1A** and **1B**.

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40. The multifunctional molecule of any of embodiments 5-18, wherein the antigen binding domain comprises the heavy chain framework regions 1-4 of Antibody A-H.2, *e.g.*, SEQ ID NO: 9; and the light chain framework regions 1-4 of Antibody A-H.2, *e.g.*, SEQ ID NO: 11, or as shown in **FIGs. 1A** and **1B**.

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41. The multifunctional molecule of any of embodiments 5-18, wherein the antigen binding domain comprises:

a VH domain comprising the amino acid sequence of SEQ ID NO: 9, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence of SEQ ID NO: 9, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 9; and/or

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a VL domain comprising the amino acid sequence of SEQ ID NO: 10, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence of SEQ ID NO: 10, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 10.

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42. The multifunctional molecule of any of embodiments 5-18, wherein the antigen binding domain comprises:

a VH domain comprising the amino acid sequence of SEQ ID NO: 9, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence of SEQ ID NO: 9, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 9; and/or

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a VL domain comprising the amino acid sequence of SEQ ID NO: 11, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence of SEQ ID NO: 11, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 11.

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43. The multifunctional molecule of any of embodiments 1-4, wherein the antigen binding domain specifically binds to TCR β V12 (e.g., TCR β V12-3*01).

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44. The multifunctional molecule of embodiment 43, wherein the antigen binding domain comprises at least one (e.g., one, two, three, or four) variable region or an antigen-binding fragment thereof, as described in **Table 2A**, or encoded by the nucleotide sequence in **Table 2A**, or a sequence substantially identical (e.g., at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences.

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45. The multifunctional molecule of either of embodiments 43 or 44, wherein the antigen binding domain comprises at least one, two, or three CDRs (or collectively all of the CDRs) from a heavy chain variable region comprising an amino acid sequence shown in **Table 2A**, or encoded by a nucleotide sequence shown in **Table 2A** (or a sequence with one, two, three, four, five, six or more changes, e.g., amino acid substitutions or deletions, relative to the amino acid sequence shown in **Table 2A**, or encoded by a nucleotide sequence shown in **Table 2A**).

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46. The multifunctional molecule of any of embodiments 43-45, wherein the antigen binding domain comprises at least one, two, or three CDRs (or collectively all of the CDRs) from a light chain variable region comprising an amino acid sequence shown in **Table 2A**, or encoded by a nucleotide sequence shown in **Table 2A** (or a sequence with one, two, three, four, five, six or more changes, e.g., amino acid substitutions or deletions, relative to the amino acid sequence shown in **Table 2A**, or encoded by a nucleotide sequence shown in **Table 2A**).

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47. The multifunctional molecule of any of embodiments 43-46, wherein the antigen binding domain comprises:

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(i) one, two or all of a light chain complementarity determining region 1 (LC CDR1), a light chain complementarity determining region 2 (LC CDR2), and a light chain complementarity determining region 3 (LC CDR3) of SEQ ID NO: 16, SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO: 29, or SEQ ID NO: 30, and/or

(ii) one, two or all of a heavy chain complementarity determining region 1 (HC CDR1), heavy chain complementarity determining region 2 (HC CDR2), and a heavy chain complementarity determining region 3 (HC CDR3) of SEQ ID NO: 15, SEQ ID NO: 23, SEQ ID NO: 24, or SEQ ID NO: 25.

48. The multifunctional molecule of any of embodiments 43-47, wherein the antigen binding domain comprises:

(i) a LC CDR1 amino acid sequence of SEQ ID NO: 20, a LC CDR2 amino acid sequence of SEQ ID NO: 21, or a LC CDR3 amino acid sequence of SEQ ID NO: 22; and/or

(ii) a HC CDR1 amino acid sequence of SEQ ID NO: 17, a HC CDR2 amino acid sequence of SEQ ID NO: 18, or a HC CDR3 amino acid sequence of SEQ ID NO: 19.

49. The multifunctional molecule of any of embodiments 43-47, wherein the antigen binding domain comprises:

(i) a light chain variable region (VL) comprising a LC CDR1 amino acid sequence of SEQ ID NO: 20, a LC CDR2 amino acid sequence of SEQ ID NO: 21, and a LC CDR3 amino acid sequence of SEQ ID NO: 2; and/or

(ii) a heavy chain variable region (VH) comprising a HC CDR1 amino acid sequence of SEQ ID NO: 17, a HC CDR2 amino acid sequence of SEQ ID NO: 18, and a HC CDR3 amino acid sequence of SEQ ID NO: 19.

50. The multifunctional molecule of any of embodiments 43-47, wherein the antigen binding domain comprises:

(i) a LC CDR1 amino acid sequence of SEQ ID NO: 63, a LC CDR2 amino acid sequence of SEQ ID NO: 64, or a LC CDR3 amino acid sequence of SEQ ID NO: 65; and/or

(ii) a HC CDR1 amino acid sequence of SEQ ID NO: 57, a HC CDR2 amino acid sequence of SEQ ID NO: 58, or a HC CDR3 amino acid sequence of SEQ ID NO: 59.

51. The multifunctional molecule of any of embodiments 43-47, wherein the antigen binding domain comprises:

(i) a light chain variable region (VL) comprising a LC CDR1 amino acid sequence of SEQ ID NO: 63, a LC CDR2 amino acid sequence of SEQ ID NO: 64, or a LC CDR3 amino acid sequence of SEQ ID NO: 65; and/or

(ii) a heavy chain variable region (VH) comprising a HC CDR1 amino acid sequence of SEQ ID NO: 57, a HC CDR2 amino acid sequence of SEQ ID NO: 58, or a HC CDR3 amino acid sequence of SEQ ID NO: 59.

52. The multifunctional molecule of any of embodiments 43-47, wherein the antigen binding domain comprises:

(i) a LC CDR1 amino acid sequence of SEQ ID NO: 66, a LC CDR2 amino acid sequence of SEQ ID NO: 67, or a LC CDR3 amino acid sequence of SEQ ID NO: 68; and/or

(ii) a HC CDR1 amino acid sequence of SEQ ID NO: 60, a HC CDR2 amino acid sequence of SEQ ID NO: 61, or a HC CDR3 amino acid sequence of SEQ ID NO: 62.

53. The multifunctional molecule of any of embodiments 43-47, wherein the antigen binding domain comprises:

(i) a light chain variable region (VL) comprising a LC CDR1 amino acid sequence of SEQ ID NO: 63, a LC CDR2 amino acid sequence of SEQ ID NO: 64, or a LC CDR3 amino acid sequence of SEQ ID NO: 65; and/or

(ii) a heavy chain variable region (VH) comprising a HC CDR1 amino acid sequence of SEQ ID NO: 57, a HC CDR2 amino acid sequence of SEQ ID NO: 58, or a HC CDR3 amino acid sequence of SEQ ID NO: 59.

54. The multifunctional molecule of any of embodiments 43-53, wherein the antigen binding domain comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) *e.g.*, as shown in **FIG. 2B, e.g., of SEQ ID NOs: 16 or 26-30.**

55. The multifunctional molecule of any of embodiments 43-54, wherein the antigen binding domain comprises a light chain variable region (VL) comprising a light chain framework region 2 (VLFWR2) *e.g.*, as shown in **FIG. 2B, e.g., of SEQ ID NOs: 16 or 26-30.**

56. The multifunctional molecule of any of embodiments 43-55, wherein the antigen binding domain comprises a light chain variable region (VL) comprising a light chain framework region 3 (VLFWR3) *e.g.*, as shown in **FIG. 2B, e.g., of SEQ ID NOs: 16 or 26-30.**

57. The multifunctional molecule of any of embodiments 43-56, wherein the antigen binding domain comprises a light chain variable region (VL) comprising a light chain framework region 4 (VLFWR4) *e.g.*, as shown in **FIG. 2B, e.g., of SEQ ID NOs: 16 or 26-30.**

58. The multifunctional molecule of any of embodiments 43-57, wherein the antigen binding domain comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1), a light chain framework region 2 (VLFWR2), a light chain framework region 3 (VLFWR3), and a light chain framework region 4 (VLFWR4) **of SEQ ID NO: 16.**

59. The multifunctional molecule of any of embodiments 43-57, wherein the antigen binding domain comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1), a light chain framework region 2 (VLFWR2), a light chain framework region 3 (VLFWR3), and a light chain framework region 4 (VLFWR4) **of SEQ ID NO: 26.**

60. The multifunctional molecule of any of embodiments 43-57, wherein the antigen binding domain comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1), a light chain framework region 2 (VLFWR2), a light chain framework region 3 (VLFWR3), and a light chain framework region 4 (VLFWR4) **of SEQ ID NO: 27.**

61. The multifunctional molecule of any of embodiments 43-57, wherein the antigen binding domain comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1), a light chain framework region 2 (VLFWR2), a light chain framework region 3 (VLFWR3), and a light chain framework region 4 (VLFWR4) **of SEQ ID NO: 28.**

62. The multifunctional molecule of any of embodiments 43-57, wherein the antigen binding domain comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1), a light chain framework region 2 (VLFWR2), a light chain framework region 3 (VLFWR3), and a light chain framework region 4 (VLFWR4) **of SEQ ID NO: 29.**

63. The multifunctional molecule of any of embodiments 43-57, wherein the antigen binding domain comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1), a light chain framework region 2 (VLFWR2), a light chain framework region 3 (VLFWR3), and a light chain framework region 4 (VLFWR4) **of SEQ ID NO: 30.**

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64. The multifunctional molecule of any of embodiments 43-57, wherein the antigen binding domain comprises a light chain variable domain comprising a framework region, *e.g.*, framework region 1 (VLFWR1), comprising one or more (*e.g.*, one, two, or three) changes, *e.g.*, substitutions (*e.g.*, a conservative substitution), at positions selected from 1, 2, and 4 according to Kabat numbering, wherein the change at position 1 is to Aspartic Acid, *e.g.*, a Alanine to Aspartic Acid substitution, the change at position 2 is to Asparagine, *e.g.*, an Isoleucine to Asparagine substitution, and the change at position 4 is to Leucine, *e.g.*, a Methionine to Leucine substitution.

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65. The multifunctional molecule of any of embodiments 43-57 or 64, wherein the antigen binding domain comprises a light chain variable domain comprising a framework region, *e.g.*, framework region 3 (VLFWR3), comprising one or more (*e.g.*, one, two, or three) changes, *e.g.*, substitutions (*e.g.*, a conservative substitution), at positions selected from 66, 69, and 71 according to Kabat numbering, wherein the change at position 66 is to Glycine, *e.g.*, a Lysine to Glycine substitution, the change at position 69 is to Asparagine, *e.g.*, an Tyrosine to Asparagine substitution, and the change at position 71 is to Tyrosine, *e.g.*, a Phenylalanine to Tyrosine substitution.

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66. The multifunctional molecule of any of embodiments 43-57, 64, or 65, wherein the antigen binding domain comprises a light chain comprising a framework region 1 (FR1) comprising a substitution at position 2 according to Kabat numbering, *e.g.*, a Isoleucine to Asparagine substitution; and a framework region 3 (FR3), comprising a substitution at position 69 according to Kabat numbering, *e.g.*, a Threonine to Asparagine substitution and a substitution at position 71 according to Kabat numbering, *e.g.*, a Phenylalanine to Tyrosine substitution, *e.g.*, as shown in the amino acid sequence of SEQ ID NO: 26.

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67. The multifunctional molecule of any of embodiments 43-57, 64, or 65, wherein the antigen binding domain comprises a light chain comprising (a) a framework region 1 (FR1)

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comprising a substitution at position 1 according to Kabat numbering, *e.g.*, a Alanine to Aspartic Acid substitution, and a substitution at position 2 according to Kabat numbering, *e.g.*, a Isoleucine to Asparagine substitution; and (b) a framework region 3 (FR3), comprising a substitution at position 69 according to Kabat numbering, *e.g.*, a Threonine to Asparagine substitution and a substitution at position 71 according to Kabat numbering, *e.g.*, a Phenylalanine to Tyrosine substitution, *e.g.*, as shown in the amino acid sequence of SEQ ID NO: 27.

68. The multifunctional molecule of any of embodiments 43-57, 64, or 65, wherein the antigen binding domain comprises a light chain comprising (a) a framework region 1 (FR1) comprising a substitution at position 2 according to Kabat numbering, *e.g.*, a Serine to Asparagine substitution; and a substitution at position 4 according to Kabat numbering, *e.g.*, a Methionine to Leucine substitution; and (b) a framework region 3 (FR3), comprising a substitution at position 69 according to Kabat numbering, *e.g.*, a Threonine to Asparagine substitution and a substitution at position 71 according to Kabat numbering, *e.g.*, a Phenylalanine to Tyrosine substitution, *e.g.*, as shown in the amino acid sequence of SEQ ID NO: 28.

69. The multifunctional molecule of any of embodiments 43-57, 64, or 65, wherein the antigen binding domain comprises a light chain comprising (a) a framework region 1 (FR1) comprising a substitution at position 2 according to Kabat numbering, *e.g.*, a Serine to Asparagine substitution; and (b) a framework region 3 (FR3) comprising a substitution at position 66 according to Kabat numbering, *e.g.*, a Lysine to Glycine substitution; a substitution at position 69 according to Kabat numbering, *e.g.*, a Threonine to Asparagine substitution; and a substitution at position 71 according to Kabat numbering, *e.g.*, a Alanine to Tyrosine substitution, *e.g.*, as shown in the amino acid sequence of SEQ ID NO: 29.

70. The multifunctional molecule of any of embodiments 43-69, wherein the antigen binding domain comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) *e.g.*, as shown in **FIG. 2A, e.g., of SEQ ID NOs: 15 or 23-25.**

71. The multifunctional molecule of any of embodiments 43-70, wherein the antigen binding domain comprises a heavy chain variable region (VH) comprising a heavy chain framework region 2 (VHFWR2) *e.g.*, as shown in **FIG. 2A, e.g., of SEQ ID NOs: 15 or 23-25.**

72. The multifunctional molecule of any of embodiments 43-71, wherein the antigen binding domain comprises a heavy chain variable region (VH) comprising a heavy chain framework region 3 (VHFWR3) *e.g.*, as shown in **FIG. 2A, e.g., of SEQ ID NOs: 15 or 23-25.**

5 73. The multifunctional molecule of any of embodiments 43-72, wherein the antigen binding domain comprises a heavy chain variable region (VH) comprising a heavy chain framework region 4 (VHFWR4) *e.g.*, as shown in **FIG. 2A, e.g., of SEQ ID NOs: 15 or 23-25.**

74. The multifunctional molecule of any of embodiments 43-73, wherein the antigen binding domain comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1), a heavy chain framework region 2 (VHFWR2), a heavy chain framework region 3 (VHFWR3), and a heavy chain framework region 4 (VHFWR4) **of SEQ ID NO: 23.**

75. The multifunctional molecule of any of embodiments 43-73, wherein the antigen binding domain comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1), a heavy chain framework region 2 (VHFWR2), a heavy chain framework region 3 (VHFWR3), and a heavy chain framework region 4 (VHFWR4) **of SEQ ID NO: 24.**

76. The multifunctional molecule of any of embodiments 43-73, wherein the antigen binding domain comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1), a heavy chain framework region 2 (VHFWR2), a heavy chain framework region 3 (VHFWR3), and a heavy chain framework region 4 (VHFWR4) **of SEQ ID NO: 25.**

25 77. The multifunctional molecule of any of embodiments 43-73, wherein the antigen binding domain comprises a heavy chain comprising the heavy chain framework regions 1-4 of SEQ ID NOs: 23, 24, or 25; and a light chain comprising the light chain framework regions 1-4 of SEQ ID NOs: 26, 27, 28, 29, or 30.

78. The multifunctional molecule of any of embodiments 43-73, wherein the antigen binding domain comprises:

a VH domain comprising an amino acid sequence chosen from the amino acid sequence of SEQ ID NO: 23, SEQ ID NO:24, or SEQ ID NO: 25, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 23, SEQ ID NO:24, or SEQ ID NO:25, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 23, SEQ ID NO:24, or SEQ ID NO:25; and/or

a VL domain comprising an amino acid sequence chosen from the amino acid sequence of SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO: 29, or SEQ ID NO: 30, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence of SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO: 29, or SEQ ID NO: 30, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO: 29, or SEQ ID NO: 30.

79. The multifunctional molecule of any of embodiments 43-73, wherein the antigen binding domain comprises:

a VH domain comprising the amino acid sequence of SEQ ID NO: 23, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 23, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 23; and

a VL domain comprising the amino acid sequence of SEQ ID NO: 26, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 26, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 26.

80. The multifunctional molecule of any of embodiments 43-73, wherein the antigen binding domain comprises:

a VH domain comprising the amino acid sequence of SEQ ID NO: 23, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ

ID NO: 23, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 23; and

a VL domain comprising the amino acid sequence of SEQ ID NO: 27, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 27, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 27.

81. The multifunctional molecule of any of embodiments 43-73, wherein the antigen binding domain comprises:

a VH domain comprising the amino acid sequence of SEQ ID NO: 23, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 23, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 23; and

a VL domain comprising the amino acid sequence of SEQ ID NO: 28, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 28, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 28.

82. The multifunctional molecule of any of embodiments 43-73, wherein the antigen binding domain comprises:

a VH domain comprising the amino acid sequence of SEQ ID NO: 23, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 23, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 23; and

a VL domain comprising the amino acid sequence of SEQ ID NO: 29, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 29, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 29.

83. The multifunctional molecule of any of embodiments 43-73, wherein the antigen binding domain comprises:

a VH domain comprising the amino acid sequence of SEQ ID NO: 23, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 23, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 23; and

5 a VL domain comprising the amino acid sequence of SEQ ID NO: 30, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 30, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 30.

10 84. The multifunctional molecule of any of embodiments 43-73, wherein the antigen binding domain comprises:

a VH domain comprising the amino acid sequence of SEQ ID NO: 24, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 24, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 24; and

15 a VL domain comprising the amino acid sequence of SEQ ID NO: 26, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 26, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 26.

20 85. The multifunctional molecule of any of embodiments 43-73, wherein the antigen binding domain comprises:

a VH domain comprising the amino acid sequence of SEQ ID NO: 24, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 24, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 24; and

25 a VL domain comprising the amino acid sequence of SEQ ID NO: 27, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 27, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 27.

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86. The multifunctional molecule of any of embodiments 43-73, wherein the antigen binding domain comprises:

a VH domain comprising the amino acid sequence of SEQ ID NO: 24, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 24, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 24; and

a VL domain comprising the amino acid sequence of SEQ ID NO: 28, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 28, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 28.

87. The multifunctional molecule of any of embodiments 43-73, wherein the antigen binding domain comprises:

a VH domain comprising the amino acid sequence of SEQ ID NO: 24, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 24, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 24; and

a VL domain comprising the amino acid sequence of SEQ ID NO: 29, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 29, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 29.

88. The multifunctional molecule of any of embodiments 43-73, wherein the antigen binding domain comprises:

a VH domain comprising the amino acid sequence of SEQ ID NO: 24, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 24, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 24; and

a VL domain comprising the amino acid sequence of SEQ ID NO: 30, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ

ID NO: 30, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 30.

89. The multifunctional molecule of any of embodiments 43-73, wherein the antigen binding domain comprises:

a VH domain comprising the amino acid sequence of SEQ ID NO: 25, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 25, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 25; and

a VL domain comprising the amino acid sequence of SEQ ID NO: 26, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 26, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 26.

90. The multifunctional molecule of any of embodiments 43-73, wherein the antigen binding domain comprises:

a VH domain comprising the amino acid sequence of SEQ ID NO: 25, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 25, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 25; and

a VL domain comprising the amino acid sequence of SEQ ID NO: 27, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 27, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 27.

91. The multifunctional molecule of any of embodiments 43-73, wherein the antigen binding domain comprises:

a VH domain comprising the amino acid sequence of SEQ ID NO: 25, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 25, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 25; and

a VL domain comprising the amino acid sequence of SEQ ID NO: 28, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 28, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 28.

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92. The multifunctional molecule of any of embodiments 43-73, wherein the antigen binding domain comprises:

10 a VH domain comprising the amino acid sequence of SEQ ID NO: 25, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 25, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 25; and

15 a VL domain comprising the amino acid sequence of SEQ ID NO: 29, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 29, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 29.

93. The multifunctional molecule of any of embodiments 43-73, wherein the antigen binding domain comprises:

20 a VH domain comprising the amino acid sequence of SEQ ID NO: 25, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 25, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 25; and

25 a VL domain comprising the amino acid sequence of SEQ ID NO: 30, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 30, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 30.

30 94. The multifunctional molecule of any one of embodiments 1-93, wherein the first antigen binding domain has a higher affinity for a T cell receptor comprising the TCRBV antigen, optionally wherein the K_D for the binding between the first antigen binding domain and

the T cell receptor comprising the TCRBV antigen is no more than 40%, 30%, 20%, 10%, 1%, 0.1%, or 0.01% of the K_D for the binding between the first antigen binding domain and a T cell receptor not comprising the TCRBV antigen.

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95. The multifunctional molecule of any preceding embodiment, wherein binding of the first antigen binding domain to the TCRBV antigen, e.g., on a lymphocyte (e.g., T cell), does not activate the lymphocyte, e.g., T cell.

10

96. The multifunctional molecule of any preceding embodiment, wherein binding of the first antigen binding domain to the TCRBV antigen, e.g., on a lymphocyte (e.g., T cell), does not appreciably activate lymphocyte, e.g., T cell, (e.g., as measured by T cell proliferation, expression of a T cell activation marker (e.g., CD69 or CD25), and/or expression of a cytokine (e.g., $TNF\alpha$ and $IFN\gamma$).

15

97. The multifunctional molecule of any preceding embodiment, wherein the multifunctional molecule preferentially binds to a lymphocyte comprising the TCRBV antigen over a lymphocyte not comprising the TCRBV antigen, optionally wherein the binding between the multifunctional molecule and the lymphocyte comprising the TCRBV antigen is more than 10, 20, 30, 40, or 50-fold greater than the binding between the multifunctional molecule and a lymphocyte not comprising the TCRBV antigen.

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98. The multifunctional molecule of any one of embodiments 1-97, wherein the multifunctional molecule comprises an immune cell engager chosen from an NK cell engager, a T cell engager, a B cell engager, a dendritic cell engager, or a macrophage cell engager.

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99. The multifunctional molecule of embodiment 98, wherein the immune cell engager binds to and activates an immune cell, e.g., an effector cell.

30

100. The multifunctional molecule of embodiment 98, wherein the immune cell engager binds to, but does not activate, an immune cell, e.g., an effector cell.

101. The multifunctional molecule of any one of embodiments 98-100, wherein the immune cell engager is a T cell engager, e.g., a T cell engager that mediates binding to and activation of a T cell, or a T cell engager that mediates binding to but not activation of a T cell.

5

102. The multifunctional molecule of embodiment 101, wherein the T cell engager binds to TCR α , TCR γ , TCR ζ , ICOS, CD28, CD27, HVEM, LIGHT, CD40, 4-1BB, OX40, DR3, GITR, CD30, TIM1, SLAM, CD2, CD3, or CD226, e.g., the T cell engager is an anti-CD3 antibody molecule.

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103. The multifunctional molecule of any one of embodiments 98-100, wherein the immune cell engager is an NK cell engager, e.g., an NK cell engager that mediates binding to and activation of an NK cell, or an NK cell engager that mediates binding to but not activation of an NK cell.

15

104. The multifunctional molecule of embodiment 103, wherein the NK cell engager is chosen from an antibody molecule, e.g., an antigen binding domain, or ligand that binds to (e.g., activates): NKp30, NKp40, NKp44, NKp46, NKG2D, DNAM1, DAP10, CD16 (e.g., CD16a, CD16b, or both), CRTAM, CD27, PSGL1, CD96, CD100 (SEMA4D), NKp80, CD244 (also known as SLAMF4 or 2B4), SLAMF6, SLAMF7, KIR2DS2, KIR2DS4, KIR3DS1, KIR2DS3, KIR2DS5, KIR2DS1, CD94, NKG2C, NKG2E, or CD160, e.g., the NK cell engager is an antibody molecule or ligand that binds to (e.g., activates) NKp30.

20

105. The multifunctional molecule of embodiment 103, wherein the NK cell engager is an antibody molecule, e.g., an antigen binding domain.

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106. The multifunctional molecule of either of embodiments 104 or 105, wherein the NK cell engager is capable of engaging an NK cell.

107. The multifunctional molecule of any one of embodiments 103-106, wherein the NK cell engager is an antibody molecule, e.g., an antigen binding domain, that binds to NKp30, NKp46, NKG2D, or CD16.

108. The multifunctional molecule of any preceding embodiment, wherein the multifunctional molecule:

(i) binds specifically to an epitope of NKp30, NKp46, NKG2D, or CD16, *e.g.*, the same or similar epitope as the epitope recognized by an anti-NKp30, anti-NKp46, anti-NKG2D, or anti-CD16 antibody molecule as described herein;

(ii) shows the same or similar binding affinity or specificity, or both, as an anti-NKp30, anti-NKp46, anti-NKG2D, or anti-CD16 antibody molecule as described herein;

(iii) inhibits, *e.g.*, competitively inhibits, the binding of an anti-NKp30, anti-NKp46, anti-NKG2D, or anti-CD16 antibody molecule as described herein;

(iv) binds the same or an overlapping epitope with an anti-NKp30, anti-NKp46, anti-NKG2D, or anti-CD16 antibody molecule as described herein; or

(v) competes for binding, and/or binds the same epitope, with an anti-NKp30, anti-NKp46, anti-NKG2D, or anti-CD16 antibody molecule as described herein.

109. The multifunctional molecule of any of embodiments 103-108, wherein the anti-NKp30 or anti-NKp46 antibody molecule comprises one or more CDRs, framework regions, variable domains, heavy or light chains, or an antigen binding domain chosen from Tables 7-10, or a sequence substantially identical thereto.

110. The multifunctional molecule of any of embodiments 103-109, wherein the NK cell engager is an antibody molecule, e.g., an antigen binding domain, that binds to NKp30.

111. The multifunctional molecule of any of embodiments 103-110, wherein lysis of the lymphocyte, e.g., lymphocyte comprising a TCRBV antigen corresponding to a biased TCRBV clonotype, is mediated by NKp30.

112. The multifunctional molecule of any of embodiments 103-111, wherein the multifunctional molecule does not activate the NK cell when incubated with the NK cell in the absence of the TCRBV antigen.

5 113. The multifunctional molecule of any of embodiments 103-112, wherein the multifunctional molecule activates the NK cell when the NK cell is a NKp30 expressing NK cell and when the TCRBV antigen is also present.

10 114. The multifunctional molecule of any of embodiments 103-113, wherein the multifunctional molecule does not activate the NK cell when the NK cell is not a NKp30 expressing NK cell and the TCRBV antigen is also present.

115. The multifunctional molecule of any of embodiments 103-113, wherein the NK cell engager comprises:

15 (i) a heavy chain variable region (VH) comprising a heavy chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 6000 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 amino acid sequence of SEQ ID NO: 6001 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VHCDR3 amino acid sequence of
20 SEQ ID NO: 6002 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and

 (ii) a light chain variable region (VL) comprising a light chain complementarity determining region 1 (VLCDR1) amino acid sequence of SEQ ID NO: 6063 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VLCDR2
25 amino acid sequence of SEQ ID NO: 6064 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VLCDR3 amino acid sequence of SEQ ID NO: 6065 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions).

30 116. The multifunctional molecule of embodiment 115, wherein the NK cell engager comprises:

(i) a heavy chain variable region (VH) comprising a heavy chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 6000, a VHCDR2 amino acid sequence of SEQ ID NO: 6001, and/or a VHCDR3 amino acid sequence of SEQ ID NO: 6002, and

5 (ii) a light chain variable region (VL) comprising a light chain complementarity determining region 1 (VLCDR1) amino acid sequence of SEQ ID NO: 6063, a VLCDR2 amino acid sequence of SEQ ID NO: 6064, and/or a VLCDR3 amino acid sequence of SEQ ID NO: 6065.

10 117. The multifunctional molecule of any of embodiments 103-116, wherein the NK cell engager comprises:

(1) a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6003 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6004 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6005 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VHFWR4 amino acid sequence of SEQ ID NO: 6006 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), and/or

20 (2) a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6066 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR2 amino acid sequence of SEQ ID NO: 6067 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR3 amino acid sequence of SEQ ID NO: 6068 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VLFWR4 amino acid sequence of SEQ ID NO: 6069 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).

118. The multifunctional molecule of embodiment 117, wherein the NK cell engager comprises:

(1) a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6003, a VHFWR2 amino acid sequence of SEQ ID NO: 6004, a VHFWR3 amino acid sequence of SEQ ID NO: 6005, or a VHFWR4 amino acid sequence of SEQ ID NO: 6006, and

(2) a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6066, a VLFWR2 amino acid sequence of SEQ ID NO: 6067, a VLFWR3 amino acid sequence of SEQ ID NO: 6068, or a VLFWR4 amino acid sequence of SEQ ID NO: 6069.

119. The multifunctional molecule of any one of embodiments 103-118, wherein the NK cell engager comprises:

(i) a VH comprising the amino acid sequence of SEQ ID NO: 6121 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6121), and/or

(ii) a VL comprising the amino acid sequence of SEQ ID NO: 6135 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6135).

120. The multifunctional molecule of either of embodiments 103-119, wherein the NK cell engager comprises a heavy chain comprising the amino acid sequence of SEQ ID NOs: 6148 or 6149 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NOs: 6148 or 6149).

121. The multifunctional molecule of either of embodiments 103-120, wherein the NK cell engager comprises a light chain comprising the amino acid sequence of SEQ ID NO: 6150 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6150).

122. The multifunctional molecule of either of embodiments 103-121, wherein the NK cell engager comprises a heavy chain comprising the amino acid sequence of SEQ ID NOs: 6148

or 6149 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NOs: 6148 or 6149), and a light chain comprising the amino acid sequence of SEQ ID NO: 6150 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6150).

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123. The multifunctional molecule of any of embodiments 103-116, wherein the NK cell engager comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6014 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a
10 VHFWR2 amino acid sequence of SEQ ID NO: 6015 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6016 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VHFWR4 amino acid sequence of SEQ ID NO: 6017 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations,
15 e.g., substitutions, additions, or deletions, therefrom).

124. The multifunctional molecule of embodiment 123, wherein the NK cell engager comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6014, a VHFWR2 amino acid sequence of
20 SEQ ID NO: 6015, a VHFWR3 amino acid sequence of SEQ ID NO: 6016, or a VHFWR4 amino acid sequence of SEQ ID NO: 6017.

125. The multifunctional molecule of embodiment 124, wherein the NK cell engager comprises a VH comprising the amino acid sequence of SEQ ID NO: 6123 (or an amino acid
25 sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6123).

126. The multifunctional molecule of any of embodiments 103-116, wherein the NK cell engager comprises a heavy chain variable region (VH) comprising a heavy chain framework
30 region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6018 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a

VHFWR2 amino acid sequence of SEQ ID NO: 6019 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6020 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VHFWR4 amino acid sequence of SEQ ID NO: 6021 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).

127. The multifunctional molecule of embodiment 126, wherein the NK cell engager comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6018, a VHFWR2 amino acid sequence of SEQ ID NO: 6019, a VHFWR3 amino acid sequence of SEQ ID NO: 6020, or a VHFWR4 amino acid sequence of SEQ ID NO: 6021.

128. The multifunctional molecule of embodiment 127, wherein the NK cell engager comprises a VH comprising the amino acid sequence of SEQ ID NO: 6124 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6124).

129. The multifunctional molecule of any of embodiments 103-116, wherein the NK cell engager comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6022 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6023 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6024 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VHFWR4 amino acid sequence of SEQ ID NO: 6025 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).

130. The multifunctional molecule of embodiment 129, wherein the NK cell engager comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1

(VHFWR1) amino acid sequence of SEQ ID NO: 6022, a VHFWR2 amino acid sequence of SEQ ID NO: 6023, a VHFWR3 amino acid sequence of SEQ ID NO: 6024, or a VHFWR4 amino acid sequence of SEQ ID NO: 6025.

5 131. The multifunctional molecule of embodiment 130, wherein the NK cell engager comprises a VH comprising the amino acid sequence of SEQ ID NO: 6125 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6125).

10 132. The multifunctional molecule of any of embodiments 103-116, wherein the NK cell engager comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6026 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6027 (or a sequence with no more than 1, 2, 3,
15 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6028 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VHFWR4 amino acid sequence of SEQ ID NO: 6029 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).

20 133. The multifunctional molecule of embodiment 132, wherein the NK cell engager comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6026, a VHFWR2 amino acid sequence of SEQ ID NO: 6027, a VHFWR3 amino acid sequence of SEQ ID NO: 6028, or a VHFWR4
25 amino acid sequence of SEQ ID NO: 6029.

 134. The multifunctional molecule of embodiment 133, wherein the NK cell engager comprises a VH comprising the amino acid sequence of SEQ ID NO: 6126 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID
30 NO: 6126).

135. The multifunctional molecule of any of embodiments 103-116, wherein the NK cell engager comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6030 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a
5 VHFWR2 amino acid sequence of SEQ ID NO: 6032 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6033 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VHFWR4 amino acid sequence of SEQ ID NO: 6034 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).
10

136. The multifunctional molecule of embodiment 135, wherein the NK cell engager comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6030, a VHFWR2 amino acid sequence of
15 SEQ ID NO: 6032, a VHFWR3 amino acid sequence of SEQ ID NO: 6033, or a VHFWR4 amino acid sequence of SEQ ID NO: 6034.

137. The multifunctional molecule of embodiment 136, wherein the NK cell engager comprises a VH comprising the amino acid sequence of SEQ ID NO: 6127 (or an amino acid
20 sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6127).

138. The multifunctional molecule of any of embodiments 103-116, wherein the NK cell engager comprises a heavy chain variable region (VH) comprising a heavy chain framework
25 region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6035 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6036 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6037 (or a sequence with no more than 1, 2, 3, 4, 5, or 6
30 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VHFWR4 amino acid

sequence of SEQ ID NO: 6038 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).

139. The multifunctional molecule of embodiment 138, wherein the NK cell engager
5 comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6035, a VHFWR2 amino acid sequence of SEQ ID NO: 6036, a VHFWR3 amino acid sequence of SEQ ID NO: 6037, or a VHFWR4 amino acid sequence of SEQ ID NO: 6038.

10 140. The multifunctional molecule of embodiment 139, wherein the NK cell engager comprises a VH comprising the amino acid sequence of SEQ ID NO: 6128 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6128).

15 141. The multifunctional molecule of any of embodiments 103-116 or 123-140, wherein the NK cell engager comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6077 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR2 amino acid sequence of SEQ ID NO: 6078 (or a sequence with no more than 1, 2, 3, 4,
20 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR3 amino acid sequence of SEQ ID NO: 6079 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VLFWR4 amino acid sequence of SEQ ID NO: 6080 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).

25 142. The multifunctional molecule of embodiment 141, wherein the NK cell engager comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6077, a VLFWR2 amino acid sequence of SEQ ID NO: 6078, a VLFWR3 amino acid sequence of SEQ ID NO: 6079, or a VLFWR4 amino acid
30 sequence of SEQ ID NO: 6080.

143. The multifunctional molecule of embodiment 142, wherein the NK cell engager comprises a VL comprising the amino acid sequence of SEQ ID NO: 6137 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6137).

5 144. The multifunctional molecule of any of embodiments 103-116 or 123-140, wherein the NK cell engager comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6081 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR2 amino acid sequence of SEQ ID NO: 6082 (or a sequence with no more than 1, 2, 3, 4,
10 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR3 amino acid sequence of SEQ ID NO: 6083 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VLFWR4 amino acid sequence of SEQ ID NO: 6084 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).

15 145. The multifunctional molecule of embodiment 144, wherein the NK cell engager comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6081, a VLFWR2 amino acid sequence of SEQ ID NO: 6082, a VLFWR3 amino acid sequence of SEQ ID NO: 6083, or a VLFWR4 amino acid
20 sequence of SEQ ID NO: 6084.

146. The multifunctional molecule of embodiment 145, wherein the NK cell engager comprises a VL comprising the amino acid sequence of SEQ ID NO: 6138 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6138).

25 147. The multifunctional molecule of any of embodiments 103-116 or 123-140, wherein the NK cell engager comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6085 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR2 amino acid sequence of SEQ ID NO: 6086 (or a sequence with no more than 1, 2, 3, 4,
30 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR3 amino acid sequence of SEQ ID NO: 6087 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations,

e.g., substitutions, additions, or deletions, therefrom), or a VLFWR4 amino acid sequence of SEQ ID NO: 6088 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).

5 148. The multifunctional molecule of embodiment 147, wherein the NK cell engager comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6085, a VLFWR2 amino acid sequence of SEQ ID NO: 6086, a VLFWR3 amino acid sequence of SEQ ID NO: 6087, or a VLFWR4 amino acid sequence of SEQ ID NO: 6088.

10 149. The multifunctional molecule of embodiment 148, wherein the NK cell engager comprises a VL comprising the amino acid sequence of SEQ ID NO: 6139 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6139).

15 150. The multifunctional molecule of any of embodiments 103-116 or 123-140, wherein the NK cell engager comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6089 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR2 amino acid sequence of SEQ ID NO: 6090 (or a sequence with no more than 1, 2, 3, 4,
20 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR3 amino acid sequence of SEQ ID NO: 6091 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VLFWR4 amino acid sequence of SEQ ID NO: 6092 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).

25 151. The multifunctional molecule of embodiment 150, wherein the NK cell engager comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6089, a VLFWR2 amino acid sequence of SEQ ID NO: 6090, a VLFWR3 amino acid sequence of SEQ ID NO: 6091, or a VLFWR4 amino acid
30 sequence of SEQ ID NO: 6092.

152. The multifunctional molecule of embodiment 151, wherein the NK cell engager comprises a VL comprising the amino acid sequence of SEQ ID NO: 6140 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6140).

5 153. The multifunctional molecule of any of embodiments 103-116 or 123-140, wherein the NK cell engager comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6093 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR2 amino acid sequence of SEQ ID NO: 6094 (or a sequence with no more than 1, 2, 3, 4,
10 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR3 amino acid sequence of SEQ ID NO: 6095 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VLFWR4 amino acid sequence of SEQ ID NO: 6096 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).

15 154. The multifunctional molecule of embodiment 153, wherein the NK cell engager comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6093, a VLFWR2 amino acid sequence of SEQ ID NO: 6094, a VLFWR3 amino acid sequence of SEQ ID NO: 6095, or a VLFWR4 amino acid
20 sequence of SEQ ID NO: 6096.

155. The multifunctional molecule of embodiment 154, wherein the NK cell engager comprises a VL comprising the amino acid sequence of SEQ ID NO: 6141 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6141).

25 156. The multifunctional molecule of any of embodiments 103-114, wherein the NK cell engager comprises:

(i) a heavy chain variable region (VH) comprising a heavy chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 6007 (or a sequence with
30 no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 amino acid sequence of SEQ ID NO: 6008 (or a sequence with no more than 1, 2, 3, or 4

mutations, e.g., substitutions, additions, or deletions), and/or a VHCDR3 amino acid sequence of SEQ ID NO: 6009 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and

(ii) a light chain variable region (VL) comprising a light chain complementarity
 5 determining region 1 (VLCDR1) amino acid sequence of SEQ ID NO: 6070 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VLCDR2 amino acid sequence of SEQ ID NO: 6071 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VLCDR3 amino acid sequence of
 10 additions, or deletions).

157. The multifunctional molecule of embodiment 156, wherein the NK cell engager comprises:

(i) a heavy chain variable region (VH) comprising a heavy chain complementarity
 15 determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 6007, a VHCDR2 amino acid sequence of SEQ ID NO: 6008, and/or a VHCDR3 amino acid sequence of SEQ ID NO: 6009, and

(ii) a light chain variable region (VL) comprising a light chain complementarity
 determining region 1 (VLCDR1) amino acid sequence of SEQ ID NO: 6070, a VLCDR2 amino
 20 acid sequence of SEQ ID NO: 6071, and/or a VLCDR3 amino acid sequence of SEQ ID NO: 6072.

158. The multifunctional molecule of any of embodiments 103-114, 156, or 157, wherein the NK cell engager comprises:

(1) a heavy chain variable region (VH) comprising a heavy chain framework region 1
 25 (VHFWR1) amino acid sequence of SEQ ID NO: 6010 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6011 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid
 30 sequence of SEQ ID NO: 6012 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VHFWR4 amino acid sequence of

SEQ ID NO: 6013 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), and/or

(2) a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6073 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR2 amino acid sequence of SEQ ID NO: 6074 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR3 amino acid sequence of SEQ ID NO: 6075 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VLFWR4 amino acid sequence of SEQ ID NO: 6076 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).

159. The multifunctional molecule of embodiment 158, wherein the NK cell engager comprises:

(1) a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6010, a VHFWR2 amino acid sequence of SEQ ID NO: 6011, a VHFWR3 amino acid sequence of SEQ ID NO: 6012, or a VHFWR4 amino acid sequence of SEQ ID NO: 6013, and

(3) a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6073, a VLFWR2 amino acid sequence of SEQ ID NO: 6074, a VLFWR3 amino acid sequence of SEQ ID NO: 6075, or a VLFWR4 amino acid sequence of SEQ ID NO: 6076.

160. The multifunctional molecule of any one of embodiments 103-114 or 156-159, wherein the NK cell engager comprises:

(i) a VH comprising the amino acid sequence of SEQ ID NO: 6122 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6122), and/or

(ii) a VL comprising the amino acid sequence of SEQ ID NO: 6136 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6136).

161. The multifunctional molecule of any of embodiments 103-114 or 156-160, wherein the NK cell engager comprises a heavy chain comprising the amino acid sequence of SEQ ID NOs: 6151 or 6152 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NOs: 6151 or 6152).

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162. The multifunctional molecule of any of embodiments 103-114 or 156-161, wherein the NK cell engager comprises a light chain comprising the amino acid sequence of SEQ ID NO: 6153 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6153).

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163. The multifunctional molecule of any of embodiments 103-114 or 156-162, wherein the NK cell engager comprises a heavy chain comprising the amino acid sequence of SEQ ID NOs: 6151 or 6152 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NOs: 6151 or 6152), and a light chain comprising the amino acid sequence of SEQ ID NO: 6153 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6153).

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164. The multifunctional molecule of any of embodiments 103-114, 156, or 157, wherein the NK cell engager comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6039 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6040 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6041 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VHFWR4 amino acid sequence of SEQ ID NO: 6042 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).

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165. The multifunctional molecule of embodiment 164, wherein the NK cell engager comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6039, a VHFWR2 amino acid sequence of

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SEQ ID NO: 6040, a VHFWR3 amino acid sequence of SEQ ID NO: 6041, or a VHFWR4 amino acid sequence of SEQ ID NO: 6042.

166. The multifunctional molecule of embodiment 165, wherein the NK cell engager
5 comprises a VH comprising the amino acid sequence of SEQ ID NO: 6129 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6129).

167. The multifunctional molecule of any of embodiments 103-114, 156, or 157, wherein
10 the NK cell engager comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6043 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6044 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino
15 acid sequence of SEQ ID NO: 6045 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VHFWR4 amino acid sequence of SEQ ID NO: 6046 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).

20 168. The multifunctional molecule of embodiment 167, wherein the NK cell engager comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6043, a VHFWR2 amino acid sequence of SEQ ID NO: 6044, a VHFWR3 amino acid sequence of SEQ ID NO: 6045, or a VHFWR4 amino acid sequence of SEQ ID NO: 6046.

25 169. The multifunctional molecule of embodiment 168, wherein the NK cell engager comprises a VH comprising the amino acid sequence of SEQ ID NO: 6130 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6130).

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170. The multifunctional molecule of any of embodiments 103-114, 156, or 157, wherein the NK cell engager comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6047 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6048 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6049 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VHFWR4 amino acid sequence of SEQ ID NO: 6050 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).

171. The multifunctional molecule of embodiment 170, wherein the NK cell engager comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6047, a VHFWR2 amino acid sequence of SEQ ID NO: 6048, a VHFWR3 amino acid sequence of SEQ ID NO: 6049, or a VHFWR4 amino acid sequence of SEQ ID NO: 6050.

172. The multifunctional molecule of embodiment 171, wherein the NK cell engager comprises a VH comprising the amino acid sequence of SEQ ID NO: 6131 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6131).

173. The multifunctional molecule of any of embodiments 103-114, 156, or 157, wherein the NK cell engager comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6051 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6052 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6053 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VHFWR4 amino acid

sequence of SEQ ID NO: 6054 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).

174. The multifunctional molecule of embodiment 173, wherein the NK cell engager
5 comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6051, a VHFWR2 amino acid sequence of SEQ ID NO: 6052, a VHFWR3 amino acid sequence of SEQ ID NO: 6053, or a VHFWR4 amino acid sequence of SEQ ID NO: 6054.

10 175. The multifunctional molecule of embodiment 174, wherein the NK cell engager comprises a VH comprising the amino acid sequence of SEQ ID NO: 6132 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6132).

15 176. The multifunctional molecule of any of embodiments 103-114, 156, or 157, wherein the NK cell engager comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6055 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6056 (or a sequence with no more than 1, 2, 3,
20 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6057 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VHFWR4 amino acid sequence of SEQ ID NO: 6058 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).

25 177. The multifunctional molecule of embodiment 176, wherein the NK cell engager comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6055, a VHFWR2 amino acid sequence of SEQ ID NO: 6056, a VHFWR3 amino acid sequence of SEQ ID NO: 6057, or a VHFWR4
30 amino acid sequence of SEQ ID NO: 6058.

178. The multifunctional molecule of embodiment 177, wherein the NK cell engager comprises a VH comprising the amino acid sequence of SEQ ID NO: 6133 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6133).

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179. The multifunctional molecule of any of embodiments 103-114, 156, or 157, wherein the NK cell engager comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6059 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6060 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6061 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VHFWR4 amino acid sequence of SEQ ID NO: 6062 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).

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180. The multifunctional molecule of embodiment 179, wherein the NK cell engager comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6059, a VHFWR2 amino acid sequence of SEQ ID NO: 6060, a VHFWR3 amino acid sequence of SEQ ID NO: 6061, or a VHFWR4 amino acid sequence of SEQ ID NO: 6062.

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181. The multifunctional molecule of embodiment 180, wherein the NK cell engager comprises a VH comprising the amino acid sequence of SEQ ID NO: 6134 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6134).

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182. The multifunctional molecule of any of embodiments 103-114, 156, 157, or 164-181, wherein the NK cell engager comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6097 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or

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deletions, therefrom), a VLFWR2 amino acid sequence of SEQ ID NO: 6098 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR3 amino acid sequence of SEQ ID NO: 6099 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VLFWR4 amino acid sequence of SEQ ID NO: 6100 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).

183. The multifunctional molecule of embodiment 182, wherein the NK cell engager comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6097, a VLFWR2 amino acid sequence of SEQ ID NO: 6098, a VLFWR3 amino acid sequence of SEQ ID NO: 6099, or a VLFWR4 amino acid sequence of SEQ ID NO: 6100.

184. The multifunctional molecule of embodiment 183, wherein the NK cell engager comprises a VL comprising the amino acid sequence of SEQ ID NO: 6142 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6142).

185. The multifunctional molecule of any of embodiments 103-114, 156, 157, or 164-181, wherein the NK cell engager comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6101 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR2 amino acid sequence of SEQ ID NO: 6102 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR3 amino acid sequence of SEQ ID NO: 6103 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VLFWR4 amino acid sequence of SEQ ID NO: 6104 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).

186. The multifunctional molecule of embodiment 185, wherein the NK cell engager comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6101, a VLFWR2 amino acid sequence of SEQ

ID NO: 6102, a VLFWR3 amino acid sequence of SEQ ID NO: 6103, or a VLFWR4 amino acid sequence of SEQ ID NO: 6104.

187. The multifunctional molecule of embodiment 186, wherein the NK cell engager
5 comprises a VL comprising the amino acid sequence of SEQ ID NO: 6143 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6143).

188. The multifunctional molecule of any of embodiments 103-114, 156, 157, or 164-
181, wherein the NK cell engager comprises a light chain variable region (VL) comprising a
10 light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6105 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR2 amino acid sequence of SEQ ID NO: 6106 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a
VLFWR3 amino acid sequence of SEQ ID NO: 6107 (or a sequence with no more than 1, 2, 3, 4,
15 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VLFWR4 amino acid sequence of SEQ ID NO: 6108 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).

189. The multifunctional molecule of embodiment 188, wherein the NK cell engager
20 comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6105, a VLFWR2 amino acid sequence of SEQ ID NO: 6106, a VLFWR3 amino acid sequence of SEQ ID NO: 6107, or a VLFWR4 amino acid sequence of SEQ ID NO: 6108.

25 190. The multifunctional molecule of embodiment 189, wherein the NK cell engager comprises a VL comprising the amino acid sequence of SEQ ID NO: 6144 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6144).

191. The multifunctional molecule of any of embodiments 103-114, 156, 157, or 164-
30 181, wherein the NK cell engager comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6109 (or a

sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR2 amino acid sequence of SEQ ID NO: 6110 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR3 amino acid sequence of SEQ ID NO: 6111 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VLFWR4 amino acid sequence of SEQ ID NO: 6112 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).

192. The multifunctional molecule of embodiment 191, wherein the NK cell engager comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6109, a VLFWR2 amino acid sequence of SEQ ID NO: 6110, a VLFWR3 amino acid sequence of SEQ ID NO: 6111, or a VLFWR4 amino acid sequence of SEQ ID NO: 6112.

193. The multifunctional molecule of embodiments 192, wherein the NK cell engager comprises a VL comprising the amino acid sequence of SEQ ID NO: 6145 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6145).

194. The multifunctional molecule of any of embodiments 103-114, 156, 157, or 164-181, wherein the NK cell engager comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6113 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR2 amino acid sequence of SEQ ID NO: 6114 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR3 amino acid sequence of SEQ ID NO: 6115 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VLFWR4 amino acid sequence of SEQ ID NO: 6116 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).

195. The multifunctional molecule of embodiment 194, wherein the NK cell engager comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6113, a VLFWR2 amino acid sequence of SEQ

ID NO: 6114, a VLFWR3 amino acid sequence of SEQ ID NO: 6115, or a VLFWR4 amino acid sequence of SEQ ID NO: 6116.

196. The multifunctional molecule of embodiment 195, wherein the NK cell engager
5 comprises a VL comprising the amino acid sequence of SEQ ID NO: 6146 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6146).

197. The multifunctional molecule of any of embodiments 103-114, 156, 157, or 164-
181, wherein the NK cell engager comprises a light chain variable region (VL) comprising a
10 light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6117 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR2 amino acid sequence of SEQ ID NO: 6118 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a
VLFWR3 amino acid sequence of SEQ ID NO: 6119 (or a sequence with no more than 1, 2, 3, 4,
15 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VLFWR4 amino acid sequence of SEQ ID NO: 6120 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).

198. The multifunctional molecule of embodiment 197, wherein the NK cell engager
20 comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6117, a VLFWR2 amino acid sequence of SEQ ID NO: 6118, a VLFWR3 amino acid sequence of SEQ ID NO: 6119, or a VLFWR4 amino acid sequence of SEQ ID NO: 6120.

25 199. The multifunctional molecule of embodiment 198, wherein the NK cell engager comprises a VL comprising the amino acid sequence of SEQ ID NO: 6147 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6147).

200. The multifunctional molecule of any of embodiments 103-106, wherein the NK cell
30 engager is an antibody molecule, e.g., an antigen binding domain, that binds to NKp46.

201. The multifunctional molecule of embodiment 200, wherein lysis of the lymphoma cell is mediated by NKp46.

202. The multifunctional molecule of either of embodiments 200 or 201, wherein the multifunctional molecule does not activate the NK cell when incubated with the NK cell in the absence of the TCRBV antigen (e.g., a TCRBV antigen corresponding to a biased TCRBV clonotype).

203. The multifunctional molecule of any one of embodiments 200-202, wherein the multifunctional molecule activates the NK cell when the NK cell is a NKp46 expressing NK cell and the TCRBV antigen (e.g., a TCRBV antigen corresponding to a biased TCRBV clonotype) is also present.

204. The multifunctional molecule of any one of embodiments 200-203, wherein the multifunctional molecule does not activate the NK cell when the NK cell is not a NKp46 expressing NK cell and the TCRBV antigen (e.g., a TCRBV antigen corresponding to a biased TCRBV clonotype) is also present.

205. The multifunctional molecule of any one of embodiments 200-204, wherein the NK cell engager comprises a VH comprising the amino acid sequence of SEQ ID NO: 6182 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6182).

206. The multifunctional molecule of any one of embodiments 200-205, wherein the NK cell engager comprises a VL comprising the amino acid sequence of SEQ ID NO: 6183 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6183).

207. The multifunctional molecule of 200-205, wherein the NK cell engager comprises an scFV comprising the amino acid sequence of SEQ ID NO: 6181 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6181).

208. The multifunctional molecule of any of embodiments 103-106, wherein the NK cell engager is an antibody molecule, e.g., an antigen binding domain, that binds to NKG2D.

5 209. The multifunctional molecule of embodiment 208, wherein lysis of the lymphoma cell is mediated by NKG2D.

10 210. The multifunctional molecule of either of embodiments 208 or 209, wherein the multifunctional molecule does not activate the NK cell when incubated with the NK cell in the absence of the TCRBV antigen (e.g., a TCRBV antigen corresponding to a biased TCRBV clonotype).

15 211. The multifunctional molecule of any one of embodiments 208-210, wherein the multifunctional molecule activates the NK cell when the NK cell is a NKG2D expressing NK cell and the TCRBV antigen (e.g., a TCRBV antigen corresponding to a biased TCRBV clonotype) is also present.

20 212. The multifunctional molecule of any one of embodiments 208-211, wherein the multifunctional molecule does not activate the NK cell when the NK cell is not a NKG2D expressing NK cell and the TCRBV antigen (e.g., a TCRBV antigen corresponding to a biased TCRBV clonotype) is also present.

25 213. The multifunctional molecule of any one of embodiments 208-212, wherein the NK cell engager comprises a VH comprising the amino acid sequence of SEQ ID NO: 6176 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6176).

30 214. The multifunctional molecule of any one of embodiments 208-213, wherein the NK cell engager comprises a VL comprising the amino acid sequence of SEQ ID NO: 6177 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6177).

215. The multifunctional molecule of any of embodiments 208-214, wherein the NK cell engager comprises an scFV comprising the amino acid sequence of SEQ ID NO: 6175 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6175).

216. The multifunctional molecule of any one of embodiments 208-212, wherein the NK cell engager comprises a VH comprising the amino acid sequence of SEQ ID NO: 6179 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6179).

217. The multifunctional molecule of any one of embodiments 208-212 or 216 wherein the NK cell engager comprises a VL comprising the amino acid sequence of SEQ ID NO: 6180 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6180).

218. The multifunctional molecule of any of embodiments 208-212, 216, or 217, wherein the NK cell engager comprises an scFV comprising the amino acid sequence of SEQ ID NO: 6178 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6178).

219. The multifunctional molecule of any of embodiments 103-106, wherein the NK cell engager is an antibody molecule, e.g., an antigen binding domain, that binds to CD16.

220. The multifunctional molecule of embodiment 219, wherein lysis of the lymphoma cell is mediated by CD16.

221. The multifunctional molecule of either of embodiments 219 or 220, wherein the multifunctional molecule does not activate the NK cell when incubated with the NK cell in the absence of the TCRBV antigen (e.g., a TCRBV antigen corresponding to a biased TCRBV clonotype).

222. The multifunctional molecule of any one of embodiments 219-221, wherein the multifunctional molecule activates the NK cell when the NK cell is a CD16 expressing NK cell and the TCRBV antigen (e.g., a TCRBV antigen corresponding to a biased TCRBV clonotype) is also present.

5 223. The multifunctional molecule of any one of embodiments 219-222, wherein the multifunctional molecule does not activate the NK cell when the NK cell is not a CD16 expressing NK cell and the TCRBV antigen (e.g., a TCRBV antigen corresponding to a biased TCRBV clonotype) is also present.

10 224. The multifunctional molecule of any one of embodiments 219-223, wherein the NK cell engager comprises a VH comprising the amino acid sequence of SEQ ID NO: 6185 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6185).

15 225. The multifunctional molecule of any one of embodiments 219-224, wherein the NK cell engager comprises a VL comprising the amino acid sequence of SEQ ID NO: 6186 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6186).

20 226. The multifunctional molecule of any of embodiments 219-225, wherein the NK cell engager comprises an scFV comprising the amino acid sequence of SEQ ID NO: 6184 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6184).

25 227. The multifunctional molecule of embodiment 103, wherein the NK cell engager is a ligand, optionally, the ligand further comprises an immunoglobulin constant region, e.g., an Fc region.

30 228. The multifunctional molecule of embodiment 227, wherein the NK cell engager is a ligand of NKp44 or NKp46, e.g., a viral HA.

229. The multifunctional molecule of embodiment 227, wherein the NK cell engager is a ligand of DAP10, e.g., a coreceptor for NKG2D.

230. The multifunctional molecule of embodiment 227, wherein the NK cell engager is a
5 ligand of CD16, e.g., a CD16a/b ligand, e.g., a CD16a/b ligand further comprising an antibody Fc region.

231. The multifunctional molecule of any one of embodiments 98-100, wherein the
10 immune cell engager mediates binding to, or activation of, or both of, one or more of a B cell, a macrophage, and/or a dendritic cell.

232. The multifunctional molecule of embodiment 231, wherein the immune cell
engager comprises a B cell, macrophage, and/or dendritic cell engager chosen from one or more
of CD40 ligand (CD40L) or a CD70 ligand; an antibody molecule that binds to CD40 or CD70;
15 an antibody molecule to OX40; an OX40 ligand (OX40L); an agonist of a Toll-like receptor
(e.g., a TLR4, e.g., a constitutively active TLR4 (caTLR4) or a TLR9 agonist); a 41BB; a CD2
agonist; a CD47; or a STING agonist, or a combination thereof.

233. The multifunctional molecule of any one of embodiments 98-100, wherein the
20 immune cell engager is a B cell engager, e.g., a CD40L, an OX40L, or a CD70 ligand, or an
antibody molecule that binds to OX40, CD40 or CD70.

234. The multifunctional molecule of any one of embodiments 98-100, wherein the
immune cell engager is a macrophage cell engager, e.g., a CD2 agonist; a CD40L; an OX40L; an
25 antibody molecule that binds to OX40, CD40 or CD70; an agonist of a Toll-like receptor (TLR)
(e.g., a TLR4, e.g., a constitutively active TLR4 (caTLR4) or a TLR9 agonist); CD47; or a
STING agonist.

235. The multifunctional molecule of any one of embodiments 98-100, wherein the
30 immune cell engager is a dendritic cell engager, e.g., a CD2 agonist, an OX40 antibody, an

OX40L, 41BB agonist, a Toll-like receptor agonist or a fragment thereof (e.g., a TLR4, e.g., a constitutively active TLR4 (caTLR4)), CD47 agonist, or a STING agonist.

236. The multifunctional molecule of embodiment 234 or 235, wherein the STING
5 agonist comprises a cyclic dinucleotide, e.g., a cyclic di-GMP (cdGMP), a cyclic di-AMP (cdAMP), or a combination thereof, optionally with 2',5' or 3',5' phosphate linkages, e.g., wherein the STING agonist is covalently coupled to the multifunctional molecule.

237. The multifunctional molecule of any one of embodiments 1-97, wherein the
10 multifunctional molecule comprises a cytokine molecule.

238. The multifunctional molecule of embodiment 237, wherein the cytokine molecule is
chosen from interleukin-2 (IL-2), interleukin-7 (IL-7), interleukin-12 (IL-12), interleukin-15 (IL-
15), interleukin-18 (IL-18), interleukin-21 (IL-21), or interferon gamma, or a fragment or variant
15 thereof, or a combination of any of the aforesaid cytokines.

239. The multifunctional molecule of embodiment 237 or 238, wherein the cytokine
molecule is a monomer or a dimer.

20 240. The multifunctional molecule of any one of embodiments 237-239, wherein the
cytokine molecule further comprises a receptor dimerizing domain, e.g., an IL15Ralpha
dimerizing domain.

241. The multifunctional molecule of embodiment 240, wherein the cytokine molecule
25 (e.g., IL-15) and the receptor dimerizing domain (e.g., an IL15Ralpha dimerizing domain) are
not covalently linked, e.g., are non-covalently associated.

242. The multifunctional molecule of any of embodiments 1-97, wherein the
multifunctional molecule comprises a cytokine inhibitor molecule.

243. The multifunctional molecule of embodiment 242, wherein the cytokine inhibitor molecule is a TGF-beta inhibitor.

244. The multifunctional molecule of either of embodiments 242 or 243, wherein the TGF-beta inhibitor inhibits (e.g., reduces the activity of): (i) TGF-beta 1; (ii) TGF-beta 2; (iii) TGF-beta 3; (iv) (i) and (ii); (v) (i) and (iii); (vi) (ii) and (iii); or (vii) (i), (ii), and (iii).

245. The multifunctional molecule of any of embodiments 242-244, wherein the TGF-beta inhibitor comprises a portion of a TGF-beta receptor (e.g., an extracellular domain of a TGF-beta receptor) that is capable of inhibiting (e.g., reducing the activity of) TGF-beta, or functional fragment or variant thereof.

246. The multifunctional molecule of embodiment 245, wherein the TGF-beta inhibitor comprises a portion of (i) TGFBR1; (ii) TGFBR2; (iii) TGFBR3; (iv) (i) and (ii); (v) (i) and (iii); (vi) (ii) and (iii); or (vii) (i), (ii), and (iii).

247. The multifunctional molecule of any of embodiments 242-246, wherein the TGF-beta inhibitor comprises an amino acid sequence selected from Table 16, or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity thereto.

248. The multifunctional molecule of any of embodiments 1-97, wherein the multifunctional molecule comprises a death receptor signal engager chosen from a TNF-related apoptosis-inducing ligand (TRAIL) molecule, a death receptor molecule, or an antigen binding domain that specifically binds to a death receptor.

249. The multifunctional molecule of embodiment 248, wherein the death receptor signal engager activates death receptor signaling in the lymphocyte (e.g., T cell) comprising the TCRBV antigen, e.g., and induces apoptosis or cell death in said cell.

250. The multifunctional molecule of either of embodiments 248 or 249, wherein the death receptor signal engager does not activate death receptor signaling on cells other than lymphocytes comprising the TCRBV antigen.

251. The multifunctional molecule of any of embodiments 248-250, wherein the death receptor signal engager comprises a TRAIL molecule, e.g., one or more TRAIL polypeptides or a fragment thereof.

5 252. The multifunctional molecule of embodiment 251, wherein the TRAIL molecule specifically binds to Death Receptor 4 (DR4) or Death Receptor 5 (DR5).

10 253. The multifunctional molecule of either of embodiments 251 or 252, wherein the TRAIL molecule comprises a truncated TRAIL polypeptide, e.g., relative to a wild-type TRAIL polypeptide.

15 254. The multifunctional molecule of embodiment 253, wherein the TRAIL molecule comprises at least residues corresponding to amino acids 95-281 of human TRAIL, e.g., a truncated TRAIL molecule comprising residues corresponding to amino acids 95-281 of human TRAIL.

20 255. The multifunctional molecule of embodiment 254, wherein the TRAIL molecule comprises a truncated TRAIL polypeptide comprising amino acids 95-281 of human TRAIL, e.g., and not amino acids 1-94 of human TRAIL.

25 256. The multifunctional molecule of embodiment 253, wherein the TRAIL molecule comprises at least residues corresponding to amino acids 122-281 of human TRAIL, e.g., a truncated TRAIL molecule comprising residues corresponding to amino acids 122-281 of human TRAIL.

 257. The multifunctional molecule of embodiment 256, wherein the TRAIL molecule comprises a truncated TRAIL polypeptide comprising amino acids 122-281 of human TRAIL, e.g., and not amino acids 1-121 of human TRAIL.

30 258. The multifunctional molecule of any of embodiments 251-257, wherein the death receptor signal engager comprises one, two, or three TRAIL molecules.

259. The multifunctional molecule of any of embodiments 248-250, wherein the death receptor signal engager comprises an antigen binding domain that specifically binds to a death receptor, e.g., Death Receptor 4 (DR4) or Death Receptor 5 (DR5).

5

260. The multifunctional molecule of embodiment 259, wherein the death receptor signal engager comprises one, two, or three antigen binding domains that specifically binds to a death receptor.

10

261. The multifunctional molecule of either of embodiments 259 or 260, wherein the antigen binding domain that specifically binds to a death receptor binds to DR5.

262. The multifunctional molecule of any of embodiments 259-261, wherein the antigen binding domain that specifically binds to a death receptor comprises tigatuzumab, drozitumab, or conatumumab.

15

263. The multifunctional molecule of any of embodiments 248-262, wherein the death receptor signal engager comprises an amino acid sequence selected from Table 11, or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto.

20

264. The multifunctional molecule of any of embodiments 248-263, wherein the death receptor signal engager comprises an amino acid sequence of SEQ ID NO: 6157, or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto.

25

265. The multifunctional molecule of any of embodiments 248-263, wherein the death receptor signal engager comprises an amino acid sequence of SEQ ID NO: 6158, or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto.

30

266. The multifunctional molecule of any of embodiments 248-263, wherein the death receptor signal engager comprises an amino acid sequence of SEQ ID NO: 6159, or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto.

5

267. The multifunctional molecule of any of embodiments 248-263, wherein the death receptor signal engager comprises an amino acid sequence of SEQ ID NO: 6160, or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto.

10

268. The multifunctional molecule of any of embodiments 248-263, wherein the death receptor signal engager comprises an amino acid sequence of SEQ ID NO: 6161, or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto.

15

269. The multifunctional molecule of any of embodiments 248-263, wherein the death receptor signal engager comprises an amino acid sequence of SEQ ID NO: 6162, or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto.

20

270. The multifunctional molecule of any of embodiments 248-263, wherein the death receptor signal engager comprises an amino acid sequence of SEQ ID NO: 6163, or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto.

25

271. The multifunctional molecule of any of embodiments 248-263, wherein the death receptor signal engager comprises an amino acid sequence of SEQ ID NO: 6164, or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto.

30

272. The multifunctional molecule of any of embodiments 248-263, wherein the death receptor signal engager comprises an amino acid sequence of SEQ ID NO: 6165, or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto.

5

273. The multifunctional molecule of embodiment 102, wherein the T cell engager binds to TCR β .

274. The multifunctional molecule of embodiment 273, wherein the T cell engager comprises an antigen binding domain (e.g., an antibody molecule or fragment thereof) that binds to (e.g., and in some embodiments activates) CD3.

275. The multifunctional molecule of either of embodiments 273 or 274, wherein the T cell engager does not bind to the lymphocyte comprising the TCRBV antigen.

276. The multifunctional molecule of any of embodiments 273-275, wherein the T cell engager does not activate the lymphocyte comprising the TCRBV.

20

277. The multifunctional molecule of any one of embodiments 1-276, wherein the multifunctional molecule comprises:

- (i) an immune cell engager (e.g., a T cell engager, an NK cell engager, a B cell engager, a dendritic cell engager, or a macrophage cell engager) and a cytokine molecule,
- (ii) an immune cell engager (e.g., a T cell engager, an NK cell engager, a B cell engager, a dendritic cell engager, or a macrophage cell engager) and a cytokine inhibitor molecule,
- (iii) an immune cell engager (e.g., a T cell engager, an NK cell engager, a B cell engager, a dendritic cell engager, or a macrophage cell engager) and a death receptor signal engager,
- (iv) a cytokine molecule and a death receptor signal engager,
- (v) a cytokine inhibitor molecule and a death receptor signal engager,

30

(vi) an immune cell engager (e.g., a T cell engager, an NK cell engager, a B cell engager, a dendritic cell engager, or a macrophage cell engager), a cytokine molecule, and a death receptor signal engager, or

(vii) an immune cell engager (e.g., a T cell engager, an NK cell engager, a B cell engager, a dendritic cell engager, or a macrophage cell engager), a cytokine inhibitor molecule, and a death receptor signal engager.

278. The multifunctional molecule of any one of embodiments 1-277, wherein the multifunctional molecule comprises the following configuration:

A, B-[dimerization module]-C, -D, wherein:

(a) the dimerization module comprises an immunoglobulin constant domain, *e.g.*, a heavy chain constant domain (*e.g.*, a homodimeric or heterodimeric heavy chain constant region, *e.g.*, an Fc region), or a constant domain of an immunoglobulin variable region (*e.g.*, a Fab region); and

(b) A, B, C, and D are independently absent; (i) an antigen binding domain that selectively binds to a TCRBV antigen; (ii) an immune cell engager chosen from a T cell engager, an NK cell engager, a B cell engager, a dendritic cell engager, or a macrophage cell engager; (iii) a cytokine molecule or cytokine inhibitor molecule; (iv) a death receptor signal engager; or (v) a stromal modifying moiety, provided that:

at least one, two, or three of A, B, C, and D comprises an antigen binding domain that selectively binds to a TCRBV antigen, and

any of the remaining A, B, C, and D is absent or comprises one of an immune cell engager, a cytokine molecule, a cytokine inhibitor molecule, a death receptor signal engager, or a stromal modifying moiety.

279. The multifunctional molecule of embodiment 278, wherein:

(1) A comprises an antigen binding domain that selectively binds to a TCRBV antigen, and B, C, or D comprises an immune cell engager, *e.g.*, a T cell engager, *e.g.*, an anti-CD3 antibody molecule;

(2) A comprises an antigen binding domain that selectively binds to a TCRBV antigen, and B, C, or D comprises an immune cell engager, e.g., an NK cell engager, e.g., an anti-NKp30, anti-NKp46, anti-NKG2D, or anti-CD16 antibody molecule;

5 (3) A comprises an antigen binding domain that selectively binds to a TCRBV antigen, and B, C, or D comprises a cytokine molecule;

(4) A comprises an antigen binding domain that selectively binds to a TCRBV antigen, and B, C, or D comprises a cytokine inhibitor molecule;

(5) A comprises an antigen binding domain that selectively binds to a TCRBV antigen, and B, C, or D comprises a death receptor signal engager;

10 (6) A comprises a first antigen binding domain that selectively binds to a TCRBV antigen, B comprises a second antigen binding domain that selectively binds to a TCRBV antigen, and C or D comprises an immune cell engager, e.g., a T cell engager, e.g., an anti-CD3 antibody molecule;

15 (7) A comprises a first antigen binding domain that selectively binds to a TCRBV antigen, B comprises a second antigen binding domain that selectively binds to a TCRBV antigen, and C or D comprises an immune cell engager, e.g., an NK cell engager, e.g., an anti-NKp30, anti-NKp46, anti-NKG2D, or anti-CD16 antibody molecule;

20 (8) A comprises a first antigen binding domain that selectively binds to a TCRBV antigen, B comprises a second antigen binding domain that selectively binds to a TCRBV antigen, and C or D comprises a cytokine molecule;

(9) A comprises a first antigen binding domain that selectively binds to a TCRBV antigen, B comprises a second antigen binding domain that selectively binds to a TCRBV antigen, and C or D comprises a cytokine inhibitor molecule;

25 (10) A comprises a first antigen binding domain that selectively binds to a TCRBV antigen, B comprises a second antigen binding domain that selectively binds to a TCRBV antigen, and C or D comprises a death receptor signal engager;

30 (11) A comprises a first antigen binding domain that selectively binds to a TCRBV antigen, C comprises a second antigen binding domain that selectively binds to a TCRBV antigen, and B or D comprises an immune cell engager, e.g., a T cell engager, e.g., an anti-CD3 antibody molecule;

(12) A comprises a first antigen binding domain that selectively binds to a TCRBV antigen, C comprises a second antigen binding domain that selectively binds to a TCRBV antigen, and B or D comprises an immune cell engager, e.g., an NK cell engager, e.g., an anti-NKp30, anti-NKp46, anti-NKG2D, or anti-CD16 antibody molecule;

5 (13) A comprises a first antigen binding domain that selectively binds to a TCRBV antigen, C comprises a second antigen binding domain that selectively binds to a TCRBV antigen, and B or D comprises a cytokine molecule;

(14) A comprises a first antigen binding domain that selectively binds to a TCRBV antigen, C comprises a second antigen binding domain that selectively binds to a TCRBV antigen, and B or D comprises a cytokine inhibitor molecule;

10

(15) A comprises a first antigen binding domain that selectively binds to a TCRBV antigen, C comprises a second antigen binding domain that selectively binds to a TCRBV antigen, and B or D comprises a death receptor signal engager;

(16) A comprises a first antigen binding domain that selectively binds to a TCRBV antigen, and B, C, or D comprises (a) an immune cell engager, e.g., an NK cell engager, e.g., an anti-NKp30, anti-NKp46, anti-NKG2D, or anti-CD16 antibody molecule, and (b) a cytokine molecule;

15

(17) A comprises a first antigen binding domain that selectively binds to a TCRBV antigen, and B, C, or D comprises (a) an immune cell engager, e.g., an NK cell engager, e.g., an anti-NKp30, anti-NKp46, anti-NKG2D, or anti-CD16 antibody molecule, and (b) a cytokine inhibitor molecule;

20

(18) A comprises a first antigen binding domain that selectively binds to a TCRBV antigen, and B, C, or D comprises (a) an immune cell engager, e.g., an NK cell engager, e.g., an anti-NKp30, anti-NKp46, anti-NKG2D, or anti-CD16 antibody molecule, and (b) a death receptor signal engager;

25

(19) A comprises a first antigen binding domain that selectively binds to a TCRBV antigen, and B, C, or D comprises (a) an immune cell engager, e.g., a T cell engager, e.g., an anti-CD3 antibody molecule, and (b) a cytokine molecule;

(20) A comprises a first antigen binding domain that selectively binds to a TCRBV antigen, and B, C, or D comprises (a) an immune cell engager, e.g., a T cell engager, e.g., an anti-CD3 antibody molecule, and (b) a cytokine inhibitor molecule;

30

(21) A comprises a first antigen binding domain that selectively binds to a TCRBV antigen, and B, C, or D comprises (a) an immune cell engager, e.g., a T cell engager, e.g., an anti-CD3 antibody molecule, and (b) a death receptor signal engager;

5 (22) A comprises a first antigen binding domain that selectively binds to a TCRBV antigen, and B, C, or D comprises (a) a cytokine molecule and (b) a death receptor signal engager;

(23) A comprises a first antigen binding domain that selectively binds to a TCRBV antigen, and B, C, or D comprises (a) a cytokine inhibitor molecule and (b) a death receptor
10 signal engager;

(24) A comprises a first antigen binding domain that selectively binds to a TCRBV antigen, B comprises a second antigen binding domain that selectively binds to a TCRBV antigen, and C or D comprises (a) an immune cell engager, e.g., an NK cell engager, e.g., an anti-NKp30, anti-NKp46, anti-NKG2D, or anti-CD16 antibody molecule, and (b) a cytokine
15 molecule;

(25) A comprises a first antigen binding domain that selectively binds to a TCRBV antigen, B comprises a second antigen binding domain that selectively binds to a TCRBV antigen, and C or D comprises (a) an immune cell engager, e.g., an NK cell engager, e.g., an anti-NKp30, anti-NKp46, anti-NKG2D, or anti-CD16 antibody molecule, and (b) a cytokine
20 inhibitor molecule;

(26) A comprises a first antigen binding domain that selectively binds to a TCRBV antigen, B comprises a second antigen binding domain that selectively binds to a TCRBV antigen, and C or D comprises (a) an immune cell engager, e.g., an NK cell engager, e.g., an anti-NKp30, anti-NKp46, anti-NKG2D, or anti-CD16 antibody molecule, and (b) a death
25 receptor signal engager;

(27) A comprises a first antigen binding domain that selectively binds to a TCRBV antigen, B comprises a second antigen binding domain that selectively binds to a TCRBV antigen, and C or D comprises (a) an immune cell engager, e.g., an NK cell engager, e.g., an anti-NKp30, anti-NKp46, anti-NKG2D, or anti-CD16 antibody molecule, and (b) a stromal
30 modifying moiety;

(28) A comprises a first antigen binding domain that selectively binds to a TCRBV antigen, B comprises a second antigen binding domain that selectively binds to a TCRBV antigen, and C or D comprises (a) an immune cell engager, e.g., a T cell engager, e.g., an anti-CD3 antibody molecule, and (b) a cytokine molecule;

5 (29) A comprises a first antigen binding domain that selectively binds to a TCRBV antigen, B comprises a second antigen binding domain that selectively binds to a TCRBV antigen, and C or D comprises (a) an immune cell engager, e.g., a T cell engager, e.g., an anti-CD3 antibody molecule, and (b) a cytokine inhibitor molecule;

10 (30) A comprises a first antigen binding domain that selectively binds to a TCRBV antigen, B comprises a second antigen binding domain that selectively binds to a TCRBV antigen, and C or D comprises (a) an immune cell engager, e.g., a T cell engager, e.g., an anti-CD3 antibody molecule, and (b) a death receptor signal engager;

15 (31) A comprises a first antigen binding domain that selectively binds to a TCRBV antigen, B comprises a second antigen binding domain that selectively binds to a TCRBV antigen, and C or D comprises (a) a cytokine molecule and (b) a death receptor signal engager;

(32) A comprises a first antigen binding domain that selectively binds to a TCRBV antigen, B comprises a second antigen binding domain that selectively binds to a TCRBV antigen, and C or D comprises (a) a cytokine inhibitor molecule and (b) a death receptor signal engager;

20 (33) A comprises a first antigen binding domain that selectively binds to a TCRBV antigen, C comprises a second antigen binding domain that selectively binds to a TCRBV antigen, and B or D comprises (a) an immune cell engager, e.g., an NK cell engager, e.g., an anti-NKp30, anti-NKp46, anti-NKG2D, or anti-CD16 antibody molecule, and (b) a cytokine molecule;

25 (34) A comprises a first antigen binding domain that selectively binds to a TCRBV antigen, C comprises a second antigen binding domain that selectively binds to a TCRBV antigen, and B or D comprises (a) an immune cell engager, e.g., an NK cell engager, e.g., an anti-NKp30, anti-NKp46, anti-NKG2D, or anti-CD16 antibody molecule, and (b) a cytokine inhibitor molecule;

30 (35) A comprises a first antigen binding domain that selectively binds to a TCRBV antigen, C comprises a second antigen binding domain that selectively binds to a TCRBV

antigen, and B or D comprises (a) an immune cell engager, e.g., an NK cell engager, e.g., an anti-NKp30, anti-NKp46, anti-NKG2D, or anti-CD16 antibody molecule, and (b) a death receptor signal engager;

(36) A comprises a first antigen binding domain that selectively binds to a TCRBV antigen, C comprises a second antigen binding domain that selectively binds to a TCRBV antigen, and B or D comprises (a) an immune cell engager, e.g., a T cell engager, e.g., an anti-CD3 antibody molecule, and (b) a cytokine molecule;

(37) A comprises a first antigen binding domain that selectively binds to a TCRBV antigen, C comprises a second antigen binding domain that selectively binds to a TCRBV antigen, and B or D comprises (a) an immune cell engager, e.g., a T cell engager, e.g., an anti-CD3 antibody molecule, and (b) a cytokine inhibitor molecule;

(38) A comprises a first antigen binding domain that selectively binds to a TCRBV antigen, C comprises a second antigen binding domain that selectively binds to a TCRBV antigen, and B or D comprises (a) an immune cell engager, e.g., a T cell engager, e.g., an anti-CD3 antibody molecule, and (b) a death receptor signal engager;

(39) A comprises a first antigen binding domain that selectively binds to a TCRBV antigen, C comprises a second antigen binding domain that selectively binds to a TCRBV antigen, and B or D comprises (a) a cytokine molecule and (b) a death receptor signal engager;

(40) A comprises a first antigen binding domain that selectively binds to a TCRBV antigen, C comprises a second antigen binding domain that selectively binds to a TCRBV antigen, and B or D comprises (a) a cytokine inhibitor molecule and (b) a death receptor signal engager; or

280. The multifunctional molecule of embodiment 278 or 279, wherein the dimerization module comprises one or more immunoglobulin chain constant regions (e.g., Fc regions) comprising one or more of: a paired cavity-protuberance (“knob-in-a hole”), an electrostatic interaction, or a strand-exchange.

281. The multifunctional molecule of embodiment 280, wherein the one or more immunoglobulin chain constant regions (e.g., Fc regions) comprise an amino acid substitution at a position chosen from one or more of 347, 349, 350, 351, 366, 368, 370, 392, 394, 395, 397,

398, 399, 405, 407, or 409, e.g., of the Fc region of human IgG1, optionally wherein the one or more immunoglobulin chain constant regions (e.g., Fc regions) comprise an amino acid substitution chosen from: T366S, L368A, or Y407V (e.g., corresponding to a cavity or hole), or T366W (e.g., corresponding to a protuberance or knob), or a combination thereof.

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282. The multifunctional molecule of any one of embodiments 1-281, further comprising a linker, e.g., a linker between one or more of: the antigen binding domain and the immune cell engager, the antigen binding domain and the cytokine molecule, the antigen binding domain and the stromal modifying moiety, the immune cell engager and the cytokine molecule, the immune cell engager and the stromal modifying moiety, the cytokine molecule and the stromal modifying moiety, the antigen binding domain and the dimerization module, the immune cell engager and the dimerization module, the cytokine molecule and the dimerization module, or the stromal modifying moiety and the dimerization module.

15 283. The multifunctional molecule of embodiment 282, wherein the linker is chosen from: a cleavable linker, a non-cleavable linker, a peptide linker, a flexible linker, a rigid linker, a helical linker, or a non-helical linker.

284. The multifunctional molecule of embodiment 282 or 283, wherein the linker is a peptide linker.

285. The multifunctional molecule of 284, wherein the peptide linker comprises Gly and Ser.

25 286. The multifunctional molecule of 285, wherein the peptide linker comprises an amino acid sequence chosen from SEQ ID NOs: 7248-7251 or 7252-7253 and 77-78.

287. A multifunctional molecule, comprising:

- 30 (i) a first antigen binding domain that selectively binds to a TCRBV antigen, and
(ii) an NK cell engager, e.g., an anti-NKp30, anti-NKp46, anti-NKG2D, or anti-CD16 antibody molecule.

288. The multifunctional molecule of embodiment 287, wherein the NK cell engager comprises an anti-NKp30 antibody molecule.

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289. The multifunctional molecule of embodiment 287, wherein the NK cell engager comprises an anti-NKp46 antibody molecule.

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290. A multifunctional molecule, comprising:
(i) a first antigen binding domain that binds to, e.g., selectively binds to, T cell receptor variable beta (TCRBV), e.g., a TCRBV antigen, and
(ii) a death receptor signal engager.

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291. A multifunctional molecule, comprising:
(i) a first antigen binding domain that binds to, e.g., selectively binds to, T cell receptor variable beta (TCRBV), e.g., a TCRBV antigen, and
(ii) a cytokine inhibitor molecule, e.g., TGF-beta inhibitor.

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292. The multifunctional molecule of any of embodiments 1-291, wherein the multifunctional molecule binds to the TCRBV antigen monovalently.

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293. The multifunctional molecule of any one of embodiments 1-291, wherein the multifunctional molecule binds to the TCRBV antigen multivalently, e.g., di-, tri-, tetra-, penta-, hexa-, hepta-, octa-, nona-, or deca-valently.

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294. The multifunctional molecule of any of embodiments 2-261, wherein the multifunctional molecule binds to the TCRBV antigen on a lymphocyte expressing the TCRBV antigen.

295. The multifunctional molecule of any preceding embodiment, wherein the multifunctional molecule binds, e.g., via the immune cell engager, to the immune cell monovalently.

296. The multifunctional molecule of any one of embodiments 1-294, wherein the multifunctional molecule binds, e.g., via the immune cell engager, to the immune cell multivalently, e.g., di-, tri-, tetra-, penta-, hexa-, hepta-, octa-, nona-, or deca-valently.

297. The multifunctional molecule of any preceding embodiment, further comprising a heavy chain constant region, e.g., an Fc region, that mediates antibody dependent cellular cytotoxicity (ADCC).

298. The multifunctional molecule of any preceding embodiment, further comprising a heavy chain constant region, e.g., an Fc region, that mediates complement dependent cytotoxicity (e.g., via C1q).

299. A nucleic acid molecule encoding the multifunctional molecule of any one of embodiments 1-298.

300. A vector, e.g., an expression vector, comprising the nucleic acid molecules of embodiment 299.

301. A host cell comprising the nucleic acid molecule of embodiment 299 or the vector of embodiment 300.

302. A method of making, e.g., producing, the multifunctional molecule or antibody molecule of any one of embodiments 1-298, comprising culturing the host cell of embodiment

301, under suitable conditions, e.g., conditions suitable for gene expression and/or homo- or heterodimerization.

303. A pharmaceutical composition comprising the multifunctional molecule of any one
5 of embodiments 1-298 and a pharmaceutically acceptable carrier, excipient, or stabilizer.

304. A method of treating a TCR bias, comprising administering to a subject in need
thereof the multifunctional molecule of any one of embodiments 1-298, wherein the
multifunctional molecule is administered in an amount effective to treat the TCR bias.

305. A method of treating an autoimmune disease (e.g., an autoimmune disease
associated with a TCR bias), comprising administering to a subject in need thereof the
multifunctional molecule of any one of embodiments 1-298, wherein the multifunctional
molecule is administered in an amount effective to treat the autoimmune disease.

306. The method of either of embodiments 304 or 305, further comprising identifying,
evaluating, or selecting a subject in need of treatment, wherein identifying, evaluating, or
selecting comprises determining (e.g., directly determining or indirectly determining, e.g.,
20 obtaining information regarding) whether a subject has a TCR bias or an autoimmune disease
(e.g., an autoimmune disease associated with a TCR bias).

307. The method of embodiment 306, further comprising, responsive to determining that
a subject has a TCR bias or an autoimmune disease (e.g., an autoimmune disease associated with
25 a TCR bias):

optionally, selecting the subject for treatment with a multifunctional molecule comprising
an antigen binding domain that binds to a TCRBV antigen (e.g., a TCRBV antigen
corresponding to the biased TCRBV clonotype), and

administering a multifunctional molecule comprising an antigen binding domain that
30 binds to a TCRBV antigen (e.g., a TCRBV antigen corresponding to the biased TCRBV
clonotype).

308. A method of treating a TCR bias, comprising:

responsive to determining that a subject has a TCR bias, administering to a subject in
5 need thereof the multifunctional molecule of any one of claims 1-298, wherein the
multifunctional molecule is administered in an amount effective to treat the TCR bias.

309. A method of treating an autoimmune disease (e.g., an autoimmune disease
associated with a TCR bias), comprising:

10 responsive to determining that a subject has an autoimmune disease (e.g., an autoimmune
disease associated with a TCR bias), administering to a subject in need thereof the
multifunctional molecule of any one of claims 1-298, wherein the multifunctional molecule is
administered in an amount effective to treat the autoimmune disease (e.g., an autoimmune
disease associated with a TCR bias).

310. The method of any of embodiments 304-309, wherein the subject has a TCR bias
(e.g., a biased TCRBV clonotype) and/or an autoimmune disease associated with said bias.

20 311. A method of identifying a subject in need of treatment for cancer using a
multifunctional molecule of any of embodiments 1-298, comprising determining (e.g., directly
determining or indirectly determining, e.g., obtaining information regarding) whether a subject
has a TCR bias (e.g., a biased TCRBV clonotype) and/or an autoimmune disease associated with
25 said bias, wherein:

responsive to determining that the subject has a TCR bias (e.g., a biased TCRBV
clonotype) and/or an autoimmune disease associated with said bias, identifying the subject as a
candidate for treatment using a multifunctional molecule comprising an antigen binding domain
that binds to the TCRBV antigen, and optionally not as a candidate for treatment using a
30 multifunctional molecule comprising an antigen binding domain that does not bind to the
TCRBV antigen (e.g., that binds to a different TCRBV antigen).

312. The method of embodiment 311, further comprising:

responsive to identifying the subject as a candidate for treatment using a multifunctional molecule comprising an antigen binding domain that binds to the TCRBV antigen, treating the
 5 subject with (e.g., administering to the subject) a multifunctional molecule comprising an antigen binding domain that binds to the TCRBV antigen.

313. A method of evaluating a subject in need of treatment for a TCR bias (e.g., a biased TCRBV clonotype) and/or an autoimmune disease associated with said bias, comprising
 10 determining (e.g., directly determining or indirectly determining, e.g., obtaining information regarding) whether a subject has a TCR bias.

314. The method of embodiment 313, further comprising responsive to the evaluation, treating the subject with (e.g., administering to the subject) a multifunctional molecule
 15 comprising an antigen binding domain that binds to the TCRBV antigen.

315. The method of any one of embodiments 304-314, wherein the TCR bias is associated with an autoimmune disease.

20 316. The method of embodiment 315, wherein the autoimmune disease is selected from Churg-Strauss syndrome, sarcoidosis, systemic lupus erythematosus (SLE), type 1 diabetes, autoimmune hepatitis (e.g., type 1 or type 2), primary sclerosing cholangitis, primary biliary cirrhosis, multiple sclerosis, Guillain-Barre syndrome and the AMAN (axonal & neuronal neuropathy), chronic inflammatory demyelinating polyneuropathy (CIDP), transverse myelitis,
 25 Tolosa-Hunt syndrome (THS), Devic's disease (neuromyelitis optica), paraneoplastic cerebellar degeneration (PCD), Lambert-Eaton syndrome, psoriasis, scleroderma, CREST (calcinosis, Raynaud phenomenon, esophageal dysmotility, sclerodactyly, and telangiectasia) syndrome, dermatitis herpetiformis, dermatomyositis, bullous pemphigoid, cicatricial pemphigoid/benign mucosal pemphigoid, pemphigoid gestationis, rheumatoid arthritis (RA), psoriatic arthritis,
 30 relapsing polychondritis, chronic recurrent multifocal osteomyelitis (CRMO), vasculitis, Kawasaki disease, granulomatosis with polyangiitis (GPA), Behcet's disease (vasculitis),

Takayasu's arteritis, polyarteritis nodosa, microscopic polyangiitis (MPA), leukocytoclastic vasculitis, Cogan's syndrome, uveitis, peripheral uveitis (Pars planitis), scleritis, autoimmune inner ear disease (AIED), Crohn's, ulcerative colitis (UC), Dressler's syndrome, Rheumatic fever, Evans syndrome, paroxysmal nocturnal hemoglobinuria (PNH), hemolytic anemia, thrombocytopenic purpura (TTP), polymyositis, juvenile myositis (JM), including Juvenile Dermatomyositis (JDM) and Juvenile Polymyositis (JPM), Sjogren's syndrome, ocular cicatricial pemphigoid, or Hashimoto's thyroiditis.

317. The method of any of embodiments 304-316, further comprising administering a second therapeutic treatment.

318. The method of embodiment 317, wherein the second therapeutic treatment comprises a therapeutic agent (e.g., a chemotherapeutic agent, a biologic agent, hormonal therapy), radiation, or surgery.

319. A method of treating an autoimmune disease (e.g., an autoimmune disease associated with a TCR bias), in a subject in need thereof, comprising administering to said subject an effective amount, *e.g.*, a therapeutically effective amount, of an antibody molecule which binds (e.g., specifically binds) to a T cell receptor beta variable region (TCR β V) ("anti-TCR β V antibody molecule"), thereby treating the disorder.

320. A method of depleting a population of T cells in a subject having an autoimmune disorder (e.g., an autoimmune disease associated with a TCR bias), comprising, contacting the T cell population with an effective amount of an antibody molecule which binds (e.g., specifically binds) to a T cell receptor beta variable region (TCR β V) ("anti-TCR β V antibody molecule").

321. The method of claim 320, wherein the contacting occurs in vivo or in vitro.

322. The method of any one of claims 319-321, wherein the anti-TCR β V antibody molecule:

(i) is not an antibody molecule disclosed in US Patent 5,861,155;

(ii) binds to TCR β V12 with an affinity and/or binding specificity that is less than (*e.g.*, less than about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90% or about 2-, 5-, or 10- fold) the affinity and/or binding specificity of the 16G8 murine antibody or a humanized version thereof as described in US Patent 5,861,155;

(iii) binds to TCR β V12 with an affinity and/or binding specificity that is greater than (*e.g.*, greater than about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90% or about 2-, 5-, or 10- fold) the affinity and/or binding specificity of the 16G8 murine antibody or a humanized version thereof as described in US Patent 5,861,155;

(iii) binds to TCR β V5-5*01 or TCR β V5-1*01 with an affinity and/or binding specificity that is greater than (*e.g.*, greater than about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90% or about 2-, 5-, or 10- fold) the affinity and/or binding specificity of the TM23 murine antibody or a humanized version thereof as described in US Patent 5,861,155 or

(iv) binds to TCR β V5-5*01 or TCR β V5-1*01 with an affinity and/or binding specificity that is greater than (*e.g.*, greater than about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90% or about 2-, 5-, or 10- fold) the affinity and/or binding specificity of the TM23 murine antibody or a humanized version thereof as described in US Patent 5,861,155.

323. The method of any one of claims 319-322, wherein the anti-TCR β V antibody molecule comprises an Fc region, *e.g.*, an Fc region having effector function, *e.g.*, antibody dependent cell-mediated cytotoxicity (ADCC), Antibody-dependent cellular phagocytosis (ADCP) and/or complement dependent cytotoxicity (CDC).

324. The method of any claim 323, wherein the anti-TCR β V antibody molecule comprises an Fc region with enhanced effector function, *e.g.*, as compared to a wildtype Fc region.

325. The method of any one of claims 319-324, wherein the anti-TCR β V antibody molecule comprises a human IgG1 region or a human IgG4 region.

326. The method of any one of claims 319 or 321-325, wherein the autoimmune disease is selected from Churg-Strauss syndrome, sarcoidosis, systemic lupus erythematosus (SLE), type 1 diabetes, autoimmune hepatitis (e.g., type 1 or type 2), primary sclerosing cholangitis, primary biliary cirrhosis, multiple sclerosis, Guillain-Barre syndrome and the AMAN (axonal & neuronal neuropathy), chronic inflammatory demyelinating polyneuropathy (CIDP), transverse myelitis, Tolosa-Hunt syndrome (THS), Devic's disease (neuromyelitis optica), paraneoplastic cerebellar degeneration (PCD), Lambert-Eaton syndrome, psoriasis, scleroderma, CREST (calcinosis, Raynaud phenomenon, esophageal dysmotility, sclerodactyly, and telangiectasia) syndrome, dermatitis herpetiformis, dermatomyositis, bullous pemphigoid, cicatricial pemphigoid/benign mucosal pemphigoid, pemphigoid gestationis, rheumatoid arthritis (RA), psoriatic arthritis, relapsing polychondritis, chronic recurrent multifocal osteomyelitis (CRMO), vasculitis, Kawasaki disease, granulomatosis with polyangiitis (GPA), Behcet's disease (vasculitis), Takayasu's arteritis, polyarteritis nodosa, microscopic polyangiitis (MPA), leukocytoclastic vasculitis, Cogan's syndrome, uveitis, peripheral uveitis (Pars planitis), scleritis, autoimmune inner ear disease (AIED), Crohn's, ulcerative colitis (UC), Dressler's syndrome, Rheumatic fever, Evans syndrome, paroxysmal nocturnal hemoglobinuria (PNH), hemolytic anemia, thrombocytopenic purpura (TTP), polymyositis, juvenile myositis (JM), including Juvenile Dermatomyositis (JDM) and Juvenile Polymyositis (JPM), Sjogren's syndrome, ocular cicatricial pemphigoid, or Hashimoto's thyroiditis.

327. The method of any one of claims 319-326, wherein the anti-TCR β V antibody molecule comprises an antigen binding domain comprising one or more (e.g., all three) of a LC CDR1, LC CDR2, and LC CDR3 provided in **Tables 1A, 2A, 10A, 11A, 12A or 13A**; and/or one or more (e.g., all three) of a HC CDR1, HC CDR2, and HC CDR3 provided in **Tables 1A, 2A, 10A, 11A, 12A or 13A**, or a sequence with at least 85%, 90%, 95%, 96%, 97%, 98%, or 99% identity thereto.

328. The method of any one of claims 319-327, wherein the anti-TCR β V antibody molecule comprises a variable heavy chain (VH) and/or a variable light chain (VL) provided in **Tables 1A, 2A, 10A, 11A, 12A or 13A**, or a sequence with at least 85%, 90%, 95%, 96%, 97%, 98%, or 99% identity thereto.

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

Other features and advantages of the invention will be apparent from the following detailed description and claims.

BRIEF DESCRIPTION OF THE DRAWINGS

FIGs. 1A-1B shows the alignment of the Antibody A source mouse VH and VL framework 1, CDR 1, framework 2, CDR 2, framework 3, CDR3, and framework 4 regions with their respective humanized sequences. Kabat CDRs are shown in bold, Chothia CDRs are shown in italics, and combined CDRs are shown in boxes. The framework positions that were back mutated are double underlined. **FIG. 1A** shows VH sequences for murine Antibody A (SEQ ID NO: 1) and humanized Antibody A-H (SEQ ID NO: 9). **FIG. 1B** shows VL sequences for murine Antibody A (SEQ ID NO: 2) and humanized Antibody A-H (SEQ ID NO: 10 and SEQ ID NO: 11).

FIGs. 2A-2B shows the alignment of the Antibody B source mouse VH and VL framework 1, CDR 1, framework 2, CDR 2, framework 3, CDR3, and framework 4 regions with their respective humanized sequences. Kabat CDRs are shown in bold, Chothia CDRs are shown in italics, and combined CDRs are shown in boxes. The framework positions that were back mutated are double underlined. **FIG. 2A** shows the VH sequence for murine Antibody B (SEQ ID NO: 15) and humanized VH sequences B-H.1A to B-H.1C (SEQ ID NOs: 23-25). **FIG. 2B** shows the VL sequence for murine Antibody B (SEQ ID NO: 16) and humanized VL sequences B-H.1D to B-H.1H (SEQ ID NOs: 26-30).

FIG. 3 depicts the phylogenetic tree of TCRBV gene family and subfamilies with corresponding antibodies mapped. Subfamily identities are as follows: Subfamily A: TCR β V6; Subfamily B: TCR β V10; Subfamily C: TCR β V12; Subfamily D: TCR β V5; Subfamily E: TCR β V7; Subfamily F: TCR β V11; Subfamily G: TCR β V14; Subfamily H: TCR β V16; Subfamily I: TCR β V18; Subfamily J: TCR β V9; Subfamily K: TCR β V13; Subfamily L: TCR β V4; Subfamily M: TCR β V3; Subfamily N: TCR β V2; Subfamily O: TCR β V15; Subfamily P: TCR β V30; Subfamily Q: TCR β V19; Subfamily R: TCR β V27; Subfamily S: TCR β V28; Subfamily T: TCR β V24; Subfamily U: TCR β V20; Subfamily V: TCR β V25; and Subfamily W: TCR β V29 subfamily. Subfamily members are described in detail herein in the Section titled “TCR beta V (TCR β V)”.

FIG. 4 is a graph showing binding of NKp30 antibodies to NK92 cells. Data was calculated as the percent-AF747 positive population.

FIG. 5 is a graph showing activation of NK92 cells by NKp30 antibodies. Data were generated using hamster anti-NKp30 mAbs.

DETAILED DESCRIPTION OF THE INVENTION

Disclosed herein are multifunctional molecules (also referred to herein as “multispecific molecules”) that include a plurality of (e.g., two or more) functionalities (or binding specificities), comprising (i) an antigen binding domain that binds to, e.g., selectively binds to, T cell receptor variable beta (TCRBV), e.g., a TCRBV antigen, and (ii) one, two, or all of: (a) an immune cell engager chosen from a T cell engager, an NK cell engager (e.g., a molecule that binds to NKp30, NKp46, NKG2D, or CD16), a B cell engager, a dendritic cell engager, or a macrophage cell engager; (b) a cytokine molecule or cytokine inhibitor molecule; and (c) a death receptor signal engager. In some embodiments, the antigen binding domain comprises a sequence or part of a sequence found in Tables 13 or 14. In some embodiments, the immune cell engager comprises an NK cell engager comprising a sequence or part of a sequence found in Tables 7-10. In some embodiments, the antigen binding domain comprises a sequence or part of a sequence found in Tables 13 or 14 and the immune cell engager comprises an NK cell engager comprising a sequence or part of a sequence found in Tables 7-10.

In an embodiment, the multispecific or multifunctional molecule is a bispecific (or bifunctional) molecule, a trispecific (or trifunctional) molecule, or a tetraspecific (or tetrafunctional) molecule.

5 In some embodiments, the multifunctional molecule comprises an antigen binding domain that binds a TCRBV antigen on the surface of a lymphocyte, e.g., T cell. In some embodiments, the TCRBV antigen corresponds to a biased TCRBV clonotype, e.g., TCRs comprising the TCRBV antigen may be over-represented in the TCR repertoire or lymphocyte (e.g., T cell) pool of a subject (e.g., subjects with autoimmune disease associated with TCR bias), or expressed at a level that is higher than the level in other subjects (e.g., non-autoimmune
10 disease subjects).

Without being bound by theory, the multispecific or multifunctional molecules disclosed herein are expected to localize (e.g., bridge) and/or activate an immune cell (e.g., an immune effector cell chosen from a T cell, an NK cell, a B cell, a dendritic cell or a macrophage), in the presence of a cell (e.g., a lymphocyte, e.g., T cell) expressing the TCRBV antigen (e.g., a
15 TCRBV antigen corresponding to a biased TCRBV clonotype), e.g., on the cell surface. Increasing the proximity and/or activity of the immune cell, in the presence of the cell (e.g., a lymphocyte, e.g., T cell) expressing the TCRBV antigen (e.g., a TCRBV antigen corresponding to a biased TCRBV clonotype) using the multispecific or multifunctional molecules described herein is expected to enhance an immune response against the target cell, thereby providing a
20 more effective therapy (e.g., by decreasing the level of the biased TCR and/or T cell expressing the biased TCR). In another embodiment, targeting a cell (e.g., a lymphocyte, e.g., T cell) expressing the TCRBV antigen (e.g., a TCRBV antigen corresponding to a biased TCRBV clonotype) with a multifunctional molecule also comprising a cell death inducing moiety (e.g., a death receptor signal engager) is thought to promote the death of the target cell (e.g., by
25 decreasing the level of the biased TCR and/or T cell expressing the biased TCR).

Without being bound by theory, by utilizing, in some embodiments, a multispecific or multifunctional molecule specific for a particular TCRBV antigen (e.g., a TCRBV antigen corresponding to a biased TCRBV clonotype), but not with specificity for other or all types of T cell receptors, it is expected that the deleterious effects of increasing the proximity or activity of
30 immune cells toward T cells generally or promoting cell death in T cells generally may be mitigated. In this way, it is thought that use of the multispecific or multifunctional molecules

disclosed herein may increase the proximity or activity of immune cells toward cells comprising TCRBV antigen corresponding to a biased TCRBV clonotype without necessarily increasing proximity or activity of immune cells toward T cells generally, or promote cell death in cells comprising TCRBV antigen corresponding to a biased TCRBV clonotype without necessarily increasing cell death in T cells generally.

Accordingly, provided herein are, *inter alia*, multispecific or multifunctional molecules (e.g., multispecific or multifunctional antibody molecules) that include the aforesaid moieties, nucleic acids encoding the same, methods of producing the aforesaid molecules, and methods of treating a disease or disorder, e.g., an autoimmune disease or a TCR bias, using the aforesaid molecules.

Definitions

In some embodiments, the multifunctional molecule includes an immune cell engager. “An immune cell engager” refers to one or more binding specificities that bind and/or activate an immune cell, e.g., a cell involved in an immune response. In embodiments, the immune cell is chosen from a T cell, an NK cell, a B cell, a dendritic cell, and/or the macrophage cell. The immune cell engager can be an antibody molecule, a receptor molecule (e.g., a full length receptor, receptor fragment, or fusion thereof (e.g., a receptor-Fc fusion)), or a ligand molecule (e.g., a full length ligand, ligand fragment, or fusion thereof (e.g., a ligand-Fc fusion)) that binds to the immune cell antigen (e.g., the T cell, the NK cell antigen, the B cell antigen, the dendritic cell antigen, and/or the macrophage cell antigen). In embodiments, the immune cell engager specifically binds to the target immune cell, e.g., binds preferentially to the target immune cell. For example, when the immune cell engager is an antibody molecule, it binds to an immune cell antigen (e.g., a T cell antigen, an NK cell antigen, a B cell antigen, a dendritic cell antigen, and/or a macrophage cell antigen) with a dissociation constant of less than about 10 nM.

In some embodiments, the multifunctional molecule includes a cytokine molecule. As used herein, a “cytokine molecule” refers to full length, a fragment or a variant of a cytokine; a cytokine further comprising a receptor domain, e.g., a cytokine receptor dimerizing domain; or an agonist of a cytokine receptor, e.g., an antibody molecule (e.g., an agonistic antibody) to a cytokine receptor, that elicits at least one activity of a naturally-occurring cytokine. In some embodiments the cytokine molecule is chosen from interleukin-2 (IL-2), interleukin-7 (IL-7),

interleukin-12 (IL-12), interleukin-15 (IL-15), interleukin-18 (IL-18), interleukin-21 (IL-21), or interferon gamma, or a fragment or variant thereof, or a combination of any of the aforesaid cytokines. The cytokine molecule can be a monomer or a dimer. In embodiments, the cytokine molecule can further include a cytokine receptor dimerizing domain. In other embodiments, the cytokine molecule is an agonist of a cytokine receptor, e.g., an antibody molecule (e.g., an agonistic antibody) to a cytokine receptor chosen from an IL-15Ra or IL-21R.

As used herein, the term “molecule” as used in, e.g., antibody molecule, cytokine molecule, receptor molecule, includes full-length, naturally-occurring molecules, as well as variants, e.g., functional variants (e.g., truncations, fragments, mutated (e.g., substantially similar sequences) or derivatized form thereof), so long as at least one function and/or activity of the unmodified (e.g., naturally-occurring) molecule remains.

As used herein, the term “autoimmune” disease, disorder, or condition refers to a disease where the body's immune system attacks its own cells or tissues. An autoimmune disease can result in the production of autoantibodies that are inappropriately produced and/or excessively produced to a self-antigen or autoantigen. Autoimmune diseases include, but are not limited to, cardiovascular diseases, rheumatoid diseases, glandular diseases, gastrointestinal diseases, cutaneous diseases, hepatic diseases, neurological diseases, muscular diseases, nephric diseases, diseases related to reproduction, connective tissue diseases and systemic diseases. In some embodiments, the autoimmune disease is mediated by T cells, B cells, innate immune cells (e.g., macrophages, eosinophils, or natural killer cells), or complement-mediated pathways.

Certain terms are defined below.

As used herein, the articles “a” and “an” refer to one or more than one, e.g., to at least one, of the grammatical object of the article. The use of the words “a” or “an” when used in conjunction with the term “comprising” herein may mean “one,” but it is also consistent with the meaning of “one or more,” “at least one,” and “one or more than one.”

As used herein, “about” and “approximately” generally mean an acceptable degree of error for the quantity measured given the nature or precision of the measurements. Exemplary degrees of error are within 20 percent (%), typically, within 10%, and more typically, within 5% of a given range of values.

“Antibody molecule” as used herein refers to a protein, e.g., an immunoglobulin chain or

fragment thereof, comprising at least one immunoglobulin variable domain sequence. An antibody molecule encompasses antibodies (e.g., full-length antibodies) and antibody fragments. In an embodiment, an antibody molecule comprises an antigen binding or functional fragment of a full-length antibody, or a full length immunoglobulin chain. For example, a full-length
5 antibody is an immunoglobulin (Ig) molecule (e.g., an IgG antibody) that is naturally occurring or formed by normal immunoglobulin gene fragment recombinatorial processes). In embodiments, an antibody molecule refers to an immunologically active, antigen-binding portion of an immunoglobulin molecule, such as an antibody fragment. An antibody fragment, e.g., functional fragment, is a portion of an antibody, e.g., Fab, Fab', F(ab')₂, F(ab)₂, variable fragment
10 (Fv), domain antibody (dAb), or single chain variable fragment (scFv). A functional antibody fragment binds to the same antigen as that recognized by the intact (e.g., full-length) antibody. The terms "antibody fragment" or "functional fragment" also include isolated fragments consisting of the variable regions, such as the "Fv" fragments consisting of the variable regions of the heavy and light chains or recombinant single chain polypeptide molecules in which light
15 and heavy variable regions are connected by a peptide linker ("scFv proteins"). In some embodiments, an antibody fragment does not include portions of antibodies without antigen binding activity, such as Fc fragments or single amino acid residues. Exemplary antibody molecules include full length antibodies and antibody fragments, e.g., dAb (domain antibody), single chain, Fab, Fab', and F(ab')₂ fragments, and single chain variable fragments (scFvs).

20 As used herein, an "immunoglobulin variable domain sequence" refers to an amino acid sequence which can form the structure of an immunoglobulin variable domain. For example, the sequence may include all or part of the amino acid sequence of a naturally-occurring variable domain. For example, the sequence may or may not include one, two, or more N- or C-terminal amino acids, or may include other alterations that are compatible with formation of the protein
25 structure.

In embodiments, an antibody molecule is monospecific, e.g., it comprises binding specificity for a single epitope. In some embodiments, an antibody molecule is multispecific, e.g., it comprises a plurality of immunoglobulin variable domain sequences, where a first immunoglobulin variable domain sequence has binding specificity for a first epitope and a
30 second immunoglobulin variable domain sequence has binding specificity for a second epitope. In some embodiments, an antibody molecule is a bispecific antibody molecule. "Bispecific

antibody molecule” as used herein refers to an antibody molecule that has specificity for more than one (e.g., two, three, four, or more) epitope and/or antigen.

“Antigen” (Ag) as used herein refers to a molecule that can provoke an immune response, e.g., involving activation of certain immune cells and/or antibody generation. Any

5 macromolecule, including almost all proteins or peptides, can be an antigen. Antigens can also be derived from genomic recombinant or DNA. For example, any DNA comprising a nucleotide sequence or a partial nucleotide sequence that encodes a protein capable of eliciting an immune response encodes an “antigen.” In embodiments, an antigen does not need to be encoded solely by a full-length nucleotide sequence of a gene, nor does an antigen need to be encoded by a gene
10 at all. In embodiments, an antigen can be synthesized or can be derived from a biological sample, e.g., a tissue sample, a blood sample, a cell, or a fluid with other biological components. As used, herein a “TCRBV antigen” includes any TCR variable beta chain or portion thereof that can provoke an immune response or be targeted by an antigen binding domain. In some embodiments, biased TCR clonotypes can be characterized by one or more TCRBV antigens
15 which most, e.g., all, of the cells comprising the clonotype exhibit, e.g., on their surface.

The “antigen-binding site,” or “binding portion” of an antibody molecule refers to the part of an antibody molecule, e.g., an immunoglobulin (Ig) molecule, that participates in antigen binding. In embodiments, the antigen binding site is formed by amino acid residues of the variable (V) regions of the heavy (H) and light (L) chains. Three highly divergent stretches
20 within the variable regions of the heavy and light chains, referred to as hypervariable regions, are disposed between more conserved flanking stretches called “framework regions,” (FRs). FRs are amino acid sequences that are naturally found between, and adjacent to, hypervariable regions in immunoglobulins. In embodiments, in an antibody molecule, the three hypervariable regions of a light chain and the three hypervariable regions of a heavy chain are disposed relative to each
25 other in three dimensional space to form an antigen-binding surface, which is complementary to the three-dimensional surface of a bound antigen. The three hypervariable regions of each of the heavy and light chains are referred to as “complementarity-determining regions,” or “CDRs.” The framework region and CDRs have been defined and described, e.g., in Kabat, E.A., et al. (1991) Sequences of Proteins of Immunological Interest, Fifth Edition, U.S. Department of
30 Health and Human Services, NIH Publication No. 91-3242, and Chothia, C. et al. (1987) J. Mol. Biol. 196:901-917. Each variable chain (e.g., variable heavy chain and variable light chain) is

typically made up of three CDRs and four FRs, arranged from amino-terminus to carboxy-terminus in the amino acid order: FR1, CDR1, FR2, CDR2, FR3, CDR3, and FR4.

As used herein, an “immune cell” refers to any of various cells that function in the immune system, e.g., to protect against agents of infection and foreign matter. In embodiments, this term includes leukocytes, e.g., neutrophils, eosinophils, basophils, lymphocytes, and monocytes. Innate leukocytes include phagocytes (e.g., macrophages, neutrophils, and dendritic cells), mast cells, eosinophils, basophils, and natural killer cells. Innate leukocytes identify and eliminate pathogens, either by attacking larger pathogens through contact or by engulfing and then killing microorganisms, and are mediators in the activation of an adaptive immune response. The cells of the adaptive immune system are special types of leukocytes, called lymphocytes. B cells and T cells are important types of lymphocytes and are derived from hematopoietic stem cells in the bone marrow. B cells are involved in the humoral immune response, whereas T cells are involved in cell-mediated immune response. The term “immune cell” includes immune effector cells.

“Immune effector cell,” as that term is used herein, refers to a cell that is involved in an immune response, e.g., in the promotion of an immune effector response. Examples of immune effector cells include, but are not limited to, T cells, e.g., alpha/beta T cells and gamma/delta T cells, B cells, natural killer (NK) cells, natural killer T (NK T) cells, and mast cells.

The term “effector function” or “effector response” refers to a specialized function of a cell. Effector function of a T cell, for example, may be cytolytic activity or helper activity including the secretion of cytokines.

The compositions and methods of the present invention encompass polypeptides and nucleic acids having the sequences specified, or sequences substantially identical or similar thereto, e.g., sequences at least 80%, 85%, 90%, 95% identical or higher to the sequence specified. In the context of an amino acid sequence, the term “substantially identical” is used herein to refer to a first amino acid that contains a sufficient or minimum number of amino acid residues that are i) identical to, or ii) conservative substitutions of aligned amino acid residues in a second amino acid sequence such that the first and second amino acid sequences can have a common structural domain and/or common functional activity. For example, amino acid sequences that contain a common structural domain having at least about 80%, 85%, 90%, 91%,

92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to a reference sequence, *e.g.*, a sequence provided herein.

In the context of nucleotide sequence, the term "substantially identical" is used herein to refer to a first nucleic acid sequence that contains a sufficient or minimum number of nucleotides that are identical to aligned nucleotides in a second nucleic acid sequence such that the first and second nucleotide sequences encode a polypeptide having common functional activity, or encode a common structural polypeptide domain or a common functional polypeptide activity. For example, nucleotide sequences having at least about 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to a reference sequence, *e.g.*, a sequence provided herein.

The term "variant" refers to a polypeptide that has a substantially identical amino acid sequence to a reference amino acid sequence, or is encoded by a substantially identical nucleotide sequence. In some embodiments, the variant is a functional variant.

The term "functional variant" refers to a polypeptide that has a substantially identical amino acid sequence to a reference amino acid sequence, or is encoded by a substantially identical nucleotide sequence, and is capable of having one or more activities of the reference amino acid sequence.

Calculations of homology or sequence identity between sequences (the terms are used interchangeably herein) are performed as follows.

To determine the percent identity of two amino acid sequences, or of two nucleic acid sequences, the sequences are aligned for optimal comparison purposes (*e.g.*, gaps can be introduced in one or both of a first and a second amino acid or nucleic acid sequence for optimal alignment and non-homologous sequences can be disregarded for comparison purposes). In a preferred embodiment, the length of a reference sequence aligned for comparison purposes is at least 30%, preferably at least 40%, more preferably at least 50%, 60%, and even more preferably at least 70%, 80%, 90%, 100% of the length of the reference sequence. The amino acid residues or nucleotides at corresponding amino acid positions or nucleotide positions are then compared. When a position in the first sequence is occupied by the same amino acid residue or nucleotide as the corresponding position in the second sequence, then the molecules are identical at that position (as used herein amino acid or nucleic acid "identity" is equivalent to amino acid or nucleic acid "homology").

The percent identity between the two sequences is a function of the number of identical positions shared by the sequences, taking into account the number of gaps, and the length of each gap, which need to be introduced for optimal alignment of the two sequences.

The comparison of sequences and determination of percent identity between two
 5 sequences can be accomplished using a mathematical algorithm. In a preferred embodiment, the percent identity between two amino acid sequences is determined using the Needleman and Wunsch ((1970) *J. Mol. Biol.* 48:444-453) algorithm which has been incorporated into the GAP program in the GCG software package (available at <http://www.gcg.com>), using either a Blossum 62 matrix or a PAM250 matrix, and a gap weight of 16, 14, 12, 10, 8, 6, or 4 and a
 10 length weight of 1, 2, 3, 4, 5, or 6. In yet another preferred embodiment, the percent identity between two nucleotide sequences is determined using the GAP program in the GCG software package (available at <http://www.gcg.com>), using a NWSgapdna.CMP matrix and a gap weight of 40, 50, 60, 70, or 80 and a length weight of 1, 2, 3, 4, 5, or 6. A particularly preferred set of parameters (and the one that should be used unless otherwise specified) are a Blossum 62 scoring
 15 matrix with a gap penalty of 12, a gap extend penalty of 4, and a frameshift gap penalty of 5.

The percent identity between two amino acid or nucleotide sequences can be determined using the algorithm of E. Meyers and W. Miller ((1989) *CABIOS*, 4:11-17) which has been incorporated into the ALIGN program (version 2.0), using a PAM120 weight residue table, a gap length penalty of 12 and a gap penalty of 4.

20 The nucleic acid and protein sequences described herein can be used as a "query sequence" to perform a search against public databases to, for example, identify other family members or related sequences. Such searches can be performed using the NBLAST and XBLAST programs (version 2.0) of Altschul, *et al.* (1990) *J. Mol. Biol.* 215:403-10. BLAST nucleotide searches can be performed with the NBLAST program, score = 100, wordlength = 12
 25 to obtain nucleotide sequences homologous to a nucleic acid molecule of the invention. BLAST protein searches can be performed with the XBLAST program, score = 50, wordlength = 3 to obtain amino acid sequences homologous to protein molecules of the invention. To obtain gapped alignments for comparison purposes, Gapped BLAST can be utilized as described in Altschul *et al.*, (1997) *Nucleic Acids Res.* 25:3389-3402. When utilizing BLAST and Gapped
 30 BLAST programs, the default parameters of the respective programs (*e.g.*, XBLAST and NBLAST) can be used. See <http://www.ncbi.nlm.nih.gov>.

It is understood that the molecules of the present invention may have additional conservative or non-essential amino acid substitutions, which do not have a substantial effect on their functions.

The term "amino acid" is intended to embrace all molecules, whether natural or synthetic, which include both an amino functionality and an acid functionality and capable of being included in a polymer of naturally-occurring amino acids. Exemplary amino acids include naturally-occurring amino acids; analogs, derivatives and congeners thereof; amino acid analogs having variant side chains; and all stereoisomers of any of any of the foregoing. As used herein the term "amino acid" includes both the D- or L- optical isomers and peptidomimetics.

A "conservative amino acid substitution" is one in which the amino acid residue is replaced with an amino acid residue having a similar side chain. Families of amino acid residues having similar side chains have been defined in the art. These families include amino acids with basic side chains (*e.g.*, lysine, arginine, histidine), acidic side chains (*e.g.*, aspartic acid, glutamic acid), uncharged polar side chains (*e.g.*, glycine, asparagine, glutamine, serine, threonine, tyrosine, cysteine), nonpolar side chains (*e.g.*, alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan), beta-branched side chains (*e.g.*, threonine, valine, isoleucine) and aromatic side chains (*e.g.*, tyrosine, phenylalanine, tryptophan, histidine).

The terms "polypeptide", "peptide" and "protein" (if single chain) are used interchangeably herein to refer to polymers of amino acids of any length. The polymer may be linear or branched, it may comprise modified amino acids, and it may be interrupted by non-amino acids. The terms also encompass an amino acid polymer that has been modified; for example, disulfide bond formation, glycosylation, lipidation, acetylation, phosphorylation, or any other manipulation, such as conjugation with a labeling component. The polypeptide can be isolated from natural sources, can be produced by recombinant techniques from a eukaryotic or prokaryotic host, or can be a product of synthetic procedures.

The terms "nucleic acid," "nucleic acid sequence," "nucleotide sequence," or "polynucleotide sequence," and "polynucleotide" are used interchangeably. They refer to a polymeric form of nucleotides of any length, either deoxyribonucleotides or ribonucleotides, or analogs thereof. The polynucleotide may be either single-stranded or double-stranded, and if single-stranded may be the coding strand or non-coding (antisense) strand. A polynucleotide may comprise modified nucleotides, such as methylated nucleotides and nucleotide analogs. The

sequence of nucleotides may be interrupted by non-nucleotide components. A polynucleotide may be further modified after polymerization, such as by conjugation with a labeling component. The nucleic acid may be a recombinant polynucleotide, or a polynucleotide of genomic, cDNA, semisynthetic, or synthetic origin which either does not occur in nature or is linked to another
 5 polynucleotide in a non-natural arrangement.

The term "isolated," as used herein, refers to material that is removed from its original or native environment (*e.g.*, the natural environment if it is naturally occurring). For example, a naturally-occurring polynucleotide or polypeptide present in a living animal is not isolated, but the same polynucleotide or polypeptide, separated by human intervention from some or all of the
 10 co-existing materials in the natural system, is isolated. Such polynucleotides could be part of a vector and/or such polynucleotides or polypeptides could be part of a composition, and still be isolated in that such vector or composition is not part of the environment in which it is found in nature.

Various aspects of the invention are described in further detail below. Additional
 15 definitions are set out throughout the specification.

Antibody Molecules

In one embodiment, the antibody molecule binds to a TCRBV antigen, *e.g.*, a (e.g., a TCRBV antigen corresponding to a biased TCRBV clonotype). In some embodiments, the
 20 TCRBV antigen is, *e.g.*, a mammalian, *e.g.*, a human, TCRBV antigen. In some embodiments, the antibody molecule binds to a TCRBV antigen on an lymphocyte, *e.g.*, T cell, *e.g.*, a mammalian, *e.g.*, a human, lymphocyte, *e.g.*, T cell. For example, the antibody molecule binds specifically to a TCRBV antigen expressed, *e.g.*, as part of a TCR comprising the TCRBV, on the surface of an lymphocyte, *e.g.*, T cell.

25 In an embodiment, an antibody molecule is a monospecific antibody molecule and binds a single epitope. *E.g.*, a monospecific antibody molecule having a plurality of immunoglobulin variable domain sequences, each of which binds the same epitope.

In an embodiment an antibody molecule is a multispecific or multifunctional antibody molecule, *e.g.*, it comprises a plurality of immunoglobulin variable domains sequences, wherein
 30 a first immunoglobulin variable domain sequence of the plurality has binding specificity for a first epitope and a second immunoglobulin variable domain sequence of the plurality has binding

specificity for a second epitope. In an embodiment the first and second epitopes are on the same antigen, *e.g.*, the same protein (or subunit of a multimeric protein). In an embodiment the first and second epitopes overlap. In an embodiment the first and second epitopes do not overlap. In an embodiment the first and second epitopes are on different antigens, *e.g.*, the different proteins (or different subunits of a multimeric protein). In an embodiment a multispecific antibody molecule comprises a third, fourth or fifth immunoglobulin variable domain. In an embodiment, a multispecific antibody molecule is a bispecific antibody molecule, a trispecific antibody molecule, or a tetraspecific antibody molecule.

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

In an embodiment, an antibody molecule comprises a diabody, and a single-chain molecule, as well as an antigen-binding fragment of an antibody (*e.g.*, Fab, F(ab')₂, and Fv). For example, an antibody molecule can include a heavy (H) chain variable domain sequence

(abbreviated herein as VH), and a light (L) chain variable domain sequence (abbreviated herein as VL). In an embodiment an antibody molecule comprises or consists of a heavy chain and a light chain (referred to herein as a half antibody). In another example, an antibody molecule includes two heavy (H) chain variable domain sequences and two light (L) chain variable domain sequence, thereby forming two antigen binding sites, such as Fab, Fab', F(ab')₂, Fc, Fd, Fd', Fv, single chain antibodies (scFv for example), single variable domain antibodies, diabodies (Dab) (bivalent and bispecific), and chimeric (*e.g.*, humanized) antibodies, which may be produced by the modification of whole antibodies or those synthesized *de novo* using recombinant DNA technologies. These functional antibody fragments retain the ability to selectively bind with their respective antigen or receptor. Antibodies and antibody fragments can be from any class of antibodies including, but not limited to, IgG, IgA, IgM, IgD, and IgE, and from any subclass (*e.g.*, IgG1, IgG2, IgG3, and IgG4) of antibodies. The a preparation of antibody molecules can be monoclonal or polyclonal. An antibody molecule can also be a human, humanized, CDR-grafted, or *in vitro* generated antibody. The antibody can have a heavy chain constant region chosen from, *e.g.*, IgG1, IgG2, IgG3, or IgG4. The antibody can also have a light chain chosen from, *e.g.*, kappa or lambda. The term "immunoglobulin" (Ig) is used interchangeably with the term "antibody" herein.

Examples of antigen-binding fragments of an antibody molecule include: (i) a Fab fragment, a monovalent fragment consisting of the VL, VH, CL and CH1 domains; (ii) a F(ab')₂ fragment, a bivalent fragment comprising two Fab fragments linked by a disulfide bridge at the hinge region; (iii) a Fd fragment consisting of the VH and CH1 domains; (iv) a Fv fragment consisting of the VL and VH domains of a single arm of an antibody, (v) a diabody (dAb) fragment, which consists of a VH domain; (vi) a camelid or camelized variable domain; (vii) a single chain Fv (scFv), *see e.g.*, Bird *et al.* (1988) *Science* 242:423-426; and Huston *et al.* (1988) *Proc. Natl. Acad. Sci. USA* 85:5879-5883); (viii) a single domain antibody. These antibody fragments are obtained using conventional techniques known to those with skill in the art, and the fragments are screened for utility in the same manner as are intact antibodies.

Antibody molecules include intact molecules as well as functional fragments thereof. Constant regions of the antibody molecules can be altered, *e.g.*, mutated, to modify the properties of the antibody (*e.g.*, to increase or decrease one or more of: Fc receptor binding, antibody glycosylation, the number of cysteine residues, effector cell function, or complement function).

Antibody molecules can also be single domain antibodies. Single domain antibodies can include antibodies whose complementary determining regions are part of a single domain polypeptide. Examples include, but are not limited to, heavy chain antibodies, antibodies naturally devoid of light chains, single domain antibodies derived from conventional 4-chain antibodies, engineered antibodies and single domain scaffolds other than those derived from antibodies. Single domain antibodies may be any of the art, or any future single domain antibodies. Single domain antibodies may be derived from any species including, but not limited to mouse, human, camel, llama, fish, shark, goat, rabbit, and bovine. According to another aspect of the invention, a single domain antibody is a naturally occurring single domain antibody known as heavy chain antibody devoid of light chains. Such single domain antibodies are disclosed in WO 9404678, for example. For clarity reasons, this variable domain derived from a heavy chain antibody naturally devoid of light chain is known herein as a VHH or nanobody to distinguish it from the conventional VH of four chain immunoglobulins. Such a VHH molecule can be derived from antibodies raised in *Camelidae* species, for example in camel, llama, dromedary, alpaca and guanaco. Other species besides *Camelidae* may produce heavy chain antibodies naturally devoid of light chain; such VHHs are within the scope of the invention.

The VH and VL regions can be subdivided into regions of hypervariability, termed "complementarity determining regions" (CDR), interspersed with regions that are more conserved, termed "framework regions" (FR or FW).

The extent of the framework region and CDRs has been precisely defined by a number of methods (*see*, Kabat, E. A., *et al.* (1991) Sequences of Proteins of Immunological Interest, Fifth Edition, U.S. Department of Health and Human Services, NIH Publication No. 91-3242; Chothia, C. *et al.* (1987) *J. Mol. Biol.* 196:901-917; and the AbM definition used by Oxford Molecular's AbM antibody modeling software. *See*, generally, *e.g.*, *Protein Sequence and Structure Analysis of Antibody Variable Domains*. In: Antibody Engineering Lab Manual (Ed.: Duebel, S. and Kontermann, R., Springer-Verlag, Heidelberg).

The terms "complementarity determining region," and "CDR," as used herein refer to the sequences of amino acids within antibody variable regions which confer antigen specificity and binding affinity. In general, there are three CDRs in each heavy chain variable region (HCDR1, HCDR2, HCDR3) and three CDRs in each light chain variable region (LCDR1, LCDR2, LCDR3).

The precise amino acid sequence boundaries of a given CDR can be determined using any of a number of known schemes, including those described by Kabat *et al.* (1991), "Sequences of Proteins of Immunological Interest," 5th Ed. Public Health Service, National Institutes of Health, Bethesda, MD ("Kabat" numbering scheme), Al-Lazikani *et al.*, (1997) *JMB* 273,927-948 ("Chothia" numbering scheme). As used herein, the CDRs defined according the "Chothia" number scheme are also sometimes referred to as "hypervariable loops."

For example, under Kabat, the CDR amino acid residues in the heavy chain variable domain (VH) are numbered 31-35 (HCDR1), 50-65 (HCDR2), and 95-102 (HCDR3); and the CDR amino acid residues in the light chain variable domain (VL) are numbered 24-34 (LCDR1), 50-56 (LCDR2), and 89-97 (LCDR3). Under Chothia, the CDR amino acids in the VH are numbered 26-32 (HCDR1), 52-56 (HCDR2), and 95-102 (HCDR3); and the amino acid residues in VL are numbered 26-32 (LCDR1), 50-52 (LCDR2), and 91-96 (LCDR3).

Each VH and VL typically includes three CDRs and four FRs, arranged from amino-terminus to carboxy-terminus in the following order: FR1, CDR1, FR2, CDR2, FR3, CDR3, FR4.

The antibody molecule can be a polyclonal or a monoclonal antibody.

The terms "monoclonal antibody" or "monoclonal antibody composition" as used herein refer to a preparation of antibody molecules of single molecular composition. A monoclonal antibody composition displays a single binding specificity and affinity for a particular epitope. A monoclonal antibody can be made by hybridoma technology or by methods that do not use hybridoma technology (*e.g.*, recombinant methods).

The antibody can be recombinantly produced, *e.g.*, produced by phage display or by combinatorial methods.

Phage display and combinatorial methods for generating antibodies are known in the art (as described in, *e.g.*, Ladner *et al.* U.S. Patent No. 5,223,409; Kang *et al.* International Publication No. WO 92/18619; Dower *et al.* International Publication No. WO 91/17271; Winter *et al.* International Publication WO 92/20791; Markland *et al.* International Publication No. WO 92/15679; Breitling *et al.* International Publication WO 93/01288; McCafferty *et al.* International Publication No. WO 92/01047; Garrard *et al.* International Publication No. WO 92/09690; Ladner *et al.* International Publication No. WO 90/02809; Fuchs *et al.* (1991) *Bio/Technology* 9:1370-1372; Hay *et al.* (1992) *Hum Antibod Hybridomas* 3:81-85; Huse *et al.*

(1989) *Science* 246:1275-1281; Griffiths *et al.* (1993) *EMBO J* 12:725-734; Hawkins *et al.* (1992) *J Mol Biol* 226:889-896; Clackson *et al.* (1991) *Nature* 352:624-628; Gram *et al.* (1992) *PNAS* 89:3576-3580; Garrad *et al.* (1991) *Bio/Technology* 9:1373-1377; Hoogenboom *et al.* (1991) *Nuc Acid Res* 19:4133-4137; and Barbas *et al.* (1991) *PNAS* 88:7978-7982, the contents of all of which are incorporated by reference herein).

In one embodiment, the antibody is a fully human antibody (*e.g.*, an antibody made in a mouse which has been genetically engineered to produce an antibody from a human immunoglobulin sequence), or a non-human antibody, *e.g.*, a rodent (mouse or rat), goat, primate (*e.g.*, monkey), camel antibody. Preferably, the non-human antibody is a rodent (mouse or rat antibody). Methods of producing rodent antibodies are known in the art.

Human monoclonal antibodies can be generated using transgenic mice carrying the human immunoglobulin genes rather than the mouse system. Splenocytes from these transgenic mice immunized with the antigen of interest are used to produce hybridomas that secrete human mAbs with specific affinities for epitopes from a human protein (see, *e.g.*, Wood *et al.* International Application WO 91/00906, Kucherlapati *et al.* PCT publication WO 91/10741; Lonberg *et al.* International Application WO 92/03918; Kay *et al.* International Application 92/03917; Lonberg, N. *et al.* 1994 *Nature* 368:856-859; Green, L.L. *et al.* 1994 *Nature Genet.* 7:13-21; Morrison, S.L. *et al.* 1994 *Proc. Natl. Acad. Sci. USA* 81:6851-6855; Bruggeman *et al.* 1993 *Year Immunol* 7:33-40; Tuailon *et al.* 1993 *PNAS* 90:3720-3724; Bruggeman *et al.* 1991 *Eur J Immunol* 21:1323-1326).

An antibody molecule can be one in which the variable region, or a portion thereof, *e.g.*, the CDRs, are generated in a non-human organism, *e.g.*, a rat or mouse. Chimeric, CDR-grafted, and humanized antibodies are within the invention. Antibody molecules generated in a non-human organism, *e.g.*, a rat or mouse, and then modified, *e.g.*, in the variable framework or constant region, to decrease antigenicity in a human are within the invention.

An “effectively human” protein is a protein that does substantially not evoke a neutralizing antibody response, *e.g.*, the human anti-murine antibody (HAMA) response. HAMA can be problematic in a number of circumstances, *e.g.*, if the antibody molecule is administered repeatedly, *e.g.*, in treatment of a chronic or recurrent disease condition. A HAMA response can make repeated antibody administration potentially ineffective because of an increased antibody clearance from the serum (see, *e.g.*, Saleh *et al.*, *Cancer Immunol.*

Immunother., 32:180-190 (1990)) and also because of potential allergic reactions (*see, e.g.,* LoBuglio *et al.*, *Hybridoma*, 5:5117-5123 (1986)).

Chimeric antibodies can be produced by recombinant DNA techniques known in the art (see Robinson *et al.*, International Patent Publication PCT/US86/02269; Akira, *et al.*, European Patent Application 184,187; Taniguchi, M., European Patent Application 171,496; Morrison *et al.*, European Patent Application 173,494; Neuberger *et al.*, International Application WO 86/01533; Cabilly *et al.* U.S. Patent No. 4,816,567; Cabilly *et al.*, European Patent Application 125,023; Better *et al.* (1988 *Science* 240:1041-1043); Liu *et al.* (1987) *PNAS* 84:3439-3443; Liu *et al.*, 1987, *J. Immunol.* 139:3521-3526; Sun *et al.* (1987) *PNAS* 84:214-218; Nishimura *et al.*, 1987, *Canc. Res.* 47:999-1005; Wood *et al.* (1985) *Nature* 314:446-449; and Shaw *et al.*, 1988, *J. Natl Cancer Inst.* 80:1553-1559).

A humanized or CDR-grafted antibody will have at least one or two but generally all three recipient CDRs (of heavy and or light immunoglobulin chains) replaced with a donor CDR. The antibody may be replaced with at least a portion of a non-human CDR or only some of the CDRs may be replaced with non-human CDRs. It is only necessary to replace the number of CDRs required for binding to the antigen. Preferably, the donor will be a rodent antibody, *e.g.*, a rat or mouse antibody, and the recipient will be a human framework or a human consensus framework. Typically, the immunoglobulin providing the CDRs is called the "donor" and the immunoglobulin providing the framework is called the "acceptor." In one embodiment, the donor immunoglobulin is a non-human (*e.g.*, rodent). The acceptor framework is a naturally-occurring (*e.g.*, a human) framework or a consensus framework, or a sequence about 85% or higher, preferably 90%, 95%, 99% or higher identical thereto.

As used herein, the term "consensus sequence" refers to the sequence formed from the most frequently occurring amino acids (or nucleotides) in a family of related sequences (See *e.g.*, Winnaker, *From Genes to Clones* (Verlagsgesellschaft, Weinheim, Germany 1987). In a family of proteins, each position in the consensus sequence is occupied by the amino acid occurring most frequently at that position in the family. If two amino acids occur equally frequently, either can be included in the consensus sequence. A "consensus framework" refers to the framework region in the consensus immunoglobulin sequence.

An antibody molecule can be humanized by methods known in the art (*see e.g.*, Morrison, S. L., 1985, *Science* 229:1202-1207, by Oi *et al.*, 1986, *BioTechniques* 4:214, and by

Queen *et al.* US 5,585,089, US 5,693,761 and US 5,693,762, the contents of all of which are hereby incorporated by reference).

Humanized or CDR-grafted antibody molecules can be produced by CDR-grafting or CDR substitution, wherein one, two, or all CDRs of an immunoglobulin chain can be replaced.

5 See *e.g.*, U.S. Patent 5,225,539; Jones *et al.* 1986 *Nature* 321:552-525; Verhoeven *et al.* 1988 *Science* 239:1534; Beidler *et al.* 1988 *J. Immunol.* 141:4053-4060; Winter US 5,225,539, the contents of all of which are hereby expressly incorporated by reference. Winter describes a CDR-grafting method which may be used to prepare the humanized antibodies of the present invention (UK Patent Application GB 2188638A, filed on March 26, 1987; Winter US
10 5,225,539), the contents of which is expressly incorporated by reference.

Also within the scope of the invention are humanized antibody molecules in which specific amino acids have been substituted, deleted or added. Criteria for selecting amino acids from the donor are described in US 5,585,089, *e.g.*, columns 12-16 of US 5,585,089, *e.g.*, columns 12-16 of US 5,585,089, the contents of which are hereby incorporated by reference.

15 Other techniques for humanizing antibodies are described in Padlan *et al.* EP 519596 A1, published on December 23, 1992.

The antibody molecule can be a single chain antibody. A single-chain antibody (scFV) may be engineered (see, for example, Colcher, D. *et al.* (1999) *Ann N Y Acad Sci* 880:263-80; and Reiter, Y. (1996) *Clin Cancer Res* 2:245-52). The single chain antibody can be dimerized or
20 multimerized to generate multivalent antibodies having specificities for different epitopes of the same target protein.

In yet other embodiments, the antibody molecule has a heavy chain constant region chosen from, *e.g.*, the heavy chain constant regions of IgG1, IgG2, IgG3, IgG4, IgM, IgA1, IgA2, IgD, and IgE; particularly, chosen from, *e.g.*, the (*e.g.*, human) heavy chain constant
25 regions of IgG1, IgG2, IgG3, and IgG4. In another embodiment, the antibody molecule has a light chain constant region chosen from, *e.g.*, the (*e.g.*, human) light chain constant regions of kappa or lambda. The constant region can be altered, *e.g.*, mutated, to modify the properties of the antibody (*e.g.*, to increase or decrease one or more of: Fc receptor binding, antibody glycosylation, the number of cysteine residues, effector cell function, and/or complement
30 function). In one embodiment the antibody has: effector function; and can fix complement. In other embodiments the antibody does not; recruit effector cells; or fix complement. In another

embodiment, the antibody has reduced or no ability to bind an Fc receptor. For example, it is a isotype or subtype, fragment or other mutant, which does not support binding to an Fc receptor, *e.g.*, it has a mutagenized or deleted Fc receptor binding region.

Methods for altering an antibody constant region are known in the art. Antibodies with
5 altered function, *e.g.* altered affinity for an effector ligand, such as FcR on a cell, or the C1 component of complement can be produced by replacing at least one amino acid residue in the constant portion of the antibody with a different residue (*see e.g.*, EP 388,151 A1, U.S. Pat. No. 5,624,821 and U.S. Pat. No. 5,648,260, the contents of all of which are hereby incorporated by reference). Similar type of alterations could be described which if applied to the murine, or other
10 species immunoglobulin would reduce or eliminate these functions.

An antibody molecule can be derivatized or linked to another functional molecule (*e.g.*, another peptide or protein). As used herein, a "derivatized" antibody molecule is one that has been modified. Methods of derivatization include but are not limited to the addition of a fluorescent moiety, a radionucleotide, a toxin, an enzyme or an affinity ligand such as biotin.
15 Accordingly, the antibody molecules of the invention are intended to include derivatized and otherwise modified forms of the antibodies described herein, including immunoadhesion molecules. For example, an antibody molecule can be functionally linked (by chemical coupling, genetic fusion, noncovalent association or otherwise) to one or more other molecular entities, such as another antibody (*e.g.*, a bispecific antibody or a diabody), a detectable agent, a cytotoxic
20 agent, a pharmaceutical agent, and/or a protein or peptide that can mediate association of the antibody or antibody portion with another molecule (such as a streptavidin core region or a polyhistidine tag).

One type of derivatized antibody molecule is produced by crosslinking two or more antibodies (of the same type or of different types, *e.g.*, to create bispecific antibodies). Suitable
25 crosslinkers include those that are heterobifunctional, having two distinctly reactive groups separated by an appropriate spacer (*e.g.*, m-maleimidobenzoyl-N-hydroxysuccinimide ester) or homobifunctional (*e.g.*, disuccinimidyl suberate). Such linkers are available from Pierce Chemical Company, Rockford, Ill.

Multispecific or multifunctional antibody molecules

Exemplary structures of multispecific and multifunctional molecules defined herein are described throughout. Exemplary structures are further described in: Weidle U et al. (2013) The Intriguing Options of Multispecific Antibody Formats for Treatment of Cancer. *Cancer*

5 *Genomics & Proteomics* 10: 1-18 (2013); and Spiess C et al. (2015) Alternative molecular formats and therapeutic applications for bispecific antibodies. *Molecular Immunology* 67: 95-106; the full contents of each of which is incorporated by reference herein).

In embodiments, multispecific antibody molecules can comprise more than one antigen-binding site, where different sites are specific for different antigens. In embodiments, multispecific antibody molecules can bind more than one (e.g., two or more) epitopes on the same antigen. In embodiments, multispecific antibody molecules comprise an antigen-binding site specific for a target cell (e.g., lymphocyte (e.g., T cell) comprising a TCRBV antigen corresponding to a biased TCRBV clonotype) and a different antigen-binding site specific for an immune effector cell. In one embodiment, the multispecific antibody molecule is a bispecific antibody molecule. Bispecific antibody molecules can be classified into five different structural groups: (i) bispecific immunoglobulin G (BsIgG); (ii) IgG appended with an additional antigen-binding moiety; (iii) bispecific antibody fragments; (iv) bispecific fusion proteins; and (v) bispecific antibody conjugates.

BsIgG is a format that is monovalent for each antigen. Exemplary BsIgG formats include but are not limited to crossMab, DAF (two-in-one), DAF (four-in-one), DutaMab, DT-IgG, knobs-in-holes common LC, knobs-in-holes assembly, charge pair, Fab-arm exchange, SEEDbody, triomab, LUZ-Y, Fcab, $\kappa\lambda$ -body, orthogonal Fab. See Spiess et al. Mol. Immunol. 67(2015):95-106. Exemplary BsIgGs include catumaxomab (Fresenius Biotech, Trion Pharma, Neopharm), which contains an anti-CD3 arm and an anti-EpCAM arm; and ertumaxomab (Neovii Biotech, Fresenius Biotech), which targets CD3 and HER2. In some embodiments, BsIgG comprises heavy chains that are engineered for heterodimerization. For example, heavy chains can be engineered for heterodimerization using a “knobs-into-holes” strategy, a SEED platform, a common heavy chain (e.g., in $\kappa\lambda$ -bodies), and use of heterodimeric Fc regions. See Spiess et al. Mol. Immunol. 67(2015):95-106. Strategies that have been used to avoid heavy chain pairing of homodimers in BsIgG include knobs-in-holes, duobody, azymetric, charge pair, HA-TF, SEEDbody, and differential protein A affinity. See *Id.* BsIgG can be produced by

separate expression of the component antibodies in different host cells and subsequent purification/assembly into a BsIgG. BsIgG can also be produced by expression of the component antibodies in a single host cell. BsIgG can be purified using affinity chromatography, e.g., using protein A and sequential pH elution.

5 IgG appended with an additional antigen-binding moiety is another format of bispecific antibody molecules. For example, monospecific IgG can be engineered to have bispecificity by appending an additional antigen-binding unit onto the monospecific IgG, e.g., at the N- or C-terminus of either the heavy or light chain. Exemplary additional antigen-binding units include single domain antibodies (e.g., variable heavy chain or variable light chain), engineered protein
10 scaffolds, and paired antibody variable domains (e.g., single chain variable fragments or variable fragments). *See Id.* Examples of appended IgG formats include dual variable domain IgG (DVD-Ig), IgG(H)-scFv, scFv-(H)IgG, IgG(L)-scFv, scFv-(L)IgG, IgG(L,H)-Fv, IgG(H)-V, V(H)-IgG, IgG(L)-V, V(L)-IgG, KIH IgG-scFab, 2scFv-IgG, IgG-2scFv, scFv4-Ig, zyboby, and DVI-IgG (four-in-one). *See* Spiess et al. Mol. Immunol. 67(2015):95-106. An example of an
15 IgG-scFv is MM-141 (Merrimack Pharmaceuticals), which binds IGF-1R and HER3. Examples of DVD-Ig include ABT-981 (AbbVie), which binds IL-1 α and IL-1 β ; and ABT-122 (AbbVie), which binds TNF and IL-17A.

Bispecific antibody fragments (BsAb) are a format of bispecific antibody molecules that lack some or all of the antibody constant domains. For example, some BsAb lack an Fc region.
20 In embodiments, bispecific antibody fragments include heavy and light chain regions that are connected by a peptide linker that permits efficient expression of the BsAb in a single host cell. Exemplary bispecific antibody fragments include but are not limited to nanobody, nanobody-HAS, BiTE, Diabody, DART, TandAb, scDiabody, scDiabody-CH3, Diabody-CH3, triple body, miniantibody, minibody, TriBi minibody, scFv-CH3 KIH, Fab-scFv, scFv-CH-CL-scFv, F(ab')₂,
25 F(ab')₂-scFv₂, scFv-KIH, Fab-scFv-Fc, tetravalent HCAb, scDiabody-Fc, Diabody-Fc, tandem scFv-Fc, and intrabody. *See Id.* For example, the BiTE format comprises tandem scFvs, where the component scFvs bind to CD3 on T cells and a TCRBV antigen on lymphocytes, e.g. T cells.

Bispecific fusion proteins include antibody fragments linked to other proteins, e.g., to add additional specificity and/or functionality. An example of a bispecific fusion protein is an
30 immTAC, which comprises an anti-CD3 scFv linked to an affinity-matured T-cell receptor that recognizes HLA-presented peptides. In embodiments, the dock-and-lock (DNL) method can be

used to generate bispecific antibody molecules with higher valency. Also, fusions to albumin binding proteins or human serum albumin can be extend the serum half-life of antibody fragments. *See Id.*

In embodiments, chemical conjugation, e.g., chemical conjugation of antibodies and/or antibody fragments, can be used to create BsAb molecules. *See Id.* An exemplary bispecific antibody conjugate includes the CovX-body format, in which a low molecular weight drug is conjugated site-specifically to a single reactive lysine in each Fab arm or an antibody or fragment thereof. In embodiments, the conjugation improves the serum half-life of the low molecular weight drug. An exemplary CovX-body is CVX-241 (NCT01004822), which comprises an antibody conjugated to two short peptides inhibiting either VEGF or Ang2. *See Id.*

The antibody molecules can be produced by recombinant expression, e.g., of at least one or more component, in a host system. Exemplary host systems include eukaryotic cells (e.g., mammalian cells, e.g., CHO cells, or insect cells, e.g., SF9 or S2 cells) and prokaryotic cells (e.g., *E. coli*). Bispecific antibody molecules can be produced by separate expression of the components in different host cells and subsequent purification/assembly. Alternatively, the antibody molecules can be produced by expression of the components in a single host cell. Purification of bispecific antibody molecules can be performed by various methods such as affinity chromatography, e.g., using protein A and sequential pH elution. In other embodiments, affinity tags can be used for purification, e.g., histidine-containing tag, myc tag, or streptavidin tag.

CDR-grafted scaffolds

In embodiments, the antibody molecule is a CDR-grafted scaffold domain. In embodiments, the scaffold domain is based on a fibronectin domain, e.g., fibronectin type III domain. The overall fold of the fibronectin type III (Fn3) domain is closely related to that of the smallest functional antibody fragment, the variable domain of the antibody heavy chain. There are three loops at the end of Fn3; the positions of BC, DE and FG loops approximately correspond to those of CDR1, 2 and 3 of the VH domain of an antibody. Fn3 does not have disulfide bonds; and therefore Fn3 is stable under reducing conditions, unlike antibodies and their fragments (see, e.g., WO 98/56915; WO 01/64942; WO 00/34784). An Fn3 domain can be

modified (e.g., using CDRs or hypervariable loops described herein) or varied, e.g., to select domains that bind to an antigen/marker/cell described herein.

In embodiments, a scaffold domain, e.g., a folded domain, is based on an antibody, e.g., a “minibody” scaffold created by deleting three beta strands from a heavy chain variable domain of a monoclonal antibody (see, e.g., Tramontano et al., 1994, J Mol. Recognit. 7:9; and Martin et al., 1994, EMBO J. 13:5303-5309). The “minibody” can be used to present two hypervariable loops. In embodiments, the scaffold domain is a V-like domain (see, e.g., Coia et al. WO 99/45110) or a domain derived from tendamistatin, which is a 74 residue, six-strand beta sheet sandwich held together by two disulfide bonds (see, e.g., McConnell and Hoess, 1995, J Mol. Biol. 250:460). For example, the loops of tendamistatin can be modified (e.g., using CDRs or hypervariable loops) or varied, e.g., to select domains that bind to a marker/antigen/cell described herein. Another exemplary scaffold domain is a beta-sandwich structure derived from the extracellular domain of CTLA-4 (see, e.g., WO 00/60070).

Other exemplary scaffold domains include but are not limited to T-cell receptors; MHC proteins; extracellular domains (e.g., fibronectin Type III repeats, EGF repeats); protease inhibitors (e.g., Kunitz domains, ecotin, BPTI, and so forth); TPR repeats; trifoil structures; zinc finger domains; DNA-binding proteins; particularly monomeric DNA binding proteins; RNA binding proteins; enzymes, e.g., proteases (particularly inactivated proteases), RNase; chaperones, e.g., thioredoxin, and heat shock proteins; and intracellular signaling domains (such as SH2 and SH3 domains). See, e.g., US 20040009530 and US 7,501,121, incorporated herein by reference.

In embodiments, a scaffold domain is evaluated and chosen, e.g., by one or more of the following criteria: (1) amino acid sequence, (2) sequences of several homologous domains, (3) 3-dimensional structure, and/or (4) stability data over a range of pH, temperature, salinity, organic solvent, oxidant concentration. In embodiments, the scaffold domain is a small, stable protein domain, e.g., a protein of less than 100, 70, 50, 40 or 30 amino acids. The domain may include one or more disulfide bonds or may chelate a metal, e.g., zinc.

Antibody-Based Fusions

A variety of formats can be generated which contain additional binding entities attached to the N or C terminus of antibodies. These fusions with single chain or disulfide stabilized Fvs

or Fabs result in the generation of tetravalent molecules with bivalent binding specificity for each antigen. Combinations of scFvs and scFabs with IgGs enable the production of molecules which can recognize three or more different antigens.

5 *Antibody-Fab Fusion*

Antibody-Fab fusions are bispecific antibodies comprising a traditional antibody to a first target and a Fab to a second target fused to the C terminus of the antibody heavy chain.

Commonly the antibody and the Fab will have a common light chain. Antibody fusions can be produced by (1) engineering the DNA sequence of the target fusion, and (2) transfecting the
10 target DNA into a suitable host cell to express the fusion protein. It seems like the antibody-scFv fusion may be linked by a (Gly)-Ser linker between the C-terminus of the CH3 domain and the N-terminus of the scFv, as described by Coloma, J. *et al.* (1997) *Nature Biotech* 15:159.

Antibody-scFv Fusion

15 *Antibody-scFv Fusions* are bispecific antibodies comprising a traditional antibody and a scFv of unique specificity fused to the C terminus of the antibody heavy chain. The scFv can be fused to the C terminus through the Heavy Chain of the scFv either directly or through a linker peptide. Antibody fusions can be produced by (1) engineering the DNA sequence of the target fusion, and (2) transfecting the target DNA into a suitable host cell to express the fusion protein.
20 It seems like the antibody-scFv fusion may be linked by a (Gly)-Ser linker between the C-terminus of the CH3 domain and the N-terminus of the scFv, as described by Coloma, J. *et al.* (1997) *Nature Biotech* 15:159.

Variable Domain Immunoglobulin DVD

25 A related format is the dual variable domain immunoglobulin (DVD), which are composed of VH and VL domains of a second specificity placed upon the N termini of the V domains by shorter linker sequences.

Other exemplary multispecific antibody formats include, e.g., those described in the
30 following US20160114057A1, US20130243775A1, US20140051833, US20130022601, US20150017187A1, US20120201746A1, US20150133638A1, US20130266568A1,

US20160145340A1, WO2015127158A1, US20150203591A1, US20140322221A1, US20130303396A1, US20110293613, US20130017200A1, US20160102135A1, WO2015197598A2, WO2015197582A1, US9359437, US20150018529, WO2016115274A1, WO2016087416A1, US20080069820A1, US9145588B, US7919257, and US20150232560A1.

- 5 Exemplary multispecific molecules utilizing a full antibody-Fab/scFab format include those described in the following, US9382323B2, US20140072581A1, US20140308285A1, US20130165638A1, US20130267686A1, US20140377269A1, US7741446B2, and WO1995009917A1. Exemplary multispecific molecules utilizing a domain exchange format include those described in the following, US20150315296A1, WO2016087650A1,
- 10 US20160075785A1, WO2016016299A1, US20160130347A1, US20150166670, US8703132B2, US20100316645, US8227577B2, US20130078249.

Fc-containing entities (mini-antibodies)

- Fc-containing entities, also known as mini-antibodies, can be generated by fusing scFv to
- 15 the C-termini of constant heavy region domain 3 (CH3-scFv) and/or to the hinge region (scFv-hinge-Fc) of an antibody with a different specificity. Trivalent entities can also be made which have disulfide stabilized variable domains (without peptide linker) fused to the C-terminus of CH3 domains of IgGs.

20 *Fc-containing multispecific molecules*

In some embodiments, the multispecific molecules disclosed herein includes an immunoglobulin constant region (e.g., an Fc region). Exemplary Fc regions can be chosen from the heavy chain constant regions of IgG1, IgG2, IgG3 or IgG4; more particularly, the heavy chain constant region of human IgG1, IgG2, IgG3, or IgG4.

- 25 In some embodiments, the immunoglobulin chain constant region (e.g., the Fc region) is altered, e.g., mutated, to increase or decrease one or more of: Fc receptor binding, antibody glycosylation, the number of cysteine residues, effector cell function, or complement function.

- In other embodiments, an interface of a first and second immunoglobulin chain constant regions (e.g., a first and a second Fc region) is altered, e.g., mutated, to increase or decrease
- 30 dimerization, e.g., relative to a non-engineered interface, e.g., a naturally-occurring interface. For example, dimerization of the immunoglobulin chain constant region (e.g., the Fc region) can

be enhanced by providing an Fc interface of a first and a second Fc region with one or more of: a paired protuberance-cavity (“knob-in-a hole”), an electrostatic interaction, or a strand-exchange, such that a greater ratio of heteromultimer to homomultimer forms, e.g., relative to a non-engineered interface.

5 In some embodiments, the multispecific molecules include a paired amino acid substitution at a position chosen from one or more of 347, 349, 350, 351, 366, 368, 370, 392, 394, 395, 397, 398, 399, 405, 407, or 409, e.g., of the Fc region of human IgG1. For example, the immunoglobulin chain constant region (e.g., Fc region) can include a paired amino acid substitution chosen from: T366S, L368A, or Y407V (e.g., corresponding to a cavity or hole), and
10 T366W (e.g., corresponding to a protuberance or knob).

In other embodiments, the multifunctional molecule includes a half-life extender, e.g., a human serum albumin or an antibody molecule to human serum albumin.

Heterodimerized Antibody Molecules & Methods of Making

15 Various methods of producing multispecific antibodies have been disclosed to address the problem of incorrect heavy chain pairing. Exemplary methods are described below. Exemplary multispecific antibody formats and methods of making said multispecific antibodies are also disclosed in e.g., Speiss et al. *Molecular Immunology* 67 (2015) 95–106; and Klein et al. *mAbs* 4:6, 653–663; November/December 2012; the entire contents of each of which are
20 incorporated by reference herein.

Heterodimerized bispecific antibodies are based on the natural IgG structure, wherein the two binding arms recognize different antigens. IgG derived formats that enable defined monovalent (and simultaneous) antigen binding are generated by forced heavy chain heterodimerization, combined with technologies that minimize light chain mispairing (e.g.,
25 common light chain). Forced heavy chain heterodimerization can be obtained using, e.g., knob-in-hole OR strand exchange engineered domains (SEED).

Knob-in-Hole

Knob-in-Hole as described in US 5,731,116, US 7,476,724 and Ridgway, J. *et al.* (1996)
30 *Prot. Engineering* 9(7): 617-621, broadly involves: (1) mutating the CH3 domain of one or both antibodies to promote heterodimerization; and (2) combining the mutated antibodies under

conditions that promote heterodimerization. “Knobs” or “protuberances” are typically created by replacing a small amino acid in a parental antibody with a larger amino acid (e.g., T366Y or T366W); “Holes” or “cavities” are created by replacing a larger residue in a parental antibody with a smaller amino acid (e.g., Y407T, T366S, L368A and/or Y407V).

5 For bispecific antibodies including an Fc domain, introduction of specific mutations into the constant region of the heavy chains to promote the correct heterodimerization of the Fc portion can be utilized. Several such techniques are reviewed in Klein et al. (mAbs (2012) 4:6, 1-11), the contents of which are incorporated herein by reference in their entirety. These techniques include the “knobs-into-holes” (KiH) approach which involves the introduction of a bulky
10 residue into one of the CH3 domains of one of the antibody heavy chains. This bulky residue fits into a complementary “hole” in the other CH3 domain of the paired heavy chain so as to promote correct pairing of heavy chains (see e.g., US7642228).

Exemplary KiH mutations include S354C, T366W in the “knob” heavy chain and Y349C, T366S, L368A, Y407V in the “hole” heavy chain. Other exemplary KiH mutations are
15 provided in Table 1, with additional optional stabilizing Fc cysteine mutations.

Table 1. Exemplary Fc KiH mutations and optional Cysteine mutations

Position	Knob Mutation	Hole Mutation
T366	T366W	T366S
L368	-	L368A
Y407	-	Y407V
Additional Cysteine Mutations to form a stabilizing disulfide bridge		
Position	Knob CH3	Hole CH3
S354	S354C	-
Y349	-	Y349C

Other Fc mutations are provided by Igawa and Tsunoda who identified 3 negatively
20 charged residues in the CH3 domain of one chain that pair with three positively charged residues in the CH3 domain of the other chain. These specific charged residue pairs are: E356-K439, E357-K370, D399-K409 and vice versa. By introducing at least two of the following three

mutations in chain A: E356K, E357K and D399K, as well as K370E, K409D, K439E in chain B, alone or in combination with newly identified disulfide bridges, they were able to favor very efficient heterodimerization while suppressing homodimerization at the same time (Martens T et al. A novel one-armed antic- Met antibody inhibits glioblastoma growth in vivo. Clin Cancer Res 2006; 12:6144-52; PMID:17062691). Xencor defined 41 variant pairs based on combining structural calculations and sequence information that were subsequently screened for maximal heterodimerization, defining the combination of S364H, F405A (HA) on chain A and Y349T, T394F on chain B (TF) (Moore GL et al. A novel bispecific antibody format enables simultaneous bivalent and monovalent co-engagement of distinct target antigens. MAbs 2011; 3:546-57; PMID: 22123055).

Other exemplary Fc mutations to promote heterodimerization of multispecific antibodies include those described in the following references, the contents of each of which is incorporated by reference herein, WO2016071377A1, US20140079689A1, US20160194389A1, US20160257763, WO2016071376A2, WO2015107026A1, WO2015107025A1, WO2015107015A1, US20150353636A1, US20140199294A1, US7750128B2, US20160229915A1, US20150344570A1, US8003774A1, US20150337049A1, US20150175707A1, US20140242075A1, US20130195849A1, US20120149876A1, US20140200331A1, US9309311B2, US8586713, US20140037621A1, US20130178605A1, US20140363426A1, US20140051835A1 and US20110054151A1.

Stabilizing cysteine mutations have also been used in combination with KiH and other Fc heterodimerization promoting variants, see e.g., US7183076. Other exemplary cysteine modifications include, e.g., those disclosed in US20140348839A1, US7855275B2, and US9000130B2.

Strand Exchange Engineered Domains (SEED)

Heterodimeric Fc platform that support the design of bispecific and asymmetric fusion proteins by devising strand-exchange engineered domain (SEED) C(H)3 heterodimers are known. These derivatives of human IgG and IgA C(H)3 domains create complementary human SEED C(H)3 heterodimers that are composed of alternating segments of human IgA and IgG C(H)3 sequences. The resulting pair of SEED C(H)3 domains preferentially associates to form heterodimers when expressed in mammalian cells. SEEDbody (Sb) fusion proteins consist of

[IgG1 hinge]-C(H)2-[SEED C(H)3], that may be genetically linked to one or more fusion partners (see e.g., Davis JH et al. SEEDbodies: fusion proteins based on strand exchange engineered domain (SEED) CH3 heterodimers in an Fc analogue platform for asymmetric binders or immunofusions and bispecific antibodies. Protein Eng Des Sel 2010; 23:195-202; PMID:20299542 and US8871912. The contents of each of which are incorporated by reference herein).

Duobody

“Duobody” technology to produce bispecific antibodies with correct heavy chain pairing are known. The DuoBody technology involves three basic steps to generate stable bispecific human IgG1 antibodies in a post-production exchange reaction. In a first step, two IgG1s, each containing single matched mutations in the third constant (CH3) domain, are produced separately using standard mammalian recombinant cell lines. Subsequently, these IgG1 antibodies are purified according to standard processes for recovery and purification. After production and purification (post-production), the two antibodies are recombined under tailored laboratory conditions resulting in a bispecific antibody product with a very high yield (typically >95%) (see e.g., Labrijn et al, PNAS 2013;110(13):5145-5150 and Labrijn et al. Nature Protocols 2014;9(10):2450-63, the contents of each of which are incorporated by reference herein).

Electrostatic Interactions

Methods of making multispecific antibodies using CH3 amino acid changes with charged amino acids such that homodimer formation is electrostatically unfavorable are disclosed. EP1870459 and WO 2009089004 describe other strategies for favoring heterodimer formation upon co-expression of different antibody domains in a host cell. In these methods, one or more residues that make up the heavy chain constant domain 3 (CH3), CH3-CH3 interfaces in both CH3 domains are replaced with a charged amino acid such that homodimer formation is electrostatically unfavorable and heterodimerization is electrostatically favorable. Additional methods of making multispecific molecules using electrostatic interactions are described in the following references, the contents of each of which is incorporated by reference herein, include US20100015133, US8592562B2, US9200060B2, US20140154254A1, and US9358286A1.

Common Light Chain

Light chain mispairing needs to be avoided to generate homogenous preparations of bispecific IgGs. One way to achieve this is through the use of the common light chain principle, i.e. combining two binders that share one light chain but still have separate specificities. An exemplary method of enhancing the formation of a desired bispecific antibody from a mixture of monomers is by providing a common variable light chain to interact with each of the heteromeric variable heavy chain regions of the bispecific antibody. Compositions and methods of producing bispecific antibodies with a common light chain as disclosed in, e.g., US7183076B2, US20110177073A1, EP2847231A1, WO2016079081A1, and EP3055329A1, the contents of each of which is incorporated by reference herein.

CrossMab

Another option to reduce light chain mispairing is the CrossMab technology which avoids non-specific L chain mispairing by exchanging CH1 and CL domains in the Fab of one half of the bispecific antibody. Such crossover variants retain binding specificity and affinity, but make the two arms so different that L chain mispairing is prevented. The CrossMab technology (as reviewed in Klein et al. *Supra*) involves domain swapping between heavy and light chains so as to promote the formation of the correct pairings. Briefly, to construct a bispecific IgG-like CrossMab antibody that could bind to two antigens by using two distinct light chain-heavy chain pairs, a two-step modification process is applied. First, a dimerization interface is engineered into the C-terminus of each heavy chain using a heterodimerization approach, e.g., Knob-into-hole (KiH) technology, to ensure that only a heterodimer of two distinct heavy chains from one antibody (e.g., Antibody A) and a second antibody (e.g., Antibody B) is efficiently formed. Next, the constant heavy 1 (CH1) and constant light (CL) domains of one antibody are exchanged (Antibody A), keeping the variable heavy (VH) and variable light (VL) domains consistent. The exchange of the CH1 and CL domains ensured that the modified antibody (Antibody A) light chain would only efficiently dimerize with the modified antibody (antibody A) heavy chain, while the unmodified antibody (Antibody B) light chain would only efficiently dimerize with the unmodified antibody (Antibody B) heavy chain; and thus only the desired bispecific CrossMab would be efficiently formed (see e.g., Cain, C. SciBX 4(28); doi:10.1038/scibx.2011.783, the contents of which are incorporated by reference herein).

Common Heavy Chain

An exemplary method of enhancing the formation of a desired bispecific antibody from a mixture of monomers is by providing a common variable heavy chain to interact with each of the
5 heteromeric variable light chain regions of the bispecific antibody. Compositions and methods of producing bispecific antibodies with a common heavy chain are disclosed in, e.g., US20120184716, US20130317200, and US20160264685A1, the contents of each of which is incorporated by reference herein.

Amino Acid Modifications

Alternative compositions and methods of producing multispecific antibodies with correct light chain pairing include various amino acid modifications. For example, Zymeworks describes heterodimers with one or more amino acid modifications in the CH1 and/or CL domains, one or more amino acid modifications in the VH and/or VL domains, or a combination thereof, which
15 are part of the interface between the light chain and heavy chain and create preferential pairing between each heavy chain and a desired light chain such that when the two heavy chains and two light chains of the heterodimer pair are co-expressed in a cell, the heavy chain of the first heterodimer preferentially pairs with one of the light chains rather than the other (see e.g., WO2015181805). Other exemplary methods are described in WO2016026943 (Argen-X),
20 US20150211001, US20140072581A1, US20160039947A1, and US20150368352.

Lambda/Kappa Formats

Multispecific molecules (e.g., multispecific antibody molecules) that include the lambda light chain polypeptide and a kappa light chain polypeptides, can be used to allow for
25 heterodimerization. Methods for generating bispecific antibody molecules comprising the lambda light chain polypeptide and a kappa light chain polypeptides are disclosed in PCT/US17/53053 filed on September 22, 2017, incorporated herein by reference in its entirety.

In embodiments, the multispecific molecules includes a multispecific antibody molecule, e.g., an antibody molecule comprising two binding specificities, e.g., a bispecific antibody
30 molecule. The multispecific antibody molecule includes:

a lambda light chain polypeptide 1 (LLCP1) specific for a first epitope;

a heavy chain polypeptide 1 (HCP1) specific for the first epitope;
 a kappa light chain polypeptide 2 (KLCP2) specific for a second epitope; and
 a heavy chain polypeptide 2 (HCP2) specific for the second epitope.

5 “Lambda light chain polypeptide 1 (LLCP1)”, as that term is used herein, refers to a polypeptide comprising sufficient light chain (LC) sequence, such that when combined with a cognate heavy chain variable region, can mediate specific binding to its epitope and complex with an HCP1. In an embodiment it comprises all or a fragment of a CH1 region. In an embodiment, an LLCP1 comprises LC-CDR1, LC-CDR2, LC-CDR3, FR1, FR2, FR3, FR4, and
 10 CH1, or sufficient sequence therefrom to mediate specific binding of its epitope and complex with an HCP1. LLCP1, together with its HCP1, provide specificity for a first epitope (while KLCP2, together with its HCP2, provide specificity for a second epitope). As described elsewhere herein, LLCP1 has a higher affinity for HCP1 than for HCP2.

“Kappa light chain polypeptide 2 (KLCP2)”, as that term is used herein, refers to a
 15 polypeptide comprising sufficient light chain (LC) sequence, such that when combined with a cognate heavy chain variable region, can mediate specific binding to its epitope and complex with an HCP2. In an embodiment it comprises all or a fragment of a CH1 region. In an embodiment, a KLCP2 comprises LC-CDR1, LC-CDR2, LC-CDR3, FR1, FR2, FR3, FR4, and CH1, or sufficient sequence therefrom to mediate specific binding of its epitope and complex
 20 with an HCP2. KLCP2, together with its HCP2, provide specificity for a second epitope (while LLCP1, together with its HCP1, provide specificity for a first epitope).

“Heavy chain polypeptide 1 (HCP1)”, as that term is used herein, refers to a polypeptide comprising sufficient heavy chain (HC) sequence, e.g., HC variable region sequence, such that when combined with a cognate LLCP1, can mediate specific binding to its epitope and complex
 25 with an HCP1. In an embodiment it comprises all or a fragment of a CH1 region. In an embodiment, it comprises all or a fragment of a CH2 and/or CH3 region. In an embodiment an HCP1 comprises HC-CDR1, HC-CDR2, HC-CDR3, FR1, FR2, FR3, FR4, CH1, CH2, and CH3, or sufficient sequence therefrom to: (i) mediate specific binding of its epitope and complex with an LLCP1, (ii) to complex preferentially, as described herein to LLCP1 as opposed to KLCP2;
 30 and (iii) to complex preferentially, as described herein, to an HCP2, as opposed to another

molecule of HCP1. HCP1, together with its LLC1, provide specificity for a first epitope (while KLCP2, together with its HCP2, provide specificity for a second epitope).

“Heavy chain polypeptide 2 (HCP2)”, as that term is used herein, refers to a polypeptide comprising sufficient heavy chain (HC) sequence, e.g., HC variable region sequence, such that when combined with a cognate LLC1, can mediate specific binding to its epitope and complex with an HCP1. In an embodiment it comprises all or a fragment of a CH1 region. In an embodiment it comprises all or a fragment of a CH2 and/or CH3 region. In an embodiment an HCP1 comprises HC-CDR1, HC-CDR2, HC-CDR3, FR1, FR2, FR3, FR4, CH1, CH2, and CH3, or sufficient sequence therefrom to: (i) mediate specific binding of its epitope and complex with a KLCP2, (ii) to complex preferentially, as described herein to KLCP2 as opposed to LLC1; and (iii) to complex preferentially, as described herein, to an HCP1, as opposed to another molecule of HCP2. HCP2, together with its KLCP2, provide specificity for a second epitope (while LLC1, together with its HCP1, provide specificity for a first epitope).

In some embodiments of the multispecific antibody molecule disclosed herein:

LLC1 has a higher affinity for HCP1 than for HCP2; and/or

KLCP2 has a higher affinity for HCP2 than for HCP1.

In embodiments, the affinity of LLC1 for HCP1 is sufficiently greater than its affinity for HCP2, such that under preselected conditions, e.g., in aqueous buffer, e.g., at pH 7, in saline, e.g., at pH 7, or under physiological conditions, at least 75, 80, 90, 95, 98, 99, 99.5, or 99.9 % of the multispecific antibody molecule molecules have a LLC1 complexed, or interfaced with, a HCP1.

In some embodiments of the multispecific antibody molecule disclosed herein:

the HCP1 has a greater affinity for HCP2, than for a second molecule of HCP1; and/or

the HCP2 has a greater affinity for HCP1, than for a second molecule of HCP2.

In embodiments, the affinity of HCP1 for HCP2 is sufficiently greater than its affinity for a second molecule of HCP1, such that under preselected conditions, e.g., in aqueous buffer, e.g., at pH 7, in saline, e.g., at pH 7, or under physiological conditions, at least 75%, 80, 90, 95, 98, 99, 99.5 or 99.9 % of the multispecific antibody molecule molecules have a HCP1 complexed, or interfaced with, a HCP2.

In another aspect, disclosed herein is a method for making, or producing, a multispecific antibody molecule. The method includes:

(i) providing a first heavy chain polypeptide (e.g., a heavy chain polypeptide comprising one, two, three or all of a first heavy chain variable region (first VH), a first CH1, a first heavy chain constant region (e.g., a first CH2, a first CH3, or both));

(ii) providing a second heavy chain polypeptide (e.g., a heavy chain polypeptide comprising one, two, three or all of a second heavy chain variable region (second VH), a second CH1, a second heavy chain constant region (e.g., a second CH2, a second CH3, or both));

(iii) providing a lambda chain polypeptide (e.g., a lambda light variable region (VL λ), a lambda light constant chain (VL λ), or both) that preferentially associates with the first heavy chain polypeptide (e.g., the first VH); and

(iv) providing a kappa chain polypeptide (e.g., a lambda light variable region (VL κ), a lambda light constant chain (VL κ), or both) that preferentially associates with the second heavy chain polypeptide (e.g., the second VH),

under conditions where (i)-(iv) associate.

In embodiments, the first and second heavy chain polypeptides form an Fc interface that enhances heterodimerization.

In embodiments, (i)-(iv) (e.g., nucleic acid encoding (i)-(iv)) are introduced in a single cell, e.g., a single mammalian cell, e.g., a CHO cell. In embodiments, (i)-(iv) are expressed in the cell.

In embodiments, (i)-(iv) (e.g., nucleic acid encoding (i)-(iv)) are introduced in different cells, e.g., different mammalian cells, e.g., two or more CHO cell. In embodiments, (i)-(iv) are expressed in the cells.

In one embodiment, the method further comprises purifying a cell-expressed antibody molecule, e.g., using a lambda- and/or- kappa-specific purification, e.g., affinity chromatography.

In embodiments, the method further comprises evaluating the cell-expressed multispecific antibody molecule. For example, the purified cell-expressed multispecific antibody molecule can be analyzed by techniques known in the art, include mass spectrometry. In one embodiment, the purified cell-expressed antibody molecule is cleaved, e.g., digested with papain to yield the Fab moieties and evaluated using mass spectrometry.

In embodiments, the method produces correctly paired kappa/lambda multispecific, e.g., bispecific, antibody molecules in a high yield, e.g., at least 75%, 80, 90, 95, 98, 99 99.5 or 99.9 %.

In other embodiments, the multispecific, e.g., a bispecific, antibody molecule that
5 includes:

(i) a first heavy chain polypeptide (HCP1) (e.g., a heavy chain polypeptide comprising one, two, three or all of a first heavy chain variable region (first VH), a first CH1, a first heavy chain constant region (e.g., a first CH2, a first CH3, or both)), e.g., wherein the HCP1 binds to a first epitope;

10 (ii) a second heavy chain polypeptide (HCP2) (e.g., a heavy chain polypeptide comprising one, two, three or all of a second heavy chain variable region (second VH), a second CH1, a second heavy chain constant region (e.g., a second CH2, a second CH3, or both)), e.g., wherein the HCP2 binds to a second epitope;

(iii) a lambda light chain polypeptide (LLCP1) (e.g., a lambda light variable region
15 (VL1), a lambda light constant chain (VLI), or both) that preferentially associates with the first heavy chain polypeptide (e.g., the first VH), e.g., wherein the LLCP1 binds to a first epitope; and

(iv) a kappa light chain polypeptide (KLCP2) (e.g., a lambda light variable region (VLk), a lambda light constant chain (VLk), or both) that preferentially associates with the second heavy chain polypeptide (e.g., the second VH), e.g., wherein the KLCP2 binds to a second epitope.

20 In embodiments, the first and second heavy chain polypeptides form an Fc interface that enhances heterodimerization. In embodiments, the multispecific antibody molecule has a first binding specificity that includes a hybrid VL1-CL1 heterodimerized to a first heavy chain variable region connected to the Fc constant, CH2-CH3 domain (having a knob modification) and a second binding specificity that includes a hybrid VLk-CLk heterodimerized to a second heavy
25 chain variable region connected to the Fc constant, CH2-CH3 domain (having a hole modification).

TCR beta V Antigen Binding Domains

Diversity in the immune system enables protection against a huge array of pathogens.
30 Since the germline genome is limited in size, diversity is achieved not only by the process of V(D)J recombination but also by junctional (junctions between V-D and D-J segments) deletion

of nucleotides and addition of pseudo-random, non-templated nucleotides. The TCR beta gene undergoes gene arrangement to generate diversity.

The TCR V beta repertoire varies between individuals and populations because of, *e.g.*, frequently occurring inactivating polymorphisms in functional gene segments and a large insertion/deletion-related polymorphism encompassing 2 V beta gene segments.

This disclosure provides, *inter alia*, antibody molecules and fragments thereof, that bind, *e.g.*, specifically bind, to a human TCR beta V chain (TCR β V), *e.g.*, a TCR β V gene family (also referred to as a group), *e.g.*, a TCR β V subfamily (also referred to as a subgroup), *e.g.*, as described herein. TCR beta V families and subfamilies are known in the art, *e.g.*, as described in Yassai et al., (2009) *Immunogenetics* 61(7)pp:493-502; Wei S. and Concannon P. (1994) *Human Immunology* 41(3) pp: 201-206. The antibodies described herein can be recombinant antibodies, *e.g.*, recombinant non-murine antibodies, *e.g.*, recombinant human or humanized antibodies.

In an aspect, the disclosure provides an anti-TCR β V antibody molecule that binds to human TCR β V, *e.g.*, a TCR β V family, *e.g.*, gene family or a variant thereof. In some embodiments a TCRBV gene family comprises one or more subfamilies, *e.g.*, as described herein, *e.g.*, in FIG. 3, Table 8A or Table 8B. In some embodiments, the TCR β V gene family comprises: a TCR β V6 subfamily, a TCR β V10 subfamily, a TCR β V12 subfamily, a TCR β V5 subfamily, a TCR β V7 subfamily, a TCR β V11 subfamily, a TCR β V14 subfamily, a TCR β V16 subfamily, a TCR β V18 subfamily, a TCR β V9 subfamily, a TCR β V13 subfamily, a TCR β V4 subfamily, a TCR β V3 subfamily, a TCR β V2 subfamily, a TCR β V15 subfamily, a TCR β V30 subfamily, a TCR β V19 subfamily, a TCR β V27 subfamily, a TCR β V28 subfamily, a TCR β V24 subfamily, a TCR β V20 subfamily, TCR β V25 subfamily, a TCR β V29 subfamily, a TCR β V1 subfamily, a TCR β V17 subfamily, a TCR β V21 subfamily, a TCR β V23 subfamily, or a TCR β V26 subfamily.

In some embodiments, TCR β V6 subfamily is also known as TCR β V13.1. In some embodiments, the TCR β V6 subfamily comprises: TCR β V6-4*01, TCR β V6-4*02, TCR β V6-9*01, TCR β V6-8*01, TCR β V6-5*01, TCR β V6-6*02, TCR β V6-6*01, TCR β V6-2*01, TCR β V6-3*01 or TCR β V6-1*01, or a variant thereof. In some embodiments, TCR β V6 comprises TCR β V6-4*01, or a variant thereof. In some embodiments, TCR β V6 comprises TCR β V6-4*02, or a variant thereof. In some embodiments, TCR β V6 comprises TCR β V6-9*01, or a variant thereof. In some embodiments, TCR β V6 comprises TCR β V6-8*01, or a variant thereof.

In some embodiments, TCR β V6 comprises TCR β V6-5*01, or a variant thereof. In some embodiments, TCR β V6 comprises TCR β V6-6*02, or a variant thereof. In some embodiments, TCR β V6 comprises TCR β V6-6*01, or a variant thereof. In some embodiments, TCR β V6 comprises TCR β V6-2*01, or a variant thereof. In some embodiments, TCR β V6 comprises
 5 TCR β V6-3*01, or a variant thereof. In some embodiments, TCR β V6 comprises TCR β V6-1*01, or a variant thereof.

In some embodiments, TCR β V6 comprises TCR β V6-5*01, or a variant thereof. In some embodiments, TCR β V6, *e.g.*, TCR β V6-5*01, is recognized, *e.g.*, bound, by SEQ ID NO: 1 and/or SEQ ID NO: 2. In some embodiments, TCR β V6, *e.g.*, TCR β V6-5*01, is recognized,
 10 *e.g.*, bound, by SEQ ID NO: 9 and/or SEQ ID NO: 10. In some embodiments, TCR β V6 is recognized, *e.g.*, bound, by SEQ ID NO: 9 and/or SEQ ID NO: 11.

In some embodiments, TCR β V10 subfamily is also known as TCR β V12. In some embodiments, the TCR β V10 subfamily comprises: TCR β V10-1*01, TCR β V10-1*02, TCR β V10-3*01 or TCR β V10-2*01, or a variant thereof.

15 In some embodiments, TCR β V12 subfamily is also known as TCR β V8.1. In some embodiments, the TCR β V12 subfamily comprises: TCR β V12-4*01, TCR β V12-3*01, or TCR β V12-5*01, or a variant thereof. In some embodiments, TCR β V12 is recognized, *e.g.*, bound, by SEQ ID NO: 15 and/or SEQ ID NO: 16. In some embodiments, TCR β V12 is recognized, *e.g.*, bound, by any one of SEQ ID NOs 23-25, and/or any one of SEQ ID NO: 26-30:

20 In some embodiments, the TCR β V5 subfamily is chosen from: TCR β V5-5*01, TCR β V5-6*01, TCR β V5-4*01, TCR β V5-8*01, TCR β V5-1*01, or a variant thereof.

In some embodiments, the TCR β V7 subfamily comprises TCR β V7-7*01, TCR β V7-6*01, TCR β V7 -8*02, TCR β V7 -4*01, TCR β V7-2*02, TCR β V7-2*03, TCR β V7-2*01, TCR β V7-3*01, TCR β V7-9*03, or TCR β V7-9*01, or a variant thereof.

25 In some embodiments, the TCR β V11 subfamily comprises: TCR β V11-1*01, TCR β V11-2*01 or TCR β V11-3*01, or a variant thereof.

In some embodiments, the TCR β V14 subfamily comprises TCR β V14*01, or a variant thereof.

In some embodiments, the TCR β V16 subfamily comprises TCR β V16*01, or a variant
 30 thereof.

In some embodiments, the TCR β V18 subfamily comprises TCR β V18*01, or a variant thereof.

In some embodiments, the TCR β V9 subfamily comprises TCR β V9*01 or TCR β V9*02, or a variant thereof.

5 In some embodiments, the TCR β V13 subfamily comprises TCR β V13*01, or a variant thereof.

In some embodiments, the TCR β V4 subfamily comprises TCR β V4-2*01, TCR β V4-3*01, or TCR β V4-1*01, or a variant thereof.

10 In some embodiments, the TCR β V3 subfamily comprises TCR β V3-1*01, or a variant thereof.

In some embodiments, the TCR β V2 subfamily comprises TCR β V2*01, or a variant thereof.

In some embodiments, the TCR β V15 subfamily comprises TCR β V15*01, or a variant thereof.

15 In some embodiments, the TCR β V30 subfamily comprises TCR β V30*01, or TCR β V30*02, or a variant thereof.

In some embodiments, the TCR β V19 subfamily comprises TCR β V19*01, or TCR β V19*02, or a variant thereof.

20 In some embodiments, the TCR β V27 subfamily comprises TCR β V27*01, or a variant thereof.

In some embodiments, the TCR β V28 subfamily comprises TCR β V28*01, or a variant thereof.

In some embodiments, the TCR β V24 subfamily comprises TCR β V24-1*01, or a variant thereof.

25 In some embodiments, the TCR β V20 subfamily comprises TCR β V20-1*01, or TCR β V20-1*02, or a variant thereof.

In some embodiments, the TCR β V25 subfamily comprises TCR β V25-1*01, or a variant thereof.

30 In some embodiments, the TCR β V29 subfamily comprises TCR β V29-1*01, or a variant thereof.

Table 8A: List of TCR β V subfamilies and subfamily members

Reference in Fig. 3	Subfamily	Subfamily members
A	TCR β V6 <i>Also referred to as: TCR VB 13.1</i>	TCR β V6-4*01, TCR β V6-4*02, TCR β V6-9*01, TCR β V6-8*01, TCR β V6-5*01, TCR β V6-6*02, TCR β V6-6*01, TCR β V6-2*01, TCR β V6-3*01 or TCR β V6-1*01.
B	TCR β V10 <i>Also referred to as: TCRβ V12</i>	TCR β V10-1*01, TCR β V10-1*02, TCR β V10-3*01 or TCR β V10-2*01
C	TCR β V12 <i>Also referred to as: TCRβ V8.1</i>	TCR β V12-4*01, TCR β V12-3*01, or TCR β V12-5*01
D	TCR β V5	TCR β V5-5*01, TCR β V5-6*01, TCR β V5-4*01, TCR β V5-8*01, TCR β V5-1*01
E	TCR β V7	TCR β V7-7*01, TCR β V7-6*01, TCR β V7-8*02, TCR β V7-4*01, TCR β V7-2*02, TCR β V7-2*03, TCR β V7-2*01, TCR β V7-3*01, TCR β V7-9*03, or TCR β V7-9*01
F	TCR β V11	TCR β V11-1*01, TCR β V11-2*01 or TCR β V11-3*01
G	TCR β V14	TCR β V14*01
H	TCR β V16	TCR β V16*01
I	TCR β V18	TCR β V18*01
J	TCR β V9	TCR β V9*01 or TCR β V9*02
K	TCR β V13	TCR β V13*01
L	TCR β V4	TCR β V4-2*01, TCR β V4-3*01, or TCR β V4-1*01
M	TCR β V3	TCR β V3-1*01
N	TCR β V2	TCR β V2*01
O	TCR β V15	TCR β V15*01
P	TCR β V30	TCR β V30*01, or TCR β V30*02
Q	TCR β V19	TCR β V19*01, or TCR β V19*02
R	TCR β V27	TCR β V27*01.
S	TCR β V28	TCR β V28*01.
T	TCR β V24	TCR β V24-1*01
U	TCR β V20	TCR β V20-1*01, or TCR β V20-1*02
V	TCR β V25	TCR β V25-1*01
W	TCR β V29	TCR β V29-1*01

Table 8B: Additional TCR β V subfamilies

Subfamily
TCR β V1
TCR β V17
TCR β V21
TCR β V23
TCR β V26

Anti-TCR β V antibodies

Disclosed herein, is the discovery of a novel class of antibodies, i.e. anti-TCR β V antibody molecules disclosed herein, which despite having low sequence similarity (e.g., low sequence identity among the different antibody molecules that recognize different TCR β V subfamilies), recognize a structurally conserved region, e.g., domain, on the TCR β V protein and have a similar function (e.g., a similar cytokine profile). Thus, the anti-TCR β V antibody molecules disclosed herein share a structure-function relationship.

In some embodiments, the anti-TCR β V antibody molecules disclosed herein do not recognize, e.g., bind to, an interface of a TCR β V:TCR α complex.

In some embodiments, the anti-TCR β V antibody molecules disclosed herein do not recognize, e.g., bind to, a constant region of a TCR β V protein. An exemplary antibody that binds to a constant region of a TCRBV region is JOVI.1 as described in Viney *et al.*, (*Hybridoma*. 1992 Dec;11(6):701-13).

In some embodiments, the anti-TCR β V antibody molecules disclosed herein do not recognize, e.g., bind to, one or more (e.g., all) of a complementarity determining region (e.g., CDR1, CDR2 and/or CDR3) of a TCR β V protein.

In some embodiments, the anti-TCR β V antibody molecules disclosed herein binds (e.g., specifically binds) to a TCR β V region. In some embodiments, binding of anti-TCR β V antibody molecules disclosed herein results in a cytokine profile that differs from a cytokine profile of a T cell engager that binds to a receptor or molecule other than a TCR β V region (“a non-TCR β V-binding T cell engager”). In some embodiments, the non-TCR β V-binding T cell engager comprises an antibody that binds to a CD3 molecule (e.g., CD3 epsilon (CD3e) molecule); or a

TCR alpha (TCR α) molecule. In some embodiments, the non-TCR β V-binding T cell engager is an OKT3 antibody or an SP34-2 antibody.

In an aspect, the disclosure provides an anti-TCR β V antibody molecule that binds to human TCR β V, *e.g.*, a TCR β V gene family, *e.g.*, one or more of a TCR β V subfamily, *e.g.*, as described herein, *e.g.*, in **FIG. 3**, Table 8A, or Table 8B. In some embodiments, the anti-TCR β V antibody molecule binds to one or more TCR β V subfamilies chosen from: a TCR β V6 subfamily, a TCR β V10 subfamily, a TCR β V12 subfamily, a TCR β V5 subfamily, a TCR β V7 subfamily, a TCR β V11 subfamily, a TCR β V14 subfamily, a TCR β V16 subfamily, a TCR β V18 subfamily, a TCR β V9 subfamily, a TCR β V13 subfamily, a TCR β V4 subfamily, a TCR β V3 subfamily, a TCR β V2 subfamily, a TCR β V15 subfamily, a TCR β V30 subfamily, a TCR β V19 subfamily, a TCR β V27 subfamily, a TCR β V28 subfamily, a TCR β V24 subfamily, a TCR β V20 subfamily, TCR β V25 subfamily, a TCR β V29 subfamily, a TCR β V1 subfamily, a TCR β V17 subfamily, a TCR β V21 subfamily, a TCR β V23 subfamily, or a TCR β V26 subfamily, or a variant thereof.

In some embodiments, the anti-TCR β V antibody molecule binds to a TCR β V6 subfamily comprising: TCR β V6-4*01, TCR β V6-4*02, TCR β V6-9*01, TCR β V6-8*01, TCR β V6-5*01, TCR β V6-6*02, TCR β V6-6*01, TCR β V6-2*01, TCR β V6-3*01 or TCR β V6-1*01, or a variant thereof. In some embodiments the TCR β V6 subfamily comprises TCR β V6-5*01, or a variant thereof. In some embodiments, TCR β V6 comprises TCR β V6-4*01, or a variant thereof. In some embodiments, TCR β V6 comprises TCR β V6-4*02, or a variant thereof. In some embodiments, TCR β V6 comprises TCR β V6-9*01, or a variant thereof. In some embodiments, TCR β V6 comprises TCR β V6-8*01, or a variant thereof. In some embodiments, TCR β V6 comprises TCR β V6-5*01, or a variant thereof. In some embodiments, TCR β V6 comprises TCR β V6-6*02, or a variant thereof. In some embodiments, TCR β V6 comprises TCR β V6-6*01, or a variant thereof. In some embodiments, TCR β V6 comprises TCR β V6-2*01, or a variant thereof. In some embodiments, TCR β V6 comprises TCR β V6-3*01, or a variant thereof. In some embodiments, TCR β V6 comprises TCR β V6-1*01, or a variant thereof.

In some embodiments, the anti-TCR β V antibody molecule binds to a TCR β V10 subfamily comprising: TCR β V10-1*01, TCR β V10-1*02, TCR β V10-3*01 or TCR β V10-2*01, or a variant thereof.

In some embodiments, the anti-TCR β V antibody molecule binds to a TCR β V12 subfamily comprising: TCR β V12-4*01, TCR β V12-3*01 or TCR β V12-5*01, or a variant thereof.

In some embodiments, the anti-TCR β V antibody molecule binds to a TCR β V5 subfamily comprising: TCR β V5-5*01, TCR β V5-6*01, TCR β V5-4*01, TCR β V5-8*01, TCR β V5-1*01, or a variant thereof.

In some embodiments, the anti-TCR β V antibody molecule does not bind to TCR β V12, or binds to TCR β V12 with an affinity and/or binding specificity that is less than (*e.g.*, less than about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90% or about 2-, 5-, or 10- fold) the affinity and/or binding specificity of the 16G8 murine antibody or a humanized version thereof as described in US Patent 5,861,155.

In some embodiments, the anti-TCR β V antibody molecule binds to TCR β V12 with an affinity and/or binding specificity that is greater than (*e.g.*, greater than about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90% or about 2-, 5-, or 10- fold) the affinity and/or binding specificity of the 16G8 murine antibody or a humanized version thereof as described in US Patent 5,861,155.

In some embodiments, the anti-TCR β V antibody molecule binds to a TCR β V region other than TCR β V12 (*e.g.*, TCR β V region as described herein, *e.g.*, TCR β V6 subfamily (*e.g.*, TCR β V6-5*01) with an affinity and/or binding specificity that is greater than (*e.g.*, greater than about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90% or about 2-, 5-, or 10- fold) the affinity and/or binding specificity of the 16G8 murine antibody or a humanized version thereof as described in US Patent 5,861,155.

In some embodiments, the anti-TCR β V antibody molecule does not bind to TCR β V5-5*01 or TCR β V5-1*01, or binds to TCR β V5-5*01 or TCR β V5-1*01 with an affinity and/or binding specificity that is less than (*e.g.*, less than about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90% or about 2-, 5-, or 10- fold) the affinity and/or binding specificity of murine Antibody C or a humanized version thereof as described in US Patent 5,861,155.

In some embodiments, the anti-TCR β V antibody molecule binds to TCR β V5-5*01 or TCR β V5-1*01 with an affinity and/or binding specificity that is greater than (*e.g.*, greater than about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90% or about 2-, 5-, or 10- fold) the affinity

and/or binding specificity of murine Antibody C or a humanized version thereof as described in US Patent 5,861,155.

In some embodiments, the anti-TCR β V antibody molecule binds to a TCR β V region other than TCR β V5-5*01 or TCR β V5-1*01 (*e.g.*, TCR β V region as described herein, *e.g.*, TCR β V6 subfamily (*e.g.*, TCR β V6-5*01) with an affinity and/or binding specificity that is greater than (*e.g.*, greater than about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90% or about 2-, 5-, or 10- fold) the affinity and/or binding specificity of murine Antibody C or a humanized version thereof as described in US Patent 5,861,155.

10 **Anti-TCR β V6 antibodies**

Accordingly, in one aspect, the disclosure provides an anti-TCR β V antibody molecule that binds to human TCR β V6, *e.g.*, a TCR β V6 subfamily comprising: TCR β V6-4*01, TCR β V6-4*02, TCR β V6-9*01, TCR β V6-8*01, TCR β V6-5*01, TCR β V6-6*02, TCR β V6-6*01, TCR β V6-2*01, TCR β V6-3*01 or TCR β V6-1*01. In some embodiments the TCR β V6 subfamily comprises TCR β V6-5*01 or a variant thereof. In some embodiments, TCR β V6 comprises TCR β V6-4*01, or a variant thereof. In some embodiments, TCR β V6 comprises TCR β V6-4*02, or a variant thereof. In some embodiments, TCR β V6 comprises TCR β V6-9*01, or a variant thereof. In some embodiments, TCR β V6 comprises TCR β V6-8*01, or a variant thereof. In some embodiments, TCR β V6 comprises TCR β V6-5*01, or a variant thereof. In some embodiments, TCR β V6 comprises TCR β V6-6*02, or a variant thereof. In some embodiments, TCR β V6 comprises TCR β V6-6*01, or a variant thereof. In some embodiments, TCR β V6 comprises TCR β V6-2*01, or a variant thereof. In some embodiments, TCR β V6 comprises TCR β V6-3*01, or a variant thereof. In some embodiments, TCR β V6 comprises TCR β V6-1*01, or a variant thereof.

25 In some embodiments, TCR β V6-5*01 is encoded by the nucleic acid sequence of SEQ ID NO: 43, or a sequence having 85%, 90%, 95%, 99% or more identity thereof.

SEQ ID NO: 43

ATGAGCATCGGCCTCCTGTGCTGTGCAGCCTTGTCTCTCCTGTGGGCAGGTCCAGTG
AATGCTGGTGTCACTCAGACCCCAAATTCAGGTCCTGAAGACAGGACAGAGCAT
30 GAACTGCAGTGTGCCAGGATATGAACCATGAATACATGTCCTGGTATCGACAAG

ACCCAGGCATGGGGCTGAGGCTGATTCATTACTCAGTTGGTGCTGGTATCACTGACC
 AAGGAGAAGTCCCCAATGGCTACAATGTCTCCAGATCAACCACAGAGGATTTCCCG
 CTCAGGCTGCTGTCGGCTGCTCCCTCCCAGACATCTGTGTACTTCTGTGCCAGCAGTT
 ACTC

5

In some embodiments, TCR β V6-5*01 comprises the amino acid sequence of SEQ ID NO: 44, or an amino acid sequence having 85%, 90%, 95%, 99% or more identity thereof.

SEQ ID NO: 44

10 MSIGLLCCAALSLLWAGPVNAGVTQTPKFQVLKTGQSM TLQCAQDMNHEYMSWYRQ
 DPGMGLRLIHYSVGAGITDQGEVPNGYNVSRSTTEDFPLRLLSAAPSQTSVYFCASSY

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, is a non-murine antibody molecule, *e.g.*, a human or
 15 humanized antibody molecule. In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule is a human antibody molecule. In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule is a humanized antibody molecule.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*,
 20 anti-TCR β V6-5*01) antibody molecule, is isolated or recombinant.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, comprises at least one antigen-binding region, *e.g.*, a variable region or an antigen-binding fragment thereof, from an antibody described herein, *e.g.*, an antibody chosen from any one of A-H.1 to A-H.68, *e.g.*, A-H.1, A-H.2 or A-H.68, or an
 25 antibody described in **Table 1A**, or encoded by a nucleotide sequence in **Table 1A**, or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, comprises at least one, two, three or four variable
 30 regions from an antibody described herein, *e.g.*, an antibody chosen from any one of A-H.1 to A-H.68, *e.g.*, A-H.1, A-H.2 or A-H.68, or an antibody described in **Table 1A**, or encoded by a

nucleotide sequence in **Table 1A**, or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, comprises at least one or two heavy chain variable regions from an antibody described herein, *e.g.*, an antibody chosen from any one of A-H.1 to A-H.68, *e.g.*, A-H.1, A-H.2 or A-H.68, or an antibody molecule described in **Table 1A**, or encoded by a nucleotide sequence in **Table 1A**, or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences.

In some embodiments, the anti-TCR β V antibody molecule comprises a heavy chain variable region (VH) having a consensus sequence of SEQ ID NO: 231 or 3290.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, comprises at least one or two light chain variable regions from an antibody described herein, *e.g.*, an antibody chosen from any one of A-H.1 to A-H.68, *e.g.*, A-H.1, A-H.2 or A-H.68, or an antibody described in **Table 1A**, or encoded by a nucleotide sequence in **Table 1A**, or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences.

In some embodiments, the anti-TCR β V antibody molecule comprises a light chain variable region (VL) having a consensus sequence of SEQ ID NO: 230 or 3289.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, comprises a heavy chain constant region for an IgG4, *e.g.*, a human IgG4. In still another embodiment, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule includes a heavy chain constant region for an IgG1, *e.g.*, a human IgG1. In one embodiment, the heavy chain constant region comprises an amino sequence set forth in **Table 3A**, or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) thereto.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, includes a kappa light chain constant region, *e.g.*, a human kappa light chain constant region. In one embodiment, the light chain constant region comprises an amino sequence set forth in **Table 3A**, or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) thereto.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, includes at least one, two, or three complementarity determining regions (CDRs) from a heavy chain variable region (VH) of an antibody described herein, *e.g.*, an antibody chosen from any one of A-H.1 to A-H.68, *e.g.*, A-H.1, A-H.2 or A-H.68, or an antibody described in **Table 1A**, or encoded by a nucleotide sequence in **Table 1A**, or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, includes at least one, two, or three CDRs (or collectively all of the CDRs) from a heavy chain variable region comprising an amino acid sequence shown in **Table 1A**, or encoded by a nucleotide sequence shown in **Table 1A**. In one embodiment, one or more of the CDRs (or collectively all of the CDRs) have one, two, three, four, five, six or more changes, *e.g.*, amino acid substitutions or deletions, relative to the amino acid sequence shown in **Table 1A**, or encoded by a nucleotide sequence shown in **Table 1A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, includes at least one, two, or three complementarity determining regions (CDRs) from a light chain variable region of an antibody described herein, *e.g.*, an antibody chosen from any one of A-H.1 to A-H.68, *e.g.*, A-H.1, A-H.2 or A-H.68, or an antibody described in **Table 1A**, or encoded by a nucleotide sequence in **Table 1A**, or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, includes at least one, two, or three CDRs (or collectively all of the CDRs) from a light chain variable region comprising an amino acid sequence shown in **Table 1A**, or encoded by a nucleotide sequence shown in **Table 1A**. In one embodiment, one or more of the CDRs (or collectively all of the CDRs) have one, two, three, four, five, six or more changes, *e.g.*, amino acid substitutions or deletions, relative to the amino acid sequence shown in **Table 1A**, or encoded by a nucleotide sequence shown in **Table 1A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, includes at least one, two, three, four, five or six CDRs (or collectively all of the CDRs) from a heavy and light chain variable region comprising an

amino acid sequence shown in **Table 1A**, or encoded by a nucleotide sequence shown in **Table 1A**. In one embodiment, one or more of the CDRs (or collectively all of the CDRs) have one, two, three, four, five, six or more changes, *e.g.*, amino acid substitutions or deletions, relative to the amino acid sequence shown in **Table 1A**, or encoded by a nucleotide sequence shown in **Table 1A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, molecule includes all six CDRs from an antibody described herein, *e.g.*, an antibody chosen from any one of A-H.1 to A-H.68, *e.g.*, A-H.1, A-H.2 or A-H.68, or an antibody described in **Table 1A**, or encoded by a nucleotide sequence in **Table 1A**, or closely related CDRs, *e.g.*, CDRs which are identical or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions). In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, may include any CDR described herein.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule includes at least one, two, or three CDRs according to Kabat *et al.* (*e.g.*, at least one, two, or three CDRs according to the Kabat definition as set out in **Table 1A**) from a heavy chain variable region of an antibody described herein, *e.g.*, an antibody chosen from any one of A-H.1 to A-H.68, *e.g.*, A-H.1, A-H.2 or A-H.68, or an antibody described in **Table 1A**, or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences; or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to one, two, or three CDRs according to Kabat *et al.* shown in **Table 1A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule includes at least one, two, or three CDRs according to Kabat *et al.* (*e.g.*, at least one, two, or three CDRs according to the Kabat definition as set out in **Table 1A**) from a light chain variable region of an antibody described herein, *e.g.*, an antibody chosen from any one of A-H.1 to A-H.68, *e.g.*, A-H.1, A-H.2 or A-H.68, or an antibody described in **Table 1A**, or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences; or which have at

least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to one, two, or three CDRs according to Kabat et al. shown in **Table 1A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, includes at least one, two, three, four, five, or six CDRs according to Kabat *et al.* (*e.g.*, at least one, two, three, four, five, or six CDRs according to the Kabat definition as set out in **Table 1A**) from the heavy and light chain variable regions of an antibody described herein, *e.g.*, an antibody chosen from any one of A-H.1 to A-H.68, *e.g.*, A-H.1, A-H.2 or A-H.68, or an antibody described in **Table 1A**, or encoded by a nucleotide sequence in **Table 1A**; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences; or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to one, two, three, four, five, or six CDRs according to Kabat et al. shown in **Table 1A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, includes all six CDRs according to Kabat *et al.* (*e.g.*, all six CDRs according to the Kabat definition as set out in **Table 1A**) from the heavy and light chain variable regions of an antibody described herein, *e.g.*, an antibody chosen from any one of A-H.1 to A-H.68, *e.g.*, A-H.1, A-H.2 or A-H.68, or an antibody described in **Table 1A**, or encoded by a nucleotide sequence in **Table 1A**; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences; or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to all six CDRs according to Kabat et al. shown in **Table 1A**. In one embodiment, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, may include any CDR described herein.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, includes at least one, two, or three hypervariable loops that have the same canonical structures as the corresponding hypervariable loop of an antibody described herein, *e.g.*, an antibody chosen from any one of A-H.1 to A-H.68, *e.g.*, A-H.1, A-H.2 or A-H.68, *e.g.*, the same canonical structures as at least loop 1 and/or loop 2 of

the heavy and/or light chain variable domains of an antibody described herein. See, *e.g.*, Chothia et al., (1992) J. Mol. Biol. 227:799-817; Tomlinson et al., (1992) J. Mol. Biol. 227:776-798 for descriptions of hypervariable loop canonical structures. These structures can be determined by inspection of the tables described in these references.

5 In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule includes at least one, two, or three CDRs according to Chothia et al. (*e.g.*, at least one, two, or three CDRs according to the Chothia definition as set out in **Table 1A**) from a heavy chain variable region of an antibody described herein, *e.g.*, an antibody chosen from any one of A-H.1 to A-H.68, *e.g.*, A-H.1, A-H.2 or A-H.68, or as
10 described in **Table 1A**, or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences; or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to one, two, or three CDRs according to Chothia et al. shown in **Table 1A**.

15 In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule includes at least one, two, or three CDRs according to Chothia *et al.* (*e.g.*, at least one, two, or three CDRs according to the Chothia definition as set out in **Table 1A**) from a light chain variable region of an antibody described herein, *e.g.*, an antibody chosen from any one of A-H.1 to A-H.68, *e.g.*, A-H.1, A-H.2 or A-H.68, or an antibody
20 described in **Table 1A**, or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences; or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to one, two, or three CDRs according to Chothia et al. shown in **Table 1A**.

25 In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, includes at least one, two, three, four, five, or six CDRs according to Chothia *et al.* (*e.g.*, at least one, two, three, four, five, or six CDRs according to the Chothia definition as set out in **Table 1A**) from the heavy and light chain variable regions of an antibody described herein, *e.g.*, an antibody chosen from any one of A-H.1 to A-H.68, *e.g.*, A-
30 H.1, A-H.2 or A-H.68, or an antibody described in **Table 1A**, or encoded by the nucleotide sequence in **Table 1A**; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%,

95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences; or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to one, two, three, four, five, or six CDRs according to Chothia et al. shown in **Table 1A**.

5 In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, includes all six CDRs according to Chothia *et al.* (*e.g.*, all six CDRs according to the Chothia definition as set out in **Table 1A**) from the heavy and light chain variable regions of an antibody described herein, *e.g.*, an antibody chosen from any one of A-H.1 to A-H.68, *e.g.*, A-H.1, A-H.2 or A-H.68, or an antibody described in **Table 1A**, or
10 encoded by a nucleotide sequence in **Table 1A**; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences; or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to all six CDRs according to Chothia et al. shown in **Table 1A**. In one embodiment, the anti-
15 TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, may include any CDR described herein.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, molecule includes a combination of CDRs or hypervariable loops defined according to Kabat et al., Chothia et al., or as described in **Table**
20 **1A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, can contain any combination of CDRs or hypervariable loops according to the Kabat and Chothia definitions.

In some embodiments, a combined CDR as set out in **Table 1A** is a CDR that comprises
25 a Kabat CDR and a Chothia CDR.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, molecule includes a combination of CDRs or hypervariable loops identified as combined CDRs in **Table 1A**. In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule,
30 can contain any combination of CDRs or hypervariable loops according the “combined” CDRs are described in **Table 1A**.

In an embodiment, *e.g.*, an embodiment comprising a variable region, a CDR (*e.g.*, a combined CDR, Chothia CDR or Kabat CDR), or other sequence referred to herein, *e.g.*, in **Table 1A**, the antibody molecule is a monospecific antibody molecule, a bispecific antibody molecule, a bivalent antibody molecule, a biparatopic antibody molecule, or an antibody molecule that comprises an antigen binding fragment of an antibody, *e.g.*, a half antibody or antigen binding fragment of a half antibody. In certain embodiments the antibody molecule comprises a multispecific molecule, *e.g.*, a bispecific molecule, *e.g.*, as described herein.

In an embodiment, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule includes:

(i) one, two or all of a light chain complementarity determining region 1 (LC CDR1), a light chain complementarity determining region 2 (LC CDR2), and a light chain complementarity determining region 3 (LC CDR3) of SEQ ID NO: 2, SEQ ID NO: 10 or SEQ ID NO: 11, and/or

(ii) one, two or all of a heavy chain complementarity determining region 1 (HC CDR1), heavy chain complementarity determining region 2 (HC CDR2), and a heavy chain complementarity determining region 3 (HC CDR3) of SEQ ID NO: 1 or SEQ ID NO: 9.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule comprises a LC CDR1, LC CDR2, and LC CDR3 of SEQ ID NO: 2, and a HC CDR1, HC CDR2, and HC CDR3 of SEQ ID NO: 1.

In some embodiments the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule comprises a LC CDR1, LC CDR2, and LC CDR3 of SEQ ID NO: 10, and a HC CDR1, HC CDR2, and HC CDR3 of SEQ ID NO: 9.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule comprises a LC CDR1, LC CDR2, and LC CDR3 of SEQ ID NO: 11, and a HC CDR1, HC CDR2, and HC CDR3 of SEQ ID NO: 9.

In an embodiment, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule comprises:

(i) a LC CDR1 amino acid sequence of SEQ ID NO: 6, a LC CDR2 amino acid sequence of SEQ ID NO: 7, or a LC CDR3 amino acid sequence of SEQ ID NO: 8; and/or

(ii) a HC CDR1 amino acid sequence of SEQ ID NO: 3, a HC CDR2 amino acid sequence of SEQ ID NO: 4, or a HC CDR3 amino acid sequence of SEQ ID NO: 5.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule comprises:

(i) a light chain variable region (VL) comprising a LC CDR1 amino acid sequence of SEQ ID NO: 6, a LC CDR2 amino acid sequence of SEQ ID NO: 7, or a LC CDR3 amino acid sequence of SEQ ID NO: 8; and/or

(ii) a heavy chain variable region (VH) comprising a HC CDR1 amino acid sequence of SEQ ID NO: 3, a HC CDR2 amino acid sequence of SEQ ID NO: 4, or a HC CDR3 amino acid sequence of SEQ ID NO: 5.

In an embodiment, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule comprises:

(i) a LC CDR1 amino acid sequence of SEQ ID NO: 51, a LC CDR2 amino acid sequence of SEQ ID NO: 52, or a LC CDR3 amino acid sequence of SEQ ID NO: 53; and/or

(ii) a HC CDR1 amino acid sequence of SEQ ID NO: 45, a HC CDR2 amino acid sequence of SEQ ID NO: 46, or a HC CDR3 amino acid sequence of SEQ ID NO: 47.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule comprises:

(i) a light chain variable region (VL) comprising a LC CDR1 amino acid sequence of SEQ ID NO: 51, a LC CDR2 amino acid sequence of SEQ ID NO: 52, or a LC CDR3 amino acid sequence of SEQ ID NO: 53; and/or

(ii) a heavy chain variable region (VH) comprising a HC CDR1 amino acid sequence of SEQ ID NO: 45, a HC CDR2 amino acid sequence of SEQ ID NO: 46, or a HC CDR3 amino acid sequence of SEQ ID NO: 47.

In an embodiment, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule comprises:

(i) a LC CDR1 amino acid sequence of SEQ ID NO: 54, a LC CDR2 amino acid sequence of SEQ ID NO: 55, or a LC CDR3 amino acid sequence of SEQ ID NO: 56; and/or

(ii) a HC CDR1 amino acid sequence of SEQ ID NO: 48, a HC CDR2 amino acid sequence of SEQ ID NO: 49, or a HC CDR3 amino acid sequence of SEQ ID NO: 50.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule comprises:

(i) a light chain variable region (VL) comprising a LC CDR1 amino acid sequence of SEQ ID NO: 54, a LC CDR2 amino acid sequence of SEQ ID NO: 55, or a LC CDR3 amino acid sequence of SEQ ID NO: 56; and/or

(ii) a heavy chain variable region (VH) comprising a HC CDR1 amino acid sequence of SEQ ID NO: 48, a HC CDR2 amino acid sequence of SEQ ID NO: 49, or a HC CDR3 amino acid sequence of SEQ ID NO: 50.

In one embodiment, the light or the heavy chain variable framework (*e.g.*, the region encompassing at least FR1, FR2, FR3, and optionally FR4) of the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule can be chosen from: (a) a light or heavy chain variable framework including at least 80%, 85%, 87%, 90%, 92%, 93%, 95%, 97%, 98%, or 100% of the amino acid residues from a human light or heavy chain variable framework, *e.g.*, a light or heavy chain variable framework residue from a human mature antibody, a human germline sequence, or a human consensus sequence; (b) a light or heavy chain variable framework including from 20% to 80%, 40% to 60%, 60% to 90%, or 70% to 95% of the amino acid residues from a human light or heavy chain variable framework, *e.g.*, a light or heavy chain variable framework residue from a human mature antibody, a human germline sequence, or a human consensus sequence; (c) a non-human framework (*e.g.*, a rodent framework); or (d) a non-human framework that has been modified, *e.g.*, to remove antigenic or cytotoxic determinants, *e.g.*, deimmunized, or partially humanized. In one embodiment, the light or heavy chain variable framework region (particularly FR1, FR2 and/or FR3) includes a light or heavy chain variable framework sequence at least 70, 75, 80, 85, 87, 88, 90, 92, 94, 95, 96, 97, 98, 99% identical or identical to the frameworks of a VL or VH segment of a human germline gene.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, comprises a heavy chain variable domain having at least one, two, three, four, five, six, seven, ten, fifteen, twenty or more changes, *e.g.*, amino acid substitutions or deletions, from an amino acid sequence of any one of A-H.1 to A-H.68, *e.g.*, A-H.1, A-H.2 or A-H.68, *e.g.*, the amino acid sequence of the FR region in the entire variable region, *e.g.*, shown in **FIG. 1A**, or in SEQ ID NO: 9.

Alternatively, or in combination with the heavy chain substitutions described herein, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, comprises a light chain variable domain having at least one, two, three, four, five, six, seven, ten, fifteen, twenty or more amino acid changes, *e.g.*, amino acid substitutions or
 5 deletions, from an amino acid sequence of any one of A-H.1 to A-H.68, *e.g.*, A-H.1, A-H.2 or A-H.68, *e.g.*, the amino acid sequence of the FR region in the entire variable region, *e.g.*, shown in **FIG. 1B**, or in SEQ ID NO: 10 or SEQ ID NO: 11.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, includes one, two, three, or four heavy chain
 10 framework regions shown in **FIG. 1A**, or a sequence substantially identical thereto.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, includes one, two, three, or four light chain framework regions shown in **FIG. 1B**, or a sequence substantially identical thereto.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*,
 15 anti-TCR β V6-5*01) antibody molecule, comprises the light chain framework region 1 of A-H.1 or A-H.2, *e.g.*, as shown in **FIG. 1B**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, comprises the light chain framework region 2 of A-H.1 or A-H.2, *e.g.*, as shown in **FIG. 1B**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*,
 20 anti-TCR β V6-5*01) antibody molecule, comprises the light chain framework region 3 of A-H.1 or A-H.2, *e.g.*, as shown in **FIG. 1B**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, comprises the light chain framework region 4 of A-H.1 or A-H.2, *e.g.*, as shown in **FIG. 1B**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, comprises a light chain variable domain comprising a framework region, *e.g.*, framework region 1 (FR1), comprising a change, *e.g.*, a substitution (*e.g.*, a conservative substitution) at position 10 according to Kabat numbering. In some
 30 embodiments, the FR1 comprises a Phenylalanine at position 10, *e.g.*, a Serine to Phenylalanine

substitution. In some embodiments, the substitution is relative to a human germline light chain framework region sequence.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, comprises a light chain variable domain comprising a
 5 framework region, *e.g.*, framework region 2 (FR2), comprising a change, *e.g.*, a substitution (*e.g.*, a conservative substitution) at a position disclosed herein according to Kabat numbering. In some embodiments, FR2 comprises a Histidine at position 36, *e.g.*, a substitution at position 36 according to Kabat numbering, *e.g.*, a Tyrosine to Histidine substitution. In some embodiments, FR2 comprises an Alanine at position 46, *e.g.*, a substitution at position 46 according to Kabat
 10 numbering, *e.g.*, an Arginine to Alanine substitution. In some embodiments, the substitution is relative to a human germline light chain framework region sequence.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, comprises a light chain variable domain comprising a
 15 framework region, *e.g.*, framework region 3 (FR3), comprising a change, *e.g.*, a substitution (*e.g.*, a conservative substitution) at a position disclosed herein according to Kabat numbering. In some embodiments, FR3 comprises a Phenylalanine at position 87, *e.g.*, a substitution at position 87 according to Kabat numbering, *e.g.*, a Tyrosine to Phenylalanine substitution. In some
 20 embodiments, the substitution is relative to a human germline light chain framework region sequence.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, comprises a light chain variable domain comprising: (a)
 a framework region 1 (FR1) comprising a Phenylalanine at position 10, *e.g.*, a substitution at position 10 according to Kabat numbering, *e.g.*, a Serine to Phenylalanine substitution; (b) a
 25 framework region 2 (FR2) comprising a Histidine at position 36, *e.g.*, a substitution at position 36 according to Kabat numbering, *e.g.*, a Tyrosine to Histidine substitution, and a Alanine at position 46, *e.g.*, a substitution at position 46 according to Kabat numbering, *e.g.*, an Arginine to Alanine substitution; and (c) a framework region 3 (FR3) comprising a Phenylalanine at position 87, *e.g.*, a substitution at position 87 according to Kabat numbering, *e.g.*, a Tyrosine to
 30 Phenylalanine substitution, *e.g.*, as shown in the amino acid sequence of SEQ ID NO: 10. In some embodiments, the substitution is relative to a human germline light chain framework region sequence.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, comprises a light chain variable domain comprising: (a) a framework region 2 (FR2) comprising a Histidine at position 36, *e.g.*, a substitution at position 36 according to Kabat numbering, *e.g.*, a Tyrosine to Histidine substitution, and a Alanine at position 46, *e.g.*, a substitution at position 46 according to Kabat numbering, *e.g.*, a Arginine to Alanine substitution; and (b) a framework region 3 (FR3) comprising a Phenylalanine at position 87, *e.g.*, a substitution at position 87 according to Kabat numbering, *e.g.*, a Tyrosine to Phenylalanine substitution, *e.g.*, as shown in the amino acid sequence of SEQ ID NO: 11. In some embodiments, the substitution is relative to a human germline light chain framework region sequence.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, comprises a light chain variable domain comprising: (a) a framework region 1 (FR1) comprising a change, *e.g.*, a substitution (*e.g.*, a conservative substitution) at one or more (*e.g.*, all) positions disclosed herein according to Kabat numbering, ; (b) a framework region 2 (FR2) comprising a change, *e.g.*, a substitution (*e.g.*, a conservative substitution) at one or more (*e.g.*, all) position disclosed herein according to Kabat numbering and (c) a framework region 3 (FR3) comprising a change, *e.g.*, a substitution (*e.g.*, a conservative substitution) at one or more (*e.g.*, all) position disclosed herein according to Kabat numbering. In some embodiments, the substitution is relative to a human germline light chain framework region sequence.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, comprises the heavy chain framework region 1 of A-H.1 or A-H.2, *e.g.*, as shown in **FIG. 1A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, comprises the heavy chain framework region 2 of A-H.1 or A-H.2, *e.g.*, as shown in **FIG. 1A**

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, comprises the heavy chain framework region 3 of A-H.1 or A-H.2, *e.g.*, as shown in **FIG. 1A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, comprises the heavy chain framework region 4 of A-H.1 or A-H.2, *e.g.*, as shown in **FIG. 1A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, comprises a heavy chain variable domain comprising a framework region, *e.g.*, framework region 3 (FR3), comprising a change, *e.g.*, a substitution (*e.g.*, a conservative substitution) at a position disclosed herein according to Kabat numbering. In some embodiments, FR3 comprises a Threonine at position 73, *e.g.*, a substitution at position 73 according to Kabat numbering, *e.g.*, a Glutamic Acid to Threonine substitution. In some
 5 embodiments, FR3 comprises a Glycine at position 94, *e.g.*, a substitution at position 94 according to Kabat numbering, *e.g.*, an Arginine to Glycine substitution. In some embodiments, the substitution is relative to a human germline heavy chain framework region sequence.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, comprises a heavy chain variable domain comprising a
 15 framework region 3 (FR3) comprising a Threonine at position 73, *e.g.*, a substitution at position 73 according to Kabat numbering, *e.g.*, a Glutamic Acid to Threonine substitution, and a Glycine at position 94, *e.g.*, a substitution at position 94 according to Kabat numbering, *e.g.*, a Arginine to Glycine substitution, *e.g.*, as shown in the amino acid sequence of SEQ ID NO: 10.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, comprises the heavy chain framework regions 1-4 of A-H.1 or A-H.2, *e.g.*, SEQ ID NO: 9, or as shown in **FIGs. 1A** and **1B**.
 20

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, comprises the light chain framework regions 1-4 of A-H.1, *e.g.*, SEQ ID NO: 10, or as shown in **FIGs. 1A** and **1B**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, comprises the light chain framework regions 1-4 of A-H.2, *e.g.*, SEQ ID NO: 11, or as shown in **FIGs. 1A** and **1B**.
 25

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, comprises the heavy chain framework regions 1-4 of A-H.1, *e.g.*, SEQ ID NO: 9; and the light chain framework regions 1-4 of A-H.1, *e.g.*, SEQ ID NO: 10, or as shown in **FIGs. 1A** and **1B**.
 30

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, comprises the heavy chain framework regions 1-4 of A-H.2, *e.g.*, SEQ ID NO: 9; and the light chain framework regions 1-4 of A-H.2, *e.g.*, SEQ ID NO: 11, or as shown in **FIGs. 1A** and **1B**.

5 In some embodiments, the heavy or light chain variable domain, or both, of the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, includes an amino acid sequence, which is substantially identical to an amino acid disclosed herein, *e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical to a variable region of an antibody described herein, *e.g.*, an antibody chosen from any one of A-H.1 to A-H.68, *e.g.*, A-H.1, A-H.2 or A-H.68, or as described in **Table 1A**, or encoded by the nucleotide sequence in **Table 1A**; or which differs at least 1 or 5 residues, but less than 40, 30, 20, or 10 residues, from a variable region of an antibody described herein.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, comprises at least one, two, three, or four antigen-
15 binding regions, *e.g.*, variable regions, having an amino acid sequence as set forth in **Table 1A**, or a sequence substantially identical thereto (*e.g.*, a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, or which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the sequences shown in **Table 1A**. In another embodiment, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule includes a VH
20 and/or VL domain encoded by a nucleic acid having a nucleotide sequence as set forth in **Table 1A**, or a sequence substantially identical thereto (*e.g.*, a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, or which differs by no more than 3, 6, 15, 30, or 45 nucleotides from the sequences shown in **Table 1A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, comprises:
25

a VH domain comprising the amino acid sequence of SEQ ID NO: 9, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence of SEQ ID NO: 9, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 9; and/or

30 a VL domain comprising the amino acid sequence of SEQ ID NO: 10, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence of

SEQ ID NO: 10, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 10.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, comprises:

5 a VH domain comprising the amino acid sequence of SEQ ID NO: 9, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence of SEQ ID NO: 9, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 9; and/or

10 a VL domain comprising the amino acid sequence of SEQ ID NO: 11, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence of SEQ ID NO: 11, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 11.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule is a full antibody or fragment thereof (*e.g.*, a Fab, 15 F(ab')₂, Fv, or a single chain Fv fragment (scFv)). In embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule is a monoclonal antibody or an antibody with single specificity. In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, can also be a humanized, chimeric, camelid, shark, or an *in vitro*-generated antibody molecule. In some 20 embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, is a humanized antibody molecule. The heavy and light chains of the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, can be full-length (*e.g.*, an antibody can include at least one, and preferably two, complete heavy chains, and at least one, and preferably two, complete light chains) or can 25 include an antigen-binding fragment (*e.g.*, a Fab, F(ab')₂, Fv, a single chain Fv fragment, a single domain antibody, a diabody (dAb), a bivalent antibody, or bispecific antibody or fragment thereof, a single domain variant thereof, or a camelid antibody).

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, is in the form of a multispecific molecule, *e.g.*, a 30 bispecific molecule, *e.g.*, as described herein.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, has a heavy chain constant region (Fc) chosen from, *e.g.*, the heavy chain constant regions of IgG1, IgG2, IgG3, IgG4, IgM, IgA1, IgA2, IgD, and IgE. In some embodiments, the Fc region is chosen from the heavy chain constant regions of
 5 IgG1, IgG2, IgG3, and IgG4. In some embodiments, the Fc region is chosen from the heavy chain constant region of IgG1 or IgG2 (*e.g.*, human IgG1, or IgG2). In some embodiments, the heavy chain constant region is human IgG1. In some embodiments, the Fc region comprises a Fc region variant, *e.g.*, as described herein.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, has a light chain constant region chosen from, *e.g.*, the
 10 light chain constant regions of kappa or lambda, preferably kappa (*e.g.*, human kappa). In one embodiment, the constant region is altered, *e.g.*, mutated, to modify the properties of the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule (*e.g.*, to increase or decrease one or more of: Fc receptor binding, antibody glycosylation, the
 15 number of cysteine residues, effector cell function, or complement function). For example, the constant region is mutated at positions 296 (M to Y), 298 (S to T), 300 (T to E), 477 (H to K) and 478 (N to F) to alter Fc receptor binding (*e.g.*, the mutated positions correspond to positions 132 (M to Y), 134 (S to T), 136 (T to E), 313 (H to K) and 314 (N to F) of SEQ ID NOs: 212 or 214; or positions 135 (M to Y), 137 (S to T), 139 (T to E), 316 (H to K) and 317 (N to F) of SEQ
 20 ID NOs: 215, 216, 217, or 218), *e.g.*, relative to human IgG1.

Antibody A-H.1 comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 3278 and a light chain comprising the amino acid sequence of SEQ ID NO: 72. Antibody A-H.2 comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 3278 and a light chain comprising the amino acid sequence of SEQ ID NO: 3279. Antibody A-H.68
 25 comprises the amino acid sequence of SEQ ID NO: 1337, or a sequence having at least 85%, 90%, 95%, 96%, 97%, 98%, or 99% identity thereto.

Additional exemplary humanized anti-TCRB V6 antibodies are provided in **Table 1A**. In some embodiments, the anti-TCR β V6 is antibody A, *e.g.*, humanized antibody A (antibody A-H), as provided in **Table 1A**. In some embodiments, the anti-TCR β V antibody comprises one or
 30 more (*e.g.*, all three) of a LC CDR1, LC CDR2, and LC CDR3 provided in **Table 1A**; and/or one or more (*e.g.*, all three) of a HC CDR1, HC CDR2, and HC CDR3 provided in **Table 1A**, or a

sequence with at least 85%, 90%, 95%, 96%, 97%, 98%, or 99% identity thereto. In some embodiments, antibody A comprises a variable heavy chain (VH) and/or a variable light chain (VL) provided in **Table 1A**, or a sequence with at least 85%, 90%, 95%, 96%, 97%, 98%, or 99% identity thereto.

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Table 1A: Amino acid and nucleotide sequences for murine, chimeric and humanized antibody molecules which bind to TCRVB 6, e.g., TCRVB 6-5. The antibody molecules include murine mAb Antibody A, and humanized mAb Antibody A-H Clones A-H.1 to A-H.68. The amino acid the heavy and light chain CDRs, and the amino acid and nucleotide sequences of the heavy and light chain variable regions, and the heavy and light chains are shown.

10

Antibody A (murine)		
SEQ ID NO: 3	HC CDR1 (Combined)	GYSFTTTYIH
SEQ ID NO: 4	HC CDR2 (Combined)	WFFPGSGNIKYNEKFKG
SEQ ID NO: 5	HC CDR3 (Combined)	SYYSYDVLDY
SEQ ID NO: 45	HC CDR1 (Kabat)	TTYIH
SEQ ID NO: 46	HC CDR2 (Kabat)	WFFPGSGNIKYNEKFKG
SEQ ID NO: 47	HC CDR3 (Kabat)	SYYSYDVLDY
SEQ ID NO: 48	HC CDR1 (Chothia)	GYSFTTY
SEQ ID NO: 49	HC CDR2 (Chothia)	FPGSGN
SEQ ID NO: 50	HC CDR3 (Chothia)	SYYSYDVLDY
SEQ ID NO: 1	VH	QVQLQQSGPELVKPGTSVKISCKASGYSFTT YYIHWVKQRPGQGLEWIGWFFPGSGNIKYN EKFKGKATLTADTSSSTAYMQLSSLTSEESA VYFCAGSYYSYDVLDYWGHGTTTLTVSS
SEQ ID NO: 6	LC CDR1 (Combined)	KASQNVGINVV
SEQ ID NO: 7	LC CDR2 (Combined)	SSSHRYS
SEQ ID NO: 8	LC CDR3 (Combined)	QQFKSYPLT
SEQ ID NO: 51	LC CDR1 (Kabat)	KASQNVGINVV
SEQ ID NO: 52	LC CDR2 (Kabat)	SSSHRYS
SEQ ID NO: 53	LC CDR3 (Kabat)	QQFKSYPLT
SEQ ID NO: 54	LC CDR1 (Chothia)	KASQNVGINVV
SEQ ID NO: 55	LC CDR2 (chothia)	SSSHRYS
SEQ ID NO: 56	LC CDR3 (chothia)	QQFKSYPLT
SEQ ID NO: 2	VL	DILMTQSQKFMSTSLGDRVSVSCKASQNVG INVVWHQQKPGQSPKALIYSSSHRYSGVPD

		RFTGSGSGTDFTLTINNVSQEDLAIFYCQQF KSYPLTFGAGTKLELK
Antibody A humanized (A-H antibody)		
A-H.1 antibody		
SEQ ID NO: 3	HC CDR1 (Combined)	GYSFTTYIYH
SEQ ID NO: 4	HC CDR2 (Combined)	WFFPGSGNIKYNEKFKG
SEQ ID NO: 5	HC CDR3 (Combined)	SYYSYDVLDY
SEQ ID NO: 9	VH	QVQLVQSGAEVKKPGSSVKVSCKASGYSFT TYIHWVRQAPGQGLEWMGWFFPGSGNIK YNEKFKGRVTITADTSTSTAYMELSSLRSED TAVYYCAGSYYSYDVLDYWGQGTITVTVSS
SEQ ID NO: 12	DNA VH	CAGGTGCAGCTGGTTCAGTCTGGCGCCGA AGTGAAGAAACCTGGCTCCTCCGTGAAGG TGTCCTGCAAGGCTTCCGGCTACTCCTTCA CCACCTACTACATCCACTGGGTCCGACAG GCCCCTGGACAAGGATTGGAATGGATGG GCTGGTTCTTCCCCGGCTCCGGCAACATC AAGTACAACGAGAAGTTCAAGGGCCGCG TGACCATCACCGCCGACACCTCTACCTCT ACCGCCTACATGGAAGTGTCCAGCCTGAG ATCTGAGGACACCGCCGTGTACTACTGCG CCGGCTCCTACTACTCTTACGACGTGCTG GATTACTGGGGCCAGGGCACCACAGTGAC AGTGTCTCT
SEQ ID NO: 69	VH-IgM constant delta CDC	METDTLLLVVLLLVVPGSTGQVQLVQSGA EVKKPGSSVKVSCKASGYSFTTYIHWVRQ APGQGLEWMGWFFPGSGNIKYNEKFKGRV TITADTSTSTAYMELSSLRSED TAVYYCAGS YYSYDVLDYWGQGTITVTVSSGSASAPTLFP LVSCENSPSDTSSVAVGCLAQDFLPDSITFS WKYKNNSDISSTRGFPSVLRGGKYAATSQV LLPSKDVMQGTDEHVCKVQHPNGNKEKN VPLPVIAELPPKVSFVPPRDGFFGNPRKSK LICQATGFSPRQIQVSWLREGKQVGSVTT DQVQAEAKESGPTTYKVTSTLTIKESDWLG QSMFTCRVDHRGLTFQQNASSMCVPDQDT AIRVFAIPPSFASIFLTKSTKLTLVTDLT DSVTISWTRQNGEAVKTHTNISESHPNATFS AVGEASICEDDWNSEGERFTCTVTHDGLASS LKQTISRPKGVALHRPDVYLLPPAREQLNLR ESATITCLVTGFSPADV FVQWMQRGQPLSP EKYVTSAPMPEPQAPGRYFAHSILTVSEEE

		WNTGETYTCVVAHEALPNRV TERTV DKST GKPTLYNVSLVMSDTAGTCY
SEQ ID NO: 70	VH-IgGA1	METDTLLLWVLLLWVPGSTGQVQLVQSGA EVKKPGSSVKVSKASGYSTFTYYIHWVRQ APGQGLEWMGWFFPGSGNIKYNEKFKGRV TITADTSTSTAYMELSSLRSED TAVYYCAGS YYSYDVLDYWGQGTTVTVSSASPTSPKVFP LSLCSTQPDGNVVIACLVQGFFPQEPLSVTW SESGQGV TARNFPPSQDASGDLYTTSSQLTL PATQCLAGKSVTCHVKHYTNPSQDVTVP VPSTPPTPSPSTPPTPSPSCCHPRLSLHRPALE DLLLGSEANLTCTLTGLRDASGVTF TWPSS GKSAVQGP PERDLCGCYSVSSVLP GCAEPW NHGKTFTCTAAYPESKTPLTATLSKSGNTER PEVHLLPPPSEELALNELVTLTCLARGFSPK DVLVRWLQGSQELPREKYLTWASRQEPSQ GTTTFAVTSILRVAAEDWKKGDTFSCMVG HEALPLAFTQKTIDRLAGKPTHVNVSVVMA EVDGTCY
SEQ ID NO: 71	VH-IgGA2	METDTLLLWVLLLWVPGSTGQVQLVQSGA EVKKPGSSVKVSKASGYSTFTYYIHWVRQ APGQGLEWMGWFFPGSGNIKYNEKFKGRV TITADTSTSTAYMELSSLRSED TAVYYCAGS YYSYDVLDYWGQGTTVTVSSASPTSPKVFP LSLDSTPQDGNVVVACL VQGFFPQEPLSVT WSESGQNV TARNFPPSQDASGDLYTTSSQL TLPATQCPDGKSVTCHVKHYTNSSQDVTVP CRVPPPPPCCHPRLSLHRPALEDLLLGSEAN LTCTLTGLRDASGATFTWTPSSGKSAVQGP PERDLCGCYSVSSVLP GCAQPWNHGETFTC TAAHPELKTPLTANITKSGNTERPEVHLLPP PSEELALNELVTLTCLARGFSPKDVLVRWL QGSQELPREKYLTWASRQEPSQGTTTYAVT SILRVAAEDWKKGETFSCMVGHEALPLAFT QKTIDRMAGKPTHINVSVMMAEADGTCY
SEQ ID NO: 3278	Heavy chain	METDTLLLWVLLLWVPGSTGQVQLVQSGA EVKKPGSSVKVSKASGYSTFTYYIHWVRQ APGQGLEWMGWFFPGSGNIKYNEKFKGRV TITADTSTSTAYMELSSLRSED TAVYYCAGS YYSYDVLDYWGQGTTVTVSSASTKGPSVFP LAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVVT VPSSSLGTQTYICNVNHKPSNTKVDKRV KSCDKTHTCPPCPAPELLGGPSVFLFPPKPK DTLMISRTPEVTCVVVDVSHEDPEVKFNWY VDGVEVHNAKTKPREEQYNSTYRVVSVLT

		VLHQDWLNGKEYKCKVSNKALPAPIEKTIS KAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 6	LC CDR1 (Combined)	KASQNVGINVV
SEQ ID NO: 7	LC CDR2 (Combined)	SSSHRYS
SEQ ID NO: 8	LC CDR3 (Combined)	QQFKSYPLT
SEQ ID NO: 10	VL	DIQMTQSPSFLSASVGDRVITITCKASQNVGINVWHQQKPKGKAPKALYSSSHRYSGVPSRFSGSGSGTEFTLTISSLQPEDFATYFCQQFKSYPLTFGQGTKLEIK
SEQ ID NO: 13	DNA VL	GACATCCAGATGACCCAGTCTCCATCCTTCCTGTCCGCCTCTGTGGGCGACAGAGTGACCATCACATGCAAGGCCTCTCAGAACGTGGCATCAACGTCGTGTGGCACCAGCAGAA GCCTGGCAAGGCTCCTAAGGCTCTGATCTACTCCTCCAGCCACCGGTACTCTGGCGTGCCCTCTAGATTTTCCGGCTCTGGCTCTGGCACCGAGTTTACCCTGACAATCTCCAGCCTGCAGCCTGAGGACTTCGCCACCTACTTTT GCCAGCAGTTCAAGAGCTACCCTCTGACCTTTGGCCAGGGCACCAAGCTGGAAATCAAG
SEQ ID NO: 72	VL and kappa constant region/light chain	METDTLLLWVLLLWVPGSTGDIQMTQSPSFLSASVGDRVITITCKASQNVGINVWHQQKPGKAPKALYSSSHRYSGVPSRFSGSGSGTEFTLTISSLQPEDFATYFCQQFKSYPLTFGQGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVC LLNMFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSSTLSSTLTLSKADYEKHKVYACEVTHQGLSPVTKSFNRGEC
A-H.2 antibody		
SEQ ID NO: 3	HC CDR1 (Combined)	GYSFTTYIIH
SEQ ID NO: 4	HC CDR2 (Combined)	WFFPGSGNIKYNEKFKG
SEQ ID NO: 5	HC CDR3 (Combined)	SYYSYDVLDY
SEQ ID NO: 9	VH	QVQLVQSGAEVKKPGSSVKVSCKASGYSFTTYIIHWVRQAPGQGLEWMGWFFPGSGNIKYNEKFKGRVTITADTSTSTAYMELSSLRSEDTAVYYCAGSYYSYDVLDYWGQGTTVTVSS
SEQ ID NO: 12	DNA VH	CAGGTGCAGCTGGTTCAGTCTGGCGCCGAGAGTGAAGAAACCTGGCTCCTCCGTGAAGGTGTCCTGCAAGGCTTCCGGCTACTCCTTCA

		CCACCTACTACATCCACTGGGTCCGACAG GCCCCTGGACAAGGATTGGAATGGATGG GCTGGTTCTTCCCCGGCTCCGGCAACATC AAGTACAACGAGAAGTTCAAGGGCCGCG TGACCATCACCGCCGACACCTCTACCTCT ACCGCCTACATGGAAGTGTCCAGCCTGAG ATCTGAGGACACCGCCGTGTACTACTGCG CCGGCTCCTACTACTCTTACGACGTGCTG GATTACTGGGGCCAGGGCACACAGTGAC AGTGTCTCT
SEQ ID NO: 3278	Heavy chain	METDTLLLWVLLWVPGSTGQVQLVQSGA EVKKPGSSVKVSKASGYSFTYYIHWVRQ APGQGLEWMGWFFPGSGNIKYNEKFKGRV TITADTSTSTAYMELSSLRSEDVAVYYCAGS YYSYDVL DYWGQGT TVTVSSASTKGPSVFP LAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVVT VPSSSLGTQTYICNVNHKPSNTKVDKRV KSCDKTHTCPPCPAPELLGGPSVFLFPPKPK DTLMISRTPEVTCVVVDVSHEDPEVKFNWY VDGVEVHNAKTKPREEQYNSTYRVVSVLT VLHQDWLNGKEYKCKVSNKALPAPIEKTIS KAKGQPREPQVYTLPPSREEMTKNQVSLTC LVKGFYPSDIAVEWESNGQPENNYKTPPV LDS DGSFFLYSKLTVDKSRWQQGNV FSCSV MHEALHNHYTQKSLSLSPGK
SEQ ID NO: 6	LC CDR1 (Combined)	KASQNVGINVV
SEQ ID NO: 7	LC CDR2 (Combined)	SSSHRYS
SEQ ID NO: 8	LC CDR3 (Combined)	QQFKSYPLT
SEQ ID NO: 11	VL	DIQMTQSPSSLSASVGDRTITCKASQNVGI NVVWHQQKPGKVPKALYSSSHRYSGVPSR FSGSGSGTDFTLTISLQPEDVATYFCQQFKS YPLTFGQGTKLEIK
SEQ ID NO: 14	DNA VL	GACATCCAGATGACCCAGTCTCCATCCTC TCTGTCCGCCTCTGTGGGCGACAGAGTGA CCATCACATGCAAGGCCTCTCAGAACGTG GGCATCAACGTCGTGTGGCACCAGCAGAA ACCTGGCAAGGTGCCCAAGGCTCTGATCT ACTCCTCCAGCCACAGATACTCCGGCGTG CCCTCTAGATTCTCCGGCTCTGGCTCTGGC ACCGACTTTACCCTGACAATCTCCAGCCT GCAGCCTGAGGACGTGGCCACCTACTTTT GCCAGCAGTTCAAGAGCTACCCTCTGACC TTTGGCCAGGGCACCAAGCTGGAAATCAA G

SEQ ID NO: 3279	Light chain	METDTLLLVLLLWVPGSTGDIQMTQSPSS LSASVGDRVTITCKASQNVGINVVWHQQKP GKVPKALYSSSHRYSGVPSRFSGSGSGTDF TLTISSLQPEDVATYFCQQFKSYPLTFGQGT KLEIKRTVAAPSVFIFPPSDEQLKSGTASVVC LLNNFYPREAKVQWKVDNALQSGNSQESV TEQDSKDSYSLSTLTLSKADYEKHKVYA CEVTHQGLSSPVTKSFNRGEC
A-H.3 antibody		
SEQ ID NO: 80	VH+VL	QVQLVQSGAEVKKPGSSVKVSCASGTDF KLTYIHWVRQAPGQGLEWMGRVSPGSGNT KYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAGSYYSYDVLDYWGQGTITVTVS SGGGGSGGGGSGGGGSGGGGSDIQMTQSPS FLSASVGDRVTITCKASQNVEDRVAWYQQ KPGKAPKALYSSSHRYKGVPSRFSGSGSGT EFTLTISLQPEDFATYFCQQFKSYPLTFGQG TKLEIK
SEQ ID NO: 81	VL	DIQMTQSPSFLSASVGDRVTITCKASQNVED RVAWYQQKPGKAPKALYSSSHRYKGVPSR FSGSGSGTEFTLTISLQPEDFATYFCQQFKS YPLTFGQGTKEIK
SEQ ID NO: 82	VH	QVQLVQSGAEVKKPGSSVKVSCASGTDF KLTYIHWVRQAPGQGLEWMGRVSPGSGNT KYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAGSYYSYDVLDYWGQGTITVTVS S
A-H.4		
SEQ ID NO: 83	VH+VL	QVQLVQSGAEVKKPGSSVKVSCASGTDF DKIYIHWVRQAPGQGLEWMGRISAGSGNV KYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAGSYYSYDVLDYWGQGTITVTVS SGGGGSGGGGSGGGGSGGGGSDIQMTQSPS FLSASVGDRVTITCKASQNVEDRVAWYQQ KPGKAPKALYSSSHRYKGVPSRFSGSGSGT EFTLTISLQPEDFATYFCQQFKSYPLTFGQG TKLEIK
SEQ ID NO: 84	VL	DIQMTQSPSFLSASVGDRVTITCKASQNVED RVAWYQQKPGKAPKALYSSSHRYKGVPSR FSGSGSGTEFTLTISLQPEDFATYFCQQFKS YPLTFGQGTKEIK
SEQ ID NO: 85	VH	QVQLVQSGAEVKKPGSSVKVSCASGTDF DKIYIHWVRQAPGQGLEWMGRISAGSGNV KYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAGSYYSYDVLDYWGQGTITVTVS S

A-H.5		
SEQ ID NO: 86	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGHDF RDFYIHWVRQAPGQGLEWMGRVYPGSGSY RYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAGSYYSYDVLDYWGQGTTVTVS SGGGGSGGGGSGGGGSGGGGSDIQMTQSPS FLSASVGDRVTITCKASQNVDDRVAWYQQ KPGKAPKALYSSSHRYKGVPSRFSGSGSGT EFTLTISLQPEDFATYFCQQFKSYPLTFGQG TKLEIK
SEQ ID NO: 87	VL	DIQMTQSPSFLSASVGDRVTITCKASQNVDD RVAWYQQKPGKAPKALYSSSHRYKGVPSR FSGSGSGTEFTLTISLQPEDFATYFCQQFKS YPLTFGQGGTKLEIK
SEQ ID NO: 88	VH	QVQLVQSGAEVKKPGSSVKVSCKASGHDF RDFYIHWVRQAPGQGLEWMGRVYPGSGSY RYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAGSYYSYDVLDYWGQGTTVTVS S
A-H.6		
SEQ ID NO: 89	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGHDF KLTYIHWVRQAPGQGLEWMGRISAGSGNV KYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAGSYYSYDVLDYWGQGTTVTVS SGGGGSGGGGSGGGGSGGGGSDIQMTQSPS FLSASVGDRVTITCKASQNVNDRVAWYQQ KPGKAPKALYSSSHRYKGVPSRFSGSGSGT EFTLTISLQPEDFATYFCQQFKSYPLTFGQG TKLEIK
SEQ ID NO: 90	VL	DIQMTQSPSFLSASVGDRVTITCKASQNVN RVAWYQQKPGKAPKALYSSSHRYKGVPSR FSGSGSGTEFTLTISLQPEDFATYFCQQFKS YPLTFGQGGTKLEIK
SEQ ID NO: 91	VH	QVQLVQSGAEVKKPGSSVKVSCKASGHDF KLTYIHWVRQAPGQGLEWMGRISAGSGNV KYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAGSYYSYDVLDYWGQGTTVTVS S
A-H.7		
SEQ ID NO: 92	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGTDF KLTYIHWVRQAPGQGLEWMGRIFPGSGNV KYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAGSYYSYDVLDYWGQGTTVTVS SGGGGSGGGGSGGGGSGGGGSDIQMTQSPS FLSASVGDRVTITCKASQNVENKVAWHQQ KPGKAPKALYSSSHRYKGVPSRFSGSGSGT

		EFTLTISSLQPEDFATYFCQQFKSYPLTFGQG TKLEIK
SEQ ID NO: 93	VL	DIQMTQSPSFLSASVGDRVITITCKASQNVEN KVAWHQQKPGKAPKALIYSSSHRYKGVPS RFSGSGSGTEFTLTISSLQPEDFATYFCQQFK SYPLTFGQGTKLEIK
SEQ ID NO: 94	VH	QVQLVQSGAEVKKPGSSVKVSCKASGTDF KLTYIHWVRQAPGQGLEWMGRIFPGSGNV KYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAGSYYSYDVLDYWGQGTITVTVS S
A-H.8		
SEQ ID NO: 95	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGTDF DKIYIHWVRQAPGQGLEWMGRIFAGSGNT KYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAGSYYSYDVLDYWGQGTITVTVS SGGGGSGGGGSGGGGSGGGGSDIQMTQSPS FLSASVGDRVITITCKASQNVDDRVAWYQQ KPGKAPKALIYSSSHRYKGVPSRFSGSGSGT EFTLTISSLQPEDFATYFCQQFKSYPLTFGQG TKLEIK
SEQ ID NO: 96	VL	DIQMTQSPSFLSASVGDRVITITCKASQNVDD RVAWYQQKPGKAPKALIYSSSHRYKGVPSR FSGSGSGTEFTLTISSLQPEDFATYFCQQFKS YPLTFGQGTKLEIK
SEQ ID NO: 97	VH	QVQLVQSGAEVKKPGSSVKVSCKASGTDF DKIYIHWVRQAPGQGLEWMGRIFAGSGNT KYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAGSYYSYDVLDYWGQGTITVTVS S
A-H.9		
SEQ ID NO: 98	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGHDF DKFYIHWVRQAPGQGLEWMGRVSAAGSN VKYNEKFKGRVTITADTSTSTAYMELSSLRS EDTAVYYCAGSYYSYDVLDYWGQGTITV VSSGGGGSGGGGSGGGGSGGGGSDIQMTQ SPSFLSASVGDRVITITCKASQNVGNRVAWY QQKPGKAPKALIYSSSHRYSGVPSRFSGSGS GTEFTLTISSLQPEDFATYFCQQFKSYPLTFG QGTKLEIK
SEQ ID NO: 99	VL	DIQMTQSPSFLSASVGDRVITITCKASQNVGN RVAWYQQKPGKAPKALIYSSSHRYSGVPSR FSGSGSGTEFTLTISSLQPEDFATYFCQQFKS YPLTFGQGTKLEIK

SEQ ID NO: 100	VH	QVQLVQSGAEVKKPGSSVKVSCKASGHDF DKFYIHWVRQAPGQGLEWMGRVSAGSGN VKYNEKFKGRVTITADTSTSTAYMELSSLRS EDTAVYYCAGSYYSYDVLDYWGQGTITV VSS
A-H.10		
SEQ ID NO: 101	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGHDF DKFYIHWVRQAPGQGLEWMGRIFAGSGNV KYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAGSYYSYDVLDYWGQGTITVTVS SGGGGSGGGGSGGGGSGGGGSDIQMTQSPS FLSASVGDRVTITCKASQNVGDRVAWYQQ KPGKAPKALIISSSHRYKGVPSRFSGSGSGT EFTLTISSLQPEDFATYFCQQFKSYPLTFGQG TKLEIKs
SEQ ID NO: 102	VL	DIQMTQSPSFLSASVGDRVTITCKASQNVGD RVAWYQQKPGKAPKALIISSSHRYKGVPSR FSGSGSGTEFTLTISSLQPEDFATYFCQQFKS YPLTFGQGTKEIK
SEQ ID NO: 103	VH	QVQLVQSGAEVKKPGSSVKVSCKASGHDF DKFYIHWVRQAPGQGLEWMGRIFAGSGNV KYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAGSYYSYDVLDYWGQGTITVTVS S
A-H.11		
SEQ ID NO: 104	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGTDF KLTYIHWVRQAPGQGLEWMGRVSPGSGNV KYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAGSYYSYDVLDYWGQGTITVTVS SGGGGSGGGGSGGGGSGGGGSDIQMTQSPS FLSASVGDRVTITCKASQNVGDRVAWYQQ KPGKAPKALIISSSHRYKGVPSRFSGSGSGT EFTLTISSLQPEDFATYFCQQFKSYPLTFGQG TKLEIK
SEQ ID NO: 105	VL	DIQMTQSPSFLSASVGDRVTITCKASQNVGD RVAWYQQKPGKAPKALIISSSHRYKGVPSR FSGSGSGTEFTLTISSLQPEDFATYFCQQFKS YPLTFGQGTKEIK
SEQ ID NO: 106	VH	QVQLVQSGAEVKKPGSSVKVSCKASGTDF KLTYIHWVRQAPGQGLEWMGRVSPGSGNV KYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAGSYYSYDVLDYWGQGTITVTVS S
A-H.12		
SEQ ID NO: 107	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGTDF DKIYIHWVRQAPGQGLEWMGRVSAGSGNT

		KYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAGSYYSYDVLDYWGQGTTVTVS SGGGGSGGGGSGGGGSGGGGSDIQMTQSPS FLSASVGDRVTITCKASQNVGNRVAWYQQ KPGKAPKALIYSSSHRYKGVPSRFSGSGSGT EFTLTISLQPEDFATYFCQQFKSYPLTFGQG TKLEIK
SEQ ID NO: 108	VL	DIQMTQSPSFLSASVGDRVTITCKASQNVGN RVAWYQQKPGKAPKALIYSSSHRYKGVPSR FSGSGSGTEFTLTISLQPEDFATYFCQQFKS YPLTFGQGGTKLEIK
SEQ ID NO: 109	VH	QVQLVQSGAEVKKPGSSVKVSCASGTD DKIYIHWVRQAPGQGLEWMGRVSAGSGNT KYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAGSYYSYDVLDYWGQGTTVTVS S
A-H.13		
SEQ ID NO: 110	VH+VL	QVQLVQSGAEVKKPGSSVKVSCASGTD KLTYIHWVRQAPGQGLEWMGRIFPGSGNV KYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAGSYYSYDVLDYWGQGTTVTVS SGGGGSGGGGSGGGGSGGGGSDIQMTQSPS FLSASVGDRVTITCKASQNVNDRVAWYQQ KPGKAPKALIYSSSHRYKGVPSRFSGSGSGT EFTLTISLQPEDFATYFCQQFKSYPLTFGQG TKLEIK
SEQ ID NO: 111	VL	DIQMTQSPSFLSASVGDRVTITCKASQNVN RVAWYQQKPGKAPKALIYSSSHRYKGVPSR FSGSGSGTEFTLTISLQPEDFATYFCQQFKS YPLTFGQGGTKLEIK
SEQ ID NO: 112	VH	QVQLVQSGAEVKKPGSSVKVSCASGTD KLTYIHWVRQAPGQGLEWMGRIFPGSGNV KYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAGSYYSYDVLDYWGQGTTVTVS S
A-H.14		
SEQ ID NO: 113	VH+VL	QVQLVQSGAEVKKPGSSVKVSCASGTD DKIYIHWVRQAPGQGLEWMGRISAGSGNT KYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAGSYYSYDVLDYWGQGTTVTVS SGGGGSGGGGSGGGGSGGGGSDIQMTQSPS FLSASVGDRVTITCKASQNVDDRVAWYQQ KPGKAPKALIYSSSHRYKGVPSRFSGSGSGT EFTLTISLQPEDFATYFCQQFKSYPLTFGQG TKLEIK

SEQ ID NO: 114	VL	DIQMTQSPSFLSASVGDRVTITCKASQNVDD RVAWYQQKPGKAPKALYSSSHRYKGVPSR FSGSGSGTEFTLTISLQPEDFATYFCQQFKS YPLTFGQGTKLEIK
SEQ ID NO: 115	VH	QVQLVQSGAEVKKPGSSVKVSCASGTD DKIYIHWVRQAPGQGLEWMGRISAGSGNT KYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAGSYYSYDVLDYWGQGTTVTVS S
A-H.15		
SEQ ID NO: 116	VH+VL	QVQLVQSGAEVKKPGSSVKVSCASGTD LTYIHWVRQAPGQGLEWMGRVSPGSGNTK YNEKFKGRVTITADTSTSTAYMELSSLRSE TAVYYCAGSYYSYDVLDYWGQGTTVTVSS GGGGSGGGSGGGSGGGGSDIQMTQSPSF LSASVGDRVTITCKASQNVNDKVAWHQQK PGKAPKALYSSSHRYKGVPSRFSGSGSGTE FTLTISLQPEDFATYFCQQFKSYPLTFGQGT KLEIK
SEQ ID NO: 117	VL	DIQMTQSPSFLSASVGDRVTITCKASQNVND KVAWHQQKPGKAPKALYSSSHRYKGVPS RFSGSGSGTEFTLTISLQPEDFATYFCQQFK SYPLTFGQGTKLEIK
SEQ ID NO: 118	VH	QVQLVQSGAEVKKPGSSVKVSCASGTD LTYIHWVRQAPGQGLEWMGRVSPGSGNTK YNEKFKGRVTITADTSTSTAYMELSSLRSE TAVYYCAGSYYSYDVLDYWGQGTTVTVSS
A-H.16		
SEQ ID NO: 119	VH+VL	QVQLVQSGAEVKKPGSSVKVSCASGGTFR LTYIHWVRQAPGQGLEWMGRVYPGSGNTK YNEKFKGRVTITADTSTSTAYMELSSLRSE TAVYYCAGSYYSYDVLDYWGQGTTVTVSS GGGGSGGGSGGGSGGGGSDIQMTQSPSF LSASVGDRVTITCKASQNVDDRVAWYQQK PGKAPKALYSSSHRYKGVPSRFSGSGSGTE FTLTISLQPEDFATYFCQQFKSYPLTFGQGT KLEIK
SEQ ID NO: 120	VL	DIQMTQSPSFLSASVGDRVTITCKASQNVDD RVAWYQQKPGKAPKALYSSSHRYKGVPSR FSGSGSGTEFTLTISLQPEDFATYFCQQFKS YPLTFGQGTKLEIK
SEQ ID NO: 121	VH	QVQLVQSGAEVKKPGSSVKVSCASGGTFR LTYIHWVRQAPGQGLEWMGRVYPGSGNTK YNEKFKGRVTITADTSTSTAYMELSSLRSE TAVYYCAGSYYSYDVLDYWGQGTTVTVSS
A-H.17		

SEQ ID NO: 122	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGTDFR LTYIHWVRQAPGQGLEWMGRIFPGSGNTK YNEKFKGRVTITADTSTSTAYMELSSLRSED TAVYYCAGSYYSYDVLDYWGQGTTVTVSS GGGGSGGGGSGGGGSGGGGSDIQMTQSPSF LSASVGDRVTITCKASQNVDDRVAWYQQK PGKAPKALIISSSHRYKGVPSRFSGSGSGTE FTLTISSLQPEDFATYFCQQFKSYPLTFGQGT KLEIK
SEQ ID NO: 123	VL	DIQMTQSPSFLSASVGDRVTITCKASQNVDD RVAWYQQKPGKAPKALIISSSHRYKGVPSR FSGSGSGTEFTLTISSLQPEDFATYFCQQFKS YPLTFGQGTKLEIK
SEQ ID NO: 124	VH	QVQLVQSGAEVKKPGSSVKVSCKASGTDFR LTYIHWVRQAPGQGLEWMGRIFPGSGNTK YNEKFKGRVTITADTSTSTAYMELSSLRSED TAVYYCAGSYYSYDVLDYWGQGTTVTVSS
A-H.18		
SEQ ID NO: 125	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGTDF KLTYIHWVRQAPGQGLEWMGRIFPGSGNV KYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAGSYYSYDVLDYWGQGTTVTVS SGGGGSGGGGSGGGGSGGGGSDIQMTQSPS FLSASVGDRVTITCKASQNVEDRVAWYQQ KPGKAPKALIISSSHRYKGVPSRFSGSGSGT EFTLTISSLQPEDFATYFCQQFKSYPLTFGQ TKLEIK
SEQ ID NO: 126	VL	DIQMTQSPSFLSASVGDRVTITCKASQNVED RVAWYQQKPGKAPKALIISSSHRYKGVPSR FSGSGSGTEFTLTISSLQPEDFATYFCQQFKS YPLTFGQGTKLEIK
SEQ ID NO: 127	VH	QVQLVQSGAEVKKPGSSVKVSCKASGTDF KLTYIHWVRQAPGQGLEWMGRIFPGSGNV KYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAGSYYSYDVLDYWGQGTTVTVS S
A-H.19		
SEQ ID NO: 128	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGGTFR LTYIHWVRQAPGQGLEWMGRISAGSGNVK YNEKFKGRVTITADTSTSTAYMELSSLRSED TAVYYCAGSYYSYDVLDYWGQGTTVTVSS GGGGSGGGGSGGGGSGGGGSDIQMTQSPSF LSASVGDRVTITCKASQNVGDRVAWYQQK PGKAPKALIISSSHRYKGVPSRFSGSGSGTE FTLTISSLQPEDFATYFCQQFKSYPLTFGQGT KLEIK

SEQ ID NO: 129	VL	DIQMTQSPSFLSASVGDRVTITCKASQNVGD RVAWYQQKPGKAPKALYSSSHRYKGVPSR FSGSGSGTEFTLTISSLQPEDFATYFCQQFKS YPLTFGQGTKLEIK
SEQ ID NO: 130	VH	QVQLVQSGAEVKKPGSSVKVSCASGGTFR LTYIHWVRQAPGQGLEWMGRISAGSGNVK YNEKFKGRVTITADTSTSTAYMELSSLRSED TAVYYCAGSYYSYDVLDYWGQGTITVTVSS
A-H.20		
SEQ ID NO: 131	VH+VL	QVQLVQSGAEVKKPGSSVKVSCASGGTF DKTYIHWVRQAPGQGLEWMGRISAGSGNT KYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAGSYYSYDVLDYWGQGTITVTVS SGGGGSGGGGSGGGGSGGGGSDIQMTQSPS FLSASVGDRVTITCKASQNVDDRVAWYQQ KPGKAPKALYSSSHRYKGVPSRFSGSGSGT EFTLTISSLQPEDFATYFCQQFKSYPLTFGQG TKLEIK
SEQ ID NO: 132	VL	DIQMTQSPSFLSASVGDRVTITCKASQNVDD RVAWYQQKPGKAPKALYSSSHRYKGVPSR FSGSGSGTEFTLTISSLQPEDFATYFCQQFKS YPLTFGQGTKLEIK
SEQ ID NO: 133	VH	QVQLVQSGAEVKKPGSSVKVSCASGGTF DKTYIHWVRQAPGQGLEWMGRISAGSGNT KYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAGSYYSYDVLDYWGQGTITVTVS S
A-H.21		
SEQ ID NO: 134	VH+VL	QVQLVQSGAEVKKPGSSVKVSCASGHDF DKFYIHWVRQAPGQGLEWMGRISAGSGNT KYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAGSYYSYDVLDYWGQGTITVTVS SGGGGSGGGGSGGGGSGGGGSDIQMTQSPS FLSASVGDRVTITCKASQNVDDRVAWYQQ KPGKAPKALYSSSHRYKGVPSRFSGSGSGT EFTLTISSLQPEDFATYFCQQFKSYPLTFGQG TKLEIK
SEQ ID NO: 135	VL	DIQMTQSPSFLSASVGDRVTITCKASQNVDD RVAWYQQKPGKAPKALYSSSHRYKGVPSR FSGSGSGTEFTLTISSLQPEDFATYFCQQFKS YPLTFGQGTKLEIK
SEQ ID NO: 136	VH	QVQLVQSGAEVKKPGSSVKVSCASGHDF DKFYIHWVRQAPGQGLEWMGRISAGSGNT KYNEKFKGRVTITADTSTSTAYMELSSLRSE

		DTAVYYCAGSYYSYDVLDYWGQGTTVTVS S
A-H.22		
SEQ ID NO: 137	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGTDF KLTYIHWVRQAPGQGLEWMGRISAGSGNV KYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAGSYYSYDVLDYWGQGTTVTVS SGGGGSGGGGSGGGGSGGGGSDIQMTQSPS FLSASVGDRVTITCKASQNVNKNVAWHQQ KPGKAPKALYSSSHRYKGVPSRFSGSGSGT EFTLTISLQPEDFATYFCQQFKSYPLTFGQG TKLEIK
SEQ ID NO: 138	VL	DIQMTQSPSFLSASVGDRVTITCKASQNVN KNVAWHQQKPGKAPKALYSSSHRYKGVPS RFSGSGSGTEFTLTISLQPEDFATYFCQQFK SYPLTFGQGTKLEIK
SEQ ID NO: 139	VH	QVQLVQSGAEVKKPGSSVKVSCKASGTDF KLTYIHWVRQAPGQGLEWMGRISAGSGNV KYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAGSYYSYDVLDYWGQGTTVTVS S
A-H.23		
SEQ ID NO: 140	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGHDF RLTYIHWVRQAPGQGLEWMGRISAGSGNV KYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAGSYYSYDVLDYWGQGTTVTVS SGGGGSGGGGSGGGGSGGGGSDIQMTQSPS FLSASVGDRVTITCKASQNVADRVAWYQQ KPGKAPKALYSSSHRYKGVPSRFSGSGSGT EFTLTISLQPEDFATYFCQQFKSYPLTFGQG TKLEIK
SEQ ID NO: 141	VL	DIQMTQSPSFLSASVGDRVTITCKASQNVAD RVAWYQQKPGKAPKALYSSSHRYKGVPSR FSGSGSGTEFTLTISLQPEDFATYFCQQFKS YPLTFGQGTKLEIK
SEQ ID NO: 142	VH	QVQLVQSGAEVKKPGSSVKVSCKASGHDF RLTYIHWVRQAPGQGLEWMGRISAGSGNV KYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAGSYYSYDVLDYWGQGTTVTVS S
A-H.24		
SEQ ID NO: 143	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGHDF HLWYIHWVRQAPGQGLEWMGRVSAGSGN VKYNEKFKGRVTITADTSTSTAYMELSSLRS EDTAVYYCAGSYYSYDVLDYWGQGTTVT VSSGGGGSGGGGSGGGGSGGGGSDIQMTQ

		SPSFLSASVGDRVTITCKASQNVDN KVAWH QQKPGKAPKALYSSSHRYKGVPSRFSGSGS GTEFTLTISLQPEDFATYFCQQFKSYPLTFG QGTKLEIK
SEQ ID NO: 144	VL	DIQMTQSPSFLSASVGDRVTITCKASQNVDN KVAWHQQKPGKAPKALYSSSHRYKGVPS RFSGSGSGTEFTLTISLQPEDFATYFCQQFK SYPLTFGQGTKLEIK
SEQ ID NO: 145	VH	QVQLVQSGAEVKKPGSSVKVSCASGHDF HLWYIHWVRQAPGQGLEWMGRVSAGSGN VKYNEKFKGRVTITADTSTSTAYMELSSLRS EDTAVYYCAGSYYSYDVLDYWGQGTITV VSS
A-H.25		
SEQ ID NO: 146	VH+VL	QVQLVQSGAEVKKPGSSVKVSCASGHDF HLWYIHWVRQAPGQGLEWMGRVFAGSGN TKYNEKFKGRVTITADTSTSTAYMELSSLRS EDTAVYYCAGSYYSYDVLDYWGQGTITV VSSGGGGSGGGGSGGGGSGGGGSDIQMTQ SPSFLSASVGDRVTITCKASQNVEDKVAWY QQKPGKAPKALYSSSHRYKGVPSRFSGSGS GTEFTLTISLQPEDFATYFCQQFKSYPLTFG QGTKLEIK
SEQ ID NO: 147	VL	DIQMTQSPSFLSASVGDRVTITCKASQNVED KVAWYQQKPGKAPKALYSSSHRYKGVPS RFSGSGSGTEFTLTISLQPEDFATYFCQQFK SYPLTFGQGTKLEIK
SEQ ID NO: 148	VH	QVQLVQSGAEVKKPGSSVKVSCASGHDF HLWYIHWVRQAPGQGLEWMGRVFAGSGN TKYNEKFKGRVTITADTSTSTAYMELSSLRS EDTAVYYCAGSYYSYDVLDYWGQGTITV VSS
A-H.26		
SEQ ID NO: 149	VH+VL	QVQLVQSGAEVKKPGSSVKVSCASGTDF KLTYIHWVRQAPGQGLEWMGRIFPGSGNT KYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAGSYYSYDVLDYWGQGTITVTVS SGGGGSGGGGSGGGGSGGGGSDIQMTQSPS FLSASVGDRVTITCKASQNVD DRAWYQQ KPGKAPKALYSSSHRYKGVPSRFSGSGSGT EFTLTISLQPEDFATYFCQQFKSYPLTFGQG TKLEIK
SEQ ID NO: 150	VL	DIQMTQSPSFLSASVGDRVTITCKASQNVD D RVAWYQQKPGKAPKALYSSSHRYKGVPSR FSGSGSGTEFTLTISLQPEDFATYFCQQFKS YPLTFGQGTKLEIK

SEQ ID NO: 151	VH	QVQLVQSGAEVKKPGSSVKVSCKASGTDF KLTYIHWVRQAPGQGLEWMGRIFPGSGNT KYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAGSYYSYDVLDYWGQGTITVTVS S
A-H.27		
SEQ ID NO: 153	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGTDF KLTYIHWVRQAPGQGLEWMGRVSAGSGN VKYNEKFKGRVTITADTSTSTAYMELSSLRS EDTAVYYCAGSYYSYDVLDYWGQGTITV VSSGGGGSGGGGSGGGGSGGGGSDIQMTQ SPSFLSASVGDRVTITCKASQNVGNRVAWY QQKPGKAPKALIISSSHRYKGVPSRFSGSGS GTEFTLTISLQPEDFATYFCQQFKSYPLTFG QGTKLEIK
SEQ ID NO: 154	VL	DIQMTQSPSFLSASVGDRVTITCKASQNVGN RVAWYQQKPGKAPKALIISSSHRYKGVPSR FSGSGSGTEFTLTISLQPEDFATYFCQQFKS YPLTFGQGTKLEIK
SEQ ID NO: 155	VH	QVQLVQSGAEVKKPGSSVKVSCKASGTDF KLTYIHWVRQAPGQGLEWMGRVSAGSGN VKYNEKFKGRVTITADTSTSTAYMELSSLRS EDTAVYYCAGSYYSYDVLDYWGQGTITV VSS
A-H.28		
SEQ ID NO: 156	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGTDF KLTYIHWVRQAPGQGLEWMGRISPGSGNT KYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAGSYYSYDVLDYWGQGTITVTVS SGGGGSGGGGSGGGGSGGGGSDIQMTQSPS FLSASVGDRVTITCKASQNVGDRVAWYQQ KPGKAPKALIISSSHRYKGVPSRFSGSGSGT EFTLTISLQPEDFATYFCQQFKSYPLTFGQG TKLEIK
SEQ ID NO: 157	VL	DIQMTQSPSFLSASVGDRVTITCKASQNVGD RVAWYQQKPGKAPKALIISSSHRYKGVPSR FSGSGSGTEFTLTISLQPEDFATYFCQQFKS YPLTFGQGTKLEIK
SEQ ID NO: 158	VH	QVQLVQSGAEVKKPGSSVKVSCKASGTDF KLTYIHWVRQAPGQGLEWMGRISPGSGNT KYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAGSYYSYDVLDYWGQGTITVTVS S
A-H.29		
SEQ ID NO: 159	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGHDF HLWYIHWVRQAPGQGLEWMGRISPGSGNV

		KYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAGSYYSYDVLDYWGQGTTVTVS SGGGGSGGGGSGGGGSGGGGSDIQMTQSPS FLSASVGDRVTITCKASQNVGDRVAWHQQ KPGKAPKALIYSSSHRYKGVPSRFSGSGSGT EFTLTISLQPEDFATYFCQQFKSYPLTFGQG TKLEIK
SEQ ID NO: 160	VL	DIQMTQSPSFLSASVGDRVTITCKASQNVGD RVAWHQQKPGKAPKALIYSSSHRYKGVPSR FSGSGSGTEFTLTISLQPEDFATYFCQQFKS YPLTFGQGTKEIK
SEQ ID NO: 161	VH	QVQLVQSGAEVKKPGSSVKVSCASGHDF HLWYIHWVRQAPGQGLEWMGRISPGSGNV KYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAGSYYSYDVLDYWGQGTTVTVS S
A-H.31		
SEQ ID NO: 162	VH+VL	QVQLVQSGAEVKKPGSSVKVSCASGHDF KLTYIHWVRQAPGQGLEWMGRISAGSGNV KYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAGSYYSYDVLDYWGQGTTVTVS SGGGGSGGGGSGGGGSGGGGSDIQMTQSPS FLSASVGDRVTITCKASQNVDDRVAWYQQ KPGKAPKALIYSSSHRYKGVPSRFSGSGSGT EFTLTISLQPEDFATYFCQQFKSYPLTFGQG TKLEIK
SEQ ID NO: 163	VL	DIQMTQSPSFLSASVGDRVTITCKASQNVDD RVAWYQQKPGKAPKALIYSSSHRYKGVPSR FSGSGSGTEFTLTISLQPEDFATYFCQQFKS YPLTFGQGTKEIK
SEQ ID NO: 164	VH	QVQLVQSGAEVKKPGSSVKVSCASGHDF KLTYIHWVRQAPGQGLEWMGRISAGSGNV KYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAGSYYSYDVLDYWGQGTTVTVS S
A-H.31		
SEQ ID NO: 165	VH+VL	QVQLVQSGAEVKKPGSSVKVSCASGTDF HLWYIHWVRQAPGQGLEWMGRVFAGSGS YRYNEKFKGRVTITADTSTSTAYMELSSLR EDTAVYYCAGSYYSYDVLDYWGQGTTVT VSSGGGGSGGGGSGGGGSGGGGSDIQMTQ SPSFLSASVGDRVTITCKASQNVDDRVAWY QQKPGKAPKALIYSSSHRYKGVPSRFSGSGS GTEFTLTISLQPEDFATYFCQQFKSYPLTFG QGTKEIK

SEQ ID NO: 166	VL	DIQMTQSPSFLSASVGDRVITITCKASQNVDD RVAWYQQKPGKAPKALYSSSHRYKGVPSR FSGSGSGTEFTLTISSLQPEDFATYFCQQFKS YPLTFGQGGTKLEIK
SEQ ID NO: 167	VH	QVQLVQSGAEVKKPGSSVKVSCASGTD HLWYIHWVRQAPGQGLEWMGRVFAGSGS YRYNEKFKGRVTITADTSTSTAYMELSSLRS EDTAVYYCAGSYYSYDVLDYWGQGT TVTVSS
A-H.32		
SEQ ID NO: 168	VH+VL	QVQLVQSGAEVKKPGSSVKVSCASGTD DKIYIHWVRQAPGQGLEWMGRISAGSGNT KYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAGSYYSYDVLDYWGQGT TVTVSSSGGGGSGGGGSGGGGSGGGGSDI QMTQSPSFLSASVGDRVITITCKASQNVAD RVAWYQQKPGKAPKALYSSSHRYKGVPSR FSGSGSGTEFTLTISSLQPEDFATYFCQQFKS YPLTFGQGGTKLEIK
SEQ ID NO: 169	VL	DIQMTQSPSFLSASVGDRVITITCKASQNVAD RVAWYQQKPGKAPKALYSSSHRYKGVPSR FSGSGSGTEFTLTISSLQPEDFATYFCQQFKS YPLTFGQGGTKLEIK
SEQ ID NO: 170	VH	QVQLVQSGAEVKKPGSSVKVSCASGTD DKIYIHWVRQAPGQGLEWMGRISAGSGNT KYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAGSYYSYDVLDYWGQGT TVTVSS
A-H.33		
SEQ ID NO: 171	VH+VL	QVQLVQSGAEVKKPGSSVKVSCASGTD KLTYIHWVRQAPGQGLEWMGRISAGSGNT KYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAGSYYSYDVLDYWGQGT TVTVSSSGGGGSGGGGSGGGGSGGGGSDI QMTQSPSFLSASVGDRVITITCKASQNVED RVAWYQQKPGKAPKALYSSSHRYKGVPSR FSGSGSGTEFTLTISSLQPEDFATYFCQQFKS YPLTFGQGGTKLEIK
SEQ ID NO: 172	VL	DIQMTQSPSFLSASVGDRVITITCKASQNVED RVAWYQQKPGKAPKALYSSSHRYKGVPSR FSGSGSGTEFTLTISSLQPEDFATYFCQQFKS YPLTFGQGGTKLEIK

SEQ ID NO: 173	VH	QVQLVQSGAEVKKPGSSVKVSCKASGTDF KLTYIHWVRQAPGQGLEWMGRISAGSGNT KYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAGSYYSYDVLDYWGQGTTVTVS S
A-H.34		
SEQ ID NO: 174	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGTDFR LTYIHWVRQAPGQGLEWMGRISPGSGNTK YNEKFKGRVTITADTSTSTAYMELSSLRSED TAVYYCAGSYYSYDVLDYWGQGTTVTVSS GGGGSGGGGSGGGGSGGGGSDIQMTQSPSF LSASVGDRVTITCKASQNVGNRVAWYQQK PGKAPKALIYSSSHRYKGVPSRFSGSGSGTE FTLTISLQPEDFATYFCQQFKSYPLTFGQGT KLEIK
SEQ ID NO: 175	VL	DIQMTQSPSFLSASVGDRVTITCKASQNVGN RVAWYQQKPGKAPKALIYSSSHRYKGVPSR FSGSGSGTEFTLTISLQPEDFATYFCQQFKS YPLTFGQGTKLEIK
SEQ ID NO: 176	VH	QVQLVQSGAEVKKPGSSVKVSCKASGTDFR LTYIHWVRQAPGQGLEWMGRISPGSGNTK YNEKFKGRVTITADTSTSTAYMELSSLRSED TAVYYCAGSYYSYDVLDYWGQGTTVTVSS
A-H.35		
SEQ ID NO: 177	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGHDF DKTYIHWVRQAPGQGLEWMGRVSAGSGN VKYNEKFKGRVTITADTSTSTAYMELSSLRS EDTAVYYCAGSYYSYDVLDYWGQGTTVT VSSGGGGSGGGGSGGGGSGGGGSDIQMTQ SPSFLSASVGDRVTITCKASQNVEDRVAWY QQKPGKAPKALIYSSSHRYKGVPSRFSGSGS GTEFTLTISLQPEDFATYFCQQFKSYPLTFG QGTKLEIK
SEQ ID NO: 178	VL	DIQMTQSPSFLSASVGDRVTITCKASQNVED RVAWYQQKPGKAPKALIYSSSHRYKGVPSR FSGSGSGTEFTLTISLQPEDFATYFCQQFKS YPLTFGQGTKLEIK
SEQ ID NO: 179	VH	QVQLVQSGAEVKKPGSSVKVSCKASGHDF DKTYIHWVRQAPGQGLEWMGRVSAGSGN VKYNEKFKGRVTITADTSTSTAYMELSSLRS EDTAVYYCAGSYYSYDVLDYWGQGTTVT VSS
A-H.36		

SEQ ID NO: 180	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGHDF KLTYIHWVRQAPGQGLEWMGRVSPGSGNT KYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAGSYYSYDVLDYWGQGTITVTVS SGGGGSGGGGSGGGGSGGGGSDIQMTQSPS FLSASVGDRVTITCKASQNVEDRVAWHQQ KPGKAPKALYSSSHRYKGVPSRFSGSGSGT EFTLTISLQPEDFATYFCQQFKSYPLTFGQG TKLEIK
SEQ ID NO: 181	VL	DIQMTQSPSFLSASVGDRVTITCKASQNVED RVAWHQQKPGKAPKALYSSSHRYKGVPSR FSGSGSGTEFTLTISLQPEDFATYFCQQFKS YPLTFGQGGTKLEIK
SEQ ID NO: 182	VH	QVQLVQSGAEVKKPGSSVKVSCKASGHDF KLTYIHWVRQAPGQGLEWMGRVSPGSGNT KYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAGSYYSYDVLDYWGQGTITVTVS S
A-H.37		
SEQ ID NO: 183	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGHDF DKTYIHWVRQAPGQGLEWMGRIYPGSGNV KYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAGSYYSYDVLDYWGQGTITVTVS SGGGGSGGGGSGGGGSGGGGSDIQMTQSPS FLSASVGDRVTITCKASQNVADRVAWYQQ KPGKAPKALYSSSHRYKGVPSRFSGSGSGT EFTLTISLQPEDFATYFCQQFKSYPLTFGQG TKLEIK
SEQ ID NO: 184	VL	DIQMTQSPSFLSASVGDRVTITCKASQNVAD RVAWYQQKPGKAPKALYSSSHRYKGVPSR FSGSGSGTEFTLTISLQPEDFATYFCQQFKS YPLTFGQGGTKLEIK
SEQ ID NO: 185	VH	QVQLVQSGAEVKKPGSSVKVSCKASGHDF DKTYIHWVRQAPGQGLEWMGRIYPGSGNV KYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAGSYYSYDVLDYWGQGTITVTVS S
A-H.38		
SEQ ID NO: 186	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGTDF DKTYIHWVRQAPGQGLEWMGRISAGSGNV KYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAGSYYSYDVLDYWGQGTITVTVS SGGGGSGGGGSGGGGSGGGGSDIQMTQSPS FLSASVGDRVTITCKASQNVDDRVAWYQQ

		KPGKAPKALIYSSSHRYKGVPSRFSGSGSGT EFTLTISLQPEDFATYFCQQFKSYPLTFGQG TKLEIK
SEQ ID NO: 187	VL	DIQMTQSPSFLSASVGDRVTITCKASQNVDD RVAWYQQKPGKAPKALIYSSSHRYKGVPSR FSGSGSGTEFTLTISLQPEDFATYFCQQFKS YPLTFGQGGTKLEIK
SEQ ID NO: 188	VH	QVQLVQSGAEVKKPGSSVKVSCASGTDF DKTYIHWVRQAPGQGLEWMGRISAGSGNV KYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAGSYYSYDVLDYWGQGTITVTVS S
A-H.39		
SEQ ID NO: 189	VH+VL	QVQLVQSGAEVKKPGSSVKVSCASGTDF DKIYIHWVRQAPGQGLEWMGRISAGSGNIK YNEKFKGRVTITADTSTSTAYMELSSLRSED TAVYYCAGSYYSYDVLDYWGQGTITVTVSS GGGGSGGGSGGGSGGGGSDIQMTQSPSF LSASVGDRVTITCKASQNVDDRVAWYQQK PGKAPKALIYSSSHRYKGVPSRFSGSGSGTE FTLTISLQPEDFATYFCQQFKSYPLTFGQGT KLEIK
SEQ ID NO: 190	VL	DIQMTQSPSFLSASVGDRVTITCKASQNVDD RVAWYQQKPGKAPKALIYSSSHRYKGVPSR FSGSGSGTEFTLTISLQPEDFATYFCQQFKS YPLTFGQGGTKLEIK
SEQ ID NO: 191	VH	QVQLVQSGAEVKKPGSSVKVSCASGTDF DKIYIHWVRQAPGQGLEWMGRISAGSGNIK YNEKFKGRVTITADTSTSTAYMELSSLRSED TAVYYCAGSYYSYDVLDYWGQGTITVTVSS
A-H.40		
SEQ ID NO: 192	VH+VL	QVQLVQSGAEVKKPGSSVKVSCASGTDF DKIYIHWVRQAPGQGLEWMGRISAGSGNV KYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAGSYYSYDVLDYWGQGTITVTVS SGGGSGGGSGGGSGGGGSDIQMTQSPS FLSASVGDRVTITCKASQNVGDRVAWYQQ KPGKAPKALIYSSSHRYKGVPSRFSGSGSGT EFTLTISLQPEDFATYFCQQFKSYPLTFGQG TKLEIK
SEQ ID NO: 193	VL	DIQMTQSPSFLSASVGDRVTITCKASQNVGD RVAWYQQKPGKAPKALIYSSSHRYKGVPSR

		FSGSGSGTEFTLTISLQPEDFATYFCQQFKS YPLTFGQGTKLEIK
SEQ ID NO: 194	VH	QVQLVQSGAEVKKPGSSVKVSCASGTDF DKIYIHWVRQAPGQGLEWMGRISAGSGNV KYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAGSYYSYDVLDYWGQGTTVTVS S
A-H.41		
SEQ ID NO: 195	VH+VL	QVQLVQSGAEVKKPGSSVKVSCASGGTF KLTYIHWVRQAPGQGLEWMGRVSAGSGN VKYNEKFKGRVTITADTSTSTAYMELSSLRS EDTAVYYCAGSYYSYDVLDYWGQGTTVT VSSGGGGSGGGGSGGGGSGGGGSDIQMTQ SPSFLSASVGDRVTITCKASQNVDDRVAWY QQKPGKAPKALIISSSHRYKGVPSRFSGSGS GTEFTLTISLQPEDFATYFCQQFKSYPLTFG QGTKLEIK
SEQ ID NO: 196	VL	DIQMTQSPSFLSASVGDRVTITCKASQNVDD RVAWYQQKPGKAPKALIISSSHRYKGVPSR FSGSGSGTEFTLTISLQPEDFATYFCQQFKS YPLTFGQGTKLEIK
SEQ ID NO: 197	VH	QVQLVQSGAEVKKPGSSVKVSCASGGTF KLTYIHWVRQAPGQGLEWMGRVSAGSGN VKYNEKFKGRVTITADTSTSTAYMELSSLRS EDTAVYYCAGSYYSYDVLDYWGQGTTVT VSS
A-H.42		
SEQ ID NO: 198	VH+VL	QVQLVQSGAEVKKPGSSVKVSCASGTDF KLTYIHWVRQAPGQGLEWMGRISPGSGNV KYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAGSYYSYDVLDYWGQGTTVTVS SGGGGSGGGGSGGGGSGGGGSDIQMTQSPS FLSASVGDRVTITCKASQNVNDRVAWHQQ KPGKAPKALIISSSHRYKGVPSRFSGSGSGT EFTLTISLQPEDFATYFCQQFKSYPLTFGQ TKLEIK
SEQ ID NO: 199	VL	DIQMTQSPSFLSASVGDRVTITCKASQNVN RVAWHQQKPGKAPKALIISSSHRYKGVPSR FSGSGSGTEFTLTISLQPEDFATYFCQQFKS YPLTFGQGTKLEIK
SEQ ID NO: 200	VH	QVQLVQSGAEVKKPGSSVKVSCASGTDF KLTYIHWVRQAPGQGLEWMGRISPGSGNV KYNEKFKGRVTITADTSTSTAYMELSSLRSE

		DTAVYYCAGSYYSYDVLDYWGQGTTVTVS S
A-H.43		
SEQ ID NO: 201	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGHDF DKFYIHWVRQAPGQGLEWMGRVSAGSGNT KYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAGSYYSYDVLDYWGQGTTVTVS SGGGGSGGGGSGGGGSGGGGSDIQMTQSPS FLSASVGDRVTITCKASQNVNDRVAWYQQ KPGKAPKALIISSSHRYKGVPSRFSGSGSGT EFTLTISLQPEDFATYFCQQFKSYPLTFGQG TKLEIK
SEQ ID NO: 202	VL	DIQMTQSPSFLSASVGDRVTITCKASQNVN RVAWYQQKPGKAPKALIISSSHRYKGVPSR FSGSGSGTEFTLTISLQPEDFATYFCQQFKS YPLTFGQGTKEIK
SEQ ID NO: 203	VH	QVQLVQSGAEVKKPGSSVKVSCKASGHDF DKFYIHWVRQAPGQGLEWMGRVSAGSGNT KYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAGSYYSYDVLDYWGQGTTVTVS S
A-H.44		
SEQ ID NO: 204	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGTDF DKFYIHWVRQAPGQGLEWMGRVSAGSGN VKYNEKFKGRVTITADTSTSTAYMELSSLR EDTAVYYCAGSYYSYDVLDYWGQGTTVT VSSGGGGSGGGGSGGGGSGGGGSDIQMTQ SPSFLSASVGDRVTITCKASQNVGDRVWY QQKPGKAPKALIISSSHRYKGVPSRFSGSGS GTEFTLTISLQPEDFATYFCQQFKSYPLTFG QGTKEIK
SEQ ID NO: 205	VH	QVQLVQSGAEVKKPGSSVKVSCKASGTDF DKFYIHWVRQAPGQGLEWMGRVSAGSGN VKYNEKFKGRVTITADTSTSTAYMELSSLR EDTAVYYCAGSYYSYDVLDYWGQGTTVT VSS
A-H.45		
SEQ ID NO: 206	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGYSFT TYIHWVRQAPGQGLEWMGWFSAGSGNT KYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAVSYYSDVLDYWGQGTTVTVS SGGGGSGGGGSGGGGSGGGGSDIQMTQSPS FLSASVGDRVTITCKASQNVGINVWHQQK PGKAPKALIISSSHRYSGVPSRFSGSGSGTE

		FTLTISLQPEDFATYFCQQFKSYPLTFGQGT KLEIK
SEQ ID NO: 207	VH	QVQLVQSGAEVKKPGSSVKVSCKASGYSFT TYYIHWVRQAPGQGLEWMGWFSAGSGNT KYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAVSYYSDVLDYWGQGTTVTVS S
A-H.46		
SEQ ID NO: 208	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGYSFT TYYIHWVRQAPGQGLEWMGWFSAGSGNT KYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAGSYYSYDVLDYWGQGTTVTVS SGGGGSGGGGSGGGGSGGGGSDIQMTQSPS FLSASVGDRVTITCKASQNVGINVVWHQKQK PGKAPKALIIYSSSHRYSGVPSRFSGSGSGTE FTLTISLQPEDFATYFCQQFKSYPLTFGQGT KLEIK
SEQ ID NO: 209	VH	QVQLVQSGAEVKKPGSSVKVSCKASGYSFT TYYIHWVRQAPGQGLEWMGWFSAGSGNT KYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAGSYYSYDVLDYWGQGTTVTVS S
A-H.47		
SEQ ID NO: 210	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGYSFT TYYIHWVRQAPGQGLEWMGWFFPGSGNTK YNEKFKGRVTITADTSTSTAYMELSSLRSED TAVYYCAGSYYSYDVLDYWGQGTTVTVSS GGGGSGGGGSGGGGSGGGGSDIQMTQSPSF LSASVGDRVTITCKASQNVGINVVWHQKQK GKAPKALIIYSSSHRYSGVPSRFSGSGSGTEF TLTISLQPEDFATYFCQQFKSYPLTFGQGT KLEIK
SEQ ID NO: 211	VH	QVQLVQSGAEVKKPGSSVKVSCKASGYSFT TYYIHWVRQAPGQGLEWMGWFFPGSGNTK YNEKFKGRVTITADTSTSTAYMELSSLRSED TAVYYCAGSYYSYDVLDYWGQGTTVTVSS
A-H.48		
SEQ ID NO: 212	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGYSFT TYYIHWVRQAPGQGLEWMGWFSPPGSGNTK YNEKFKGRVTITADTSTSTAYMELSSLRSED TAVYYCAVSYYSDVLDYWGQGTTVTVSS GGGGSGGGGSGGGGSGGGGSDIQMTQSPSF LSASVGDRVTITCKASQNVGINVVWHQKQK GKAPKALIIYSSSHRYSGVPSRFSGSGSGTEF

		TLTISSLQPEDFATYFCQQFKSYPLTFGQGT KLEIK
SEQ ID NO: 213	VH	QVQLVQSGAEVKKPGSSVKVSCKASGYSFT TYYIHWVRQAPGQGLEWMGWFSPPGSGNTK YNEKFKGRVTITADTSTSTAYMELSSLRSED TAVYYCAVSYYSDVLDYWGQGTTVTVSS
A-H.49		
SEQ ID NO: 214	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGYSFT TYYIHWVRQAPGQGLEWMGWFSPPGSGNTK YNEKFKGRVTITADTSTSTAYMELSSLRSED TAVYYCAGSYYSYDVLDYWGQGTTVTVSS GGGGSGGGSGGGSGGGGSDIQMTQSPSF LSASVGDRVTITCKASQNVGINVVWHQKQP GKAPKALIIYSSSHRYSGVPSRFSGSGSGTEF TLTISSLQPEDFATYFCQQFKSYPLTFGQGT KLEIK
SEQ ID NO: 215	VH	QVQLVQSGAEVKKPGSSVKVSCKASGYSFT TYYIHWVRQAPGQGLEWMGWFSPPGSGNTK YNEKFKGRVTITADTSTSTAYMELSSLRSED TAVYYCAGSYYSYDVLDYWGQGTTVTVSS
A-H.50		
SEQ ID NO: 216	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGYSFT TYYIHWVRQAPGQGLEWMGRIFPGSGNIKY NEKFKGRVTITADTSTSTAYMELSSLRSED TAVYYCAGSYYSYDVLDYWGQGTTVTVSS GGGGSGGGSGGGSGGGGSDIQMTQSPSFL SASVGDRVTITCKASQNVGINVVWHQKQP GKAPKALIIYSSSHRYSGVPSRFSGSGSGTEF TLTISSLQPEDFATYFCQQFKSYPLTFGQGT KLEIK
SEQ ID NO: 217	VH	QVQLVQSGAEVKKPGSSVKVSCKASGYSFT TYYIHWVRQAPGQGLEWMGRIFPGSGNIKY NEKFKGRVTITADTSTSTAYMELSSLRSED TAVYYCAGSYYSYDVLDYWGQGTTVTVSS
A-H.51		
SEQ ID NO: 218	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGYSFT TYYIHWVRQAPGQGLEWMGWFFPGSGNIK YNEKFKGRVTITADTSTSTAYMELSSLRSED TAVYYCAGSIYSAGVLDYWGQGTTVTVSS GGGGSGGGSGGGSGGGGSDIQMTQSPSF LSASVGDRVTITCKASQNVGINVVWHQKQP GKAPKALIIYSSSHRYSGVPSRFSGSGSGTEF

		TLTISSLQPEDFATYFCQQFKSYPLTFGQGT KLEIK
SEQ ID NO: 219	VH	QVQLVQSGAEVKKPGSSVKVSCKASGYSFT TYYIHWVRQAPGQGLEWMGWFFPGSGNIK YNEKFKGRVTITADTSTSTAYMELSSLRSED TAVYYCAGSIYSAGVLDYWGQGTTVTVSS
A-H.52		
SEQ ID NO: 220	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGYSFT LGYIHWVRQAPGQGLEWMGWFFPGSGNIK YNEKFKGRVTITADTSTSTAYMELSSLRSED TAVYYCAGSYYSYDVLDYWGQGTTVTVSS GGGGSGGGSGGGSGGGGSDIQMTQSPSF LSASVGDRVTITCKASQNVGINVVWHQQKP GKAPKALIIYSSSHRYSGVPSRFSGSGSGTEF TLTISSLQPEDFATYFCQQFKSYPLTFGQGT KLEIK
SEQ ID NO: 221	VH	QVQLVQSGAEVKKPGSSVKVSCKASGYSFT LGYIHWVRQAPGQGLEWMGWFFPGSGNIK YNEKFKGRVTITADTSTSTAYMELSSLRSED TAVYYCAGSYYSYDVLDYWGQGTTVTVSS
A-H.53		
SEQ ID NO: 222	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGYSFR LTYIHWVRQAPGQGLEWMGWFFPGSGNIK YNEKFKGRVTITADTSTSTAYMELSSLRSED TAVYYCAGSYYSYDVLDYWGQGTTVTVSS GGGGSGGGSGGGSGGGGSDIQMTQSPSF LSASVGDRVTITCKASQNVGINVVWHQQKP GKAPKALIIYSSSHRYSGVPSRFSGSGSGTEF TLTISSLQPEDFATYFCQQFKSYPLTFGQGT KLEIK
SEQ ID NO: 223	VH	QVQLVQSGAEVKKPGSSVKVSCKASGYSFR LTYIHWVRQAPGQGLEWMGWFFPGSGNIK YNEKFKGRVTITADTSTSTAYMELSSLRSED TAVYYCAGSYYSYDVLDYWGQGTTVTVSS
A-H.54		
SEQ ID NO: 224	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGYSFH NWIYIHWVRQAPGQGLEWMGWFFPGSGNI KYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAGSYYSYDVLDYWGQGTTVTVS SGGGSGGGSGGGSGGGGSDIQMTQSPS FLSASVGDRVTITCKASQNVGINVVWHQQK PGKAPKALIIYSSSHRYSGVPSRFSGSGSGTE

		FTLTISSLQPEDFATYFCQQFKSYPLTFGQGT KLEIK
SEQ ID NO: 225	VH	QVQLVQSGAEVKKPGSSVKVSCKASGYSFH NWIYHWVRQAPGQGLEWMGWFFPGSGNI KYNEKFKGRVTITADTSTSTAYMELSSLRSE DTAVYYCAGSYYSYDVLDYWGQGTTVTVS S
A-H.55 antibody		
SEQ ID NO: 3	HC CDR1 (Combined)	GYSFTTYIYH
SEQ ID NO: 4	HC CDR2 (Combined)	WFFPGSGNIKYNEKFKG
SEQ ID NO: 5	HC CDR3 (Combined)	SYYSYDVLDY
SEQ ID NO: 45	HC CDR1 (Kabat)	TYIYH
SEQ ID NO: 46	HC CDR2 (Kabat)	WFFPGSGNIKYNEKFKG
SEQ ID NO: 47	HC CDR3 (Kabat)	SYYSYDVLDY
SEQ ID NO: 48	HC CDR1 (Chothia)	GYSFTTY
SEQ ID NO: 49	HC CDR2 (Chothia)	FPGSGN
SEQ ID NO: 50	HC CDR3 (Chothia)	SYYSYDVLDY
SEQ ID NO: 1100	VH	QVQLVQSGAEVKKPGSSVKVSCKASGYSFTTY YIHWVRQAPGQGLEWMGWFFPGSGNIKYNEK KGRVTITADTSTSTAYMELSSLRSEDTAVYYCA GSYYSYDVLDYWGQGTTVTVSS
SEQ ID NO: 6	LC CDR1 (Combined)	KASQNVGINVV
SEQ ID NO: 7	LC CDR2 (Combined)	SSSHRYS
SEQ ID NO: 8	LC CDR3 (Combined)	QQFKSYPLT
SEQ ID NO: 51	LC CDR1 (Kabat)	KASQNVGINVV
SEQ ID NO: 52	LC CDR2 (Kabat)	SSSHRYS
SEQ ID NO: 53	LC CDR3 (Kabat)	QQFKSYPLT
SEQ ID NO: 54	LC CDR1 (Chothia)	KASQNVGINVV
SEQ ID NO: 55	LC CDR2 (chothia)	SSSHRYS
SEQ ID NO: 56	LC CDR3 (chothia)	QQFKSYPLT
SEQ ID NO: 1101	VL	QSVLTQPPSVSEAPRQRVTISCKASQNVGINVV WHQQLPGKAPKALIYSSSHRYSGVSDRFSGSGS GTSFSLAISGLQSEDEADYFCQQFKSYPLTFGTG TKVTVL
A-H.56		
SEQ ID NO: 1309	VH+ VL (ScFv)	QVQLVQSGAEVKKPGSSVKVSCKASGHDFDKF YIHWVRQAPGQGLEWMGRVSAGSGNVKYNEK FKGRVTITADTSTSTAYMELSSLRSEDTAVYYC AGSYYSYDVLDYWGQGTTVTVSSGGGGSGGG GSGGGGSGGGGSDIQTQSPSFLSASVGDRVIT TCKASQNVGNRVAWYQQKPGKAPKALIYSSSH RYKGVPSRFSGSGSGTEFTLTISSLQPEDFATYFC QQFKSYPLTFGQGTKLEIK

A-H.57		
SEQ ID NO: 1326	VH+ VL (ScFv)	QVQLVQSGAEVKKPGSSVKVSCKASGHDFRLT YIHWVRQAPGQGLEWMGRVSAGSGNTKYNEK FKGRVTITADTSTSTAYMELSSLRSEDNAVYYC AVSYYSYDVLDYWGQGTITVTVSSGGGGSGGG GSGGGGSGGGGSDIQMTQSPSFLSASVGDRVIT TCKASQNVGDRVVWHQQKPGKAPKALIISSSH RYKGVPSRFSGSGSGTEFTLTISLQPEDFATYFC QQFKSYPLTFGQGTKLEIK
A-H.58		
SEQ ID NO: 1327	VH+ VL (ScFv)	QVQLVQSGAEVKKPGSSVKVSCKASGHDFRLT YIHWVRQAPGQGLEWMGRVSAGSGNVKYNEK FKGRVTITADTSTSTAYMELSSLRSEDNAVYYC AVSYYSYDVLDYWGQGTITVTVSSGGGGSGGG GSGGGGSGGGGSDIQMTQSPSFLSASVGDRVIT TCKASQNVGNRVVWHQQKPGKAPKALIISSSH RYKGVPSRFSGSGSGTEFTLTISLQPEDFATYFC QQFKSYPLTFGQGTKLEIK
A-H.59		
SEQ ID NO: 1328	VH+ VL (ScFv)	QVQLVQSGAEVKKPGSSVKVSCKASGHDFRLT YIHWVRQAPGQGLEWMGRIYAGSGNVKYNEK FKGRVTITADTSTSTAYMELSSLRSEDNAVYYC AVSYYSYDVLDYWGQGTITVTVSSGGGGSGGG GSGGGGSGGGGSDIQMTQSPSFLSASVGDRVIT TCKASQNVADRVVWHQQKPGKAPKALIISSSH RYKGVPSRFSGSGSGTEFTLTISLQPEDFATYFC QQFKSYPLTFGQGTKLEIK
A-H.60		
SEQ ID NO: 1329	VH+ VL (ScFv)	QVQLVQSGAEVKKPGSSVKVSCKASGHDFKLT YIHWVRQAPGQGLEWMGRVSAGSGNTKYNEK FKGRVTITADTSTSTAYMELSSLRSEDNAVYYC AVSYYSYDVLDYWGQGTITVTVSSGGGGSGGG GSGGGGSGGGGSDIQMTQSPSFLSASVGDRVIT TCKASQNVGDRVAWHQQKPGKAPKALIISSSH RYKGVPSRFSGSGSGTEFTLTISLQPEDFATYFC QQFKSYPLTFGQGTKLEIK
A-H.61		
SEQ ID NO: 1330	VH+ VL (ScFv)	QVQLVQSGAEVKKPGSSVKVSCKASGHDFKLT YIHWVRQAPGQGLEWMGRVSAGSGNTKYNEK FKGRVTITADTSTSTAYMELSSLRSEDNAVYYC AVSYYSYDVLDYWGQGTITVTVSSGGGGSGGG GSGGGGSGGGGSDIQMTQSPSFLSASVGDRVIT TCKASQNVNDRVAWHQQKPGKAPKALIISSSH RYKGVPSRFSGSGSGTEFTLTISLQPEDFATYFC QQFKSYPLTFGQGTKLEIK
A-H.62		
SEQ ID NO: 1331	VH+ VL (ScFv)	QVQLVQSGAEVKKPGSSVKVSCKASGHDFRLT YIHWVRQAPGQGLEWMGRVSAGSGNVKYNEK FKGRVTITADTSTSTAYMELSSLRSEDNAVYYC AVSYYSYDVLDYWGQGTITVTVSSGGGGSGGG

		GSGGGGSGGGGSDIQMTQSPSFLSASVGDRVITI TCKASQNVADRVVWHQQKPGKAPKALIYSSSH RYKGVPSRFSGSGSGTEFTLTISLQPEDFATYFC QQFKSYPLTFGQGTKLEIK
A-H.63		
SEQ ID NO: 1332	VH+ VL (ScFv)	QVQLVQSGAEVKKPGSSVKVSCASGHDFRLT YIHWVRQAPGQGLEWMGRVYAGSGNTKYNEK FKGRVTITADTSTSTAYMELSSLRSEDNAVYYC AVSYYSYDVL DYWGQGT TVTVSSGGGGSGGG GSGGGGSGGGGSDIQMTQSPSFLSASVGDRVITI TCKASQNVEDRVVWHQQKPGKAPKALIYSSSH RYKGVPSRFSGSGSGTEFTLTISLQPEDFATYFC QQFKSYPLTFGQGTKLEIK
A-H.64		
SEQ ID NO: 1333	VH+ VL (ScFv)	QVQLVQSGAEVKKPGSSVKVSCASGHDFKLT YIHWVRQAPGQGLEWMGRVSAGSGNTKYNEK FKGRVTITADTSTSTAYMELSSLRSEDNAVYYC AVSYYSYDVL DYWGQGT TVTVSSGGGGSGGG GSGGGGSGGGGSDIQMTQSPSFLSASVGDRVITI TCKASQNVADRVVWHQQKPGKAPKALIYSSSH RYKGVPSRFSGSGSGTEFTLTISLQPEDFATYFC QQFKSYPLTFGQGTKLEIK
A-H.65		
SEQ ID NO: 1334	VH+ VL (ScFv)	QVQLVQSGAEVKKPGSSVKVSCASGHDFKLT YIHWVRQAPGQGLEWMGRISAGSGNTKYNEKF KGRVTITADTSTSTAYMELSSLRSEDNAVYYCA VSYYSYDVL DYWGQGT TVTVSSGGGGSGGGGS GGGGSGGGGSDIQMTQSPSFLSASVGDRVITITC KASQNVGDRVVWHQQKPGKAPKALIYSSSHRY KGVPSRFSGSGSGTEFTLTISLQPEDFATYFCQQ FKSYPLTFGQGTKLEIK
A-H.66		
SEQ ID NO: 1335	VH+ VL (ScFv)	QVQLVQSGAEVKKPGSSVKVSCASGHDFKLT YIHWVRQAPGQGLEWMGRIYAGSGNTKYNEKF KGRVTITADTSTSTAYMELSSLRSEDNAVYYCA VSYYSYDVL DYWGQGT TVTVSSGGGGSGGGGS GGGGSGGGGSDIQMTQSPSFLSASVGDRVITITC KASQNVGDRVVWHQQKPGKAPKALIYSSSHRY KGVPSRFSGSGSGTEFTLTISLQPEDFATYFCQQ FKSYPLTFGQGTKLEIK
A-H.67		
SEQ ID NO: 1336	VH+ VL (ScFv)	QVQLVQSGAEVKKPGSSVKVSCASGTDFKLT YIHWVRQAPGQGLEWMGRIFPGSGNVKYNEKF KGRVTITADTSTSTAYMELSSLRSEDNAVYYCA VSYYSYDVL DYWGQGT TVTVSSGGGGSGGGGS GGGGSGGGGSDIQMTQSPSFLSASVGDRVITITC KASQNVNDRVAWYQQKPGKAPKALIYSSSHRY KGVPSRFSGSGSGTEFTLTISLQPEDFATYFCQQ FKSYPLTFGQGTKLEIK

A-H.68		
SEQ ID NO: 1337	VH+ VL (ScFv)	QVQLVQSGAEVKKPGSSVKVSCKASGHDFRLT YIHWVRQAPGQGLEWMGRISAGSGNVKYNEKF KGRVTITADTSTSTAYMELSSLRSEDTAVYYCA VSYYSYDVL DYWGQGT TTVTVSSGGGGSGGGGS GGGGSGGGGSDIQMTQSPSFLSASVGDRVITC KASQNVADRV AWYQQKPGKAPKALYSSSHRY KGVPSRFSGSGSGTEFTLTISLQPEDFATYFCQQ FKSYPLTFGQGTKLEIK
A-H.69		
SEQ ID NO: 1344	VH+ VL (ScFv)	QVQLVQSGAEVKKPGSSVKVSCKASGTDF KLTYIHWVRQAPGQGLEWMGRIFPGSGNV KYNEKF KGRVTITADTSTSTAYMELSSLRSE DTAVYYCAGSYYSYDVL DYWGQGT TTVTVS SGGGSGGGGSGGGGSGGGGSDIQMTQSPS FLSASVGDRVITCKASQNV DNRV AWYQQ KPGKAPKALYSSSHRYKGVPSRFSGSGSGT EFTLTISLQPEDFATYFCQQFKSYPLTFGQG TKLEIK
A-H humanized-matured VH		
SEQ ID NO: 1310	VH-humanized matured 1	QVQLVQSGAEVKKPGSSVKVSCKASGTDFKLT YIHWVRQAPGQGLEWMGRIFPGSGNVKYNEKF KGRVTITADTSTSTAYMELSSLRSEDTAVYYCA GSYYSYDVL DYWGQGT TTVTVSS
SEQ ID NO: 1311	VH-humanized matured 2	QVQLVQSGAEVKKPGSSVKVSCKASGTDFKLT YIHWVRQAPGQGLEWMGRIFPGSGNVKYNEKF KGRVTITADTSTSTAYMELSSLRSEDTAVYYCA VSYYSYDVL DYWGQGT TTVTVSS
SEQ ID NO: 1312	VH-humanized matured 3	QVQLVQSGAEVKKPGSSVKVSCKASGHDFRLT YIHWVRQAPGQGLEWMGRISAGSGNVKYNEKF KGRVTITADTSTSTAYMELSSLRSEDTAVYYCA VSYYSYDVL DYWGQGT TTVTVSS
A-H humanized-matured VL		
SEQ ID NO: 1313	VL-humanized matured 1	DIQMTQSPSFLSASVGDRVITCKASQNV DNRV AWYQQKPGKAPKALYSSSHRYKGVPSRFSGSG SGTEFTLTISLQPEDFATYFCQQFKSYPLTFGQG TKLEIK
SEQ ID NO: 1314	VL-humanized matured 2	DIQMTQSPSFLSASVGDRVITCKASQNVADRV AWYQQKPGKAPKALYSSSHRYKGVPSRFSGSG SGTEFTLTISLQPEDFATYFCQQFKSYPLTFGQG TKLEIK

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule comprises a VH and/or a VL of an antibody described in **Table 1A**, or a sequence with at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or more identity thereto.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule comprises a VH and a VL of an antibody described in **Table 1A**, or a sequence with at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or more identity thereto.

Alignment of affinity matured humanized Antibody A-H VL sequences (SEQ ID NOS 3377-3389, respectively, in order of appearance)

	a5-VL	DIQMTQSPSF ¹ LSASVGDRVTITCKASQNVNENKVAWHQQKPGKAPKALIYSSSHRYKGVPS	60
	c1d2d4-VL	DIQMTQSPSF ¹ LSASVGDRVTITCKASQNVNENKVAWHQQKPGKAPKALIYSSSHRYKGVPS	60
5	h3-VL	DIQMTQSPSF ¹ LSASVGDRVTITCKASQNVNENKVAWHQQKPGKAPKALIYSSSHRYKGVPS	60
	f5-VL	DIQMTQSPSF ¹ LSASVGDRVTITCKASQNVNENKVAWHQQKPGKAPKALIYSSSHRYKGVPS	60
	e4b6g3c6h2c2d1a6c3a3e6d6g2-VL	DIQMTQSPSF ¹ LSASVGDRVTITCKASQNVNENKVAWHQQKPGKAPKALIYSSSHRYKGVPS	60
	e3-VL	DIQMTQSPSF ¹ LSASVGDRVTITCKASQNVNENKVAWHQQKPGKAPKALIYSSSHRYKGVPS	60
	d5-VL	DIQMTQSPSF ¹ LSASVGDRVTITCKASQNVNENKVAWHQQKPGKAPKALIYSSSHRYKGVPS	60
10	d3f1g1-VL	DIQMTQSPSF ¹ LSASVGDRVTITCKASQNVNENKVAWHQQKPGKAPKALIYSSSHRYKGVPS	60
	c4f4f2a2a1-VL	DIQMTQSPSF ¹ LSASVGDRVTITCKASQNVNENKVAWHQQKPGKAPKALIYSSSHRYKGVPS	60
	b5h4a4-VL	DIQMTQSPSF ¹ LSASVGDRVTITCKASQNVNENKVAWHQQKPGKAPKALIYSSSHRYKGVPS	60
	b2c5b3e2g4h6-VL	DIQMTQSPSF ¹ LSASVGDRVTITCKASQNVNENKVAWHQQKPGKAPKALIYSSSHRYKGVPS	60
	b1-VL	DIQMTQSPSF ¹ LSASVGDRVTITCKASQNVNENKVAWHQQKPGKAPKALIYSSSHRYKGVPS	60
15	b4e1f3-VL	DIQMTQSPSF ¹ LSASVGDRVTITCKASQNVNENKVAWHQQKPGKAPKALIYSSSHRYKGVPS	60
		***** : : *****. ****	

20

	a5-VL	RFSGSGSGTEFTLTISSLQPEDFATYFCQQFKSYPLTFGQGTKLEIK	107
	c1d2d4-VL	RFSGSGSGTEFTLTISSLQPEDFATYFCQQFKSYPLTFGQGTKLEIK	107
	h3-VL	RFSGSGSGTEFTLTISSLQPEDFATYFCQQFKSYPLTFGQGTKLEIK	107
25	f5-VL	RFSGSGSGTEFTLTISSLQPEDFATYFCQQFKSYPLTFGQGTKLEIK	107
	e4b6g3c6h2c2d1a6c3a3e6d6g2-VL	RFSGSGSGTEFTLTISSLQPEDFATYFCQQFKSYPLTFGQGTKLEIK	107
	e3-VL	RFSGSGSGTEFTLTISSLQPEDFATYFCQQFKSYPLTFGQGTKLEIK	107
	d5-VL	RFSGSGSGTEFTLTISSLQPEDFATYFCQQFKSYPLTFGQGTKLEIK	107
	d3f1g1-VL	RFSGSGSGTEFTLTISSLQPEDFATYFCQQFKSYPLTFGQGTKLEIK	107
30	c4f4f2a2a1-VL	RFSGSGSGTEFTLTISSLQPEDFATYFCQQFKSYPLTFGQGTKLEIK	107
	b5h4a4-VL	RFSGSGSGTEFTLTISSLQPEDFATYFCQQFKSYPLTFGQGTKLEIK	107
	b2c5b3e2g4h6-VL	RFSGSGSGTEFTLTISSLQPEDFATYFCQQFKSYPLTFGQGTKLEIK	107
	b1-VL	RFSGSGSGTEFTLTISSLQPEDFATYFCQQFKSYPLTFGQGTKLEIK	107
35	b4e1f3-VL	RFSGSGSGTEFTLTISSLQPEDFATYFCQQFKSYPLTFGQGTKLEIK	107

Consensus VL: SEQ ID NO: 230

DIQMTQSPSFLSASVGDRVTITCKASQNV G/E/A/D N/D R/K VAW Y/H QQKPGKAPKALYSSSHRY K/S
GVPSRFGSGSGTEFTLTISSLQPEDFATYFCQQFKSYPLTFGQGTKLEIK

Consensus VL: SEQ ID NO: 3289

DIQMTQSPSFLSASVGDRVTITCKASQNVX₁X₂X₃VAWX₄QQKPGKAPKALYSSSHRYX₅

5 GVPSRFGSGSGTEFTLTISSLQPEDFATYFCQQFKSYPLTFGQGTKLEIK, wherein X₁ is G, E, A or D; X₂ is N or D; X₃ is R or K; X₄ is Y or H; and X₅ is K or S

Alignment of affinity matured humanized Antibody A-H VH sequences (SEQ ID NOS 3390-3436, respectively, in order of appearance)

10	A-H. 52-VH	QVQLVQSGAEVKKPKGSSVKVSKASGYSTLTGYIHWVRQAPQGQLEWMGWFFPGSGNIKY 60
	A-H. 53-VH	QVQLVQSGAEVKKPKGSSVKVSKASGYSFRLTYIHWVRQAPQGQLEWMGWFFPGSGNIKY 60
	A-H. 54-VH	QVQLVQSGAEVKKPKGSSVKVSKASGYSFHNWYIHWVRQAPQGQLEWMGWFFPGSGNIKY 60
	A-H. 51-VH	QVQLVQSGAEVKKPKGSSVKVSKASGYSTTTYIHWVRQAPQGQLEWMGWFFPGSGNIKY 60
	A-H. 50-VH	QVQLVQSGAEVKKPKGSSVKVSKASGYSTTTYIHWVRQAPQGQLEWMGRIFPGSGNIKY 60
15	A-H. 47-VH	QVQLVQSGAEVKKPKGSSVKVSKASGYSTTTYIHWVRQAPQGQLEWMGWFFPGSGNTKY 60
	A-H. 49-VH	QVQLVQSGAEVKKPKGSSVKVSKASGYSTTTYIHWVRQAPQGQLEWMGWFFPGSGNTKY 60
	A-H. 48-VH	QVQLVQSGAEVKKPKGSSVKVSKASGYSTTTYIHWVRQAPQGQLEWMGWFFPGSGNTKY 60
	A-H. 45-VH	QVQLVQSGAEVKKPKGSSVKVSKASGYSTTTYIHWVRQAPQGQLEWMGWFFSAGSGNTKY 60
20	A-H. 46-VH	QVQLVQSGAEVKKPKGSSVKVSKASGGTFRITYIHWVRQAPQGQLEWMGRVYPGSGNTKY 60
	c2-VH	QVQLVQSGAEVKKPKGSSVKVSKASGHDFKITYIHWVRQAPQGQLEWMGRVSPGSGNTKY 60
	f5-VH	QVQLVQSGAEVKKPKGSSVKVSKASGTDFRLTYIHWVRQAPQGQLEWMGRISPGSGNTKY 60
	f3-VH	QVQLVQSGAEVKKPKGSSVKVSKASGTDFRLTYIHWVRQAPQGQLEWMGRISPGSGNTKY 60
	e2-VH	QVQLVQSGAEVKKPKGSSVKVSKASGTDFKITYIHWVRQAPQGQLEWMGRISPGSGNTKY 60
25	e1-VH	QVQLVQSGAEVKKPKGSSVKVSKASGTDFKITYIHWVRQAPQGQLEWMGRVSAAGSGNVKY 60
	c1-VH	QVQLVQSGAEVKKPKGSSVKVSKASGTDFRLTYIHWVRQAPQGQLEWMGRVSPGSGNTKY 60
	a1-VH	QVQLVQSGAEVKKPKGSSVKVSKASGTDFKITYIHWVRQAPQGQLEWMGRVSPGSGNTKY 60
	b3-VH	QVQLVQSGAEVKKPKGSSVKVSKASGTDFKITYIHWVRQAPQGQLEWMGRVSPGSGNVKY 60
	h3-VH	QVQLVQSGAEVKKPKGSSVKVSKASGTDFKITYIHWVRQAPQGQLEWMGRISPGSGNVKY 60
30	c3-VH	QVQLVQSGAEVKKPKGSSVKVSKASGTDFRLTYIHWVRQAPQGQLEWMGRIFPGSGNTKY 60
	a5b5c4-VH	QVQLVQSGAEVKKPKGSSVKVSKASGTDFKITYIHWVRQAPQGQLEWMGRIFPGSGNVKY 60
	d6-VH	QVQLVQSGAEVKKPKGSSVKVSKASGTDFKITYIHWVRQAPQGQLEWMGRIFPGSGNTKY 60
	h2-VH	QVQLVQSGAEVKKPKGSSVKVSKASGGTFRITYIHWVRQAPQGQLEWMGRVSAAGSGNVKY 60
	c5-VH	QVQLVQSGAEVKKPKGSSVKVSKASGGTFRITYIHWVRQAPQGQLEWMGRISAGSGNVKY 60
35	f2-VH	QVQLVQSGAEVKKPKGSSVKVSKASGTDFKITYIHWVRQAPQGQLEWMGRISAGSGNTKY 60
	d3-VH	QVQLVQSGAEVKKPKGSSVKVSKASGHDFRLTYIHWVRQAPQGQLEWMGRISAGSGNVKY 60
	a4e4-VH	QVQLVQSGAEVKKPKGSSVKVSKASGHDFKITYIHWVRQAPQGQLEWMGRISAGSGNVKY 60
	d2-VH	QVQLVQSGAEVKKPKGSSVKVSKASGTDFKITYIHWVRQAPQGQLEWMGRISAGSGNVKY 60

g1-VH QVQLVQSGAEVKKPKGSSVKVSKASGHDFDKTYIHWVRQAPQGQGLEWMGRIFAGSGNVKY 60
c6-VH QVQLVQSGAEVKKPKGSSVKVSKASGGTDFDKTYIHWVRQAPQGQGLEWMGRISAGSGNTKY 60
g2-VH QVQLVQSGAEVKKPKGSSVKVSKASGTDFDKTYIHWVRQAPQGQGLEWMGRISAGSGNVKY 60
b4-VH QVQLVQSGAEVKKPKGSSVKVSKASGTDFDKIYIHWVRQAPQGQGLEWMGRVSAGSGNTKY 60
a6-VH QVQLVQSGAEVKKPKGSSVKVSKASGTDFDKIYIHWVRQAPQGQGLEWMGRIFAGSGNTKY 60
a2g4-VH QVQLVQSGAEVKKPKGSSVKVSKASGTDFDKIYIHWVRQAPQGQGLEWMGRISAGSGNVKY 60
b6f1-VH QVQLVQSGAEVKKPKGSSVKVSKASGTDFDKIYIHWVRQAPQGQGLEWMGRISAGSGNTKY 60
g3-VH QVQLVQSGAEVKKPKGSSVKVSKASGTDFDKIYIHWVRQAPQGQGLEWMGRISAGSGNIKY 60
d1-VH QVQLVQSGAEVKKPKGSSVKVSKASGHDFDKFYIHWVRQAPQGQGLEWMGRISAGSGNTKY 60
h4-VH QVQLVQSGAEVKKPKGSSVKVSKASGHDFDKFYIHWVRQAPQGQGLEWMGRVSAGSGNTKY 60
b2-VH QVQLVQSGAEVKKPKGSSVKVSKASGHDFDKFYIHWVRQAPQGQGLEWMGRIFAGSGNVKY 60
h6-VH QVQLVQSGAEVKKPKGSSVKVSKASGTDFDKFYIHWVRQAPQGQGLEWMGRVSAGSGNVKY 60
b1-VH QVQLVQSGAEVKKPKGSSVKVSKASGHDFDKFYIHWVRQAPQGQGLEWMGRVSAGSGNVKY 60
f4-VH QVQLVQSGAEVKKPKGSSVKVSKASGHDFDKTYIHWVRQAPQGQGLEWMGRVSAGSGNVKY 60
a3-VH QVQLVQSGAEVKKPKGSSVKVSKASGHDFRDFYIHWVRQAPQGQGLEWMGRVYPGSGSYRY 60
e6-VH QVQLVQSGAEVKKPKGSSVKVSKASGTDFHLWYIHWVRQAPQGQGLEWMGRVFAAGSGSYRY 60
e3-VH QVQLVQSGAEVKKPKGSSVKVSKASGHDFHLWYIHWVRQAPQGQGLEWMGRISPAGSGNVKY 60
d4-VH QVQLVQSGAEVKKPKGSSVKVSKASGHDFHLWYIHWVRQAPQGQGLEWMGRVSAGSGNVKY 60
d5-VH QVQLVQSGAEVKKPKGSSVKVSKASGHDFHLWYIHWVRQAPQGQGLEWMGRVFAAGSGNTKY 60
***** * ***** . ***. : *

A-H. 52-VH NEKFKGRVTITADTSTSTAYMELSSLRSEDNAVYACAGSYISYDVLVDYWGQGTITVTVSS 119
A-H. 53-VH NEKFKGRVTITADTSTSTAYMELSSLRSEDNAVYACAGSYISYDVLVDYWGQGTITVTVSS 119
A-H. 54-VH NEKFKGRVTITADTSTSTAYMELSSLRSEDNAVYACAGSYISYDVLVDYWGQGTITVTVSS 119
A-H. 51-VH NEKFKGRVTITADTSTSTAYMELSSLRSEDNAVYACAGSIYSAGVLVDYWGQGTITVTVSS 119
A-H. 50-VH NEKFKGRVTITADTSTSTAYMELSSLRSEDNAVYACAGSYISYDVLVDYWGQGTITVTVSS 119
A-H. 47-VH NEKFKGRVTITADTSTSTAYMELSSLRSEDNAVYACAGSYISYDVLVDYWGQGTITVTVSS 119
A-H. 49-VH NEKFKGRVTITADTSTSTAYMELSSLRSEDNAVYACAGSYISYDVLVDYWGQGTITVTVSS 119
A-H. 48-VH NEKFKGRVTITADTSTSTAYMELSSLRSEDNAVYCAVSYISYDVLVDYWGQGTITVTVSS 119
A-H. 45-VH NEKFKGRVTITADTSTSTAYMELSSLRSEDNAVYCAVSYISYDVLVDYWGQGTITVTVSS 119
A-H. 46-VH NEKFKGRVTITADTSTSTAYMELSSLRSEDNAVYACAGSYISYDVLVDYWGQGTITVTVSS 119
c2-VH NEKFKGRVTITADTSTSTAYMELSSLRSEDNAVYACAGSYISYDVLVDYWGQGTITVTVSS 119
f5-VH NEKFKGRVTITADTSTSTAYMELSSLRSEDNAVYACAGSYISYDVLVDYWGQGTITVTVSS 119
f3-VH NEKFKGRVTITADTSTSTAYMELSSLRSEDNAVYACAGSYISYDVLVDYWGQGTITVTVSS 119
e2-VH NEKFKGRVTITADTSTSTAYMELSSLRSEDNAVYACAGSYISYDVLVDYWGQGTITVTVSS 119
e1-VH NEKFKGRVTITADTSTSTAYMELSSLRSEDNAVYACAGSYISYDVLVDYWGQGTITVTVSS 119
c1-VH NEKFKGRVTITADTSTSTAYMELSSLRSEDNAVYACAGSYISYDVLVDYWGQGTITVTVSS 119
a1-VH NEKFKGRVTITADTSTSTAYMELSSLRSEDNAVYACAGSYISYDVLVDYWGQGTITVTVSS 119
b3-VH NEKFKGRVTITADTSTSTAYMELSSLRSEDNAVYACAGSYISYDVLVDYWGQGTITVTVSS 119

Attorney Docket: E2070-7024WO

h3-VH	NEKFKGRVTITADTSTSTAYMELSSLRSED	TAVVYCAGSYYSYDVLDYWGQGT	TTVTVSS	119
c3-VH	NEKFKGRVTITADTSTSTAYMELSSLRSED	TAVVYCAGSYYSYDVLDYWGQGT	TTVTVSS	119
a5b5c4-VH	NEKFKGRVTITADTSTSTAYMELSSLRSED	TAVVYCAGSYYSYDVLDYWGQGT	TTVTVSS	119
d6-VH	NEKFKGRVTITADTSTSTAYMELSSLRSED	TAVVYCAGSYYSYDVLDYWGQGT	TTVTVSS	119
h2-VH	NEKFKGRVTITADTSTSTAYMELSSLRSED	TAVVYCAGSYYSYDVLDYWGQGT	TTVTVSS	119
c5-VH	NEKFKGRVTITADTSTSTAYMELSSLRSED	TAVVYCAGSYYSYDVLDYWGQGT	TTVTVSS	119
f2-VH	NEKFKGRVTITADTSTSTAYMELSSLRSED	TAVVYCAGSYYSYDVLDYWGQGT	TTVTVSS	119
d3-VH	NEKFKGRVTITADTSTSTAYMELSSLRSED	TAVVYCAGSYYSYDVLDYWGQGT	TTVTVSS	119
a4e4-VH	NEKFKGRVTITADTSTSTAYMELSSLRSED	TAVVYCAGSYYSYDVLDYWGQGT	TTVTVSS	119
d2-VH	NEKFKGRVTITADTSTSTAYMELSSLRSED	TAVVYCAGSYYSYDVLDYWGQGT	TTVTVSS	119
g1-VH	NEKFKGRVTITADTSTSTAYMELSSLRSED	TAVVYCAGSYYSYDVLDYWGQGT	TTVTVSS	119
c6-VH	NEKFKGRVTITADTSTSTAYMELSSLRSED	TAVVYCAGSYYSYDVLDYWGQGT	TTVTVSS	119
g2-VH	NEKFKGRVTITADTSTSTAYMELSSLRSED	TAVVYCAGSYYSYDVLDYWGQGT	TTVTVSS	119
b4-VH	NEKFKGRVTITADTSTSTAYMELSSLRSED	TAVVYCAGSYYSYDVLDYWGQGT	TTVTVSS	119
a6-VH	NEKFKGRVTITADTSTSTAYMELSSLRSED	TAVVYCAGSYYSYDVLDYWGQGT	TTVTVSS	119
a2g4-VH	NEKFKGRVTITADTSTSTAYMELSSLRSED	TAVVYCAGSYYSYDVLDYWGQGT	TTVTVSS	119
b6f1-VH	NEKFKGRVTITADTSTSTAYMELSSLRSED	TAVVYCAGSYYSYDVLDYWGQGT	TTVTVSS	119
g3-VH	NEKFKGRVTITADTSTSTAYMELSSLRSED	TAVVYCAGSYYSYDVLDYWGQGT	TTVTVSS	119
d1-VH	NEKFKGRVTITADTSTSTAYMELSSLRSED	TAVVYCAGSYYSYDVLDYWGQGT	TTVTVSS	119
h4-VH	NEKFKGRVTITADTSTSTAYMELSSLRSED	TAVVYCAGSYYSYDVLDYWGQGT	TTVTVSS	119
b2-VH	NEKFKGRVTITADTSTSTAYMELSSLRSED	TAVVYCAGSYYSYDVLDYWGQGT	TTVTVSS	119
h6-VH	NEKFKGRVTITADTSTSTAYMELSSLRSED	TAVVYCAGSYYSYDVLDYWGQGT	TTVTVSS	119
b1-VH	NEKFKGRVTITADTSTSTAYMELSSLRSED	TAVVYCAGSYYSYDVLDYWGQGT	TTVTVSS	119
f4-VH	NEKFKGRVTITADTSTSTAYMELSSLRSED	TAVVYCAGSYYSYDVLDYWGQGT	TTVTVSS	119
a3-VH	NEKFKGRVTITADTSTSTAYMELSSLRSED	TAVVYCAGSYYSYDVLDYWGQGT	TTVTVSS	119
e6-VH	NEKFKGRVTITADTSTSTAYMELSSLRSED	TAVVYCAGSYYSYDVLDYWGQGT	TTVTVSS	119
e3-VH	NEKFKGRVTITADTSTSTAYMELSSLRSED	TAVVYCAGSYYSYDVLDYWGQGT	TTVTVSS	119
d4-VH	NEKFKGRVTITADTSTSTAYMELSSLRSED	TAVVYCAGSYYSYDVLDYWGQGT	TTVTVSS	119
d5-VH	NEKFKGRVTITADTSTSTAYMELSSLRSED	TAVVYCAGSYYSYDVLDYWGQGT	TTVTVSS	119
	*****	*****	*****	

35	Consensus VH: SEQ ID NO: 231
	QVQLVQSGAEVKKPGSSVKVCKASG H/T/G/Y D/T/S F H/R/D/K/T L/D/K/T/N W/F/T/I/Y/G YIHWVRQAPGQGLEWMG
	R/W V/I/F F/S/Y A/P GSG N/S T/V/Y/I K/R YNEKFKGRVTITADTSTSTAYMELSSLRSED
	TAVVYCAGSYYSYDVLDYWGQGT

Attorney Docket: E2070-7024WO

Consensus VH: SEQ ID NO: 3290

QVQLVQSGAEVKKPGSSVKVSCKASGX₁X₂FX₃X₄X₅YIHWVVRQAPGQGLEWMGX₆X₇X₈X₉GSGX₁₀X₁₁X₁₂YNEKFKGRVTIT
 ADTSTSTAYMESSLRSEDTAVYYCAX₁₃SX₁₄YSX₁₅X₁₆VLDYWQGTTTVTVSS, wherein: X1 is H or T or G or Y; X2 is D or
 T or S; X3 is H or R or D or K or T; X4 is L or D or K or T or N; X5 is W or F or T or Y or G; X6 is R or W; X7 is V or I or F;
 X8 is F or S or Y; X9 is A or P; X10 is N or S; X11 is T or V or Y or I; X12 is K or R; X13 is G or V; X14 is Y or I; X15 is Y or A;
 and X16 is D or G

In some embodiments, an anti-TCRVb antibody disclosed herein has an antigen binding domain having a VL having a consensus sequence of SEQ ID NO: 230, wherein position 30 is G, E, A or D; position 31 is N or D; position 32 is R or K; position 36 is Y or H; and/or position 56 is K or S.

5 In some embodiments, an anti-TCRVb antibody disclosed herein has an antigen binding domain having a VH having a consensus sequence of SEQ ID NO: 231, wherein: position 27 is H or T or G or Y; position 28 is D or T or S; position 30 is H or R or D or K or T; position 31 is L or D or K or T or N; position 32 is W or F or T or I or Y or G; position 49 is R or W; position 50 is V or I or F; position 51 is F or S or Y; position 52 is A or P; position 56 is N or S; position 10 57 is T or V or Y or I; position 58 is K or R; position 97 is G or V; position 99 is Y or I; position 102 is Y or A; and/or position 103 is D or G.

Anti-TCR β V12 antibodies

Accordingly, in one aspect, the disclosure provides an anti-TCR β V antibody molecule 15 that binds to human TCR β V12, *e.g.*, a TCR β V12 subfamily comprising: TCR β V12-4*01, TCR β V12-3*01 or TCR β V12-5*01. In some embodiments the TCR β V12 subfamily comprises TCR β V12-4*01. In some embodiments the TCR β V12 subfamily comprises TCR β V12-3*01.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule, is a non-murine antibody molecule, *e.g.*, a human or humanized antibody molecule. In 20 some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule is a human antibody molecule. In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule is a humanized antibody molecule.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule, is isolated or recombinant.

25 In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule, comprises at least one antigen-binding region, *e.g.*, a variable region or an antigen-binding fragment thereof, from an antibody described herein, *e.g.*, an antibody described in **Table 2A**, or encoded by a nucleotide sequence in **Table 2A**, or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of 30 the aforesaid sequences.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule, comprises at least one, two, three or four variable regions from an antibody described herein, *e.g.*, an antibody as described in **Table 2A**, or encoded by a nucleotide sequence in **Table 2A**, or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%,
5 99% or higher identical) to any of the aforesaid sequences.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule, comprises at least one or two heavy chain variable regions from an antibody described herein, *e.g.*, an antibody as described in **Table 2A**, or encoded by a nucleotide sequence in **Table 2A**, or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%,
10 99% or higher identical) to any of the aforesaid sequences.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule, comprises at least one or two light chain variable regions from an antibody described herein, *e.g.*, an antibody as described in **Table 2A**, or encoded by a nucleotide sequence in **Table 2A**, or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%,
15 99% or higher identical) to any of the aforesaid sequences.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule, comprises a heavy chain constant region for an IgG4, *e.g.*, a human IgG4. In still another embodiment, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule, includes a heavy chain constant region for an IgG1, *e.g.*, a human IgG1. In one
20 embodiment, the heavy chain constant region comprises an amino sequence set forth in **Table 3A**, or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) thereto.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule, includes a kappa light chain constant region, *e.g.*, a human kappa light chain constant
25 region. In one embodiment, the light chain constant region comprises an amino sequence set forth in **Table 3A**, or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) thereto.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule, includes at least one, two, or three complementarity determining regions (CDRs) from
30 a heavy chain variable region of an antibody described herein, *e.g.*, an antibody as described in

Table 2A, or encoded by the nucleotide sequence in **Table 2A**, or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule, includes at least one, two, or three CDRs (or collectively all of the CDRs) from a heavy chain variable region comprising an amino acid sequence shown in **Table 2A**, or encoded by a nucleotide sequence shown in **Table 2A**. In one embodiment, one or more of the CDRs (or collectively all of the CDRs) have one, two, three, four, five, six or more changes, *e.g.*, amino acid substitutions or deletions, relative to the amino acid sequence shown in **Table 2A**, or encoded by a nucleotide sequence shown in **Table 2A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule, includes at least one, two, or three complementarity determining regions (CDRs) from a light chain variable region of an antibody described herein, *e.g.*, an antibody as described in **Table 2A**, or encoded by the nucleotide sequence in **Table 2A**, or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule, includes at least one, two, or three CDRs (or collectively all of the CDRs) from a light chain variable region comprising an amino acid sequence shown in **Table 2A**, or encoded by a nucleotide sequence shown in **Table 2A**. In one embodiment, one or more of the CDRs (or collectively all of the CDRs) have one, two, three, four, five, six or more changes, *e.g.*, amino acid substitutions or deletions, relative to the amino acid sequence shown in **Table 2A**, or encoded by a nucleotide sequence shown in **Table 2A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule, includes at least one, two, three, four, five or six CDRs (or collectively all of the CDRs) from a heavy and light chain variable region comprising an amino acid sequence shown in **Table 2A**, or encoded by a nucleotide sequence shown in **Table 2A**. In one embodiment, one or more of the CDRs (or collectively all of the CDRs) have one, two, three, four, five, six or more changes, *e.g.*, amino acid substitutions or deletions, relative to the amino acid sequence shown in **Table 2A**, or encoded by a nucleotide sequence shown in **Table 2A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule, molecule includes all six CDRs from an antibody described herein, *e.g.*, an antibody as described in **Table 2A**, or encoded by the nucleotide sequence in **Table 2A**, or closely related CDRs, *e.g.*, CDRs which are identical or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions). In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule, may include any CDR described herein.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule includes at least one, two, or three CDRs according to Kabat *et al.* (*e.g.*, at least one, two, or three CDRs according to the Kabat definition as set out in **Table 2A**) from a heavy chain variable region of an antibody described herein, *e.g.*, an antibody chosen as described in **Table 2A**, or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences; or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to one, two, or three CDRs according to Kabat *et al.* shown in **Table 2A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule includes at least one, two, or three CDRs according to Kabat *et al.* (*e.g.*, at least one, two, or three CDRs according to the Kabat definition as set out in **Table 2A**) from a light chain variable region of an antibody described herein, *e.g.*, an antibody as described in **Table 2A**, or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences; or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to one, two, or three CDRs according to Kabat *et al.* shown in **Table 2A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule includes at least one, two, three, four, five, or six CDRs according to Kabat *et al.* (*e.g.*, at least one, two, three, four, five, or six CDRs according to the Kabat definition as set out in **Table 2A**) from the heavy and light chain variable regions of an antibody described herein, *e.g.*, an antibody as described in **Table 2A**, or encoded by the nucleotide sequence in **Table 2A**; or a

sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences; or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to one, two, three, four, five, or six CDRs according to Kabat et al. shown in **Table 2A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule includes all six CDRs according to Kabat *et al.* (*e.g.*, all six CDRs according to the Kabat definition as set out in **Table 2A**) from the heavy and light chain variable regions of an antibody described herein, *e.g.*, an antibody as described in **Table 2A**, or encoded by the nucleotide sequence in **Table 2A**; or encoded by the nucleotide sequence in **Table 2A**; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences; or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to all six CDRs according to Kabat et al. shown in **Table 2A**. In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule may include any CDR described herein.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule includes at least one, two, or three hypervariable loops that have the same canonical structures as the corresponding hypervariable loop of an antibody described herein, *e.g.*, an antibody described in **Table 2A**, *e.g.*, the same canonical structures as at least loop 1 and/or loop 2 of the heavy and/or light chain variable domains of an antibody described herein. See, *e.g.*, Chothia et al., (1992) J. Mol. Biol. 227:799-817; Tomlinson et al., (1992) J. Mol. Biol. 227:776-798 for descriptions of hypervariable loop canonical structures. These structures can be determined by inspection of the tables described in these references.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule includes at least one, two, or three CDRs according to Chothia *et al.* (*e.g.*, at least one, two, or three CDRs according to the Chothia definition as set out in **Table 2A**) from a heavy chain variable region of an antibody described herein, *e.g.*, an antibody chosen as described in **Table 2A**, or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences; or which have at least one

amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to one, two, or three CDRs according to Chothia et al. shown in **Table 2A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule includes at least one, two, or three CDRs according to Chothia *et al.* (*e.g.*, at least one, two, or three CDRs according to the Chothia definition as set out in **Table 2A**) from a light chain variable region of an antibody described herein, *e.g.*, an antibody as described in **Table 2A**, or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences; or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to one, two, or three CDRs according to Chothia et al. shown in **Table 2A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule includes at least one, two, three, four, five, or six CDRs according to Chothia *et al.* (*e.g.*, at least one, two, three, four, five, or six CDRs according to the Chothia definition as set out in **Table 2A**) from the heavy and light chain variable regions of an antibody described herein, *e.g.*, an antibody as described in **Table 2A**, or encoded by the nucleotide sequence in **Table 2A**; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences; or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to one, two, three, four, five, or six CDRs according to Chothia et al. shown in **Table 2A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule includes all six CDRs according to Chothia *et al.* (*e.g.*, all six CDRs according to the Chothia definition as set out in **Table 2A**) from the heavy and light chain variable regions of an antibody described herein, *e.g.*, an antibody as described in **Table 2A**, or encoded by the nucleotide sequence in **Table 2A**; or encoded by the nucleotide sequence in **Table 2A**; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences; or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or

insertions, *e.g.*, conservative substitutions) relative to all six CDRs according to Chothia et al. shown in **Table 2A**. In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule may include any CDR described herein.

5 In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule includes at least one, two, or three CDRs according to a combined CDR (*e.g.*, at least one, two, or three CDRs according to the combined CDR definition as set out in **Table 2A**) from a heavy chain variable region of an antibody described herein, *e.g.*, an antibody chosen as described in **Table 2A**, or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%,
10 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences; or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to one, two, or three CDRs according to combined CDR shown in **Table 2A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody
15 molecule includes at least one, two, or three CDRs according to a combined CDR (*e.g.*, at least one, two, or three CDRs according to the combined CDR definition as set out in **Table 2A**) from a light chain variable region of an antibody described herein, *e.g.*, an antibody as described in **Table 2A**, or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%,
20 98%, 99% or higher identical) to any of the aforesaid sequences; or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to one, two, or three CDRs according to a combined CDR shown in **Table 2A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule includes at least one, two, three, four, five, or six CDRs according to a combined CDR.
25 (*e.g.*, at least one, two, three, four, five, or six CDRs according to the combined CDR definition as set out in **Table 2A**) from the heavy and light chain variable regions of an antibody described herein, *e.g.*, an antibody as described in **Table 2A**, or encoded by the nucleotide sequence in **Table 2A**; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%,
30 98%, 99% or higher identical) to any of the aforesaid sequences; or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions,

deletions, or insertions, *e.g.*, conservative substitutions) relative to one, two, three, four, five, or six CDRs according to a combined CDR shown in **Table 2A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule includes all six CDRs according to a combined CDR (*e.g.*, all six CDRs according to the combined CDR definition as set out in **Table 2A**) from the heavy and light chain variable regions of an antibody described herein, *e.g.*, an antibody as described in **Table 2A**, or encoded by the nucleotide sequence in **Table 2A**; or encoded by the nucleotide sequence in **Table 2A**; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences; or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to all six CDRs according to a combined CDR shown in **Table 2A**. In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule may include any CDR described herein.

In some embodiments, a combined CDR as set out in **Table 1A** is a CDR that comprises a Kabat CDR and a Chothia CDR.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule, molecule includes a combination of CDRs or hypervariable loops identified as combined CDRs in **Table 1A**. In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule, can contain any combination of CDRs or hypervariable loops according the “combined” CDRs are described in **Table 1A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule includes a combination of CDRs or hypervariable loops defined according to the Kabat et al. and Chothia et al., or as described in **Table 1A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule can contain any combination of CDRs or hypervariable loops according to the Kabat and Chothia definitions.

In an embodiment, *e.g.*, an embodiment comprising a variable region, a CDR (*e.g.*, a combined CDR, Chothia CDR or Kabat CDR), or other sequence referred to herein, *e.g.*, in **Table 2A**, the antibody molecule is a monospecific antibody molecule, a bispecific antibody

molecule, a bivalent antibody molecule, a biparatopic antibody molecule, or an antibody molecule that comprises an antigen binding fragment of an antibody, *e.g.*, a half antibody or antigen binding fragment of a half antibody. In certain embodiments the antibody molecule comprises a multispecific molecule, *e.g.*, a bispecific molecule, *e.g.*, as described herein.

5 In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule includes:

(i) one, two or all of a light chain complementarity determining region 1 (LC CDR1), a light chain complementarity determining region 2 (LC CDR2), and a light chain complementarity determining region 3 (LC CDR3) of SEQ ID NO: 16, SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO: 29 or SEQ ID NO: 30, and/or

(ii) one, two or all of a heavy chain complementarity determining region 1 (HC CDR1), heavy chain complementarity determining region 2 (HC CDR2), and a heavy chain complementarity determining region 3 (HC CDR3) of SEQ ID NO: 15, SEQ ID NO: 23, SEQ ID NO: 24, or SEQ ID NO: 25.

15 In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises:

(i) a LC CDR1 amino acid sequence of SEQ ID NO: 20, a LC CDR2 amino acid sequence of SEQ ID NO: 21, or a LC CDR3 amino acid sequence of SEQ ID NO: 22; and/or

(ii) a HC CDR1 amino acid sequence of SEQ ID NO: 17, a HC CDR2 amino acid sequence of SEQ ID NO: 18, or a HC CDR3 amino acid sequence of SEQ ID NO: 19.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises:

(i) a light chain variable region (VL) comprising a LC CDR1 amino acid sequence of SEQ ID NO: 20, a LC CDR2 amino acid sequence of SEQ ID NO: 21, and a LC CDR3 amino acid sequence of SEQ ID NO: 2; and/or

(ii) a heavy chain variable region (VH) comprising a HC CDR1 amino acid sequence of SEQ ID NO: 17, a HC CDR2 amino acid sequence of SEQ ID NO: 18, and a HC CDR3 amino acid sequence of SEQ ID NO: 19.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises:

(i) a LC CDR1 amino acid sequence of SEQ ID NO: 63, a LC CDR2 amino acid sequence of SEQ ID NO: 64, or a LC CDR3 amino acid sequence of SEQ ID NO: 65; and/or

(ii) a HC CDR1 amino acid sequence of SEQ ID NO: 57, a HC CDR2 amino acid sequence of SEQ ID NO: 58, or a HC CDR3 amino acid sequence of SEQ ID NO: 59.

5 In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises:

(i) a light chain variable region (VL) comprising a LC CDR1 amino acid sequence of SEQ ID NO: 63, a LC CDR2 amino acid sequence of SEQ ID NO: 64, or a LC CDR3 amino acid sequence of SEQ ID NO: 65; and/or

10 (ii) a heavy chain variable region (VH) comprising a HC CDR1 amino acid sequence of SEQ ID NO: 57, a HC CDR2 amino acid sequence of SEQ ID NO: 58, or a HC CDR3 amino acid sequence of SEQ ID NO: 59.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises:

15 (i) a LC CDR1 amino acid sequence of SEQ ID NO: 66, a LC CDR2 amino acid sequence of SEQ ID NO: 67, or a LC CDR3 amino acid sequence of SEQ ID NO: 68; and/or

(ii) a HC CDR1 amino acid sequence of SEQ ID NO: 60, a HC CDR2 amino acid sequence of SEQ ID NO: 61, or a HC CDR3 amino acid sequence of SEQ ID NO: 62.

20 In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises:

(i) a light chain variable region (VL) comprising a LC CDR1 amino acid sequence of SEQ ID NO: 63, a LC CDR2 amino acid sequence of SEQ ID NO: 64, or a LC CDR3 amino acid sequence of SEQ ID NO: 65; and/or

25 (ii) a heavy chain variable region (VH) comprising a HC CDR1 amino acid sequence of SEQ ID NO: 57, a HC CDR2 amino acid sequence of SEQ ID NO: 58, or a HC CDR3 amino acid sequence of SEQ ID NO: 59.

30 In one embodiment, the light or the heavy chain variable framework (*e.g.*, the region encompassing at least FR1, FR2, FR3, and optionally FR4) of the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule can be chosen from: (a) a light or heavy chain

variable framework including at least 80%, 85%, 87%, 90%, 92%, 93%, 95%, 97%, 98%, or 100% of the amino acid residues from a human light or heavy chain variable framework, *e.g.*, a light or heavy chain variable framework residue from a human mature antibody, a human germline sequence, or a human consensus sequence; (b) a light or heavy chain variable framework including from 20% to 80%, 40% to 60%, 60% to 90%, or 70% to 95% of the amino acid residues from a human light or heavy chain variable framework, *e.g.*, a light or heavy chain variable framework residue from a human mature antibody, a human germline sequence, or a human consensus sequence; (c) a non-human framework (*e.g.*, a rodent framework); or (d) a non-human framework that has been modified, *e.g.*, to remove antigenic or cytotoxic determinants, *e.g.*, deimmunized, or partially humanized. In one embodiment, the light or heavy chain variable framework region (particularly FR1, FR2 and/or FR3) includes a light or heavy chain variable framework sequence at least 70, 75, 80, 85, 87, 88, 90, 92, 94, 95, 96, 97, 98, 99% identical or identical to the frameworks of a VL or VH segment of a human germline gene.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule, comprises a heavy chain variable domain having at least one, two, three, four, five, six, seven, ten, fifteen, twenty or more changes, *e.g.*, amino acid substitutions or deletions, from an amino acid sequence described in **Table 2A** *e.g.*, the amino acid sequence of the FR region in the entire variable region, *e.g.*, shown in **FIGs. 2A** and **2B**, or in SEQ ID NOs: 23-25.

Alternatively, or in combination with the heavy chain substitutions described herein the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises a light chain variable domain having at least one, two, three, four, five, six, seven, ten, fifteen, twenty or more amino acid changes, *e.g.*, amino acid substitutions or deletions, from an amino acid sequence of an antibody described herein *e.g.*, the amino acid sequence of the FR region in the entire variable region, *e.g.*, shown in **FIGs. 2A** and **2B**, or in SEQ ID NOs: 26-30.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule includes one, two, three, or four heavy chain framework regions shown in **FIG. 2A**, or a sequence substantially identical thereto.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule includes one, two, three, or four light chain framework regions shown in **FIG. 2B**, or a sequence substantially identical thereto.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises the light chain framework region 1 *e.g.*, as shown in **FIG. 2B**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises the light chain framework region 2 *e.g.*, as shown in **FIG. 2B**.

5 In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises the light chain framework region 3, *e.g.*, as shown in **FIG. 2B**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises the light chain framework region 4, *e.g.*, as shown in **FIG. 2B**.

10 In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises a light chain comprising a framework region, *e.g.*, framework region 1 (FR1), comprising a change, *e.g.*, a substitution (*e.g.*, a conservative substitution) at one or more, *e.g.*, all, position disclosed herein according to Kabat numbering. In some embodiments, FR1 comprises an Aspartic Acid at position 1, *e.g.*, a substitution at position 1 according to Kabat numbering, *e.g.*, an Alanine to Aspartic Acid substitution. In some embodiments, FR1 comprises
15 an Asparagine at position 2, *e.g.*, a substitution at position 2 according to Kabat numbering, *e.g.*, an Isoleucine to Asparagine substitution, Serine to Asparagine substitution or Tyrosine to Asparagine substitution. In some embodiments, FR1 comprises a Leucine at position 4, *e.g.*, a substitution at position 4 according to Kabat numbering, *e.g.*, a Methionine to Leucine substitution.

20 In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises a light chain comprising a framework region, *e.g.*, framework region 1 (FR1), comprising a substitution at position 1 according to Kabat numbering, *e.g.*, an Alanine to Aspartic Acid substitution, a substitution at position 2 according to Kabat numbering, *e.g.*, an Isoleucine to Asparagine substitution, Serine to Asparagine substitution or Tyrosine to
25 Asparagine substitution, and a substitution at position 4 according to Kabat numbering, *e.g.*, a Methionine to Leucine substitution. In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises a light chain comprising a framework region, *e.g.*, framework region 1 (FR1), comprising a substitution at position 1 according to Kabat numbering, *e.g.*, an Alanine to Aspartic Acid substitution, and a substitution at position 2
30 according to Kabat numbering, *e.g.*, an Isoleucine to Asparagine substitution, Serine to

Asparagine substitution or Tyrosine to Asparagine substitution. In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises a light chain comprising a framework region, *e.g.*, framework region 1 (FR1), comprising a substitution at position 1 according to Kabat numbering, *e.g.*, an Alanine to Aspartic Acid substitution, and a substitution at position 4 according to Kabat numbering, *e.g.*, a Methionine to Leucine substitution. In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises a light chain comprising a framework region, *e.g.*, framework region 1 (FR1), comprising a substitution at position 2 according to Kabat numbering, *e.g.*, an Isoleucine to Asparagine substitution, Serine to Asparagine substitution or Tyrosine to Asparagine substitution, and a substitution at position 4 according to Kabat numbering, *e.g.*, a Methionine to Leucine substitution. In some embodiments, the substitution is relative to a human germline light chain framework region sequence.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises a light chain comprising a framework region, *e.g.*, framework region 3 (FR3), comprising a change, *e.g.*, a substitution (*e.g.*, a conservative substitution) at one or more, *e.g.*, all, position disclosed herein according to Kabat numbering. In some embodiments, FR3 comprises a Glycine at position 66, *e.g.*, a substitution at position 66 according to Kabat numbering, *e.g.*, a Lysine to Glycine substitution, or a Serine to Glycine substitution. In some embodiments, FR3 comprises an Asparagine at position 69, *e.g.*, a substitution at position 69 according to Kabat numbering, *e.g.*, a Tyrosine to Asparagine substitution. In some embodiments, FR3 comprises a Tyrosine at position 71, *e.g.*, a substitution at position 71 according to Kabat numbering, *e.g.*, a Phenylalanine to Tyrosine substitution, or an Alanine to Tyrosine substitution.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises a light chain comprising a framework region, *e.g.*, framework region 3 (FR3), comprising a substitution at position 66 according to Kabat numbering, *e.g.*, a Lysine to Glycine substitution, or a Serine to Glycine substitution, and a substitution at position 69 according to Kabat numbering, *e.g.*, a Tyrosine to Asparagine substitution. . In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises a light chain comprising a framework region, *e.g.*, framework region 3 (FR3),

comprising a substitution at position 66 according to Kabat numbering, *e.g.*, Lysine to Glycine substitution, or a Serine to Glycine substitution, and a substitution at position 71 according to Kabat numbering, *e.g.*, a Phenylalanine to Tyrosine substitution, or an Alanine to Tyrosine substitution. In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises a light chain comprising a framework region, *e.g.*, framework region 3 (FR3), comprising a substitution at position 69 according to Kabat numbering, *e.g.*, a Tyrosine to Asparagine substitution and a substitution at position 71 according to Kabat numbering, *e.g.*, a Phenylalanine to Tyrosine substitution, or an Alanine to Tyrosine substitution. In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises a light chain comprising a framework region, *e.g.*, framework region 3 (FR3), comprising a substitution at position 66 according to Kabat numbering, *e.g.*, a Lysine to Glycine substitution, or a Serine to Glycine substitution, a substitution at position 69 according to Kabat numbering, *e.g.*, a Tyrosine to Asparagine substitution and a substitution at position 71 according to Kabat numbering, *e.g.*, a Phenylalanine to Tyrosine substitution, or an Alanine to Tyrosine substitution. In some embodiments, the substitution is relative to a human germline light chain framework region sequence.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises a light chain comprising: a framework region 1 (FR1) comprising a substitution at position 2 according to Kabat numbering, *e.g.*, a Isoleucine to Asparagine substitution; and a framework region 3 (FR3), comprising a substitution at position 69 according to Kabat numbering, *e.g.*, a Threonine to Asparagine substitution and a substitution at position 71 according to Kabat numbering, *e.g.*, a Phenylalanine to Tyrosine substitution, *e.g.*, as shown in the amino acid sequence of SEQ ID NO: 26. In some embodiments, the substitution is relative to a human germline light chain framework region sequence.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises a light chain comprising: (a) a framework region 1 (FR1) comprising a substitution at position 1 according to Kabat numbering, *e.g.*, a Alanine to Aspartic Acid substitution, and a substitution at position 2 according to Kabat numbering, *e.g.*, a Isoleucine to Asparagine substitution; and (b) a framework region 3 (FR3), comprising a substitution at

position 69 according to Kabat numbering, *e.g.*, a Threonine to Asparagine substitution and a substitution at position 71 according to Kabat numbering, *e.g.*, a Phenylalanine to Tyrosine substitution, *e.g.*, as shown in the amino acid sequence of SEQ ID NO: 27. In some embodiments, the substitution is relative to a human germline light chain framework region sequence.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises a light chain comprising: (a) a framework region 1 (FR1) comprising a substitution at position 2 according to Kabat numbering, *e.g.*, a Serine to Asparagine substitution; and a substitution at position 4 according to Kabat numbering, *e.g.*, a Methionine to Leucine substitution; and (b) a framework region 3 (FR3), comprising a substitution at position 69 according to Kabat numbering, *e.g.*, a Threonine to Asparagine substitution and a substitution at position 71 according to Kabat numbering, *e.g.*, a Phenylalanine to Tyrosine substitution, *e.g.*, as shown in the amino acid sequence of SEQ ID NO: 28. In some embodiments, the substitution is relative to a human germline light chain framework region sequence.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises a light chain comprising: (a) a framework region 1 (FR1) comprising a substitution at position 2 according to Kabat numbering, *e.g.*, a Serine to Asparagine substitution; and (b) a framework region 3 (FR3) comprising a substitution at position 66 according to Kabat numbering, *e.g.*, a Lysine to Glycine substitution; a substitution at position 69 according to Kabat numbering, *e.g.*, a Threonine to Asparagine substitution; and a substitution at position 71 according to Kabat numbering, *e.g.*, a Alanine to Tyrosine substitution, *e.g.*, as shown in the amino acid sequence of SEQ ID NO: 29. In some embodiments, the substitution is relative to a human germline light chain framework region sequence.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises a light chain comprising: (a) a framework region 1 (FR1) comprising a substitution at position 2 according to Kabat numbering, *e.g.*, a Tyrosine to Asparagine substitution; and (b) a framework region 3 (FR3) comprising a substitution at position 66 according to Kabat numbering, *e.g.*, a Serine to Glycine substitution; a substitution at position 69 according to Kabat numbering, *e.g.*, a Threonine to Asparagine substitution; and a substitution at position 71 according to Kabat numbering, *e.g.*, a Alanine to Tyrosine substitution, *e.g.*, as

shown in the amino acid sequence of SEQ ID NO: 29. In some embodiments, the substitution is relative to a human germline light chain framework region sequence.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises a light chain variable domain comprising: (a) a framework region 1 (FR1) comprising a change, *e.g.*, a substitution (*e.g.*, a conservative substitution) at one or more (*e.g.*, all) positions disclosed herein according to Kabat numbering, and (b) a framework region 3 (FR3) comprising a change, *e.g.*, a substitution (*e.g.*, a conservative substitution) at one or more (*e.g.*, all) position disclosed herein according to Kabat numbering. In some embodiments, the substitution is relative to a human germline light chain framework region sequence.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises the heavy chain framework region 1, *e.g.*, as shown in **FIG. 2A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises the heavy chain framework region 2, *e.g.*, as shown in **FIG. 2A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises the heavy chain framework region 3, *e.g.*, as shown in **FIG. 2A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises the heavy chain framework region 4, *e.g.*, as shown in **FIG. 2A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises the heavy chain framework regions 1-4, *e.g.*, SEQ ID NOS: 20-23, or as shown in **FIG. 2A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises the light chain framework regions 1-4, *e.g.*, SEQ ID NOS: 26-30, or as shown in **FIG. 2B**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises the heavy chain framework regions 1-4, *e.g.*, SEQ ID NOS: 23-25; and the light chain framework regions 1-4, *e.g.*, SEQ ID NOS: 26-30, or as shown in **FIGs. 2A and 2B**.

In some embodiments, the heavy or light chain variable domain, or both, of , the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule includes an amino acid sequence, which is substantially identical to an amino acid disclosed herein, *e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical to a variable region of an antibody
 5 described herein, *e.g.*, an antibody as described in **Table 2A**, or encoded by the nucleotide sequence in **Table 2A**; or which differs at least 1 or 5 residues, but less than 40, 30, 20, or 10 residues, from a variable region of an antibody described herein.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises at least one, two, three, or four antigen-binding regions, *e.g.*, variable
 10 regions, having an amino acid sequence as set forth in **Table 2A**, or a sequence substantially identical thereto (*e.g.*, a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, or which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the sequences shown in **Table 2A**. In another embodiment, , the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule includes a VH and/or VL domain encoded by a nucleic acid
 15 having a nucleotide sequence as set forth in **Table 2A**, or a sequence substantially identical thereto (*e.g.*, a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, or which differs by no more than 3, 6, 15, 30, or 45 nucleotides from the sequences shown in **Table 2A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises:

20 a VH domain comprising an amino acid sequence chosen from the amino acid sequence of SEQ ID NO: 23, SEQ ID NO: 24 or SEQ ID NO: 25, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 23, SEQ ID NO: 24 or SEQ ID NO: 25, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 23, SEQ ID NO: 24, or
 25 SEQ ID NO: 25; and/or

a VL domain comprising an amino acid sequence chosen from the amino acid sequence of SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO: 29, or SEQ ID NO: 30, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence of SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO: 29, or SEQ ID NO:
 30 30, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid

residues from the amino acid sequence of SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO: 29, or SEQ ID NO: 30.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises:

5 a VH domain comprising the amino acid sequence of SEQ ID NO: 23, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 23, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 23; and

10 a VL domain comprising the amino acid sequence of SEQ ID NO: 26, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 26, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 26.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises:

15 a VH domain comprising the amino acid sequence of SEQ ID NO: 23, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 23, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 23; and

20 a VL domain comprising the amino acid sequence of SEQ ID NO: 27, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 27, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 27.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises:

25 a VH domain comprising the amino acid sequence of SEQ ID NO: 23, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 23, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 23; and

30 a VL domain comprising the amino acid sequence of SEQ ID NO: 28, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ

ID NO: 28, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 28.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises:

5 a VH domain comprising the amino acid sequence of SEQ ID NO: 23, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 23, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 23; and

10 a VL domain comprising the amino acid sequence of SEQ ID NO: 29, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 29, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 29.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises:

15 a VH domain comprising the amino acid sequence of SEQ ID NO: 23, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 23, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 23; and

20 a VL domain comprising the amino acid sequence of SEQ ID NO: 30, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 30, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 30.

25 In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises:

a VH domain comprising the amino acid sequence of SEQ ID NO: 24, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 24, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 24; and

a VL domain comprising the amino acid sequence of SEQ ID NO: 26, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 26, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 26.

5 In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises:

a VH domain comprising the amino acid sequence of SEQ ID NO: 24, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 24, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 24; and

a VL domain comprising the amino acid sequence of SEQ ID NO: 27, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 27, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 27.

15 In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises:

a VH domain comprising the amino acid sequence of SEQ ID NO: 24, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 24, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 24; and

a VL domain comprising the amino acid sequence of SEQ ID NO: 28, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 28, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 28.

25 In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises:

a VH domain comprising the amino acid sequence of SEQ ID NO: 24, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 24, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 24; and

a VL domain comprising the amino acid sequence of SEQ ID NO: 29, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 29, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 29.

5 In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises:

a VH domain comprising the amino acid sequence of SEQ ID NO: 24, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 24, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 24; and

10 a VL domain comprising the amino acid sequence of SEQ ID NO: 30, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 30, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 30.

15 In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises:

a VH domain comprising the amino acid sequence of SEQ ID NO: 25, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 25, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 25; and

20 a VL domain comprising the amino acid sequence of SEQ ID NO: 26, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 26, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 26.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises:

a VH domain comprising the amino acid sequence of SEQ ID NO: 25, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ

ID NO: 25, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 25; and

5 a VL domain comprising the amino acid sequence of SEQ ID NO: 27, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 27, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 27.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises:

10 a VH domain comprising the amino acid sequence of SEQ ID NO: 25, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 25, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 25; and

15 a VL domain comprising the amino acid sequence of SEQ ID NO: 28, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 28, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 28.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises:

20 a VH domain comprising the amino acid sequence of SEQ ID NO: 25, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 25, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 25; and

25 a VL domain comprising the amino acid sequence of SEQ ID NO: 29, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 29, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 29.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises:

30 a VH domain comprising the amino acid sequence of SEQ ID NO: 25, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ

ID NO: 25, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 25; and

a VL domain comprising the amino acid sequence of SEQ ID NO: 30, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 30, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 30.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule is a full antibody or fragment thereof (*e.g.*, a Fab, F(ab')₂, Fv, or a single chain Fv fragment (scFv)). In embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule is a monoclonal antibody or an antibody with single specificity. In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule, can also be a humanized, chimeric, camelid, shark, or an *in vitro*-generated antibody molecule. In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule is a humanized antibody molecule. The heavy and light chains of the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule can be full-length (*e.g.*, an antibody can include at least one, and preferably two, complete heavy chains, and at least one, and preferably two, complete light chains) or can include an antigen-binding fragment (*e.g.*, a Fab, F(ab')₂, Fv, a single chain Fv fragment, a single domain antibody, a diabody (dAb), a bivalent antibody, or bispecific antibody or fragment thereof, a single domain variant thereof, or a camelid antibody).

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule is in the form of a multispecific molecule, *e.g.*, a bispecific molecule, *e.g.*, as described herein.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule has a heavy chain constant region (Fc) chosen from, *e.g.*, the heavy chain constant regions of IgG1, IgG2, IgG3, IgG4, IgM, IgA1, IgA2, IgD, and IgE. In some embodiments, the Fc region is chosen from the heavy chain constant regions of IgG1, IgG2, IgG3, and IgG4. In some embodiments, the Fc region is chosen from the heavy chain constant region of IgG1 or

IgG2 (*e.g.*, human IgG1, or IgG2). In some embodiments, the heavy chain constant region is human IgG1.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule has a light chain constant region chosen from, *e.g.*, the light chain constant regions of kappa or lambda, preferably kappa (*e.g.*, human kappa). In one embodiment, the constant region is altered, *e.g.*, mutated, to modify the properties of the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule (*e.g.*, to increase or decrease one or more of: Fc receptor binding, antibody glycosylation, the number of cysteine residues, effector cell function, or complement function). For example, the constant region is mutated at positions 296 (M to Y), 298 (S to T), 300 (T to E), 477 (H to K) and 478 (N to F) to alter Fc receptor binding (*e.g.*, the mutated positions correspond to positions 132 (M to Y), 134 (S to T), 136 (T to E), 313 (H to K) and 314 (N to F) of SEQ ID NOs: 212 or 214; or positions 135 (M to Y), 137 (S to T), 139 (T to E), 316 (H to K) and 317 (N to F) of SEQ ID NOs: 215, 216, 217, or 218).

Antibody B-H.1 comprises a first chain comprising the amino acid sequence of SEQ ID NO: 3280 and a second chain comprising the amino acid sequence of SEQ ID NO: 3281.

Additional exemplary anti-TCR β V12 antibodies of the disclosure are provided in **Table 2A**. In some embodiments, the anti-TCR β V12 is antibody B, *e.g.*, humanized antibody B (antibody B-H), as provided in **Table 2A**. In some embodiments, the anti-TCR β V antibody comprises one or more (*e.g.*, all three) of a LC CDR1, LC CDR2, and LC CDR3 provided in **Table 2A**; and/or one or more (*e.g.*, all three) of a HC CDR1, HC CDR2, and HC CDR3 provided in **Table 2A**, or a sequence with at least 95% identity thereto. In some embodiments, antibody B comprises a variable heavy chain (VH) and/or a variable light chain (VL) provided in **Table 2A**, or a sequence with at least 95% identity thereto.

Table 2A: Amino acid and nucleotide sequences for murine and humanized antibody molecules which bind to TCRVB 12, e.g., TCRVB 12-3 or TCRVB 12-4. The antibody molecules include murine mAb Antibody B and humanized mAb Antibody B-H.1 to B-H.6. The amino acid the heavy and light chain CDRs, and the amino acid and nucleotide sequences of the heavy and light chain variable regions, and the heavy and light chains are shown.

Antibody B (murine)		
SEQ ID NO: 17	HC CDR1 (Combined)	GFTFSNFGMH
SEQ ID NO: 18	HC CDR2 (Combined)	YISSGSSTIYYADTLKG
SEQ ID NO: 19	HC CDR3 (Combined)	RGEGAMDY
SEQ ID NO: 57	HC CDR1 (Kabat)	NFGMH
SEQ ID NO: 58	HC CDR2 (Kabat)	YISSGSSTIYYADTLKG
SEQ ID NO: 59	HC CDR3 (Kabat)	RGEGAMDY
SEQ ID NO: 60	HC CDR1 (Chothia)	GFTFSNF
SEQ ID NO: 61	HC CDR2 (Chothia)	SSGSST
SEQ ID NO: 62	HC CDR3 (Chothia)	RGEGAMDY
SEQ ID NO: 15	VH	DVQLVESGGGLVQPGGSRKLSAASGF TFSNFGMHWVRQAPDKGLEWVAYISS GSSTIYYADTLKGRFTISRDNPKNTLFL QMTSLRSEDAMYYCARRGEGAMDY WGQGTSTVTVSS
SEQ ID NO: 20	LC CDR1 (Combined)	RASSSVNYIY
SEQ ID NO: 21	LC CDR2 (Combined)	YTSNLAP
SEQ ID NO: 22	LC CDR3 (Combined)	QQFTSSPFT
SEQ ID NO: 63	LC CDR1 (Kabat)	RASSSVNYIY
SEQ ID NO: 64	LC CDR2 (Kabat)	YTSNLAP
SEQ ID NO: 65	LC CDR3 (Kabat)	QQFTSSPFT
SEQ ID NO: 66	LC CDR1 (Chothia)	RASSSVNYIY
SEQ ID NO: 67	LC CDR2 (Chothia)	YTSNLAP
SEQ ID NO: 68	LC CDR3 (Chothia)	QQFTSSPFT
SEQ ID NO: 16	VL	ENVLTQSPAIMSASLGEKVTMSCRASSS VNYIYWYQQKSDASPGLWIYYTSNLAP GVPTRFSGSGSGNSYSLTISSEMEGEDAA TYYCQQFTSSPFTFGSGTKLEIK
Antibody B humanized (B-H)		
Antibody B-H.1A HC-1		
SEQ ID NO: 17	HC CDR1 (Combined)	GFTFSNFGMH
SEQ ID NO: 18	HC CDR2 (Combined)	YISSGSSTIYYADTLKG
SEQ ID NO: 19	HC CDR3 (Combined)	RGEGAMDY
SEQ ID NO: 23	VH	EVQLVESGGGLVQPGGSLRLSAASGF TFSNFGMHWVRQAPGKLEWVSYISSG SSTIYYADTLKGRFTISRDNKNSLYLQ MNSLRAEDTAVYYCARRGEGAMDYW GQGTSTVTVSS
SEQ ID NO: 31	DNA VH	GAGGTGCAGCTGGTTGAATCTGGCGG AGGATTGGTTCAGCCTGGCGGCTCTCT

		GAGACTGTCTTGTGCCGCTTCTGGCTT CACCTTCTCCAACCTTCGGCATGCACTG GGTCCGACAGGCCCCCTGGAAAAGGAC TGGAATGGGTGTCCTACATCTCCTCCG GCTCCTCCACCATCTACTACGCTGACA CCCTGAAGGGCAGATTCACCATCTCT CGGGACAACGCCAAGAACTCCCTGTA CCTGCAGATGAACAGCCTGAGAGCCG AGGACACCGCCGTGTACTACTGTGCT AGAAGAGGCGAGGGCGCCATGGATTA TTGGGGCCAGGGAACCACAGTGACCG TGCTAGC
Antibody B-H.1B HC-2		
SEQ ID NO: 17	HC CDR1 (Combined)	GFTFSNFGMH
SEQ ID NO: 18	HC CDR2 (Combined)	YISSGSSTIYYADTLKG
SEQ ID NO: 19	HC CDR3 (Combined)	RGEGAMDY
SEQ ID NO: 24	VH	EVQLVESGGGLVQPGGSLRLSCAASGF TFSNFGMHWVRQAPGKLEWVSYISSG SSTIYYADTLKGRFTISRDN SKNTLYLQ MNSLRAEDTAVYYCARRGEGAMDYW GQGT TVTVSS
SEQ ID NO: 32	DNA VH	GAGGTGCAGCTGGTTGAATCTGGCGG AGGATTGGTTCAGCCTGGCGGCTCTCT GAGACTGTCTTGTGCCGCTTCTGGCTT CACCTTCTCCAACCTTCGGCATGCACTG GGTCCGACAGGCCCCCTGGAAAAGGAC TGGAATGGGTGTCCTACATCTCCTCCG GCTCCTCCACCATCTACTACGCTGACA CCCTGAAGGGCAGATTCACCATCAGC CGGGACAAC TCCAAGAACACCCTGTA CCTGCAGATGAACTCCCTGAGAGCCG AGGACACCGCCGTGTACTACTGTGCT AGAAGAGGCGAGGGCGCCATGGATTA TTGGGGCCAGGGAACCACAGTGACCG TGCTAGC
Antibody B-H.1C HC-3		
SEQ ID NO: 17	HC CDR1 (Combined)	GFTFSNFGMH
SEQ ID NO: 18	HC CDR2 (Combined)	YISSGSSTIYYADTLKG
SEQ ID NO: 19	HC CDR3 (Combined)	RGEGAMDY
SEQ ID NO: 25	VH	QVQLVESGGGVVQPGRSLRLSCAASGF TFSNFGMHWVRQAPGKLEWVAYISS GSSTIYYADTLKGRFTISRDN SKNTLYL QMNSLRAEDTAVYYCARRGEGAMDY WGQGT TVTVSS
SEQ ID NO: 33	DNA VH	CAGGTGCAGCTGGTGGAATCTGGTG CGGAGTTGTGCAGCCTGGCAGATCCC TGAGACTGTCTTGTGCCGCTCTGGCT TCACCTTCTCCAACCTTCGGCATGCACT GGGTCCGACAGGCCCCCTGGAAAAGGA

		TTGGAGTGGGTCGCCTACATCTCCTCC GGCTCCTCCACCATCTACTACGCTGAC ACCCTGAAGGGCAGATTACCATCAG CCGGGACAACCTCCAAGAACACCCTGT ACCTGCAGATGAACTCCCTGAGAGCC GAGGACACCGCCGTGTACTACTGTGC TAGAAGAGGCGAGGGCGCCATGGATT ATTGGGGCCAGGGAACCACAGTGACC GTGTCTAGC
Antibody B-H.1D LC-1		
SEQ ID NO: 20	LC CDR1 (Combined)	RASSSVNYIY
SEQ ID NO: 21	LC CDR2 (Combined)	YTSNLAP
SEQ ID NO: 22	LC CDR3(Combined)	QQFTSSPFT
SEQ ID NO: 26	VL	DNQLTQSPSFLSASVGDRVITICRASSS VNYIYWYQQKPGKAPKLLIYYTSNLAP GVPSRFSGSGSGNEYTLTISSLQPEDFAT YYCQQFTSSPFTFGQGTKLEIK
SEQ ID NO: 34	DNA VL	GATAACCAGCTGACCCAGTCTCCTAG CTTCCTGTCTGCCTCTGTGGGCGACAG AGTGACAATTACCTGCCGGGCCTCCT CCTCCGTGAACTACATCTACTGGTATC AGCAGAAGCCCGGCAAGGCCCTAAG CTGCTGATCTACTACACCTCCAATCTG GCCCCTGGCGTGCCCTCTAGATTTTCC GGATCTGGCTCCGGCAACGAGTATAC CCTGACAATCTCCAGCCTGCAGCCTG AGGACTTCGCCACCTACTACTGCCAG CAGTTCACCTCCTCTCCATTACCTTT GGCCAGGGCACCAAGCTGGAAATCAA A
Antibody B-H.1E LC-2		
SEQ ID NO: 20	LC CDR1 (Combined)	RASSSVNYIY
SEQ ID NO: 21	LC CDR2 (Combined)	YTSNLAP
SEQ ID NO: 22	LC CDR3(Combined)	QQFTSSPFT
SEQ ID NO: 27	VL	DNQLTQSPSSLSASVGDRVITICRASSS VNYIYWYQQKPGKAPKLLIYYTSNLAP GVPSRFSGSGSGNDYTLTISSLQPEDFAT YYCQQFTSSPFTFGQGTKLEIK
SEQ ID NO: 35	DNA VL	ATAACCAGCTGACCCAGTCTCCTTCCA GCCTGTCTGCTTCTGTGGGCGACAGA GTGACAATTACCTGCCGGGCCTCCTCC TCCGTGAACTACATCTACTGGTATCAG CAGAAGCCCGGCAAGGCCCTAAGCT GCTGATCTACTACACCTCCAATCTGGC CCCTGGCGTGCCCTCTAGATTTTCCGG ATCTGGCTCCGGCAACGACTATACCC TGACAATCTCCAGCCTGCAGCCTGAG GACTTCGCCACCTACTACTGCCAGCA

		GTTCACCTCCTCTCCATTCACCTTTGG CCAGGGCACCAAGCTGGAAATCAAA
Antibody B-H.1F LC-3		
SEQ ID NO: 20	LC CDR1 (Combined)	RASSSVNYIY
SEQ ID NO: 21	LC CDR2 (Combined)	YTSNLAP
SEQ ID NO: 22	LC CDR3(Combined)	QQFTSSPFT
SEQ ID NO: 28	VL	ENVLTQSPATLSVSPGERATLSCRASSS VNYIYWYQQKPGQAPRLLIYYTSNLAP GIPARFSGSGSGNEYTLTISSLQSEDFAV YYCQQFTSSPFTFGQGTKLEIK
SEQ ID NO: 36	DNA VL	GAGAATGTGCTGACCCAGTCTCCTGC CACACTGTCTGTTAGCCCTGGCGAGA GAGCTACCCTGAGCTGCAGAGCCTCT TCCTCCGTGAACTACATCTACTGGTAT CAGCAGAAGCCCGGCCAGGCTCCTAG ACTGCTGATCTACTACACCTCCAATCT GGCCCCTGGCATCCCTGCCAGATTTTC CGGATCTGGCTCCGGCAACGAGTATA CCCTGACCATCTCCAGCCTGCAGTCCG AGGACTTTGCTGTGTACTATTGCCAGC AGTTCACAAGCAGCCCTTTCACCTTTG GCCAGGGCACCAAGCTGGAAATCAAA
Antibody B-H.1G LC-4		
SEQ ID NO: 20	LC CDR1 (Combined)	RASSSVNYIY
SEQ ID NO: 21	LC CDR2 (Combined)	YTSNLAP
SEQ ID NO: 22	LC CDR3(Combined)	QQFTSSPFT
SEQ ID NO: 29	VL	QNVLTQPPSASGTPGQRVITSCRASSSV NYIYWYQQLPGTAPKLLIYYTSNLAPG VPDRFSGSGSGNSYSLAISGLRSEDEAD YYCQQFTSSPFTFGTGKVTVL
SEQ ID NO: 37	DNA VL	CAGAATGTGCTGACCCAACCTCCTTCC GCCTCTGGCACACCTGGACAGAGAGT GACAATCTCCTGCCGGGCCTCCTCCTC CGTGAACCTACATCTACTGGTATCAGC AGCTGCCCGGCACCGCTCCTAAACTG CTGATCTACTACACCTCCAATCTGGCC CCTGGCGTGCCCGATAGATTTTCCGG ATCTGGCTCCGGCAACTCCTACAGCCT GGCTATCTCTGGCCTGAGATCTGAGG ACGAGGCCGACTACTACTGCCAGCAG TTCACCTCCTCTCCATTCACCTTTGGC ACCGGCACCAAAGTGACAGTTCTT
Antibody B-H.1H LC-5		
SEQ ID NO: 20	LC CDR1 (Combined)	RASSSVNYIY
SEQ ID NO: 21	LC CDR2 (Combined)	YTSNLAP
SEQ ID NO: 22	LC CDR3(Combined)	QQFTSSPFT
SEQ ID NO: 30	VL	SNELTQPPSVSVSPGQTARITCRASSSVN YIYWYQQKSGQAPVLVIYYTSNLAPGIP

		ERFSGSGSGNMYTLTISGAQVEDEADY YCQQFTSSPFTFGTGTKVTVL
SEQ ID NO: 38	DNA VL	TCTAATGAGCTGACCCAGCCTCCTTCC GTGTCCGTGTCTCCTGGACAGACCGC CAGAATTACCTGCCGGGCCTCCTCCTC CGTGAACCTACATCTACTGGTATCAGC AGAAGTCCGGCCAGGCTCCTGTGCTC GTGATCTACTACACCTCCAATCTGGCC CCTGGCATCCCTGAGAGATTCTCCGG ATCTGGCTCCGGCAACATGTACACCC TGACCATCTCTGGCGCCCAGGTGGAA GATGAGGCCGACTACTACTGCCAGCA GTTACCTCCTCTCCATTCACCTTTGG CACCGGCACCAAAGTGACAGTTCTT
Antibody B-H.1		
SEQ ID NO: 3280	Chain1: Fc only	METDTLLLWVLLLWVPGSTGDKTHTCP PCPAPELLGGPSVFLFPPKPKDTLMISRT PEVTCVVDVSHEDPEVKFNWYVDGV EVHNAKTKPREEQYNSTYRVVSVLTVL HQDWLNGKEYKCKVSNKALPAPIEKTI SKAKGQPREPQVYTLPPCREEMTKNQV SLWCLVKGFYPSDIAVEWESNGQPENN YKTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNRTQKSLSLS PGK
SEQ ID NO: 3281	Chain2: humanized B-H scFv	METDTLLLWVLLLWVPGSTGEVQLVES GGGLVQPGGSLRLSCAASGFTFSNFGM HWVRQAPGKGLEWVSYISSGSSTIYYA DTLKGRFTISRDN SKNTLYLQMNSLRA EDTAVYYCARRGEGAMDYWGQGTTV TVSSGGGGSGGGGSGGGGSGGGGSDN QLTQSPSFLSASVGDRVITICRASSVN YIYWYQQKPGKAPKLLIYYTSNLAPGV PSRFSGSGSGNEYTLTISSLQPEDFATYY CQQFTSSPFTFGQGTKLEIKGGGGSDKT HTCPPCPAPELLGGPSVFLFPPKPKDTL MISRTPEVTCVVDVSHEDPEVKFNWY VDGVEVHNAKTKPREEQYNSTYRVVS VLTVLHQDWLNGKEYKCKVSNKALPA PIEKTISKAKGQPREPVCTLPPSREEMT KNQVSLSCAVKGFYPSDIAVEWESNGQ PENNYKTPPVLDSDGSFFLVSKLTVDK SRWQQGNVFSCSVMHEALHNHYTQKS LSLSPGKGGGGSGGGGSGLNDIFEAQKI EWHE
SEQ ID NO: 1343	scFv	EVQLVESGGGLVQPGGSLRLSCAASGF TFSNFGMHWRQAPGKGLEWVSYISSG SSTIYYADTLKGRFTISRDN SKNTLYLQ MNSLRAEDTAVYYCARRGEGAMDYW

		GQGTTVTVSSGGGGSGGGGSGGGGSG GGGSDNQLTQSPSFLSASVGDRVITICR ASSSVNYIYWYQQKPGKAPKLLIYYS NLAPGVPSRFSGSGSGNEYTLTISSLQPE DFATYYCQQFTSSPFTFGQGTKLEIK
Antibody B-H.2		
SEQ ID NO: 1338	scFv	EVQLVESGGGLVQPGGSLRLSCAASGF TFSNFGMHWVRQAPGKGLEWVSYISSG SSTIYYADTLKGRFTISRDN SKNTLYLQ MNSLRAEDTAVYYCARRGEGAMDYW GQGTTVTVSSGGGGSGGGGSGGGGSG GGGSDNQLTQSPSSLSASVGDRVITICR ASSSVNYIYWYQQKPGKAPKLLIYYS NLAPGVPSRFSGSGSGNDYTLTISSLQPE DFATYYCQQFTSSPFTFGQGTKLEIK
Antibody B-H.3		
SEQ ID NO: 1339	scFv	EVQLVESGGGLVQPGGSLRLSCAASGF TFSNFGMHWVRQAPGKGLEWVSYISSG SSTIYYADTLKGRFTISRDN SKNTLYLQ MNSLRAEDTAVYYCARRGEGAMDYW GQGTTVTVSSGGGGSGGGGSGGGGSG GGGSSNELTQPPSVSVSPGQTARITCRA SSSVNYIYWYQQKSGQAPVLVIYYTSN LAPGIPERFSGSGSGNMYTLTISGAQVE DEADYYCQQFTSSPFTFGTGTGKVTVL
Antibody B-H.4		
SEQ ID NO: 1340	scFv	QVQLVESGGGVVQPGRSLRLSCAASGF TFSNFGMHWVRQAPGKGLEWVAYISS GSSTIYYADTLKGRFTISRDN SKNTLYL QMNSLRAEDTAVYYCARRGEGAMDY WGQGTTVTVSSGGGGSGGGGSGGGGS GGGGSDNQLTQSPSFLSASVGDRVITIC RASSSVNYIYWYQQKPGKAPKLLIYYT SNLAPGVPSRFSGSGSGNEYTLTISSLQP EDFATYYCQQFTSSPFTFGQGTKLEIK
Antibody B-H.5		
SEQ ID NO: 1341	scFv	QVQLVESGGGVVQPGRSLRLSCAASGF TFSNFGMHWVRQAPGKGLEWVAYISS GSSTIYYADTLKGRFTISRDN SKNTLYL QMNSLRAEDTAVYYCARRGEGAMDY WGQGTTVTVSSGGGGSGGGGSGGGGS GGGGSDNQLTQSPSSLSASVGDRVITIC RASSSVNYIYWYQQKPGKAPKLLIYYT SNLAPGVPSRFSGSGSGNDYTLTISSLQP EDFATYYCQQFTSSPFTFGQGTKLEIK
Antibody B-H.6		
SEQ ID NO: 1342	scFv	QVQLVESGGGVVQPGRSLRLSCAASGF TFSNFGMHWVRQAPGKGLEWVAYISS GSSTIYYADTLKGRFTISRDN SKNTLYL

		QMNSLRAEDTAVYYCARRGEGAMDY WGQGTTVTVSSGGGGSGGGGSGGGGS GGGGSSNELTQPPSVSVSPGQTARITCR ASSSVNYIYWYQQKSGQAPVLVIYYTS NLAPGIPERFSGSGSGNMYTLTISGAQV EDEADYYCQQFTSSPFTFGTGKTVTL

Table 3A. Constant region amino acid sequences of human IgG heavy chains and human kappa light chain

Human kappa constant region SEQ ID NO: 39	LC	RTVAAPSVFI FPPSDEQLKS GTASVVCLLN NFYPREAKVQ WKVDNALQSG NSQESVTEQD SKDSTYSLSS TLTLISKADYE KHKVYACEVT HQGLSSPVTK SFNRGEC
IgG4 (S228P) mutant constant region (EU Numbering) SEQ ID NO: 40	HC	ASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGAL TSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYTCNVDHKPSNT KVDKRVESKYGPCCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEV TCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVV SVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQV YTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKT TPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQ KSLSLSLG
IgG1 wild type SEQ ID NO: 41	HC	ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGAL TSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTK VDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEV TCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYR VVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP QVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNY KTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHY TQKSLSLSPGK
IgG1 (N297A) mutant constant region (EU Numbering) SEQ ID NO: 42	HC	ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGAL TSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTK VDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEV TCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYR VVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP QVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNY KTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHY TQKSLSLSPGK
IgM constant delta CDC (P311A, P313S) SEQ ID NO: 73	HC	GSASAPTLFPLVSCENSPSDTSSVAVGCLAQDFLPDSITFSWKYKNN SDISSTRGFPSVLRGGKYAATSQVLLPSKDVMQGTDEHVVCVKVQH PNGNKEKNVPLPVIAELPPKVSFVPPRDGFFGNPRKSKLICQATGF SPRQIQVSWLREGKQVGSVTTDQVQAEAKESGPTTYKVTSTLTIK ESDWLGQSMFTCRVDHRGLTFQQNASSMCPDQDPAIRVFAIPPSF ASIFLTKSTKLTCLVTDLTITYDSVTISWTRQNGEAVKTHTNISESH NATFSAVGEASICEDDWSGERFTCTVTHTDLASSLKQTISRPKG ALHRPDVYLLPPAREQLNLRESATITCLVTGFSPADVQVQWMQRG QPLSPEKYVTSAPEPQAPGRYFAHSILTVSEEEWNTGETYTCVV AHEALPNRVTERTVDKSTGKPTLYNVSLVMSDTAGTCY
IgGA1 SEQ ID NO: 74	HC	ASPTSPKVFPLSLCSTQPDGNVVIACLVQGGFPQEPLSVTWSESGQG VTARNFPPSQDASGDLTYTSSQLTLPATQCLAGKSVTCHVKHYTNP

		SQDVTVPVPCVPSTPPTPSPSTPPTPSPSCCHPRLSLHRPALEDLLLGSE ANLTCTLTGLRDASGVTFTWTPSSGKSAVQGPPERDLCGCYSVSSV LPGCAEPWNHGKTFTCTAAYPESKTPLTATLSKSGNTFRPEVHLLP PPSEELALNELVTLTCLARGFSPKDVLRWLQGSQELPREKYLTW ASRQEPSQGTTTFAVTSILRVA AEDWKKGDTFSCMVGHEALPLAF TQKTIDRLAGKPTHVNVSVVMAEVDGTCY
IgGA2 SEQ ID NO: 75	HC	ASPTSPKVFPLSLDSTPQDGNVVVACL VQGFFPQEPLSVTWSESGQ NVTARNFPPSQDASGDLYTTSSQLTLPATQCPDGKSVTCHVKHYT NSSQDVTVPVPCRVPPPPPCCHPRLSLHRPALEDLLLGSEANLTCTLTG LRDASGATFTWTPSSGKSAVQGPPERDLCGCYSVSSVLPGCAQPW NHGETFTCTAAHPELKTPLTANITKSGNTFRPEVHLLPPPSEELALN ELVTLTCLARGFSPKDVLRWLQGSQELPREKYLTWASRQEPSQG TTTYAVTSILRVA AEDWKKGETFSCMVGHEALPLAFTQKTIDRMA GKPTHINVSVMMAEADGTCY
Human Ig_J chain SEQ ID NO: 76	HC	MKNHLLFWGVLAVFIKAVHVKAQEDERIVLVDNKCKCARITSRIIR SSEDPNEDIVERNIRIIVPLNNRENISDPTSPLRTRFVYHLSDLCKKC DPTEVELDNQIVTATQSNICDEDSATETCYTYDRNKCYTAVVPLVY GGETKMMVETALTPDACYPD

Anti-TCR β V5 antibodies

Accordingly, in one aspect, the disclosure provides an anti-TCR β V antibody molecule that binds to human TCR β V5. In some embodiments, the TCR β V5 subfamily comprises TCR β V5-5*01, TCR β V5-6*01, TCR β V5-4*01, TCR β V5-8*01, TCR β V5-1*01, or a variant thereof.

Exemplary anti-TCR β V5 antibodies of the disclosure are provided in **Table 10A**. In some embodiments, the anti-TCR β V5 is antibody C, e.g., humanized antibody C (antibody C-H), as provided in **Table 10A**. In some embodiments, the anti-TCR β V antibody comprises one or more (e.g., all three) of a LC CDR1, LC CDR2, and LC CDR3 provided in **Table 10A**; and/or one or more (e.g., all three) of a HC CDR1, HC CDR2, and HC CDR3 provided in **Table 10A**, or a sequence with at least 95% identity thereto. In some embodiments, antibody C comprises a variable heavy chain (VH) and/or a variable light chain (VL) provided in **Table 10A**, or a sequence with at least 95% identity thereto.

Table 10A: Amino acid sequences for anti TCR β V5 antibodies

Amino acid and nucleotide sequences for murine and humanized antibody molecules which bind to TCRVB 5 (e.g., TCRVB 5-5 or TCRVB 5-6). The amino acid the heavy and light chain CDRs, and the amino acid and nucleotide sequences of the heavy and light chain variable regions, and the heavy and light chains are shown.

Murine antibody C		
SEQ ID NO: 1315	HC CDR1 (Kabat)	AYGVN
SEQ ID NO: 1316	HC CDR2 (Kabat)	MIWGDGNTDYN SALKS
SEQ ID NO: 1317	HC CDR3 (Kabat)	DRVTATLYAMDY
SEQ ID NO: 1318	HC CDR1 (Chothia)	GFSLTAY
SEQ ID NO: 1319	HC CDR2 (Chothia)	WGDGN
SEQ ID NO: 1317	HC CDR3 (Chothia)	DRVTATLYAMDY
SEQ ID NO: 1320	HC CDR1 (Combined)	GFSLTAYGVN
SEQ ID NO: 1316	HC CDR2 (Combined)	MIWGDGNTDYN SALKS
SEQ ID NO: 1317	HC CDR3(Combined)	DRVTATLYAMDY
SEQ ID NO: 1321	LC CDR1 (Kabat)	SASQGISNYLN
SEQ ID NO: 1322	LC CDR2 (Kabat)	YTSSLHS
SEQ ID NO: 1323	LC CDR3 (Kabat)	QQYSKLPRT
SEQ ID NO: 1321	LC CDR1 (Chothia)	SASQGISNYLN
SEQ ID NO: 1322	LC CDR2 (Chothia)	YTSSLHS
SEQ ID NO: 1323	LC CDR3 (Chothia)	QQYSKLPRT
SEQ ID NO: 1321	LC CDR1 (Combined)	SASQGISNYLN
SEQ ID NO: 1322	LC CDR2 (Combined)	YTSSLHS
SEQ ID NO: 1323	LC CDR3(Combined)	QQYSKLPRT
SEQ ID NO: 232	VH	DIQMTQTSSLSASLGDRVTISCSASQGISNYLN WYQQKPDGTVKLLIYYTSSLHSGVPSRFSGSGSG TDYSLTISNLEPEDIATYYCQQYSKLPRTFGGGT KVEIK
SEQ ID NO: 233	VL	QVQLKESGPGLVAPSQSL SITCTVSGFSLTAYGV NWVRQPPGKGLEWLGMIWGDGNTDYN SALKS RLSISKDNSKSQVFLKMNSLQTD D TARY YCARD RVTATLYAMDYWGQGTSTVSS
Humanized antibody C		
C-H-1 antibody		
SEQ ID NO: 1315	HC CDR1 (Kabat)	AYGVN
SEQ ID NO: 1316	HC CDR2 (Kabat)	MIWGDGNTDYN SALKS
SEQ ID NO: 1317	HC CDR3 (Kabat)	DRVTATLYAMDY
SEQ ID NO: 1318	HC CDR1 (Chothia)	GFSLTAY
SEQ ID NO: 1319	HC CDR2 (Chothia)	WGDGN
SEQ ID NO: 1317	HC CDR3 (Chothia)	DRVTATLYAMDY
SEQ ID NO: 1320	HC CDR1 (Combined)	GFSLTAYGVN

SEQ ID NO: 1316	HC CDR2 (Combined)	MIWGDGNTDYN SALKS	
SEQ ID NO: 1317	HC CDR3(Combined)	DRV TATLYAMDY	
SEQ ID NO: 1321	LC CDR1 (Kabat)	SASQGISNYLN	
SEQ ID NO: 1322	LC CDR2 (Kabat)	YTSSLHS	
SEQ ID NO: 1323	LC CDR3 (Kabat)	QQYSKL PRT	
SEQ ID NO: 1321	LC CDR1 (Chothia)	SASQGISNYLN	
SEQ ID NO: 1322	LC CDR2 (Chothia)	YTSSLHS	
SEQ ID NO: 1323	LC CDR3 (Chothia)	QQYSKL PRT	
SEQ ID NO: 1321	LC CDR1 (Combined)	SASQGISNYLN	
SEQ ID NO: 1322	LC CDR2 (Combined)	YTSSLHS	
SEQ ID NO: 1323	LC CDR3(Combined)	QQYSKL PRT	
SEQ ID NO: 1324	VL	DIQMTQSPSSLSASVGDRVTITCSASQGISNYLNW YQQTPGKAPKLLIYYTSSLHSGVPSRFSGSGSGTD YTFTISLQPEDIATYYCQQYSKL PRTFGGQTKLQI T	
SEQ ID NO: 1325	VH	QVQLQESGPGLVRPSQTL SLTCTVSGFSLTAYGV NWVRQPPGRGLEWLGMIWGDGNTDYN SALKSR VTMLKDTSKNQFSLRLSSVTAADTAVYYCARDR VTATLYAMDYW GQGS LVTVSS	
Humanized antibody C Variable light chain (VL)			
SEQ ID NO: 3000	VL	C-H- VL.1	DIQMTQSPSFLSASVGDRVTITCSASQGISNYLN WYQQKPGKAVKLLIYYTSSLHSGVPSRFSGSGS GTEYTLTISLQPEDFATYYCQQYSKL PRTFGGG TKVEIK
SEQ ID NO: 3001	VL	C-H- VL.2	DIQMTQSPSSLSASVGDRVTITCSASQGISNYLNWYQ QKPGKAVKLLIYYTSSLHSGVPSRFSGSGSGTDYTLT ISLQPEDFATYYCQQYSKL PRTFGGGTKVEIK
SEQ ID NO: 3002	VL	C-H- VL.3	DIQMTQSPSSLSASVGDRVTITCSASQGISNYLNWYQ QKPGKVVKLLIYYTSSLHSGVPSRFSGSGSGTDYTLT ISLQPEDVATYYCQQYSKL PRTFGGGTKVEIK
SEQ ID NO: 3003	VL	C-H- VL.4	DIQMTQSPSSLSASVGDRVTITCSASQGISNYLNWYQ QKPGQAVKLLIYYTSSLHSGVPSRFSGSGSGTDYTLT ISLQPEDVATYYCQQYSKL PRTFGGGTKVEIK
SEQ ID NO: 3004	VL	C-H- VL.5	DIQMTQSPSSLSASVGDRVTITCSASQGISNYLNWYQ QKPGKAVKLLIYYTSSLHSGVPSRFSGSGSGTDYFT ISLQPEDIATYYCQQYSKL PRTFGGGTKVEIK
SEQ ID NO: 3005	VL	C-H- VL.6	DIQMTQSPSSLSASVGDRVTITCSASQGISNYLNWYQ QKPGKTVKLLIYYTSSLHSGIPSRFSGSGSGTDYTLT IRSLQPEDFATYYCQQYSKL PRTFGGGTKVEIK

SEQ ID NO: 3006	VL	C-H-VL.7	AIQMTQSPSSLSASVGDRVITITCSASQGISNYLNWYQ QKPGKAVKLLIYYTSSLHSGVPSRFSGSGSGTDYTLT ISLQPEDFATYYCQQYSKLPRTFGGGTKVEIK
SEQ ID NO: 3007	VL	C-H-VL.8	DIQMTQSPSSVSASVGDRVITITCSASQGISNYLNWYQ QKPGKAVKLLIYYTSSLHSGVPSRFSGSGSGTDYTLT ISLQPEDFATYYCQQYSKLPRTFGGGTKVEIK
SEQ ID NO: 3008	VL	C-H-VL.9	DIQMTQSPSSLSASVGDRVITITCSASQGISNYLNWYQ QKPGKAVKRLIYYTSSLHSGVPSRFSGSGSGTEYTLT ISNLQPEDFATYYCQQYSKLPRTFGGGTKVEIK
SEQ ID NO: 3009	VL	C-H-VL.10	AIRMTQSPFSLASVGDRVITITCSASQGISNYLNWYQ QKPAKAVKLFIIYYTSSLHSGVPSRFSGSGSGTDYTLT ISLQPEDFATYYCQQYSKLPRTFGGGTKVEIK
SEQ ID NO: 3010	VL	C-H-VL.11	DIQMTQSPSSLSASVGDRVITITCSASQGISNYLNWYQ QKPGKAVKRLIYYTSSLHSGVPSRFSGSGSGTEYTLT ISLQPEDFATYYCQQYSKLPRTFGGGTKVEIK
SEQ ID NO: 3011	VL	C-H-VL.12	DIQMTQSPSTLSASVGDRVITITCSASQGISNYLNWYQ QKPGKAVKLLIYYTSSLHSGVPSRFSGSGSGTEYTLT ISLQPDDEFATYYCQQYSKLPRTFGGGTKVEIK
SEQ ID NO: 3012	VL	C-H-VL.13	DIQMTQSPSSLSASVGDRVITITCSASQGISNYLNWYQ QKPGKAVKSLIYYTSSLHSGVPSRFSGSGSGTDYTLT ISLQPEDFATYYCQQYSKLPRTFGGGTKVEIK
SEQ ID NO: 3013	VL	C-H-VL.14	DIQMTQSPSSLSASVGDRVITITCSASQGISNYLNWYQ QKPGKAVKSLIYYTSSLHSGVPSKFSGSGSGTDYTLT ISLQPEDFATYYCQQYSKLPRTFGGGTKVEIK
SEQ ID NO: 3014	VL	C-H-VL.15	DIQMTQSPSSLSASVGDRVITITCSASQGISNYLNWYQ QKPEKAVKSLIYYTSSLHSGVPSRFSGSGSGTDYTLT ISLQPEDFATYYCQQYSKLPRTFGGGTKVEIK
SEQ ID NO: 3015	VL	C-H-VL.16	DIQMTQSPSAMSASVGDRVITITCSASQGISNYLNWYQ QKPGKVVKRLIYYTSSLHSGVPSRFSGSGSGTEYTLT ISLQPEDFATYYCQQYSKLPRTFGGGTKVEIK
SEQ ID NO: 3016	VL	C-H-VL.17	DIVMTQSPDSLAVSLGERATINCSASQGISNYLNWYQ QKPGQPVKLLIYYTSSLHSGVPDRFSGSGSGTDYTLT ISLQAEDVAVYYCQQYSKLPRTFGGGTKVEIK
SEQ ID NO: 3017	VL	C-H-VL.18	EIVMTQSPGTLSPGERATLSCSASQGISNYLNWYQ QKPGQAVKLLIYYTSSLHSGIPDRFSGSGSGTDYTLT ISRLEPEDFAVYYCQQYSKLPRTFGGGTKVEIK
SEQ ID NO: 3018	VL	C-H-VL.19	EIVMTQSPPTLSLSPGERVTLSASQGISNYLNWYQ QKPGQAVKLLIYYTSSLHSGIPARFSGSGSGTDYTLT ISLQPEDFAVYYCQQYSKLPRTFGGGTKVEIK
SEQ ID NO: 3019	VL	C-H-VL.20	EIVMTQSPPTLSLSPGERVTLSASQGISNYLNWYQ QKPGQAVKLLIYYTSSLHSSIPARFSGSGSGTDYTLT ISLQPEDFAVYYCQQYSKLPRTFGGGTKVEIK
SEQ ID NO: 3020	VL	C-H-VL.21	EIVMTQSPATLSLSPGERATLSCSASQGISNYLNWYQ QKPGQAVKLLIYYTSSLHSGIPARFSGSGSGTDYTLT ISLLEPEDFAVYYCQQYSKLPRTFGGGTKVEIK
SEQ ID NO: 3021	VL	C-H-VL.22	EIVMTQSPATLSLSPGERATLSCSASQGISNYLNWYQ QKPGQAVKLLIYYTSSLHSGIPARFSGSGSGTDYTLT ISRLEPEDFAVYYCQQYSKLPRTFGGGTKVEIK

SEQ ID NO: 3022	VL	C-H-VL.23	EIVMTQSPATLSLSPGERATLSCSASQGISNYLNWYQ QKPGQAVKLLIYYTSSLHSGIPDRFSGSGSGTDYTLT ISRLEPEDFAVYYCQQYSKLPRTFGGGTKVEIK
SEQ ID NO: 3023	VL	C-H-VL.24	EIVMTQSPATLSLSPGERATLSCSASQGISNYLNWYQ QKPGQAVKLLIYYTSSLHSGIPDRFSGSGSGTDYTLT ISRLEPEDFAVYYCQQYSKLPRTFGGGTKVEIK
SEQ ID NO: 3024	VL	C-H-VL.25	DIQMIQSPSFLSASVGDVSIICSASQGISNYLNWYL QKPGKSVKLLIYYTSSLHSGVSSRFSGRSGTDYTLT IISLKPEDFAAYYCQQYSKLPRTFGGGTKVEIK
SEQ ID NO: 3025	VL	C-H-VL.26	EIVMTQSPATLSLSPGERATLSCSASQGISNYLNWYQ QKPGQAVKLLIYYTSSLHSGIPARFSGSGSGTDYTLT ISSLQPEDFAVYYCQQYSKLPRTFGGGTKVEIK
SEQ ID NO: 3026	VL	C-H-VL.27	EIVMTQSPATLSLSPGERATLSCSASQGISNYLNWYQ QKPGQAVKLLIYYTSSLHSGIPARFSGSGPGTDYTLT ISSLEPEDFAVYYCQQYSKLPRTFGGGTKVEIK
SEQ ID NO: 3027	VL	C-H-VL.28	DIVMTQTPLSLSVTPGQPASISCSASQGISNYLNWYL QKPGQSVKLLIYYTSSLHSGVPDRFSGSGSGTDYTLK ISRVEAEDVGVYYCQQYSKLPRTFGGGTKVEIK
SEQ ID NO: 3028	VL	C-H-VL.29	DIVMTQTPLSLSVTPGQPASISCSASQGISNYLNWYL QKPGQPVKLLIYYTSSLHSGVPDRFSGSGSGTDYTLK ISRVEAEDVGVYYCQQYSKLPRTFGGGTKVEIK
SEQ ID NO: 3029	VL	C-H-VL.30	DIVMTQSPAFLSVTPGKEVITITCSASQGISNYLNWYQ QKPDQAVKLLIYYTSSLHSGVPSRFSGSGSGTDYTFT ISSLEAEDAATYYCQQYSKLPRTFGGGTKVEIK
SEQ ID NO: 3030	VL	C-H-VL.31	DIVMTQSPLSLPVTGPGEPAISCSASQGISNYLNWYL QKPGQSVKLLIYYTSSLHSGVPDRFSGSGSGTDYTLK ISRVEAEDVGVYYCQQYSKLPRTFGGGTKVEIK
SEQ ID NO: 3031	VL	C-H-VL.32	DIVMTQTPLSLPVTGPGEPAISCSASQGISNYLNWYL QKPGQSVKLLIYYTSSLHSGVPDRFSGSGSGTDYTLK ISRVEAEDVGVYYCQQYSKLPRTFGGGTKVEIK
SEQ ID NO: 3032	VL	C-H-VL.33	EIVMTQSPATLSVSPGERATLSCSASQGISNYLNWYQ QKPGQAVKLLIYYTSSLHSGIPARFSGSGSGTEYTLT ISILQSEDFAVYYCQQYSKLPRTFGGGTKVEIK
SEQ ID NO: 3033	VL	C-H-VL.34	EIVMTQSPATLSVSPGERATLSCSASQGISNYLNWYQ QKPGQAVKLLIYYTSSLHSGIPARFSGSGSGTEYTLT ISSLQSEDFAVYYCQQYSKLPRTFGGGTKVEIK
SEQ ID NO: 3034	VL	C-H-VL.35	DIVMTQSPLSLPVTLGQPASISCSASQGISNYLNWYQ QRPQGQSVKRLIYYTSSLHSGVPDRFSGSGSGTDYTLK ISRVEAEDVGVYYCQQYSKLPRTFGGGTKVEIK
SEQ ID NO: 3035	VL	C-H-VL.36	EITMTQSPAFM SATPGDKVNISCSASQGISNYLNWYQ QKPGQAVKFI IYYTSSLHSGIPPRFSGSGYGTDTLT INNIESEDAAYYYCQQYSKLPRTFGGGTKVEIK
SEQ ID NO: 3036	VL	C-H-VL.37	DIVMTQTPLSSPVTLGQPASISCSASQGISNYLNWYQ QRPQGQPVKLLIYYTSSLHSGVPDRFSGSGAGTDYTLK ISRVEAEDVGVYYCQQYSKLPRTFGGGTKVEIK
SEQ ID NO: 3037	VL	C-H-VL.38	EIVMTQSPDFQSVTPKEKVITITCSASQGISNYLNWYQ QKPDQSVKLLIYYTSSLHSGVPSRFSGSGSGTDYTLT INSLEAEDAATYYCQQYSKLPRTFGGGTKVEIK

SEQ ID NO: 3038	VL	C-H-VL.39	EIVMTQTPLSL SITPGEQASISCSASQGISNYLNWYL QKARPVVKLLIYYTSSLHSGVPDRFSGSGSGTDYTLK ISRVEAEDFGVYYCQQYSKLPRTFGGGTKVEIK
SEQ ID NO: 3039	VL	C-H-VL.40	EIVMTQTPLSL SITPGEQASMSCSASQGISNYLNWYL QKARPVVKLLIYYTSSLHSGVPDRFSGSGSGTDYTLK ISRVEAEDFGVYYCQQYSKLPRTFGGGTKVEIK
Humanized antibody C Variable HEAVY chain (VH)			
SEQ ID NO: 3040	VH	C-H-VH.1	QVTLKESGPVLVKPTETLTCTVSGFSLTAYGVNWV RQPPGKALEWLGMIWGDGNTDYN SALKSRLTISKDNS KSQVVLTMNMDPVD TATYYCARDRV TATLYAMDYWG QGT LVT VSS
SEQ ID NO: 3041	VH	C-H-VH.2	QVTLKESGPALVKPTETLTCTVSGFSLTAYGVNWV RQPPGKALEWLGMIWGDGNTDYN SALKSRLIISKDNS KSQVVLTMNMDPVD TATYYCARDRV TATLYAMDYWG QGT LVT VSS
SEQ ID NO: 3042	VH	C-H-VH.3	QVTLKESGPALVKPTQTLTCTVSGFSLTAYGVNWV RQPPGKALEWLGMIWGDGNTDYN SALKSRLTISKDNS KSQVVLTMNMDPVD TATYYCARDRV TATLYAMDYWG QGT LVT VSS
SEQ ID NO: 3043	VH	C-H-VH.4	QVQLQESGPGLVKPSGTL SLTCAVSGFSLTAYGVNWV RQPPGKGLEWLGMIWGDGNTDYN SALKSRLTISKDNS KSQVSLKLSSVTAAD TAVYYCARDRV TATLYAMDYWG QGT LVT VSS
SEQ ID NO: 3044	VH	C-H-VH.5	QVTLKESGPTLVKPTQTLTCTVSGFSLTAYGVNWV RQPPGKALEWLGMIWGDGNTDYN SALKSRLTITKDNS KSQVVLTMNMDPVD TATYYCARDRV TATLYAMDYWG QGT LVT VSS
SEQ ID NO: 3045	VH	C-H-VH.6	QVTLKESGPALVKPTQTLTCTVSGFSLTAYGVNWV RQPPGKALEWLGMIWGDGNTDYN SALKSRLTITKDNS KSQVVLTMNMDPVD TATYYCARDRV TATLYAMDYWG QGT LVT VSS
SEQ ID NO: 3046	VH	C-H-VH.7	QVQLQESGPGLVKPSQTL SLTCTVSGFSLTAYGVNWV RQPPGKGLEWLGMIWGDGNTDYN SALKSRLTISKDNS KSQVSLKLSSVTAAD TAVYYCARDRV TATLYAMDYWG QGT LVT VSS
SEQ ID NO: 3047	VH	C-H-VH.8	QVQLQESGPGLVKPSQTL SLTCTVSGFSLTAYGVNWV RQPPGKGLEWLGMIWGDGNTDYN SALKSRLTISKDNS KSQVSLKLSSVTAAD TAVYYCARDRV TATLYAMDYWG QGT LVT VSS
SEQ ID NO: 3048	VH	C-H-VH.9	QVQLQESGPGLVKPSQTL SLTCAVSGFSLTAYGVNWV RQPPGKGLEWLGMIWGDGNTDYN SALKSRLTISKDNS KSQVSLKLSSVTAAD TAVYYCARDRV TATLYAMDYWG QGT LVT VSS
SEQ ID NO: 3049	VH	C-H-VH.10	QVQLQESGPGLVKPSDTL SLTCTVSGFSLTAYGVNWV RQPPGKGLEWLGMIWGDGNTDYN SALKSRLTISKDNS KSQVSLKLSSVTAAD TAVYYCARDRV TATLYAMDYWG QGT LVT VSS
SEQ ID NO: 3050	VH	C-H-VH.11	QVQLQESGPGLVKPSQTL SLTCTVSGFSLTAYGVNWV RQHPGKGLEWLGMIWGDGNTDYN SALKSRLTISKDNS

			KSQVSLKLSSVTAADTAVYYCARDRVATATLYAMDYWG QGTLLVTVSS
SEQ ID NO: 3051	VH	C-H- VH.12	QVQLQESGPGGLVKPSQTLSTCTVSGFSLTAYGVNHW RQPPGKGLEWLGMIWGDGNTDYNALKSRLTISKDNS KSQVSLKLSSVTAADTAVYYCARDRVATATLYAMDYWG QGTLLVTVSS
SEQ ID NO: 3052	VH	C-H- VH.13	QVQLQESGPGGLVKPSQTLSTCAVSGFSLTAYGVNHW RQPPGKGLEWLGMIWGDGNTDYNALKSRLTISKDNS KSQVSLKLSSVTAADTAVYYCARDRVATATLYAMDYWG QGTLLVTVSS
SEQ ID NO: 3053	VH	C-H- VH.14	QVQLQESGPGGLVKPSETLSLTCTVSGFSLTAYGVNHW RQPPGKGLEWLGMIWGDGNTDYNALKSRLTISKDNS KSHVSLKLSSVTAADTAVYYCARDRVATATLYAMDYWG QGTLLVTVSS
SEQ ID NO: 3054	VH	C-H- VH.15	QVQLQESGPGGLVKPSETLSLTCAVSGFSLTAYGVNHW RQPPGKGLEWLGMIWGDGNTDYNALKSRLTISKDNS KSQVSLKLSSVTAADTAVYYCARDRVATATLYAMDYWG QGTLLVTVSS
SEQ ID NO: 3055	VH	C-H- VH.16	QVQLQESGPGGLVKPSQTLSTCAVYGFSLTAYGVNHW RQPPGKGLEWLGMIWGDGNTDYNALKSRLTISKDNS KSQVSLKLSSVTAADTAVYYCARDRVATATLYAMDYWG QGTLLVTVSS
SEQ ID NO: 3056	VH	C-H- VH.17	RVQLQESGPGGLVKPSETLSLTCTVSGFSLTAYGVNHW RQPPGKGLEWLGMIWGDGNTDYNALKSRLTISKDNS KSQVPLKLSSVTAADTAVYYCARDRVATATLYAMDYWG QGTLLVTVSS
SEQ ID NO: 3057	VH	C-H- VH.18	QVQLQESGPGGLVKPSQTLSTCTVSGFSLTAYGVNHW RQHPGKGLEWLGMIWGDGNTDYNALKSLTISKDNS KSQVSLKLSSVTAADTAVYYCARDRVATATLYAMDYWG QGTLLVTVSS
SEQ ID NO: 3058	VH	C-H- VH.19	QVQLQESGPGGLVKPSDTLSLTCAVSGFSLTAYGVNHW RQPPGKGLEWLGMIWGDGNTDYNALKSRLTISKDNS KSQVSLKLSSVTALDTAVYYCARDRVATATLYAMDYWG QGTLLVTVSS
SEQ ID NO: 3059	VH	C-H- VH.20	QVQLQESGPGGLVKPSDTLSLTCAVSGFSLTAYGVNHW RQPPGKGLEWLGMIWGDGNTDYNALKSRLTISKDNS KSQVSLKLSSVTAADTAVYYCARDRVATATLYAMDYWG QGTLLVTVSS
SEQ ID NO: 3060	VH	C-H- VH.21	QVQLQESGSGGLVKPSQTLSTCAVSGFSLTAYGVNHW RQPPGKGLEWLGMIWGDGNTDYNALKSRLTISKDNS KSQVSLKLSSVTAADTAVYYCARDRVATATLYAMDYWG QGTLLVTVSS
SEQ ID NO: 3061	VH	C-H- VH.22	EVQLVESGGGLVQPGSRSLRLSCTVSGFSLTAYGVNHW RQAPGKGLEWLGMIWGDGNTDYNALKSRLTISKDNS KSIVYLQMNSLKTEDTAVYYCARDRVATATLYAMDYWG QGTLLVTVSS
SEQ ID NO: 3062	VH	C-H- VH.23	EVQLVESGGGLVQPGPSLRLSCTVSGFSLTAYGVNHW RQAPGKGLEWLGMIWGDGNTDYNALKSRLTISKDNS KSIVYLQMNSLKTEDTAVYYCARDRVATATLYAMDYWG QGTLLVTVSS

SEQ ID NO: 3063	VH	C-H-VH.24	QVQLQESGSGLVKPSQTLSLTCAVSGFSLTAYGVNWV RQSPGKGLEWLGMIWGDGNTDYNALKSRLTISKDNS KSQVSLKLSSVTAADTAVYYCARDRTATLYAMDYWG QGTLVTVSS
SEQ ID NO: 3064	VH	C-H-VH.25	QVQLQESGPGVLKPSSETLSLTCTVSGFSLTAYGVNWV RQPAGKGLEWLGMIWGDGNTDYNALKSRLTISKDNS KSQVSLKLSSVTAADTAVYYCARDRTATLYAMDYWG QGTLVTVSS
SEQ ID NO: 3065	VH	C-H-VH.26	EVQLVESGGGLVKPGRSLRLSCTVSGFSLTAYGVNWV RQAPGKGLEWLGMIWGDGNTDYNALKSRLTISKDNS KSIVYLQMNSLKTEDTAVYYCARDRTATLYAMDYWG QGTLVTVSS
SEQ ID NO: 3066	VH	C-H-VH.27	QVQLQESGPGVLKPSSETLSLTCAVYGFSLTAYGVNWV RQPPGKGLEWLGMIWGDGNTDYNALKSRLTISKDNS KSQVYLKLSSVTAADTAVYYCARDRTATLYAMDYWG QGTLVTVSS
SEQ ID NO: 3067	VH	C-H-VH.28	QVQLQESGPGVLKPSDTLSLTCAVSGFSLTAYGVNWV RQPPGKGLEWLGMIWGDGNTDYNALKSRLTISKDNS KSQVSLKLSSVTAADTAVYYCARDRTATLYAMDYWG QGTLVTVSS
SEQ ID NO: 3068	VH	C-H-VH.29	EVQLVESGGGLVQPGGSLRLSCAVSGFSLTAYGVNWV RQAPGKGLEWLGMIWGDGNTDYNALKSRLTISKDNS KSSVYLQMNSLKTEDTAVYYCARDRTATLYAMDYWG QGTLVTVSS
SEQ ID NO: 3069	VH	C-H-VH.30	EVQLVESGGGLVKPGGSLRLSCAVSGFSLTAYGVNWV RQAPGKGLEWLGMIWGDGNTDYNALKSRLTISKDNS KSTVYLQMNSLKTEDTAVYYCARDRTATLYAMDYWG QGTLVTVSS
SEQ ID NO: 3070	VH	C-H-VH.31	QVQLQQSGPGLVKPSQTLSLTCAVSGFSLTAYGVNWV RQSPSRGLEWLGMIWGDGNTDYNALKSRLTINKDNS KSQVSLQLNSVTPEDTAVYYCARDRTATLYAMDYWG QGTLVTVSS
SEQ ID NO: 3071	VH	C-H-VH.32	QVQLVESGGGLVQPGGSLRLSCSVSGFSLTAYGVNWV RQAPGKGLEWLGMIWGDGNTDYNALKSRLTISKDNS KSTVYLQMNSLRAEDTAVYYCARDRTATLYAMDYWG QGTLVTVSS
SEQ ID NO: 3072	VH	C-H-VH.33	QVQLQQWGAGLLKPSETLSLTCAVYGFSLTAYGVNWV RQPPGKGLEWLGMIWGDGNTDYNALKSRLTISKDNS KSQVSLKLSSVTAADTAVYYCARDRTATLYAMDYWG QGTLVTVSS
SEQ ID NO: 3073	VH	C-H-VH.34	QVQLVESGGGVVQPGRSLRLSCAVSGFSLTAYGVNWV RQAPGKGLEWLGMIWGDGNTDYNALKSRLTISKDNS TSTVFLQMNSLRAEDTAVYYCARDRTATLYAMDYWG QGTLVTVSS
SEQ ID NO: 3074	VH	C-H-VH.35	EVQLVESGGGLVQPGGSLRLSCAVSGFSLTAYGVNWV RQAPGKGLEWLGMIWGDGNTDYNALKSRLTISKDNS KSTVYLQMNSLRAEDTAVYYCARDRTATLYAMDYWG QGTLVTVSS
SEQ ID NO: 3075	VH	C-H-VH.36	EVQLVESGGGLVQPGGSLRLSCAVSGFSLTAYGVNWV RQAPGKGLEWLGMIWGDGNTDYNALKSRLTISKDNA

			KSSVYLQMNSLRDEDTAVYYCARDRVATATLYAMDYWG QGTLLTVSS
SEQ ID NO: 3076	VH	C-H- VH.37	EVQLLESGGGLVQPGGSLRLSCAVSGFSLTAYGVNWV RQAPGKGLEWLGMIWGDGNTDYNALKSRLTISKDNS KSTVYLQMNSLRAEDTAVYYCARDRVATATLYAMDYWG QGTLLTVSS
SEQ ID NO: 3077	VH	C-H- VH.38	QVQLVESGGGLVKPGGSLRLSCAVSGFSLTAYGVNWV RQAPGKGLEWLGMIWGDGNTDYNALKSRLTISKDNA KSSVYLQMNSLRAEDTAVYYCARDRVATATLYAMDYWG QGTLLTVSS
SEQ ID NO: 3078	VH	C-H- VH.39	EVQLVESGGGLVQPGGSLKLSCAVSGFSLTAYGVNWV RQASGKGLEWLGMIWGDGNTDYNALKSRLTISKDNS KSTVYLQMNSLKTEDTAVYYCARDRVATATLYAMDYWG QGTLLTVSS
SEQ ID NO: 3079	VH	C-H- VH.40	QVQLLESGGGLVKPGGSLRLSCAVSGFSLTAYGVNWV RQAPGKGLEWLGMIWGDGNTDYNALKSRLTISKDNA KSSVYLQMNSLRAEDTAVYYCARDRVATATLYAMDYWG QGTLLTVSS
SEQ ID NO: 3080	VH	C-H- VH.41	QVQLVESGGGVVQPGSLRLSCAVSGFSLTAYGVNWV RQAPGKGLEWLGMIWGDGNTDYNALKSRLTISKDNS KSTVYLQMNSLRAEDTAVYYCARDRVATATLYAMDYWG QGTLLTVSS
SEQ ID NO: 3081	VH	C-H- VH.42	QVQLVESGGGVVQPGSLRLSCAVSGFSLTAYGVNWV RQAPGKGLEWLGMIWGDGNTDYNALKSRLTISKDNS KSRVYLQMNSLRAEDTAVYYCARDRVATATLYAMDYWG QGTLLTVSS
SEQ ID NO: 3082	VH	C-H- VH.43	QVQLVESGGGVVQPGSLRLSCAVSGFSLTAYGVNWV RQAPGKGLEWLGMIWGDGNTDYNALKSRLAISKDNS KSTVYLQMNSLRAEDTAVYYCARDRVATATLYAMDYWG QGTLLTVSS
SEQ ID NO: 3083	VH	C-H- VH.44	QVQLVESGGGVVQPGGSLRLSCAVSGFSLTAYGVNWV RQAPGKGLEWLGMIWGDGNTDYNALKSRLTISKDNS KSTVYLQMNSLRAEDTAVYYCARDRVATATLYAMDYWG QGTLLTVSS
SEQ ID NO: 3084	VH	C-H- VH.45	EVQLVESGGGLVQPGGSLRLSCAVSGFSLTAYGVNWV RQAPGKGLEWLGMIWGDGNTDYNALKSRLTISKDNA KSTVYLQMNSLRAEDTAVYYCARDRVATATLYAMDYWG QGTLLTVSS
SEQ ID NO: 3085	VH	C-H- VH.46	EVQLVESGGGLVQPGGSLRLSCAVSGFSLTAYGVNWV RQAPGKGLEWLGMIWGDGNTDYNALKSRLTISKDNA KSSVYLQMNSLRAEDTAVYYCARDRVATATLYAMDYWG QGTLLTVSS
SEQ ID NO: 3086	VH	C-H- VH.47	EVQLVESGGVVVQPGGSLRLSCAVSGFSLTAYGVNWV RQAPGKGLEWLGMIWGDGNTDYNALKSRLTISKDNS KSSVYLQMNSLRTEDTALYYCARDRVATATLYAMDYWG QGTLLTVSS
SEQ ID NO: 3087	VH	C-H- VH.48	EVQLVESGGGLVQPGGSLRLSCAVSGFSLTAYGVNWV RQAPGKGLEWLGMIWGDGNTDYNALKSRLTISKHNS KSTVYLQMNSLRAEDTAVYYCARDRVATATLYAMDYWG QGTLLTVSS

SEQ ID NO: 3088	VH	C-H-VH.49	EVQLVESGGGLVKPGGSLRLSCAVSGFSLTAYGVNWW RQAPGKGLEWLGMIWGDGNTDYN SALKSRLTISKDNA KSSVYLQMNSLRAEDTAVYYCARDRV TATLYAMDYWG QGTLVTVSS
SEQ ID NO: 3089	VH	C-H-VH.50	EVQLVESGGGLIQPGGSLRLSCAVSGFSLTAYGVNWW RQPPGKGLEWLGMIWGDGNTDYN SALKSRLTISKDNS KSTVYLQMNSLRAEDTAVYYCARDRV TATLYAMDYWG QGTLVTVSS

Exemplary anti-TCR β V5 antibodies of the disclosure are provided in **Table 11A**. In some embodiments, the anti-TCR β V5 is antibody E, e.g., humanized antibody E (antibody E-H), as provided in **Table 11A**. In some embodiments, the anti-TCR β V antibody comprises one or more (e.g., all three) of a LC CDR1, LC CDR2, and LC CDR3 provided in **Table 11A**; and/or one or more (e.g., all three) of a HC CDR1, HC CDR2, and HC CDR3 provided in **Table 11A**, or a sequence with at least 95% identity thereto. In some embodiments, antibody E comprises a variable heavy chain (VH) and/or a variable light chain (VL) provided in **Table 11A**, or a sequence with at least 95% identity thereto.

In some embodiments, antibody E comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 3284 and/or a light chain comprising the amino acid sequence of SEQ ID NO: 3285, or sequence with at least 95% identity thereto.

Table 11A: Amino acid sequences for anti TCR β V5 antibodies

Amino acid and nucleotide sequences for murine and humanized antibody molecules which bind to TCRVB 5 (e.g., TCRVB 5-5 or TCRVB 5-6). The amino acid the heavy and light chain CDRs, and the amino acid and nucleotide sequences of the heavy and light chain variable regions, and the heavy and light chains are shown.

Murine antibody E		
SEQ ID NO: 1298	HC CDR1 (Kabat)	SSWMN
SEQ ID NO: 1299	HC CDR2 (Kabat)	RIYPGDGDTKYNGKFKG
SEQ ID NO: 1300	HC CDR3 (Kabat)	RGTGGWYFDV
SEQ ID NO: 1302	HC CDR1 (Chothia)	GYAFSSS
SEQ ID NO: 1303	HC CDR2 (Chothia)	YPGDGD
SEQ ID NO: 1301	HC CDR3 (Chothia)	RGTGGWYFDV
SEQ ID NO: 1304	HC CDR1 (Combined)	GYAFSSSWMN

SEQ ID NO: 1299	HC CDR2 (Combined))	RIYPGDGDTKYNGKFKG
SEQ ID NO: 1301	HC CDR3(Combined)	RGTGGWYFDV
SEQ ID NO: 1305	LC CDR1 (Kabat)	RASESVDSSGNSFMH
SEQ ID NO: 1306	LC CDR2 (Kabat)	RASNLES
SEQ ID NO: 1307	LC CDR3 (Kabat)	QQSFDDPFT
SEQ ID NO: 1308	LC CDR1 (Chothia)	SESVDSSGNSF
SEQ ID NO: 1306	LC CDR2 (Chothia)	RASNLES
SEQ ID NO: 1307	LC CDR3 (Chothia)	QQSFDDPFT
SEQ ID NO: 1305	LC CDR1 (Combined)	RASESVDSSGNSFMH
SEQ ID NO: 1306	LC CDR2 (Combined)	RASNLES
SEQ ID NO: 1307	LC CDR3(Combined)	QQSFDDPFT
SEQ ID NO: 3091	VH	QVQLQQSGPELVKPGASVKISCKASGYAFSSSW MNWVKQRPGQGLEWIGRIYPGDGDTKYNGKFK GKATLTADKSSSTAYMHLSSLTSVDSAVYFCAR RGTGGWYFDVWGAGTTVTVSS
SEQ ID NO: 3284	Heavy chain	METDTLLLWVLLLWVPGSTGQVQLQQSGPELV KPGASVKISCKASGYAFSSSWMNWVKQRPGQ LEWIGRIYPGDGDTKYNGKFKGKATLTADKSS TAYMHLSSLTSVDSAVYFCARRGTGGWYFDVW GAGTTVTVSSAKTTAPSVYPLAPVCGDTTGSSVT LGCLVKGYFPEPVTLTWNSGSLSSGVHTFPAVL QSDLYTLSSSVTVTSSTWPSQSITCNVAHPASSTK VDKKIEPRGPTIKPCPPCKCPAPNLLGGPSVFIFPP KIKDVLMSLSPIVTCVVVDVSEDDPDVQISWV NNVEVHTAQTTQTHREDYNSTLRVVSALPIQH QDWMMSGKEFKCKVNNKDLPAPIERTISKPKGS VRA PQVYVLPPEEEMTKKQVTLTCMVTDFMP EDIY VEW TNNGKTELNYKNTEPVLDSDGSYF MYSKL RVEKKNWVERN SYSCSVVHEGLHNH HTTKSFSRTPGK
SEQ ID NO: 3092	VL	DIVLTQSPASLAVSLGQRATISCRASESVDSSGNS FMHWYQQKPGQPPQLLIYRASNLESGIPARFSGS GSRTDFTLTINPVEADDVATFYCQQSFDDPFTFG SGTKLEIK
SEQ ID NO: 3285	Light chain	METDTLLLWVLLLWVPGSTGDIVLTQSPASLAV SLGQRATISCRASESVDSSGNSFMHWYQQKPGQ PPQLLIYRASNLESGIPARFSGSGSRTDFTLTINP VEADDVATFYCQQSFDDPFTFGSGTKLEIKRADA APTVSIFPPSSEQLTSGGASVVCFLNNFYPKDIN V KWKIDGSERQNGVLNSWTDQDSKDSTYSMSSTL TLTKDEYERHNSYTCEATHKTSTSPIVKSFNRNE C
Humanized antibody E (E-H antibody)		
Variable light chain (VL)		

SEQ ID NO: 3093	VL	E-H.1	DIVLTQSPDLSLAVSLGERATINCRASESVDSGGNS FMHWYQQKPGQPPQLLIYRASNLESGVPDRFSGSG SRTDFTLTISLQAEDVAVYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3094	VL	E-H.2	EIVLTQSPATLSLSPGERATLSCRASESVDSSGNS FMHWYQQKPGQAPQLLIYRASNLESGIPARFSGSG SRTDFTLTISLLEPEDFAVYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3095	VL	E-H.3	EIVLTQSPATLSLSPGERATLSCRASESVDSSGNS FMHWYQQKPGQAPQLLIYRASNLESGIPARFSGSG SRTDFTLTISRLEPEDFAVYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3096	VL	E-H.4	EIVLTQSPATLSLSPGERATLSCRASESVDSSGNS FMHWYQQKPGQAPQLLIYRASNLESGIPARFSGSG SRTDFTLTISLQPEDFAVYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3097	VL	E-H.5	DIQLTQSPSSLSASVGDRVITITCRASESVDSGGNS FMHWYQQKPGQAPQLLIYRASNLESGVPSRFSGSG SRTDFTLTISLQPEDVATYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3098	VL	E-H.6	EIVLTQSPATLSLSPGERATLSCRASESVDSSGNS FMHWYQQKPGQAPQLLIYRASNLESGIPARFSGSG PRTDFTLTISLLEPEDFAVYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3099	VL	E-H.7	EIVLTQSPATLSLSPGERATLSCRASESVDSSGNS FMHWYQQKPGQAPQLLIYRASNLESGIPDRFSGSG SRTDFTLTISRLEPEDFAVYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3100	VL	E-H.8	DIQLTQSPSSLSASVGDRVITITCRASESVDSGGNS FMHWYQQKPGKVPQLLIYRASNLESGVPSRFSGSG SRTDFTLTISLQPEDVATYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3101	VL	E-H.9	DIQLTQSPSSLSASVGDRVITITCRASESVDSGGNS FMHWYQQKPGKTPQLLIYRASNLESGIPSRFSGSG SRTDFTLTIRSLQPEDFATYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3102	VL	E-H.10	EIVLTQSPGTLSPGERATLSCRASESVDSSGNS FMHWYQQKPGQAPQLLIYRASNLESGIPDRFSGSG SRTDFTLTISRLEPEDFAVYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3103	VL	E-H.11	EIVLTQSPATLSLSPGERATLSCRASESVDSSGNS FMHWYQQKPGGLAPQLLIYRASNLESGIPDRFSGSG SRTDFTLTISRLEPEDFAVYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3104	VL	E-H.12	DIQLTQSPSSLSASVGDRVITITCRASESVDSGGNS FMHWYQQKPGKAPQLLIYRASNLESGVPSRFSGSG SRTDFTLTISLQPEDFATYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3105	VL	E-H.13	DIQLTQSPSSVSASVGDRVITITCRASESVDSGGNS FMHWYQQKPGKAPQLLIYRASNLESGVPSRFSGSG

			SRTDFTLTISLQPEDFATYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3106	VL	E-H.14	AIQLTQSPSSLSASVGDRVTITCRASESVDSSGNS FMHWYQQKPGKAPQLLIYRASNLESGVPSRFSGSG SRTDFTLTISLQPEDFATYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3107	VL	E-H.15	DIQLTQSPSFLSASVGDRVTITCRASESVDSSGNS FMHWYQQKPGKAPQLLIYRASNLESGVPSRFSGSG SRTEFTLTISLQPEDFATYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3108	VL	E-H.16	DIQLTQSPSSLSASVGDRVTITCRASESVDSSGNS FMHWYQQKPGKAPQLLIYRASNLESGVPSRFSGSG SRTDFTLTISLQPEDFATYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3109	VL	E-H.17	EIVLTQSPATLSVSPGERATLSCRASESVDSSGNS FMHWYQQKPGQAPQLLIYRASNLESGIPARFSGSG SRTEFTLTISILQSEDFAVYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3110	VL	E-H.18	EIVLTQSPATLSVSPGERATLSCRASESVDSSGNS FMHWYQQKPGQAPQLLIYRASNLESGIPARFSGSG SRTEFTLTISLQSEDFAVYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3111	VL	E-H.19	AIRLTQSPFSLASVGDRVTITCRASESVDSSGNS FMHWYQQKPAKAPQLFIYRASNLESGVPSRFSGSG SRTDFTLTISLQPEDFATYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3112	VL	E-H.20	DIQLTQSPSSLSASVGDRVTITCRASESVDSSGNS FMHWYQQKPGKAPQSLIYRASNLESGVPSRFSGSG SRTDFTLTISLQPEDFATYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3113	VL	E-H.21	DIQLTQSPSSLSASVGDRVTITCRASESVDSSGNS FMHWYQQKPGKAPQRLIYRASNLESGVPSRFSGSG SRTEFTLTISNLQPEDFATYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3114	VL	E-H.22	DIQLTQSPSTLSASVGDRVTITCRASESVDSSGNS FMHWYQQKPGKAPQLLIYRASNLESGVPSRFSGSG SRTEFTLTISLQPDDFATYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3115	VL	E-H.23	EIVLTQSPDFQSVTPKEKVTITCRASESVDSSGNS FMHWYQQKPDQSPQLLIYRASNLESGVPSRFSGSG SRTDFTLTINSLEAEDAATYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3116	VL	E-H.24	DIQLTQSPSSLSASVGDRVTITCRASESVDSSGNS FMHWYQQKPGKAPQSLIYRASNLESGVPSKFSGSG SRTDFTLTISLQPEDFATYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3117	VL	E-H.25	DIQLTQSPSSLSASVGDRVTITCRASESVDSSGNS FMHWYQQKPGKAPQRLIYRASNLESGVPSRFSGSG SRTEFTLTISLQPEDFATYYCQQSFDDPFTFGQG TKLEIK

SEQ ID NO: 3118	VL	E-H.26	DIVLTQTPLSLSVTPGQPASISCRASESVDSGGNS FMHWYLQKPGQPPQLLIYRASNLESGVPDRFSGSG SRTDFTLKISRVEAEDVGVYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3119	VL	E-H.27	DIQLTQSPSSLSASVGDRVTITCRASESVDSGGNS FMHWYQQKPEKAPQSLIYRASNLESGVPSRFSGSG SRTDFTLTISLQPEDFATYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3120	VL	E-H.28	EIVLTQSPPTLSLSPGERVTLSRASESVDSGGNS FMHWYQQKPGQAPQLLIYRASNLESGIPARFSGSG SRTDFTLTISLQPEDFAVYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3121	VL	E-H.29	DIQLTQSPSAMSASVGDRVTITCRASESVDSGGNS FMHWYQQKPGKVPQRLIYRASNLESGVPSRFSGSG SRTEFTLTISLQPEDFATYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3122	VL	E-H.30	DIVLTQSPSLPVTGPGEASISCRASESVDSGGNS FMHWYLQKPGQSPQLLIYRASNLESGVPDRFSGSG SRTDFTLKISRVEAEDVGVYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3123	VL	E-H.31	DIVLTQTPLSLPVTGPGEASISCRASESVDSGGNS FMHWYLQKPGQSPQLLIYRASNLESGVPDRFSGSG SRTDFTLKISRVEAEDVGVYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3124	VL	E-H.32	DIVLTQTPLSLSVTPGQPASISCRASESVDSGGNS FMHWYLQKPGQSPQLLIYRASNLESGVPDRFSGSG SRTDFTLKISRVEAEDVGVYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3125	VL	E-H.33	EIVLTQSPPTLSLSPGERVTLSRASESVDSGGNS FMHWYQQKPGQAPQLLIYRASNLESSIPARFSGSG SRTDFTLTISLQPEDFAVYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3126	VL	E-H.34	DIVLTQSPSLPVTLGQPASISCRASESVDSGGNS FMHWYQQRPGQSPQRLIYRASNLESGVPDRFSGSG SRTDFTLKISRVEAEDVGVYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3127	VL	E-H.35	DIVLTQTPLSSPVTLGQPASISCRASESVDSGGNS FMHWYQQRPGQPPQLLIYRASNLESGVPDRFSGSG ARTDFTLKISRVEAEDVGVYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3128	VL	E-H.36	DIVLTQSPAFLSVTPGEKVTITCRASESVDSGGNS FMHWYQQKPDQAPQLLIYRASNLESGVPSRFSGSG SRTDFTFTISLLEAEDAATYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3129	VL	E-H.37	DIQLIQSPSFLSASVGDRVSIICRASESVDSGGNS FMHWYLQKPGKSPQLFIYRASNLESGVSSRFSGRG SRTDFTLTIIISLKPEDFAAYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3130	VL	E-H.38	EIVLTQTPLSLSITPGEQASISCRASESVDSGGNS FMHWYLQKARPVPQLLIYRASNLESGVPDRFSGSG

			SRTDFTLKISRVEAEDFGVYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3131	VL	E-H.39	EIVLTQTPLSL SITPGEQASMSCRASESVDSGNS FMHWYLQKARPVPQLLIYRASNL ESGVPDRFSGSG SRTDFTLKISRVEAEDFGVYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3132	VL	E-H.40	EITLTQSPAFMSATPGDKVNISCRASESVDSGNS FMHWYQQKPG EAPQFI IYRASNL SGIPPRFSGSG YRTDFTLTINNIESEDAAYYCQQSFDDPFTFGQG TKLEIK
Variable HEAVY chain (VH)			
SEQ ID NO: 3133	VH	E-H.1	QVQLVQSGAEVKKPGASVKV SCKASGYAFSSSWMN WVRQAPGQGLEWIGRIYPGDGDTKYNGKFKGRATL TADKSTSTAYMELSSLRSED TAVYYCARRGTGGWY FDVWGQGTTTVTVSS
SEQ ID NO: 3134	VH	E-H.2	QVQLVQSGAEVKKPGSSVKV SCKASGYAFSSSWMN WVRQAPGQGLEWIGRIYPGDGDTKYNGKFKGRATL TADKSTSTAYMELSSLRSED TAVYYCARRGTGGWY FDVWGQGTTTVTVSS
SEQ ID NO: 3135	VH	E-H.3	QVQLVQSGAEVKKPGASVKV SCKASGYAFSSSWMN WVRQAPGKGLEWIGRIYPGDGDTKYNGKFKGRATL TADKSTSTAYMELSSLRSED TAVYYCARRGTGGWY FDVWGQGTTTVTVSS
SEQ ID NO: 3136	VH	E-H.4	QVQLVQSGAEVKKPGASVKV SCKASGYAFSSSWMN WVRQAPGQLEWIGRIYPGDGDTKYNGKFKGRATL TADKSI STAYMELSSLRSED TATYYCARRGTGGWY FDVWGQGTTTVTVSS
SEQ ID NO: 3137	VH	E-H.5	EVQLVQSGAEVKKPGATVKI SCKASGYAFSSSWMN WVQQAPGKGLEWIGRIYPGDGDTKYNGKFKGRATL TADKSTSTAYMELSSLRSED TAVYYCARRGTGGWY FDVWGQGTTTVTVSS
SEQ ID NO: 3138	VH	E-H.6	QVQLVQSGAEVKKKTGSSVKV SCKASGYAFSSSWMN WVRQAPGQALEWIGRIYPGDGDTKYNGKFKGRATL TADKSMSTAYMELSSLRSED TAMY CARRGTGGWY FDVWGQGTTTVTVSS
SEQ ID NO: 3139	VH	E-H.7	QVQLVQSGAEVKKPGASVKV SCKASGYAFSSSWMN WVRQAPGQRLEWIGRIYPGDGDTKYNGKFKGRATL TADKSASTAYMELSSLRSED MAVYYCARRGTGGWY FDVWGQGTTTVTVSS
SEQ ID NO: 3140	VH	E-H.8	QVQLVQSGAEVKKPGASVKV SCKASGYAFSSSWMN WVRQAPGQGLEWIGRIYPGDGDTKYNGKFKGRATL TADKSTSTAYMELRSLRSDDM AVYYCARRGTGGWY FDVWGQGTTTVTVSS
SEQ ID NO: 3141	VH	E-H.9	QVQLVQSGAEVKKPGASVKV SCKASGYAFSSSWMN WVRQAPGQRLEWIGRIYPGDGDTKYNGKFKGRATL TADKSASTAYMELSSLRSED TAVYYCARRGTGGWY FDVWGQGTTTVTVSS
SEQ ID NO: 3142	VH	E-H.10	QVQLVQSGAEVKKPGASVKV SCKASGYAFSSSWMN WVRQAPGQGLEWIGRIYPGDGDTKYNGKFKGRATL

			TADKSTSTAYMELRSLRSDDTAVYYCARRGTGGWY FDVWGQGT TVTVSS
SEQ ID NO: 3143	VH	E-H.11	QVQLVQSGAEVKKPGASVKVSCASGYAFSSSWMN WVRQAPGQGLEWIGRIYPGDGDTKYNGKFKGRATL TADKSI STAYMELRSLRSDDTAVYYCARRGTGGWY FDVWGQGT TVTVSS
SEQ ID NO: 3144	VH	E-H.12	QVQLVQSGAEVKKPGASVKVSCASGYAFSSSWMN WVRQAPGQGLEWIGRIYPGDGDTKYNGKFKGRATL TADKSI STAYMELRSLRSDDTVVYYCARRGTGGWY FDVWGQGT TVTVSS
SEQ ID NO: 3145	VH	E-H.13	QVQLVQSGAEVKKPGASVKVSCASGYAFSSSWMN WVRQAPGQGLEWIGRIYPGDGDTKYNGKFKGWATL TADKSI STAYMELRSLRSDDTAVYYCARRGTGGWY FDVWGQGT TVTVSS
SEQ ID NO: 3146	VH	E-H.14	QVQLVQSGAEVKKPGASVKVSCASGYAFSSSWMN WVRQATGQGLEWIGRIYPGDGDTKYNGKFKGRATL TANKSI STAYMELSSLRSED TAVYYCARRGTGGWY FDVWGQGT TVTVSS
SEQ ID NO: 3147	VH	E-H.15	QVQLVQSGSELKKPGASVKVSCASGYAFSSSWMN WVRQAPGQGLEWIGRIYPGDGDTKYNGKFKGRAVL SADKSVSTAYLQISSLKAEDTAVYYCARRGTGGWY FDVWGQGT TVTVSS
SEQ ID NO: 3148	VH	E-H.16	QVQLVQSGPEVKKPGTSVKVSCASGYAFSSSWMN WVRQARGQRLWIGRIYPGDGDTKYNGKFKGRATL TADKSTSTAYMELSSLRSED TAVYYCARRGTGGWY FDVWGQGT TVTVSS
SEQ ID NO: 3149	VH	E-H.17	EVQLVQSGAEVKKPGESLKISCKASGYAFSSSWMN WVRQMPGKGLEWIGRIYPGDGDTKYNGKFKGQATL SADKSI STAYLQWSSLKASDTAMYYCARRGTGGWY FDVWGQGT TVTVSS
SEQ ID NO: 3150	VH	E-H.18	QVQLVQSGSELKKPGASVKVSCASGYAFSSSWMN WVRQAPGQGLEWIGRIYPGDGDTKYNGKFKGRAVL SADKSVSMAYLQISSLKAEDTAVYYCARRGTGGWY FDVWGQGT TVTVSS
SEQ ID NO: 3151	VH	E-H.19	QVQLVQSGHEVKKQPGASVKVSCASGYAFSSSWMN WVPQAPGQGLEWIGRIYPGDGDTKYNGKFKGRAVL SADKSASTAYLQISSLKAEDMAMYYCARRGTGGWY FDVWGQGT TVTVSS
SEQ ID NO: 3152	VH	E-H.20	EVQLVQSGAEVKKPGESLKISCKASGYAFSSSWMN WVRQMPGKGLEWIGRIYPGDGDTKYNGKFKGQATL SADKPI STAYLQWSSLKASDTAMYYCARRGTGGWY FDVWGQGT TVTVSS
SEQ ID NO: 3153	VH	E-H.21	EVQLVQSGAEVKKPGESLRISCKASGYAFSSSWMN WVRQMPGKGLEWIGRIYPGDGDTKYNGKFKGQATL SADKSI STAYLQWSSLKASDTAMYYCARRGTGGWY FDVWGQGT TVTVSS
SEQ ID NO: 3154	VH	E-H.22	EVQLVQSGAEVKKPGESLRISCKASGYAFSSSWMN WVRQMPGKGLEWIGRIYPGDGDTKYNGKFKGHATL SADKSI STAYLQWSSLKASDTAMYYCARRGTGGWY FDVWGQGT TVTVSS

SEQ ID NO: 3155	VH	E-H.23	QVQLVQSGAEVKKTGSSSVKVSCKASGYAFSSSWMN WVRQAPRQALEWIGRIYPGDGDTKYNGKFKGRATL TADKSMSTAYMELSSLRSEDAMYYCARRGTGGWY FDVWGQGTITVTVSS
SEQ ID NO: 3156	VH	E-H.24	EVQLVESGGGLVQPGRSLRLSCTASGYAFSSSWMN WVRQAPGKGLEWIGRIYPGDGDTKYNGKFKGRATL SADKSKSIAYLQMNSLKTEDTAVYYCARRGTGGWY FDVWGQGTITVTVSS
SEQ ID NO: 3157	VH	E-H.25	EVQLVESGGGLVQPGPSLRLSCTASGYAFSSSWMN WVRQAPGKGLEWIGRIYPGDGDTKYNGKFKGRATL SADKSKSIAYLQMNSLKTEDTAVYYCARRGTGGWY FDVWGQGTITVTVSS
SEQ ID NO: 3158	VH	E-H.26	QVQLQESGPGLVKPSQTLSTCTASGYAFSSSWMN WVRQPPGKGLEWIGRIYPGDGDTKYNGKFKGRATL SADKSKSQASLKLSSVTAADTAVYYCARRGTGGWY FDVWGQGTITVTVSS
SEQ ID NO: 3159	VH	E-H.27	QVQLQESGPGLVKPSGTLSTCAASGYAFSSSWMN WVRQPPGKGLEWIGRIYPGDGDTKYNGKFKGRATL SADKSKSQASLKLSSVTAADTAVYYCARRGTGGWY FDVWGQGTITVTVSS
SEQ ID NO: 3160	VH	E-H.28	EVQLVESGGGLVQPGRSLRLSCTASGYAFSSSWMN WVRQAPGKGLEWIGRIYPGDGDTKYNGKFKGRATL SADKSKSIAYLQMNSLKTEDTAVYYCARRGTGGWY FDVWGQGTITVTVSS
SEQ ID NO: 3161	VH	E-H.29	EVQLVESGGGLVQPGGSLKLSAASGYAFSSSWMN WVRQASGKGLEWIGRIYPGDGDTKYNGKFKGRATL SADKSKSTAYLQMNSLKTEDTAVYYCARRGTGGWY FDVWGQGTITVTVSS
SEQ ID NO: 3162	VH	E-H.30	QVQLQESGPGLVKPSQTLSTCAASGYAFSSSWMN WVRQPPGKGLEWIGRIYPGDGDTKYNGKFKGRATL SADKSKSQASLKLSSVTAADTAVYYCARRGTGGWY FDVWGQGTITVTVSS
SEQ ID NO: 3163	VH	E-H.31	EVQLVESGGGLVQPGGSLRLSCTASGYAFSSSWMN WVRQAPGKGLEWIGRIYPGDGDTKYNGKFKGRATL SADKSKSTAYLQMNSLKTEDTAVYYCARRGTGGWY FDVWGQGTITVTVSS
SEQ ID NO: 3164	VH	E-H.32	EVQLVESGGALVQPGGSLRLSCTASGYAFSSSWMN WVRQAPGKGLEWIGRIYPGDGDTKYNGKFKGRATL SADKSKSTAYLQMNSLKTEDTAVYYCARRGTGGWY FDVWGQGTITVTVSS
SEQ ID NO: 3165	VH	E-H.33	QVQLQESGPGLVKPSQTLSTCAAYGYAFSSSWMN WVRQPPGKGLEWIGRIYPGDGDTKYNGKFKGRATL SADKSKSQASLKLSSVTAADTAVYYCARRGTGGWY FDVWGQGTITVTVSS
SEQ ID NO: 3166	VH	E-H.34	QVQLQESGSLVQPSQTLSTCAASGYAFSSSWMN WVRQPPGKGLEWIGRIYPGDGDTKYNGKFKGRATL SADKSKSQASLKLSSVTAADTAVYYCARRGTGGWY FDVWGQGTITVTVSS
SEQ ID NO: 3167	VH	E-H.35	EVQLVESGGGLVQPGGSLRLSCTASGYAFSSSWMN WVRQAPGKGLEWIGRIYPGDGDTKYNGKFKGRATL

			SADKSKSSAYLQMNSLKTEDTAVYYCARRGTGGWY FDVWGQGT TVTVSS
SEQ ID NO: 3168	VH	E-H.36	QVQLQESGPGGLVKPSDTLSLTCTASGYAFSSSWMN WVRQPPGKGLEWIGRIYPGDGDTKYNGKFKGRATL SADKSKSQASLKLSSVTAADTAVYYCARRGTGGWY FDVWGQGT TVTVSS
SEQ ID NO: 3169	VH	E-H.37	QVQLQESGPGGLVKPSQTLSTLTCTASGYAFSSSWMN WVRQHPGKGLEWIGRIYPGDGDTKYNGKFKGRATL SADKSKSQASLKLSSVTAADTAVYYCARRGTGGWY FDVWGQGT TVTVSS
SEQ ID NO: 3170	VH	E-H.38	QVQLQESGPGGLVKPSQTLSTLTCTASGYAFSSSWMN WVRQHPGKGLEWIGRIYPGDGDTKYNGKFKGLATL SADKSKSQASLKLSSVTAADTAVYYCARRGTGGWY FDVWGQGT TVTVSS
SEQ ID NO: 3171	VH	E-H.39	QVQLVESGGGVVQPGRSRLRLSCAASGYAFSSSWMN WVRQAPGKGLEWIGRIYPGDGDTKYNGKFKGRATL SADKSKSTAYLQMSSLRAEDTAVYYCARRGTGGWY FDVWGQGT TVTVSS
SEQ ID NO: 3172	VH	E-H.40	QVQLVESGGGLVKPGGSLRLSCAASGYAFSSSWMN WVRQAPGKGLEWIGRIYPGDGDTKYNGKFKGRATL SADKAKSSAYLQMNSLRAEDTAVYYCARRGTGGWY FDVWGQGT TVTVSS
SEQ ID NO: 3173	VH	E-H.41	QVQLVESGGGLVQPGGSLRLSCSASGYAFSSSWMN WVRQAPGKGLEWIGRIYPGDGDTKYNGKFKGRATL SADKSKSTAYLQMNSLRAEDTAVYYCARRGTGGWY FDVWGQGT TVTVSS
SEQ ID NO: 3174	VH	E-H.42	QVQLLES GGGLVKPGGSLRLSCAASGYAFSSSWMN WVRQAPGKGLEWIGRIYPGDGDTKYNGKFKGRATL SADKAKSSAYLQMNSLRAEDTAVYYCARRGTGGWY FDVWGQGT TVTVSS
SEQ ID NO: 3175	VH	E-H.43	EVQLVESGGGLVQPGGSLRLSCSASGYAFSSSWMN WVRQAPGKGLEWIGRIYPGDGDTKYNGKFKGRATL SADKSKSTAYLQMSSLRAEDTAVYYCARRGTGGWY FDVWGQGT TVTVSS
SEQ ID NO: 3176	VH	E-H.44	QVQLQESGPGGLVKPSDTLSLTCAASGYAFSSSWMN WVRQPPGKGLEWIGRIYPGDGDTKYNGKFKGRATL SADKSKSQASLKLSSVTAVDTAVYYCARRGTGGWY FDVWGQGT TVTVSS
SEQ ID NO: 3177	VH	E-H.45	QVQLQESGPGGLVKPSQTLSTLTCAASGYAFSSSWMN WVRQPPGKGLEWIGRIYPGDGDTKYNGKFKGRATL SADKSKSQASLKLSSVTAVDTAVYYCARRGTGGWY FDVWGQGT TVTVSS
SEQ ID NO: 3178	VH	E-H.46	EVQLVESGGGLVQPGGSLRLSCSASGYAFSSSWMN WVRQAPGKGLEWIGRIYPGDGDTKYNGKFKGRATL SADKSKSTAYVQMSSLRAEDTAVYYCARRGTGGWY FDVWGQGT TVTVSS
SEQ ID NO: 3179	VH	E-H.47	QVQLVDSGGGVVQPGRSRLRLSCAASGYAFSSSWMN WVRQAPGKGLEWIGRIYPGDGDTKYNGKFKGRATL SADKSKSTAYLQMNSLRAEDTAVYYCARRGTGGWY FDVWGQGT TVTVSS

SEQ ID NO: 3180	VH	E-H.48	QVQLVESGGGVVQPGRSLRLSCAASGYAFSSSWMN WVRQAPGKGLEWIGRIYPGDGDTKYNGKFGRATL SADKSKSTAYLQMNSLRAEGTAVYYCARRGTGGWY FDVWGQGTITVTVSS
SEQ ID NO: 3181	VH	E-H.49	QVQLVESGGGVVQPGRSLRLSCAASGYAFSSSWMN WVRQAPGKGLEWIGRIYPGDGDTKYNGKFGRATL SADKSKSTAYLQMNSLRAEDTAVYYCARRGTGGWY FDVWGQGTITVTVSS
SEQ ID NO: 3182	VH	E-H.50	EVQLVESGGGLVQPGGSLRLSCAASGYAFSSSWMN WVRQAPGKGLEWIGRIYPGDGDTKYNGKFGRATL SADKSKSTAYLQMNSLRAEDTAVYYCARRGTGGWY FDVWGQGTITVTVSS

In some embodiments, the anti-TCR β V5 antibody molecule comprises a VH and/or a VL of an antibody described in **Table 10A**, or a sequence with at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or more identity thereto.

5 In some embodiments, the anti-TCR β V5 antibody molecule comprises a VH and a VL of an antibody described in **Table 10A**, or a sequence with at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or more identity thereto.

In some embodiments, the anti-TCR β V5 antibody molecule comprises a VH and/or a VL of an antibody described in **Table 11A**, or a sequence with at least 80%, 85%, 90%, 95%,
10 96%, 97%, 98%, 99% or more identity thereto.

In some embodiments, the anti-TCR β V5 antibody molecule comprises a VH and a VL of an antibody described in **Table 11A**, or a sequence with at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or more identity thereto.

15 **Anti-TCR β V10 antibodies**

Accordingly, in one aspect, the disclosure provides an anti-TCR β V antibody molecule that binds to a human TCR β V10 subfamily member. In some embodiments, TCR β V10 subfamily is also known as TCR β V12. In some embodiments, the TCR β V10 subfamily comprises: TCR β V10-1*01, TCR β V10-1*02, TCR β V10-3*01 or TCR β V10-2*01, or a
20 variant thereof.

Exemplary anti-TCR β V10 antibodies of the disclosure are provided in **Table 12A**. In some embodiments, the anti-TCR β V10 is antibody D, e.g., humanized antibody D (antibody D-H), as provided in **Table 12A**. In some embodiments, antibody D comprises one or more (e.g.,

three) light chain CDRs and/or one or more (e.g., three) heavy chain CDRs provided in **Table 12A**, or a sequence with at least 95% identity thereto. In some embodiments, antibody D comprises a variable heavy chain (VH) and/or a variable light chain (VL) provided in **Table 12A**, or a sequence with at least 95% identity thereto.

5

Table 12A: Amino acid sequences for anti TCR β V10 antibodies

Amino acid and nucleotide sequences for murine and humanized antibody molecules which bind to TCRBV 10 (e.g., TCRBV 10-1, TCRBV 10-2 or TCRBV 10-3). The amino acid the heavy and light chain CDRs, and the amino acid and nucleotide sequences of the heavy and light chain variable regions, and the heavy and light chains are shown.

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Murine antibody D		
SEQ ID NO: 1288	HC CDR1 (Kabat)	SYGMS
SEQ ID NO: 1289	HC CDR2 (Kabat)	LISSGGSYTTYTDSVKG
SEQ ID NO: 1290	HC CDR3 (Kabat)	HGGNFFDY
SEQ ID NO: 1291	HC CDR1 (Chothia)	GFTFRSY
SEQ ID NO: 1292	HC CDR2 (Chothia)	SSGGSY
SEQ ID NO: 1290	HC CDR3 (Chothia)	HGGNFFDY
SEQ ID NO: 1293	HC CDR1 (Combined)	GFTFRSYGMS
SEQ ID NO: 1289	HC CDR2 (Combined))	LISSGGSYTTYTDSVKG
SEQ ID NO: 1290	HC CDR3(Combined)	HGGNFFDY
SEQ ID NO: 1294	LC CDR1 (Kabat)	SVSSSVSYM
SEQ ID NO: 1295	LC CDR2 (Kabat)	DTSKLAS
SEQ ID NO: 1296	LC CDR3 (Kabat)	QQWSSNPQYT
SEQ ID NO: 1297	LC CDR1 (Chothia)	SSSVSY
SEQ ID NO: 1295	LC CDR2 (Chothia)	DTSKLAS
SEQ ID NO: 1296	LC CDR3 (Chothia)	QQWSSNPQYT

SEQ ID NO: 1294	LC CDR1 (Combined)	SVSSSVSYMH	
SEQ ID NO: 1295	LC CDR2 (Combined)	DTSKLAS	
SEQ ID NO: 1296	LC CDR3 (Combined)	QQWSSNPQYT	
SEQ ID NO: 3183	VH	EVQLVESGGDLVKPGGSLKLSCAVSGFTFRSYGMS WVRQTPDKRLEWVALISSGGSYTYYTDSVKGRFTI SRDNAKNTLYLQMSSLKSEDTAIYYCSRHGNNFFD YWGQGTTLTVSS	
SEQ ID NO: 3184	VL	QIVLTQSPSIMSASPGEKVTMTCSVSSSVSYMHWY QQKSGTSPKRWIYDTSKLASGVPARFSGSGSGTSYS LTISSMEAEDAATYYCQQWSSNPQYTFGGGTKLEI K	
Humanized antibody D (D-H antibody)			
Variable light chain (VL)			
SEQ ID NO: 3185	VL	D-VL-H.1	DIVLTQSPAFLSVTPGEKVTITCSVSSSVSYMHWY QQKPDQAPKLLIYDTSKLASGVPSRFSGSGSGTDY TFTISSLEAEDAATYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3186	VL	D-VL-H.2	AIQLTQSPSSLSASVGDRVTITCSVSSSVSYMHWY QQKPGKAPKLLIYDTSKLASGVPSRFSGSGSGTDY TLTISSLQPEDFATYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3187	VL	D-VL-H.3	DIQLTQSPSFLSASVGDRVTITCSVSSSVSYMHWY QQKPGKAPKLLIYDTSKLASGVPSRFSGSGSGTEY TLTISSLQPEDFATYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3188	VL	D-VL-H.4	DIQLTQSPSSLSASVGDRVTITCSVSSSVSYMHWY QQKPGKAPKLLIYDTSKLASGVPSRFSGSGSGTDY TLTISSLQPEDFATYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3189	VL	D-VL-H.5	DIQLTQSPSSVSASVGDRVTITCSVSSSVSYMHWY QQKPGKAPKLLIYDTSKLASGVPSRFSGSGSGTDY TLTISSLQPEDFATYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3190	VL	D- VL-H.6	DIQLTQSPSSLSASVGDRVTITCSVSSSVSYMHWY QQKPGKVPKLLIYDTSKLASGVPSRFSGSGSGTDY TLTISSLQPEDVATYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3191	VL	D- VL-H.7	DIQLTQSPSSLSASVGDRVTITCSVSSSVSYMHWY QQKPGQAPKLLIYDTSKLASGVPSRFSGSGSGTDY TLTISSLQPEDVATYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3192	VL	D- VL-H.8	EIVLTQSPDFQSVTPKEKVTITCSVSSSVSYMHWY QQKPDQSPKLLIYDTSKLASGVPSRFSGSGSGTDY TLTINSLEAEDAATYYCQQWSSNPQYTFGQGTKLE IK

SEQ ID NO: 3193	VL	D- VL-H.9	AIRLTQSPFSLASVGDRTITCSVSSSVSYMHWY QQKPAKAPKLFYDTSKLAGVPSRFSGSGSGTDY TLTISSLQPEDFATYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3194	VL	D- VL-H.10	DIQLTQSPSSLASVGDRTITCSVSSSVSYMHWY QQKPGKAPKLLIYDTSKLAGVPSRFSGSGSGTDY TFTISSLQPEDATYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3195	VL	D- VL-H.11	EIVLTQSPATLSLSPGERATLSCSVSSSVSYMHWY QQKPGQAPKLLIYDTSKLAGIPARFSGSGSGTDY TLTISSLEPEDFAVYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3196	VL	D- VL-H.12	DIQLTQSPSTLSASVGDRTITCSVSSSVSYMHWY QQKPGKAPKLLIYDTSKLAGVPSRFSGSGSGTEY TLTISSLQPDDEFATYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3197	VL	D- VL-H.13	DIQLTQSPSSLASVGDRTITCSVSSSVSYMHWY QQKPGKTPKLLIYDTSKLAGIPSRFSGSGSGTDY TLTIRSLQPEDFATYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3198	VL	D- VL-H.14	EIVLTQSPPTLSLSPGERVTLSVSSSVSYMHWY QQKPGQAPKLLIYDTSKLAGIPARFSGSGSGTDY TLTISSLQPEDFAVYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3199	VL	D- VL-H.15	DIQLTQSPSSLASVGDRTITCSVSSSVSYMHWY QQKPGKAPKRLIYDTSKLAGVPSRFSGSGSGTEY TLTISSLQPEDFATYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3200	VL	D- VL-H.16	EIVLTQSPATLSLSPGERATLSCSVSSSVSYMHWY QQKPGQAPKLLIYDTSKLAGIPARFSGSGPGTDY TLTISSLEPEDFAVYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3201	VL	D- VL-H.17	EIVLTQSPATLSLSPGERATLSCSVSSSVSYMHWY QQKPGQAPKLLIYDTSKLAGIPARFSGSGSGTDY TLTISRLEPEDFAVYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3202	VL	D- VL-H.18	EIVLTQSPATLSLSPGERATLSCSVSSSVSYMHWY QQKPGQAPKLLIYDTSKLAGIPARFSGSGSGTDY TLTISSLQPEDFAVYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3203	VL	D- VL-H.19	EIVLTQSPATLSVSPGERATLSCSVSSSVSYMHWY QQKPGQAPKLLIYDTSKLAGIPARFSGSGSGTEY TLTISSLQSEDFAVYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3204	VL	D- VL-H.20	EIVLTQSPATLSVSPGERATLSCSVSSSVSYMHWY QQKPGQAPKLLIYDTSKLAGIPARFSGSGSGTEY TLTISILQSEDFAVYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3205	VL	D- VL-H.21	EIVLTQSPPTLSLSPGERVTLSVSSSVSYMHWY QQKPGQAPKLLIYDTSKLASSIPARFSGSGSGTDY

			TLTISSLQPEDFAVYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3206	VL	D- VL- H.22	DIQLTQSPSSLSASVGDRVTITCSVSSSVSYMHWHY QQKPGKAPKSLIYDTSKLAGVPSRFSGSGSGTDY TLTISSLQPEDFATYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3207	VL	D- VL- H.23	DIQLTQSPSSLSASVGDRVTITCSVSSSVSYMHWHY QQKPGKAPKRLIYDTSKLAGVPSRFSGSGSGTEY TLTISNLQPEDFATYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3208	VL	D- VL- H.24	DIQLTQSPSAMSASVGDRVTITCSVSSSVSYMHWHY QQKPGKVPKRLIYDTSKLAGVPSRFSGSGSGTEY TLTISSLQPEDFATYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3209	VL	D- VL- H.25	EIVLTQSPATLSLSPGERATLSCSVSSSVSYMHWHY QQKPGQAPKLLIYDTSKLAGIPDRFSGSGSGTDY TLTISRLEPEDFAVYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3210	VL	D- VL- H.26	EIVLTQSPATLSLSPGERATLSCSVSSSVSYMHWHY QQKPGKAPKLLIYDTSKLAGIPDRFSGSGSGTDY TLTISRLEPEDFAVYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3211	VL	D- VL- H.27	EIVLTQSPGTLSLSPGERATLSCSVSSSVSYMHWHY QQKPGQAPKLLIYDTSKLAGIPDRFSGSGSGTDY TLTISRLEPEDFAVYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3212	VL	D- VL- H.28	DIQLTQSPSSLSASVGDRVTITCSVSSSVSYMHWHY QQKPGKAPKSLIYDTSKLAGVPSKFSGSGSGTDY TLTISSLQPEDFATYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3213	VL	D- VL- H.29	DIQLTQSPSSLSASVGDRVTITCSVSSSVSYMHWHY QQKPEKAPKSLIYDTSKLAGVPSRFSGSGSGTDY TLTISSLQPEDFATYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3214	VL	D- VL- H.30	DIVLTQSPDSLAVSLGERATINCSVSSSVSYMHWHY QQKPGQPPKLLIYDTSKLAGVPDRFSGSGSGTDY TLTISSLQAEDVAVYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3215	VL	D- VL- H.31	EIVLTQTPLSLSLITPGEQASMSVSSSVSYMHWHY LQKARPVPKLLIYDTSKLAGVPDRFSGSGSGTDY TLKISRVEAEDFGVYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3216	VL	D- VL- H.32	EIVLTQTPLSLSLITPGEQASISVSSSVSYMHWHY LQKARPVPKLLIYDTSKLAGVPDRFSGSGSGTDY TLKISRVEAEDFGVYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3217	VL	D- VL- H.33	DIVLTQSPLSLPVTGPGEPAISVSSSVSYMHWHY LQKPGQSPKLLIYDTSKLAGVPDRFSGSGSGTDY TLKISRVEAEDVGYYCQQWSSNPQYTFGQGTKLE IK

SEQ ID NO: 3218	VL	D- VL-H.34	DIVLTQSPFLSLPVTLGQPASISCSVSSSVSYMHY QQRPQGQSPKRLIYDTSKLGVPDRFSGSGSGTDY TLKISRVEAEDVGVYYCQQWSSNPQYTFGGGTKLE IK
SEQ ID NO: 3219	VL	D- VL-H.35	DIVLTQTPLSLPVTGPGEPAISCSVSSSVSYMHY LQKPGQSPKLLIYDTSKLGVPDRFSGSGSGTDY TLKISRVEAEDVGVYYCQQWSSNPQYTFGGGTKLE IK
SEQ ID NO: 3220	VL	D- VL-H.36	DIVLTQTPLSLSVTPGQPASISCSVSSSVSYMHY LQKPGQSPKLLIYDTSKLGVPDRFSGSGSGTDY TLKISRVEAEDVGVYYCQQWSSNPQYTFGGGTKLE IK
SEQ ID NO: 3221	VL	D- VL-H.37	DIVLTQTPLSLSVTPGQPASISCSVSSSVSYMHY LQKPGQPPKLLIYDTSKLGVPDRFSGSGSGTDY TLKISRVEAEDVGVYYCQQWSSNPQYTFGGGTKLE IK
SEQ ID NO: 3222	VL	D- VL-H.38	DIQLIQSPSFLSASVGDRVSIICSVSSSVSYMHY LQKPGKSPKLFYDTSKLGVSRRFSGRSGSGTDY TLTIISLKPEDFAAYYCQQWSSNPQYTFGGGTKLE IK
SEQ ID NO: 3223	VL	D- VL-H.39	DIVLTQTPLSSPVTLGQPASISCSVSSSVSYMHY QQRPQGPPKLLIYDTSKLGVPDRFSGSGAGTDY TLKISRVEAEDVGVYYCQQWSSNPQYTFGGGTKLE IK
SEQ ID NO: 3224	VL	D- VL-H.40	EITLTQSPAFMSATPGDKVNISCSVSSSVSYMHY QQKPGEPKFIYDTSKLGIPPRFSGSGYGTDY TLTINNIESEDAAYYYCQQWSSNPQYTFGGGTKLE IK
Variable HEAVY chain (VH)			
SEQ ID NO: 3225	VH	D- VH-H.1	EVQLVESGGGLVKPGGSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNSKNTLYLQMNSLKTEDTAVYYCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3226	VH	D- VH-H.2	EVQLVESGGALVKPGGSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNSKNTLYLQMNSLKTEDTAVYYCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3227	VH	D- VH-H.3	EVQLVESGGGLVQPGGSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNAKNTLYLQMNSLRAEDTAVYYCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3228	VH	D- VH-H.4	EVQLVESGGGLVQPGGSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNAKNSLYLQMNSLRAEDTAVYYCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3229	VH	D- VH-H.5	EVQLVESGGGLVQPGGSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNSKNSLYLQMNSLKTEDTAVYYCSRHGGNFFD YWGQGTITVTVSS

SEQ ID NO: 3230	VH	D- VH-H.6	EVQLVESGGGLVQPGGSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNAKNSLYLQMNSLRAEDMAVYYCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3231	VH	D- VH-H.7	EVQLVESGGGLVQPGGSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNAKNTLYLQMNSLRAEDMAVYYCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3232	VH	D- VH-H.8	EVQLVESGGGLVKPGRSLRLSCTVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNSKNILYLQMNSLKTEDTAVYYCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3233	VH	D- VH-H.9	EVQLVESGGGLVKPGGSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNAKNSLYLQMNSLRAEDTAVYYCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3234	VH	D- VH- H.10	EVQLVESGGGLVQPGGSLKLSCAVSGFTFRSYGMS WVRQASGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNSKNTLYLQMNSLKTEDTAVYYCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3235	VH	D- VH- H.11	QVQLVESGGGVVQPGGSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNSKNTLYLQMNSLRAEDTAVYYCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3236	VH	D- VH- H.12	QVQLVESGGGVVQPGRSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNSKNTLYLQMSSLRAEDTAVYYCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3237	VH	D- VH- H.13	EVQLVESGGGLVQPGGSLRLSCPVSFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNANNSLYLQMNSLRAEDTAVYYCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3238	VH	D- VH- H.14	EVQLVESGGGLVQPGRSLRLSCTVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNSKNILYLQMNSLKTEDTAVYYCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3239	VH	D- VH- H.15	EVQLVESGGGLVQPGPSLRLSCTVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNSKNILYLQMNSLKTEDTAVYYCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3240	VH	D- VH- H.16	EVQLVESGGGLVQPGGSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNSKNTLYLQMNSLRAEDTAVYYCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3241	VH	D- VH- H.17	EVQLVESGGGLVQPGGSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNAKNSLYLQMNSLRDEDTAVYYCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3242	VH	D- VH- H.18	QVQLVESGGGLVKPGGSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI

			SRDNAKNSLYLQMNSLRAEDTAVYYCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3243	VH	D- VH- H.19	QVQLVESGGGVVQPGRSRLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNSKNTLYLQMNSLRAEDTAVYYCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3244	VH	D- VH- H.20	EVQLLESGGGLVQPGGSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNSKNTLYLQMNSLRAEDTAVYYCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3245	VH	D- VH- H.21	EVQLVESGGGLVQPGGSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRHNSKNTLYLQMNSLRAEDTAVYYCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3246	VH	D- VH- H.22	EVQLVESGGGLIQPGGSLRLSCAVSGFTFRSYGMS WVRQPPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNSKNTLYLQMNSLRAEDTAVYYCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3247	VH	D- VH- H.23	EVQLVESGGGLIQPGGSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNSKNTLYLQMNSLRAEDTAVYYCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3248	VH	D- VH- H.24	EVQLVESGGGLVQPGRSRLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNAKNSLYLQMNSLRAEDTALYYCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3249	VH	D- VH- H.25	QVQLVESGGGVVQPGRSRLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNSKNRLYLQMNSLRAEDTAVYYCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3250	VH	D- VH- H.26	QVQLVESGGGVVQPGRSRLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNSKNTLYLQMNSLRAEGTAVYYCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3251	VH	D- VH- H.27	QVQLVESGGGVVQPGRSRLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFAI SRDNSKNTLYLQMNSLRAEDTAVYYCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3252	VH	D- VH- H.28	QVQLVDSGGGVVQPGRSRLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNSKNTLYLQMNSLRAEDTAVYYCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3253	VH	D- VH- H.29	EVQLVESGGGVVRPGGSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNAKNSLYLQMNSLRAEDTALYHCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3254	VH	D- VH- H.30	EVQLVESGGVVVQPGGSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNSKNSLYLQMNSLRAEDTALYYCSRHGGNFFD YWGQGTITVTVSS

SEQ ID NO: 3255	VH	D- VH- H.31	EVQLVESGGGVVQPGGSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNSKNSLYLQMNSLRTEDTALYYCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3256	VH	D- VH- H.32	EVQLVESGGGVVQPGGSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNSKNSLYLQMNSLRTEDTALYYCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3257	VH	D- VH- H.33	EVQLVETGGGLIQPGGSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNSKNTLYLQMNSLRAEDTAVYYCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3258	VH	D- VH- H.34	EVQLVESGGGLVQPGGSLRLSCAVSGFTFRSYGMS WVRQATGKGLEWVALISSGGSYTTYTDSVKGRFTI SRENAKNSLYLQMNSLRAGDTAVYYCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3259	VH	D- VH- H.35	EVQLVESRGVLVQPGGSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNSKNTLHLQMNSLRAEDTAVYYCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3260	VH	D- VH- H.36	EVQLVESGGGLVQPGRSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNAKNSLYLQMNSLRAEDMALYYCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3261	VH	D- VH- H.37	QVQLVESGGGLVQPGGSLRLSCSVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNSKNTLYLQMNSLRAEDTAVYYCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3262	VH	D- VH- H.38	EVQLVESGGGLVQPGGSLRLSCSVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNSKNTLYLQMSSLRAEDTAVYYCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3263	VH	D- VH- H.39	QVQLVESGGGVVQPGRSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNSTNTLFLQMNSLRAEDTAVYYCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3264	VH	D- VH- H.40	QVQLLESGGGLVKPGGSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNAKNSLYLQMNSLRAEDTAVYYCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3265	VH	D- VH- H.41	EVQLVESGEGLVQPGGSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNSKNTLYLQMGSLRAEDMAVYYCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3266	VH	D- VH- H.42	EVQLVESGGGLVQPGGSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNSKNTLYLQMGSLRAEDMAVYYCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3267	VH	D- VH- H.43	EVQLVESGGGLVQPGGSLRLSCSVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI

			SRDNSKNTLYVQMSSLRAEDTAVYYCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3268	VH	D- VH- H.44	EVQLVESGGGLVQPGGSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFII SRDNSRNSLYLQKNRRRAEDMAVYYCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3269	VH	D- VH- H.45	EVQLVESGGGLVQPGGSLRLSCAVSGFTFRSYGMS WVHQAPGKGLEWVALISSGGSYTTYTDSVKGRFII SRDNSRNTLYLQTNLSRAEDTAVYYCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3270	VH	D- VH- H.46	EVHLVESGGGLVQPGGALRLSCAVSGFTFRSYGMS WVRQATGKGLEWVALISSGGSYTTYTDSVKGRFTI SRENAKNSLYLQMNSLRAGDTAVYYCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3271	VH	D- VH- H.47	EVQLVESGGGLVQPRGSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNSKNTLYLQMNNLRAEGTAVYYCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3272	VH	D- VH- H.48	EVQLVESGGGLVQPRGSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNSKNTLYLQMNNLRAEGTAAYYCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3273	VH	D- VH- H.49	QVQLVQSGAEVKKPGASVKVCKVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI TRDNSTNTLYMELSSLRSEDVAVYYCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3274	VH	D- VH- H.50	QVQLVQSGSELKKPGASVKVCKVSGFTFRSYGMS WVRQAPGQGLEWVALISSGGSYTTYTDSVKGRFVI SRDNSVNTLYLQISSSLKAEDTAVYYCSRHGGNFFD YWGQGTITVTVSS

In some embodiments, the anti-TCR β V10 antibody molecule comprises a VH or a VL of an antibody described in **Table 12A**, or a sequence with at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or more identity thereto.

- 5 In some embodiments, the anti-TCR β V10 antibody molecule comprises a VH and a VL of an antibody described in **Table 12A**, or a sequence with at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or more identity thereto.

Additional anti-TCRV β antibodies

- 10 Additional exemplary anti-TCR β V antibodies of the disclosure are provided in **Table 13A**. In some embodiments, the anti-TCR β V antibody is a humanized antibody, e.g., as provided in **Table 13A**. In some embodiments, the anti-TCR β V antibody comprises one or more (e.g., all

three) of a LC CDR1, LC CDR2, and LC CDR3 provided in **Table 13A**; and/or one or more (e.g., all three) of a HC CDR1, HC CDR2, and HC CDR3 provided in **Table 13A**, or a sequence with at least 95% identity thereto. In some embodiments, the anti-TCR β V antibody comprises a variable heavy chain (VH) and/or a variable light chain (VL) provided in **Table 13A**, or a sequence with at least 95% identity thereto.

Table 13A: Amino acid sequences for additional anti-TCR β V antibodies

Amino acid and nucleotide sequences for murine and humanized antibody molecules which bind to various TCRVB families are disclosed. The amino acid the heavy and light chain CDRs, and the amino acid and nucleotide sequences of the heavy and light chain variable regions, and the heavy and light chains are shown. Antibodies disclosed in the table include, MPB2D5, CAS1.1.3, IMMU222, REA1062, JOVI-3 and IMMU546. MPB2D5 binds human TCR β V 20-1 (TCR β V2 per old nomenclature). CAS1.1.3 binds human TCR β V 27 (TCR β V14 per old nomenclature). IMMU 222 binds human TCR β V 6-5, TCR β V 6-6, or TCR β V 6-9 (TCR β V13.1 per old nomenclature). REA1062 binds human TCR β V 5-1). JOVI-3 binds human TCR β V 28 (TCR β V3.1 per old nomenclature). IMMU546 binds human TCR β V 2.

Antibody G (murine) binds to human TCRVβ 20-1		
SEQ ID NO: 1102	HC CDR1 (Kabat)	SAYMH
SEQ ID NO: 1103	HC CDR2 (Kabat)	RIDPATGKTKYAPKFQA
SEQ ID NO: 1104	HC CDR3 (Kabat)	SLNWDYGLDY
SEQ ID NO: 1105	HC CDR1 (Chothia)	GFNIKSA
SEQ ID NO: 1106	HC CDR2 (Chothia)	DPATGK
SEQ ID NO: 1104	HC CDR3 (Chothia)	SLNWDYGLDY
SEQ ID NO: 7289	HC CDR1 (Combined)	GFNIKSA YMH
SEQ ID NO: 1103	HC CDR2 (Combined)	RIDPATGKTKYAPKFQA
SEQ ID NO: 1104	HC CDR3 (Combined)	SLNWDYGLDY
SEQ ID NO: 1107	LC CDR1 (Kabat)	RASKSVSILGTHLIH
SEQ ID NO: 1108	LC CDR2 (Kabat)	AASNLES
SEQ ID NO: 1109	LC CDR3 (Kabat)	QQSIEDPWT
SEQ ID NO: 1110	LC CDR1 (Chothia)	SKSVSILGTHL
SEQ ID NO: 1108	LC CDR2 (Chothia)	AASNLES
SEQ ID NO: 1109	LC CDR3 (Chothia)	QQSIEDPWT
SEQ ID NO: 1107	LC CDR1 (Combined)	RASKSVSILGTHLIH
SEQ ID NO: 1108	LC CDR2 (Combined)	AASNLES
SEQ ID NO: 1109	LC CDR3(Combined)	QQSIEDPWT
SEQ ID NO: 1111	VL	DIVLTQSPASLA VSLGQRATISCRASKSVSILGTHL IHWYQQKPGQP PPKLLIYAASNLESGV PARFSGSGS

		ETVFTLNIHPVEEEDAATYFCQQSIEDPWTFGGGT KLGK
SEQ ID NO: 1112	VH	EVQLQQSVADLVRPGASLKLSTASGFNIKSA YMHVVIQRPDQGPCLGRIDPATGKTKYAPKFQ AKATITADTSSNTAYLQLSSLTSEDTAIYYCT RSLNWDYGLDYWGQGTSTVTVSS
Antibody G-H (humanized) VHs binds to human TCRVβ 20-1		
SEQ ID NO: 1113	VH - 1	QVQLVQSGAEVKKPGASVKVSKASGFNIKSA YMHVVRQAPGQGLEWMGRIDPATGKTKYAPKF QARVTMTADTSTNTAYMELSSLRSEDTAVYYC ARSLNWDYGLDYWGQGTSLTVTVSS
SEQ ID NO: 1114	VH - 2	QVQLVQSGAEVKKPGASVKVSKASGFNIKSA YMHVVRQAPGQEPGCMGRIDPATGKTKYAPKF QARVTMTADTSINTAYTELSSLRSEDTATYYC ARSLNWDYGLDYWGQGTSLTVTVSS
SEQ ID NO: 1115	VH - 3	QVQLVQSGAEVKKPGSSVKVSKASGFNIKSA YMHVVRQAPGQGLEWMGRIDPATGKTKYAPKF QARVTITADTSTNTAYMELSSLRSEDTAVYYC ARSLNWDYGLDYWGQGTSLTVTVSS
SEQ ID NO: 1116	VH - 4	QVQLVQSGAEVKKPGASVKVSKASGFNIKSA YMHVVRQAPGQRLEWMGRIDPATGKTKYAPKF QARVTITADTSANTAYMELSSLRSEDTAVYYC ARSLNWDYGLDYWGQGTSLTVTVSS
Antibody G-H (humanized) VLs binds to human TCRVβ 20-1		
SEQ ID NO: 1117	VL - 1	EIVLTQSPATLSLSPGERATLSCRASKSVSILG THLIHWYQQKPGQAPRLLIYAASNLESGIPAR FSGSGSETDFTLTISLSEPEDFAVYFCQQSIE DPFGGGTKVEIK
SEQ ID NO: 1118	VL - 2	EIVLTQSPATLSLSPGERATLSCRASKSVSILG THLIHWYQQKPGGLAPRLLIYAASNLESGIPDR FSGSGSETDFTLTISRLEPEDFAVYFCQQSIE DPFGGGTKVEIK
SEQ ID NO: 1119	VL - 3	EIVLTQSPGTLTLSPGERATLSCRASKSVSILG THLIHWYQQKPGQAPRLLIYAASNLESGIPDR FSGSGSETDFTLTISRLEPEDFAVYFCQQSIE DPFGGGTKVEIK
Antibody H (murine) binds to human TCRVβ 27		
SEQ ID NO: 1120	HC CDR1 (Kabat)	DTYMY
SEQ ID NO: 1121	HC CDR2 (Kabat)	RIDPANGNTKYDPKFQD
SEQ ID NO: 1122	HC CDR3 (Kabat)	GSYYYAMDY
SEQ ID NO: 1123	HC CDR1 (Chothia)	GFKTEDT
SEQ ID NO: 1124	HC CDR2 (Chothia)	DPANGN
SEQ ID NO: 1122	HC CDR3 (Chothia)	GSYYYAMDY
SEQ ID NO: 1125	HC CDR1 (Combined)	GFKTEDTYMY
SEQ ID NO: 1121	HC CDR2 (Combined)	RIDPANGNTKYDPKFQD
SEQ ID NO: 1122	HC CDR3 (Combined)	GSYYYAMDY
SEQ ID NO: 1126	LC CDR1 (Kabat)	RASEVDSYGNFSMH
SEQ ID NO: 1127	LC CDR2 (Kabat)	RASNLES
SEQ ID NO: 1128	LC CDR3 (Kabat)	QQSNEDPYT

SEQ ID NO: 7290	LC CDR1 (Chothia)	SESVDSYGNSF
SEQ ID NO: 1127	LC CDR2 (Chothia)	RASNLES
SEQ ID NO: 1128	LC CDR3 (Chothia)	QQSNEDPYT
SEQ ID NO: 1126	LC CDR1 (Combined)	RASESVDSYGNSFMH
SEQ ID NO: 1127	LC CDR2 (Combined)	RASNLES
SEQ ID NO: 1128	LC CDR3(Combined)	QQSNEDPYT
SEQ ID NO: 1129	VL	DIVLTQSPASLAVSLGQRATISCRASESVDSYGNSF MHWYQQKPGQPPKLLIYRASNLESGIPARFSGSGS RTDFTLTINPVEADDVATYYCQQSNEDPYTFGGG TKLEIK
SEQ ID NO: 1130	VH	EVQLQQSGAELVKPGASVKLSCTASGFKTEDTYM YWVKQRPEQGLEWIGRIDPANGNTKYDPKFQDK ATITADSSSNTAYLQLSSLPS EDTAVYYCARGSY YAMDYWGQGTSTVTVSS
Antibody H-H (humanized) VHs binds to human TCRVβ 27		
SEQ ID NO: 1131	VH - 1	QVQLVQSGAEVKKPGSSVKVSKASGFKTEDTY MYWVRQAPGQGLEWIGRIDPANGNTKYDPKFQD RATITADSSNTAYMELSSLRSED TAVYYCARGS YYYAMDYWGQGTSLTVTVSS
SEQ ID NO: 1132	VH - 2	QVQLVQSGAEVKKPGASVKVSKASGFKTEDTY MYWVRQAPGQRLEWIGRIDPANGNTKYDPKFQD RATITADSSANTAYMELSSLRSED TAVYYCARGS YYYAMDYWGQGTSLTVTVSS
SEQ ID NO: 1133	VH - 3	EVQLVESGGGLVQPGGSLKLSAASGFKTEDTYM YWVRQASGKGLEWIGRIDPANGNTKYDPKFQDR ATISADSSKNTAYLQMNSLKTED TAVYYCARGSY YYAMDYWGQGTSLTVTVSS
SEQ ID NO: 1134	VH - 4	EVQLVQSGAEVKKPGESLRISCKASGFKTEDTYM YWVRQMPGKGLEWIGRIDPANGNTKYDPKFQDQ ATISADSSINTAYLQWSSLKASDTAMYYCARGSY YYAMDYWGQGTSLTVTVSS
SEQ ID NO: 1135	VH - 5	QVQLVQSGSELKKPGASVKVSKASGFKTEDTY MYWVRQAPGQGLEWIGRIDPANGNTKYDPKFQD RAVISADSSVNTAYLQISSLKAED TAVYYCARGS YYYAMDYWGQGTSLTVTVSS
Antibody H-H (humanized) VLs Binds to human TCRVβ 27		
SEQ ID NO: 1136	VL - 1	DIVLTQSPDSLAVSLGERATINCRASESVDSYGNS FMHWYQQKPGQPPKLLIYRASNLESGVPDRFSGS GSRTDFTLTISSLQAEDVAVYYCQQSNEDPYTFGQ GTKLEIK
SEQ ID NO: 1137	VL - 2	EIVLTQSPATLSLSPGERATLSCRASESVD SYGNSF MHWYQQKPGQAPKLLIYRASNLESGIPARFSGSG SRTDFTLTISRLEPEDFAVYYCQQSNEDPYTFGQG TKLEIK
SEQ ID NO: 1138	VL - 3	DIQLTQSPSSLSASVGDRVITITCRASESVDSYGNSF MHWYQQKPGQAPKLLIYRASNLESGVPSRFSGSG SRTDFTLTISSLQPEDVATYYCQQSNEDPYTFGQG TKLEIK

SEQ ID NO: 1139	VL - 4	AIQLTQSPSSLSASVGDRVITITCRASESVDSYGNSF MHWYQQKPGKAPKLLIYRASNLSEGVPSRFSGSG SRTDFTLTISLQPEDFATYYCQQSNEDPYTFGQG TKLEIK
SEQ ID NO: 1140	VL - 5	EIVLTQSPDFQSVTPKEKVTITCRASESVDSYGNSF MHWYQQKPDQSPKLLIYRASNLSEGVPSRFSGSG SRTDFTLTINSLEAEDAATYYCQQSNEDPYTFGQG TKLEIK
Antibody I(murine) binds to human TCRVβ 6-5,6-6,6-9		
SEQ ID NO: 1141	HC CDR1 (Kabat)	SYAMS
SEQ ID NO: 1142	HC CDR2 (Kabat)	HISNGGDYIYYADTVKG
SEQ ID NO: 1143	HC CDR3 (Kabat)	PSYYSDPWFFDV
SEQ ID NO: 1144	HC CDR1 (Chothia)	GFTFRSY
SEQ ID NO: 1145	HC CDR2 (Chothia)	SNGGDY
SEQ ID NO: 1143	HC CDR3 (Chothia)	PSYYSDPWFFDV
SEQ ID NO: 1146	HC CDR1 (Combined)	GFTFRSYAMS
SEQ ID NO: 1142	HC CDR2 (Combined)	HISNGGDYIYYADTVKG
SEQ ID NO: 1143	HC CDR3(Combined)	PSYYSDPWFFDV
SEQ ID NO: 1147	LC CDR1 (Kabat)	SAGSSVSFMH
SEQ ID NO: 1148	LC CDR2 (Kabat)	DTSKLAS
SEQ ID NO: 1149	LC CDR3 (Kabat)	LQSGGFPLT
SEQ ID NO: 1150	LC CDR1 (Chothia)	GSSVSF
SEQ ID NO: 1148	LC CDR2 (Chothia)	DTSKLAS
SEQ ID NO: 1149	LC CDR3 (Chothia)	LQSGGFPLT
SEQ ID NO: 1147	LC CDR1 (Combined)	SAGSSVSFMH
SEQ ID NO: 1148	LC CDR2 (Combined)	DTSKLAS
SEQ ID NO: 1149	LC CDR3(Combined)	LQSGGFPLT
SEQ ID NO: 1151	VL	ENVLTQSPAIMASAPGEKVTMTCSAGSSVSFMHW YQQSSTSPKLWIYDTSKLASGVPGRFSGSGSGNS FSLTISSMEAEDVAIYYCLQSGGFPLTFGSGTKLEI K
SEQ ID NO: 1152	VH	DVKLVESGGLVQPGGSLRLSCAASGFTFRSYAM SWVRQTPPEKRLWVAHISNGGDYIYYADTVKGR FTISRDNARNLTLYLQMSSLKSEDTAMYYCTRPSY YSDPWFFDVWGTTTTVTVSS
Antibody I-H (humanized) VHs Binds to human TCRVβ 6-5,6-6,6-9		
SEQ ID NO: 1153	VH - 1	EVQLVESGGGLVQPGGSLRLSCAASGFTFRSYAM SWVRQAPGKGLEWVAHISNGGDYIYYADTVKGR FTISRDNAKNSLYLQMNSLRAEDTAVYYCTRPSY YSDPWFFDVWGQGTITVTVSS
SEQ ID NO: 1154	VH - 2	QVQLVESGGGVVQPGSLRLSCAASGFTFRSYAM SWVRQAPGKGLEWVAHISNGGDYIYYADTVKGR FTISRDNSKNTLYLQMSSLRAEDTAVYYCTRPSY YSDPWFFDVWGQGTITVTVSS
SEQ ID NO: 1155	VH - 3	EVQLVESGGGLVQPGGSLRLSCAASGFTFRSYAM SWVRQAPGKGLEWVAHISNGGDYIYYADTVKGR FTISRDNSKNTLYLQMNSLRAEDTAVYYCTRPSY YSDPWFFDVWGQGTITVTVSS

SEQ ID NO: 1156	VH - 4	QVQLVQSGSELKKPGASVKVSCASGFTFRSYAM SWVRQAPGQGLEWVAHISNGGDYIYYADTVKGR FVISRDNSVNTLYLQISSLKAEDTAVYYCTRPSYY SDPWFFDVWGQGTTVTVSS
SEQ ID NO: 1157	VH - 5	QVQLVQSGAEVKKPGASVKVSCASGFTFRSYA MSWVRQAPGQRLEWVAHISNGGDYIYYADTVKG RFTITRDNSANTLYMELSSLRSEDVAVYYCTRPSY YSDPWFFDVWGQGTTVTVSS
Antibody I-H (humanized) VLs Binds to human TCRVβ 6-5,6-6,6-9		
SEQ ID NO: 1158	VL - 1	ENVLTQSPATLSLSPGERATLSCSAGSSVSFMHWY QQKPGQAPKLLIYDTSKLASGIPARFSGSGSGNDF TLTISSLEPEDFAVYYCLQSGGFPLTFGQGGTKLEIK
SEQ ID NO: 1159	VL - 2	ENVLTQSPDFQSVTPKEKVTITCSAGSSVSFMHW YQQKPDQSPKLLIYDTSKLASGVPSRFSGSGSGND FTLTINSLEAEDAATYYCLQSGGFPLTFGQGGTKLEI K
SEQ ID NO: 1160	VL - 3	DNQLTQSPSSLSASVGDRVTITCSAGSSVSFMHW YQQKPGKVPKLLIYDTSKLASGVPSRFSGSGSGND FTLTISLQPEDVATYYCLQSGGFPLTFGQGGTKLEI K
SEQ ID NO: 1161	VL - 4	ANQLTQSPSSLSASVGDRVTITCSAGSSVSFMHW YQQKPGKAPKLLIYDTSKLASGVPSRFSGSGSGND FTLTISLQPEDFATYYCLQSGGFPLTFGQGGTKLEI K
SEQ ID NO: 1162	VL - 5	DNVLTQSPDSLAVSLGERATINCSAGSSVSFMHW YQQKPGQPPKLLIYDTSKLASGVPDFRSGSGSGND FTLTISLQAEDVAVYYCLQSGGFPLTFGQGGTKLE IK
Antibody IJ (murine), Binds to human TCRVβ 5-1		
SEQ ID NO: 1163	HC CDR1 (Kabat)	DYNIH
SEQ ID NO: 1164	HC CDR2 (Kabat)	YINPYNGRTGYNQKFKA
SEQ ID NO: 1165	HC CDR3 (Kabat)	WDGSSYFDY
SEQ ID NO: 1166	HC CDR1 (Chothia)	GYTFTDYNIH
SEQ ID NO: 1167	HC CDR2 (Chothia)	NPYNGR
SEQ ID NO: 1165	HC CDR3 (Chothia)	WDGSSYFDY
SEQ ID NO: 1166	HC CDR1 (Combined)	GYTFTDYNIH
SEQ ID NO: 1164	HC CDR2 (Combined)	YINPYNGRTGYNQKFKA
SEQ ID NO: 1165	HC CDR3(Combined)	WDGSSYFDY
SEQ ID NO: 1168	LC CDR1 (Kabat)	SASSSVSYMH
SEQ ID NO: 1169	LC CDR2 (Kabat)	EISKLAS
SEQ ID NO: 1170	LC CDR3 (Kabat)	QQWNYPLLT
SEQ ID NO: 1297	LC CDR1 (Chothia)	SSSVSY
SEQ ID NO: 1169	LC CDR2 (Chothia)	EISKLAS
SEQ ID NO: 1170	LC CDR3 (Chothia)	QQWNYPLLT
SEQ ID NO: 1168	LC CDR1 (Combined)	SASSSVSYMH
SEQ ID NO: 1169	LC CDR2 (Combined)	EISKLAS
SEQ ID NO: 1170	LC CDR3(Combined)	QQWNYPLLT

SEQ ID NO: 1171	VL	EIVLTQSPAITAASLGQKVTITCSASSSVSYMHWY QQKSGTSPKPWIYEISKLASGVPARFSGSGSGTSY SLTISSMEAEDAAIYYCQQWNYPLLTFGAGTKLE LK
SEQ ID NO: 1172	VH	EVQLQQSGPVLVKPGASVRMSCKASGYTFTDYN HWVKQSHGRSLEWVGYPYNGRTGYNQKFKA KATLTVDKSSSTAYMDLRSLTSEDSAVYYCARW DGSSYFDYWGQGTTTLTVSS
Antibody J-H(humanized) VHs Binds to human TCRVβ 5-1		
SEQ ID NO: 1173	VH - 1	QVQLVQSGAEVKKPGSSVKVSCASGYTFTDYN HWVRQAPGQGLEWVGYPYNGRTGYNQKFKA RATLTVDKSTSTAYMELSSLRSEDTAVYYCARW DGSSYFDYWGQGTTTVTVSS
SEQ ID NO: 1174	VH - 2	QVQLVQSGAEVKKPGASVKVSCASGYTFTDYN HWVRQAPGQGLEWVGYPYNGRTGYNQKFKA RATLTVDKSTSTAYMELRSLRSDDMAVYYCARW DGSSYFDYWGQGTTTVTVSS
SEQ ID NO: 1175	VH - 3	QVQLVQSGAEVKKPGASVKVSCASGYTFTDYN HWVRQATGQGLEWVGYPYNGRTGYNQKFKA RATLTVNKSISTAYMELSSLRSEDTAVYYCARW DGSSYFDYWGQGTTTVTVSS
SEQ ID NO: 1176	VH - 4	EVQLVESGGGLVQPGRSLRLSCTASGYTFTDYN HWVRQAPGKGLEWVGYPYNGRTGYNQKFKA ATLSVDKSKSIAYLQMNSLKTEDTAVYYCARW DGSSYFDYWGQGTTTVTVSS
SEQ ID NO: 1177	VH - 5	QVQLVQSGSELKKPGASVKVSCASGYTFTDYN HWVRQAPGQGLEWVGYPYNGRTGYNQKFKA RAVLSVDKSVSTAYLQISSLKAEDTAVYYCARW DGSSYFDYWGQGTTTVTVSS
Antibody J-H (humanized) VLs Binds to human TCRVβ 5-1		
SEQ ID NO: 1178	VL - 1	EIVLTQSPATLSLSPGERATLSCSASSSVSYMHWY QQKPGQAPKLLIYEISKLASGIPARFSGSGSGTDYT LTISLLEPEDFAVYYCQQWNYPLLTFGQGGTKLEIK
SEQ ID NO: 1179	VL - 2	EIVLTQSPATLSLSPGERATLSCSASSSVSYMHWY QQKPGQAPKLLIYEISKLASGIPARFSGSGSGTDYT LTISRLEPEDFAVYYCQQWNYPLLTFGQGGTKLEIK
SEQ ID NO: 1180	VL - 3	EIVLTQSPDFQSVTPKEKVTITCSASSSVSYMHWY QQKPDQSPKLLIYEISKLASGVPSRFSGSGSGTDYT LTINSLEAEDAATYYCQQWNYPLLTFGQGGTKLEI K
SEQ ID NO: 1181	VL - 4	DIQLTQSPSFLSASVGDRVITITCSASSSVSYMHWY QQKPGKAPKLLIYEISKLASGVPSRFSGSGSGTEYT LTISLQPEDFATYYCQQWNYPLLTFGQGGTKLEIK
SEQ ID NO: 1182	VL - 5	AIQLTQSPSSLSASVGDRVITITCSASSSVSYMHWY QQKPGKAPKLLIYEISKLASGVPSRFSGSGSGTDY TLTISLQPEDFATYYCQQWNYPLLTFGQGGTKLEI K

SEQ ID NO: 1183	VL - 6	AIRLTQSPFSLASVSGDRVITITCSASSSVSYMHWY QQKPAKAPKLFIEISKLASGVPSRFSGSGSGTDY TLTISSLQPEDFATYYCQQWNYPLLTFGQGGTKLEI K
SEQ ID NO: 1184	VL - 7	DIVLTQSPDSLAVSLGERATINCSASSSVSYMHWY QQKPGQPPKLLIYEISKLASGVDPDRFSGSGSGTDY TLTISSLQAEDVAVYYCQQWNYPLLTFGQGGTKLE IK
Antibody K (murine), binds to human TCRVβ 28		
SEQ ID NO: 1185	HC CDR1 (Kabat)	GSWMN
SEQ ID NO: 1186	HC CDR2 (Kabat)	RIYPGDGD TDYSGKFKG
SEQ ID NO: 1187	HC CDR3 (Kabat)	SGYFNYVPVFDY
SEQ ID NO: 1188	HC CDR1 (Chothia)	GYTFSGS
SEQ ID NO: 1189	HC CDR2 (Chothia)	YPGDGD
SEQ ID NO: 1187	HC CDR3 (Chothia)	SGYFNYVPVFDY
SEQ ID NO: 1190	HC CDR1 (Combined)	GYTFSGSWMN
SEQ ID NO: 1186	HC CDR2 (Combined)	RIYPGDGD TDYSGKFKG
SEQ ID NO: 1187	HC CDR3 (Combined)	SGYFNYVPVFDY
SEQ ID NO: 1191	LC CDR1 (Kabat)	SANSTVGYIH
SEQ ID NO: 1192	LC CDR2 (Kabat)	TTSNLAS
SEQ ID NO: 1193	LC CDR3 (Kabat)	HQWSFYPT
SEQ ID NO: 1194	LC CDR1 (Chothia)	NSTVGY
SEQ ID NO: 1192	LC CDR2 (Chothia)	TTSNLAS
SEQ ID NO: 1193	LC CDR3 (Chothia)	HQWSFYPT
SEQ ID NO: 1191	LC CDR1 (Combined)	SANSTVGYIH
SEQ ID NO: 1192	LC CDR2 (Combined)	TTSNLAS
SEQ ID NO: 1193	LC CDR3 (Combined)	HQWSFYPT
SEQ ID NO: 1195	VL	QIVLTQSPAIMSASLGEEIALTCSANSTVGYIHWY QQKSGTSPKLLIYTTSNLASGVPSRFSGSGSGTFYS LTISSVEAEDAADYFCHQWSFYPTFGGGTKLEIK
SEQ ID NO: 1196	VH	QIQLQQSGPEVVKPGASVQISCKASGYTFSGSW NWVKQRPGKGLEWIGRIYPGDGD TDYSGKFKGR ATLTADKSSSTAYMRLSSLTSEDSAVYFCARSGYF NYVPVFDYWGQGTTLVSS
Antibody K-H(humanized) VHs Binds to human TCRVβ 28		
SEQ ID NO: 1197	VH - 1	QIQLVQSGAEVKKPGASVKVSCKASGYTFSGSW MNWVRQAPGQGLEWIGRIYPGDGD TDYSGKFKG RATLTADKSTSTAYMELSSLRSED TAVYYCARSG YFNYVPVFDYWGQGT TTVTVSS
SEQ ID NO: 1198	VH - 2	QIQLVQSGAEVKKPGSSVKVSCKASGYTFSGSW NWVRQAPGQGLEWIGRIYPGDGD TDYSGKFKGR ATLTADKSTSTAYMELSSLRSED TAVYYCARSGY FNYVPVFDYWGQGT TTVTVSS
SEQ ID NO: 1199	VH - 3	EIQLVQSGAEVKKPGESLKISCKASGYTFSGSW NWVRQMPGKGLEWIGRIYPGDGD TDYSGKFKGQ ATLSADKSISTAYLQWSSLKASDTAMYYCARSGY FNYVPVFDYWGQGT TTVTVSS

SEQ ID NO: 1200	VH - 4	QIQLVQSGSELKKPGASVKVSCKASGYTFSGSWM NWVRQAPGQGLEWIGRIYPGDGTDYSGKFKGR AVLSADKSVSTAYLQISSLKAEDTAVYYCARSGY FNYVPVFDYWGQGTTVTVSS
SEQ ID NO: 1201	VH - 5	QIQLVQSGSELKKPGASVKVSCKASGYTFSGSWM NWVRQAPGQGLEWIGRIYPGDGTDYSGKFKGR AVLSADKSVSMAYLQISSLKAEDTAVYYCARSGY FNYVPVFDYWGQGTTVTVSS
SEQ ID NO: 1202	VH - 6	EIQLVESGGGLVQPGRSLRLSCTASGYTFSGSWM NWVRQAPGKGLEWIGRIYPGDGTDYSGKFKGR ATLSADKSKSIAYLQMNSLKTEDTAVYYCARSGY FNYVPVFDYWGQGTTVTVSS
Antibody K-H (humanized) VLs Binds to human TCRVβ 28		
SEQ ID NO: 1203	VL - 1	EIVLTQSPATLSLSPGERATLSCSANSTVGYIHWY QQKPGQAPKLLIYTTSNLAGIPARFSGSGSGTDY TLTISSLEPEDFAVYFCHQWSFYPTFGQGTKLEIK
SEQ ID NO: 1204	VL - 2	DIQLTQSPSFLSASVGDRVITITCSANSTVGYIHWY QQKPGKAPKLLIYTTSNLAGVPSRFSGSGSGTEY TLTISSLQPEDFATYFCHQWSFYPTFGQGTKLEIK
SEQ ID NO: 1205	VL - 3	EIVLTQSPATLSLSPGERATLSCSANSTVGYIHWY QQKPGQAPKLLIYTTSNLAGIPARFSGSGPGTDY TLTISSLEPEDFAVYFCHQWSFYPTFGQGTKLEIK
SEQ ID NO: 1206	VL - 4	DIVLTQSPDSLAVSLGERATINCSANSTVGYIHWY QQKPGQPPKLLIYTTSNLAGVPDRFSGSGSGTDY TLTISSLQAEDVAVYFCHQWSFYPTFGQGTKLEIK
SEQ ID NO: 1207	VL - 5	EIVLTQSPDFQSVTPKEKVTITCSANSTVGYIHWY QQKPDQSPKLLIYTTSNLAGVPSRFSGSGSGTDY TLTINSLEAEDAATYFCHQWSFYPTFGQGTKLEIK
Antibody L (murine), binds to human TCRVβ 4-1,4-2,4-3		
SEQ ID NO: 1208	HC CDR1 (Kabat)	DYYMY
SEQ ID NO: 1209	HC CDR2 (Kabat)	TISGGGSYTYSPDSVKG
SEQ ID NO: 1210	HC CDR3 (Kabat)	ERDIYYGNFNAMVY
SEQ ID NO: 1211	HC CDR1 (Chothia)	GFTFSDY
SEQ ID NO: 1212	HC CDR2 (Chothia)	SGGGSY
SEQ ID NO: 1210	HC CDR3 (Chothia)	ERDIYYGNFNAMVY
SEQ ID NO: 1213	HC CDR1 (Combined)	GFTFSDYYMY
SEQ ID NO: 1209	HC CDR2 (Combined)	TISGGGSYTYSPDSVKG
SEQ ID NO: 1210	HC CDR3(Combined)	ERDIYYGNFNAMVY
SEQ ID NO: 1214	LC CDR1 (Kabat)	RASKSVSTSGYSYMH
SEQ ID NO: 1215	LC CDR2 (Kabat)	LASNLES
SEQ ID NO: 1216	LC CDR3 (Kabat)	QHSRDLPWT
SEQ ID NO: 1217	LC CDR1 (Chothia)	SKSVSTSGYSY
SEQ ID NO: 1215	LC CDR2 (Chothia)	LASNLES
SEQ ID NO: 1216	LC CDR3 (Chothia)	QHSRDLPWT
SEQ ID NO: 1214	LC CDR1 (Combined)	RASKSVSTSGYSYMH
SEQ ID NO: 1215	LC CDR2 (Combined)	LASNLES
SEQ ID NO: 1216	LC CDR3(Combined)	QHSRDLPWT

SEQ ID NO: 1218	VL	DIVLTQSPVSLTVSLGQRATISCRASKSVSTSGYSY MHWYQQKPGQPPKLLIYLASNLESGVPARFSGSG SGTDFTLNIHPVEEEDAATYYCQHSRDLPWTFGG GTKLEIK
SEQ ID NO: 1219	VH	EVQLVESGGGLVKPGGSLKLSAASGFTFSDYYM YWVRQTPEKRLVWVATISGGGSYTYSPDSVKGRF TISRDNKNNLYLQMSSLRSEDAMYFCARERDI YYGNFNAMVYWGRGTSVTVSS
Antibody L-H (humanized) VHs Binds to human TCRVβ 4-1,4-2,4-3		
SEQ ID NO: 1220	VH - 1	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDYYM YWVRQAPGKGLEWVATISGGGSYTYSPDSVKGR FTISRDNKNTLYLQMNSLRAEDTAVYYCARERD IYYGNFNAMVYWGRGTLTVSS
SEQ ID NO: 1221	VH - 2	EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYYM YWVRQAPGKGLEWVATISGGGSYTYSPDSVKGR FTISRDNKNSLYLQMNSLRAEDTAVYYCARERD IYYGNFNAMVYWGRGTLTVSS
SEQ ID NO: 1222	VH - 3	QVQLVESGGGVVQPGSLRLSCAASGFTFSDYY MYWVRQAPGKGLEWVATISGGGSYTYSPDSVK GRFTISRDNKNTLYLQMNSLRAEDTAVYYCAR ERDIYYGNFNAMVYWGRGTLTVSS
SEQ ID NO: 1223	VH - 4	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYM YWVRQAPGKGLEWVATISGGGSYTYSPDSVKGRF TISRDNKNSLYLQMNSLRAEDTAVYYCARERDI YYGNFNAMVYWGRGTLTVSS
Antibody L-H(humanized) VLs Binds to human TCRVβ 4-1,4-2,4-3		
SEQ ID NO: 1224	VL - 1	EIVLTQSPGTLSPGERATLSCRASKSVSTSGYSY MHWYQQKPGQAPRLIYLASNLESGIPDRFSGSGS GTDFTLTISRLEPEDFAVYYCQHSRDLPWTFGGGT KVEIK
SEQ ID NO: 1225	VL - 2	EIVLTQSPATLSPGERATLSCRASKSVSTSGYSY MHWYQQKPGQAPRLIYLASNLESGIPARFSGSGS GTDFTLTISLLEPEDFAVYYCQHSRDLPWTFGGGT KVEIK
SEQ ID NO: 1226	VL - 3	DIQLTQSPSTLSASVGDRVTITCRASKSVSTSGYSY MHWYQQKPGKAPKLLIYLASNLESGVPSRFSGSG SGTEFTLTISLQPDDEFATYYCQHSRDLPWTFGGG TKVEIK
SEQ ID NO: 1227	VL - 4	AIQLTQSPSSLSASVGDRVTITCRASKSVSTSGYSY MHWYQQKPGKAPKLLIYLASNLESGVPSRFSGSG SGTDFTLTISLQPEDFAVYYCQHSRDLPWTFGGG TKVEIK
Antibody M (murine), binds to human TCRVβ 19		
SEQ ID NO: 1229	HC CDR1 (Kabat)	GYFWN
SEQ ID NO: 1230	HC CDR2 (Kabat)	YISYDGSNNYNPSLKN
SEQ ID NO: 1231	HC CDR3 (Kabat)	PSPGTGYAVDY
SEQ ID NO: 1232	HC CDR1 (Chothia)	GYSITSGY

SEQ ID NO: 1233	HC CDR2 (Chothia)	SYDGSN
SEQ ID NO: 1231	HC CDR3 (Chothia)	PSPGTGYAVDY
SEQ ID NO: 1234	HC CDR1 (Combined)	GYSITSGYFWN
SEQ ID NO: 1230	HC CDR2 (Combined)	YISYDGSNNYNPSLKN
SEQ ID NO: 1231	HC CDR3(Combined)	PSPGTGYAVDY
SEQ ID NO: 1235	LC CDR1 (Kabat)	RSSQSLVHSNGNTYLH
SEQ ID NO: 1236	LC CDR2 (Kabat)	KVSNRFS
SEQ ID NO: 1237	LC CDR3 (Kabat)	SQSTHVPFT
SEQ ID NO: 1238	LC CDR1 (Chothia)	SQSLVHSNGNTY
SEQ ID NO: 1236	LC CDR2 (Chothia)	KVSNRFS
SEQ ID NO: 1237	LC CDR3 (Chothia)	SQSTHVPFT
SEQ ID NO: 1235	LC CDR1 (Combined)	RSSQSLVHSNGNTYLH
SEQ ID NO: 1236	LC CDR2 (Combined)	KVSNRFS
SEQ ID NO: 1237	LC CDR3(Combined)	SQSTHVPFT
SEQ ID NO: 1239	VL	NVVMQTPLSLPVSLGDQASISCRSSQSLVHSNGN TYLHWYLYKPGQSPKFLIYKVSNRFSGVPDRFSG GGSGTEFTLKISRVEAEDLGVYFCSQSTHVPFTFG SGTKLEIK
SEQ ID NO: 1240	VH	NVQLQESGPGLVKPSQSLSLTCSVAGYSITSGYFW NWIRQFPGNKLEWMGYISYDGSNNYNPSLKNRISI TRDTSKNQFFLKLNSVTTEDATYYCASPSPGTGY AVDYWGQGTSTVTVSS
Antibody M-H (humanized) VHs Binds to human TCRVβ 19		
SEQ ID NO: 1241	VH - 1	QVQLQESGPGLVKPSSETLSLTCTVSGYSITSGYFW NWIRQPPGKGLEWIGYISYDGSNNYNPSLKNRVTI SRDTSKNQFSLKLSSVTAADTAVYYCASPSPGTG YAVDYWGQGTSLTVTVSS
SEQ ID NO: 1242	VH - 2	QVQLQESGPGLVKPSSETLSLTCTVSGYSITSGYFW NWIRQPPGKGLEWIGYISYDGSNNYNPSLKNRVTI SRDTSKNQFSLKLSSVTAADTAVYYCASPSPGTG YAVDYWGQGTSLTVTVSS
SEQ ID NO: 1243	VH - 3	QVQLVESGGGLVQPGGSLRLSCSVSGYSITSGYF WNWVRQAPGKGLEWVGYSYDGSNNYNPSLKN RFTISRDTSKNTFYLMNSLRAEDTAVYYCASPS GTGYAVDYWGQGTSLTVTVSS
Antibody M-H (humanized) VLs Binds to human TCRVβ 19		
SEQ ID NO: 1244	VL - 1	VVMTQSPGTLSPGERATLSCRSSQSLVHSNGNT YLHWYQQKPGQAPRFLIYKVSNRFSGIPDRFSGSG SGTDFTLTISRLEPEDFAVYFCSQSTHVPFTFGQGT KLEIK
SEQ ID NO: 1245	VL - 2	EVVMTQSPATLSLSPGERATLSCRSSQSLVHSNGN TYLHWYQQKPGQAPRFLIYKVSNRFSGIPARFSGS GSGTDFTLTISLEPEDFAVYFCSQSTHVPFTFGQG TKLEIK
SEQ ID NO: 1246	VL - 3	EVVMTQSPATLSVSPGERATLSCRSSQSLVHSNGN TYLHWYQQKPGQAPRFLIYKVSNRFSGIPARFSGS

		GSgteftLTlssLQSEdFAVYfCSQSThVPFTFGQG TKLEIK
SEQ ID NO: 1247	VL - 4	DVQMTQSPSSLSASVGDRVTITCRSSQSLVHSNGN TYLHWYQQKPGKAPKFLIYKVSNRFSGVPSRFSG SGSGTDFTFTISSLQPEDIATYFCSQSTHVPFTFGQ GTKLEIK
Antibody N(murine), binds to human TCRVβ 9		
SEQ ID NO: 1248	HC CDR1 (Kabat)	DYIVH
SEQ ID NO: 1249	HC CDR2 (Kabat)	WINTYTGTPTYADDFEG
SEQ ID NO: 1250	HC CDR3 (Kabat)	SWRRGIRGIGFDY
SEQ ID NO: 1251	HC CDR1 (Chothia)	GYTFTDY
SEQ ID NO: 1252	HC CDR2 (Chothia)	NTYTGT
SEQ ID NO: 1250	HC CDR3 (Chothia)	SWRRGIRGIGFDY
SEQ ID NO: 1253	HC CDR1 (Combined)	GYTFTDYIVH
SEQ ID NO: 1249	HC CDR2 (Combined)	WINTYTGTPTYADDFEG
SEQ ID NO: 1250	HC CDR3(Combined)	SWRRGIRGIGFDY
SEQ ID NO: 1254	LC CDR1 (Kabat)	KASKSINKYLA
SEQ ID NO: 1255	LC CDR2 (Kabat)	DGSTLQS
SEQ ID NO: 1256	LC CDR3 (Kabat)	QQHNEYPPPT
SEQ ID NO: 1257	LC CDR1 (Chothia)	SKSINKY
SEQ ID NO: 1255	LC CDR2 (Chothia)	DGSTLQS
SEQ ID NO: 1256	LC CDR3 (Chothia)	QQHNEYPPPT
SEQ ID NO: 1254	LC CDR1 (Combined)	KASKSINKYLA
SEQ ID NO: 1255	LC CDR2 (Combined)	DGSTLQS
SEQ ID NO: 1256	LC CDR3(Combined)	QQHNEYPPPT
SEQ ID NO: 1258	VL	DVQMTQSPYNLAASPGESVSINCKASKSINKYLA WYQQKPGKPNKLLIYDGSTLQSGIPSRFSGSGSGT DFTLTIRGLEPEDFGLYYCQQHNEYPPPTFGAGTKL ELK
SEQ ID NO: 1259	VH	QLQLVQSGPELREPGEsvKISCKASGYTFTDYIVH WVKQAPGKGLKWMGWINTYTGTPTYADDFEGR FVFSLEASASTANLQISNLKNEdTATYFCARSWRR GIRGIGFDYWGQGVMVTVSS
Antibody N-H (humanized) VH's Binds to human TCRVβ 9		
SEQ ID NO: 1260	VH - 1	QLQLVQSGAEVKKPGASVKVSCKASGYTFTDYIV HWVRQAPGQGLEWMGWINTYTGTPTYADDFEG WVTMTLDASISTAYMELSLRSDDTAVYYCARS WRRGIRGIGFDYWGQGMVTVSS
SEQ ID NO: 1261	VH - 2	QLQLVQSGAEVKKPGASVKVSCKASGYTFTDYIV HWVRQAPGQGLEWMGWINTYTGTPTYADDFEG RVTMTLDASTAYMELSSLRSEDtAVYYCARS WRRGIRGIGFDYWGQGMVTVSS
SEQ ID NO: 1262	VH - 3	QLQLVQSGAEVKKPGASVKVSCKASGYTFTDYIV HWVRQAPGQRLEWMGWINTYTGTPTYADDFEG RVTITLDASASTAYMELSSLRSEdMAVYYCARSW RRGIRGIGFDYWGQGMVTVSS

SEQ ID NO: 1263	VH - 4	QLQLVQSGAEVKKPGASVKVSCKASGYTFTDYIV HWVRQATGQGLEWMGWINTYTGTPTYADDFEG RVTMTLNASISTAYMELSSLRSED TAVYYCARSW RRGIRGIGFDYWGQGTMTVTVSS
Antibody N-H (humanized) VL's Binds to human TCRVβ 9		
SEQ ID NO: 1264	VL - 1	EVVMTQSPGTLSPGERATLSC KASKSINKYLA WYQQKPGQAPRLLIYDGSTLQSGIPDRFSGSGSGT DFTLTISRLEPEDFAVYYCQQHNEYPPFTFGQGTKL EIK
SEQ ID NO: 1265	VL - 2	EVVMTQSPATLSLSPGERATLSC KASKSINKYLA WYQQKPGQAPRLLIYDGSTLQSGIPARFSGSGSGT DFTLTISLLEPEDFAVYYCQQHNEYPPFTFGQGTKL EIK
SEQ ID NO: 1266	VL - 3	DVQMTQSPSSLSASVGDRVTITCKASKSINKYLA WYQQKPGKAPKLLIYDGSTLQSGVPSRFSGSGSG TDFTLTISLQPEDFATYYCQQHNEYPPFTFGQGTK LEIK
SEQ ID NO: 1267	VL - 4	AVRMTQSPSSFSASTGDRVTITCKASKSINKYLAW YQQKPGKAPKLLIYDGSTLQSGVPSRFSGSGSGTD FTLTISCLQSEDFATYYCQQHNEYPPFTFGQGTKLEI K
Antibody O (murine) binds to TRVβ 11-2		
SEQ ID NO: 1268	HC CDR1 (Kabat)	NYGVH
SEQ ID NO: 1269	HC CDR2 (Kabat)	VIWSDGSTDYDTAFIS
SEQ ID NO: 1270	HC CDR3 (Kabat)	RAVVADFDY
SEQ ID NO: 1271	HC CDR1 (Chothia)	GFSLTN
SEQ ID NO: 1272	HC CDR2 (Chothia)	VIWSDGSTD
SEQ ID NO: 1270	HC CDR3 (Chothia)	RAVVADFDY
SEQ ID NO: 1273	HC CDR1 (combined)	GFSLTNYGVH
SEQ ID NO: 1269	HC CDR2 (combined)	VIWSDGSTDYDTAFIS
SEQ ID NO: 1270	HC CDR3 (combined)	RAVVADFDY
SEQ ID NO: 1274	VH	QVQLKQSGPGLLQPSQSL SITCTVSGFSLTNYGVH WVRQSPGKGLEWLGVIWSDGSTDYDTAFISRLSIS KDNSKSKVFFKLNSLQADDTAIYYCARRAVVADF DYWGQGTTTLTVSS
SEQ ID NO: 1275	LC CDR1 (Kabat)	KASKEVTIFGSISALH
SEQ ID NO: 1276	LC CDR2 (Kabat)	NGAKLES
SEQ ID NO: 1277	LC CDR3 (Kabat)	LQNKEVPFT
SEQ ID NO: 1275	LC CDR1 (Chothia)	KASKEVTIFGSISALH
SEQ ID NO: 1276	LC CDR2 (Chothia)	NGAKLES
SEQ ID NO: 1277	LC CDR3 (Chothia)	LQNKEVPFT
SEQ ID NO: 1275	LC CDR1 (combined)	KASKEVTIFGSISALH
SEQ ID NO: 1276	LC CDR2 (combined)	NGAKLES
SEQ ID NO: 1277	LC CDR3 (combined)	LQNKEVPFT
SEQ ID NO: 1278	VL	DIVLTQSPASLAVSLGQKATISCKASKEVTIFGSIS ALHWYQQKPGQP KLIYNGAKLES GVSARFSDS GSQNRSPFGNQLSFTLT IAPVEADDAATYYCLQN KEVPFTFGSGTKLEIK

Antibody O-H (humanized) VL binds to TRVβ 11-2		
SEQ ID NO: 1279	VL-1	DIVLTQSPDSLAVSLGERATINCKASKEVTIFGSIS ALHWYQQKPGQPPKLLYNGAKLESGVSARFGVP DRFSRSGSGLDFTLTISLQAEDVAVYYCLQNKE VPFTFGQGTKLEIK
SEQ ID NO: 1280	VL-2	EIVLTQSPDFQSVTPKEKVTITCKASKEVTIFGSIS ALHWYQQKPDQSPKLLYNGAKLESGVSARFGVP SRFSRSGSGLDFTLTINSLEAEDAATYYCLQNKE VPFTFGQGTKLEIK
SEQ ID NO: 1281	VL-3	AIQLTQSPSSLSASVGDRVITITCKASKEVTIFGSIS ALHWYQQKPGKAPKLLYNGAKLESGVSARFGV PSRFSRSGSGLDFTLTISLQPEDFATYYCLQNKE VPFTFGQGTKLEIK
SEQ ID NO: 1282	VL-4	DIVLTQTPLSLSVTPGQPASISCKASKEVTIFGSIS ALHWYQLKPGQPPKLLYNGAKLESGVSARFGVP DRFSRSGSGLDFTLKISRVEAEDVGVYYCLQNKE VPFTFGQGTKLEIK
Antibody O-H (humanized) VH, binds to TRVβ 11-2		
SEQ ID NO: 1283	VH-1	QVTLKESGPVLVKPTETLTCTVSGFSLTNYGV HWVRQPPGKALEWLGVIWSDGSTDYDTAFISRL TISKDNSKSQVVLMTNMDPVDATYYCARRAV VADFDYWGQGTTVTVSS
SEQ ID NO: 1284	VH-2	QVQLQESGPGLVKPSGTLSTCAVSGFSLTNYGV HWVRQPPGKGLEWLGVIWSDGSTDYDTAFISRL TISKDNSKSQVSLKLSSVTAADTAVYYCARRAV VADFDYWGQGTTVTVSS
SEQ ID NO: 1285	VH-3	QVQLQQSGPGLVKPSQTLSTCAVSGFSLTNYGV HWVRQSPSRGLEWLGVIWSDGSTDYDTAFISRLT INKDNSKSQVSLQLNSVTPEDTAVYYCARRAV ADFDYWGQGTTVTVSS
SEQ ID NO: 1286	VH-4	EVQLVESGGGLVQPGPSLRLSCTVSGFSLTNYGV HWVRQAPGKGLEWLGVIWSDGSTDYDTAFISRL TISKDNSKSIVYLQMNSLKTEDTAVYYCARRAV VADFDYWGQGTTVTVSS
SEQ ID NO: 1287	VH-5	EVQLVQSGAEVKKPGESLRISCKVSGFSLTNYGV HWVRQMPGKGLEWLGVIWSDGSTDYDTAFISQL TISKDNSISTVYLQWSSLKASDTAMYYCARRAV VADFDYWGQGTTVTVSS
IMMU546 binds to TRBV 2		

Cytokine Molecules and Cytokine Inhibitor Molecules

Cytokines are generally polypeptides that influence cellular activity, for example, through signal transduction pathways. Accordingly, a cytokine of the multispecific or multifunctional polypeptide is useful and can be associated with receptor-mediated signaling that transmits a signal from outside the cell membrane to modulate a response within the cell. Cytokines are proteinaceous signaling compounds that are mediators of the immune response. They control many different cellular functions including proliferation, differentiation and cell survival/apoptosis; cytokines are also involved in several pathophysiological processes including viral infections and autoimmune diseases. Cytokines are synthesized under various stimuli by a variety of cells of both the innate (monocytes, macrophages, dendritic cells) and adaptive (T- and B-cells) immune systems. Cytokines can be classified into two groups: pro- and anti-inflammatory. Pro-inflammatory cytokines, including IFN γ , IL-1, IL-6 and TNF- α , are predominantly derived from the innate immune cells and Th1 cells. Anti-inflammatory cytokines, including IL-10, IL-4, IL-13 and IL-5, are synthesized from Th2 immune cells.

The present disclosure provides, *inter alia*, multispecific (e.g., bi-, tri-, quad- specific) or multifunctional molecules, that include, e.g., are engineered to contain, one or more cytokine molecules, e.g., immunomodulatory (e.g., proinflammatory) cytokines and variants, e.g., functional variants, thereof. Accordingly, in some embodiments, the cytokine molecule is an interleukin or a variant, e.g., a functional variant thereof. In some embodiments the interleukin is a proinflammatory interleukin. In some embodiments the interleukin is chosen from interleukin-2 (IL-2), interleukin-12 (IL-12), interleukin-15 (IL-15), interleukin-18 (IL-18), interleukin-21 (IL-21), interleukin-7 (IL-7), or interferon gamma. In some embodiments, the cytokine molecule is a proinflammatory cytokine.

In certain embodiments, the cytokine is a single chain cytokine. In certain embodiments, the cytokine is a multichain cytokine (e.g., the cytokine comprises 2 or more (e.g., 2) polypeptide chains. An exemplary multichain cytokine is IL-12.

Examples of useful cytokines include, but are not limited to, GM-CSF, IL-1 α , IL-1 β , IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-10, IL-12, IL-21, IFN- α , IFN- β , IFN- γ , MIP-1 α , MIP-1 β , TGF- β , TNF- α , and TNF β . In one embodiment the cytokine of the multispecific or multifunctional polypeptide is a cytokine selected from the group of GM-CSF, IL-2, IL-7, IL-8,

IL-10, IL-12, IL-15, IL-21, IFN- α , IFN- γ , MIP-1 α , MIP-1 β and TGF- β . In one embodiment the cytokine of the i the multispecific or multifunctional polypeptide is a cytokine selected from the group of IL-2, IL-7, IL-10, IL-12, IL-15, IFN- α , and IFN- γ . In certain embodiments the cytokine is mutated to remove N- and/or O-glycosylation sites. Elimination of glycosylation increases
 5 homogeneity of the product obtainable in recombinant production.

In one embodiment, the cytokine of the multispecific or multifunctional polypeptide is IL-2. In a specific embodiment, the IL-2 cytokine can elicit one or more of the cellular responses selected from the group consisting of: proliferation in an activated T lymphocyte cell, differentiation in an activated T lymphocyte cell, cytotoxic T cell (CTL) activity, proliferation in
 10 an activated B cell, differentiation in an activated B cell, proliferation in a natural killer (NK) cell, differentiation in a NK cell, cytokine secretion by an activated T cell or an NK cell, and NK/lymphocyte activated killer (LAK) antitumor cytotoxicity. In another particular embodiment the IL-2 cytokine is a mutant IL-2 cytokine having reduced binding affinity to the .alpha.-subunit of the IL-2 receptor. Together with the .beta.- and .gamma.-subunits (also known as CD122 and
 15 CD132, respectively), the .alpha.-subunit (also known as CD25) forms the heterotrimeric high-affinity IL-2 receptor, while the dimeric receptor consisting only of the β - and γ -subunits is termed the intermediate-affinity IL-2 receptor. As described in PCT patent application number PCT/EP2012/051991, which is incorporated herein by reference in its entirety, a mutant IL-2 polypeptide with reduced binding to the .alpha.-subunit of the IL-2 receptor has a reduced ability
 20 to induce IL-2 signaling in regulatory T cells, induces less activation-induced cell death (AICD) in T cells, and has a reduced toxicity profile in vivo, compared to a wild-type IL-2 polypeptide. The use of such an cytokine with reduced toxicity is particularly advantageous in a multispecific or multifunctional polypeptide according to the invention, having a long serum half-life due to the presence of an Fc domain. In one embodiment, the mutant IL-2 cytokine of the multispecific
 25 or multifunctional polypeptide according to the invention comprises at least one amino acid mutation that reduces or abolishes the affinity of the mutant IL-2 cytokine to the .alpha.-subunit of the IL-2 receptor (CD25) but preserves the affinity of the mutant IL-2 cytokine to the intermediate-affinity IL-2 receptor (consisting of the β and γ subunits of the IL-2 receptor), compared to the non-mutated IL-2 cytokine. In one embodiment the one or more amino acid
 30 mutations are amino acid substitutions. In a specific embodiment, the mutant IL-2 cytokine

comprises one, two or three amino acid substitutions at one, two or three position(s) selected from the positions corresponding to residue 42, 45, and 72 of human IL-2. In a more specific embodiment, the mutant IL-2 cytokine comprises three amino acid substitutions at the positions corresponding to residue 42, 45 and 72 of human IL-2. In an even more specific embodiment, the mutant IL-2 cytokine is human IL-2 comprising the amino acid substitutions F42A, Y45A and L72G. In one embodiment the mutant IL-2 cytokine additionally comprises an amino acid mutation at a position corresponding to position 3 of human IL-2, which eliminates the O-glycosylation site of IL-2. Particularly, said additional amino acid mutation is an amino acid substitution replacing a threonine residue by an alanine residue. A particular mutant IL-2 cytokine useful in the invention comprises four amino acid substitutions at positions corresponding to residues 3, 42, 45 and 72 of human IL-2. Specific amino acid substitutions are T3A, F42A, Y45A and L72G. As demonstrated in PCT patent application number PCT/EP2012/051991 and in the appended Examples, said quadruple mutant IL-2 polypeptide (IL-2 qm) exhibits no detectable binding to CD25, reduced ability to induce apoptosis in T cells, reduced ability to induce IL-2 signaling in T.sub.reg cells, and a reduced toxicity profile in vivo. However, it retains ability to activate IL-2 signaling in effector cells, to induce proliferation of effector cells, and to generate IFN- γ as a secondary cytokine by NK cells.

The IL-2 or mutant IL-2 cytokine according to any of the above embodiments may comprise additional mutations that provide further advantages such as increased expression or stability. For example, the cysteine at position 125 may be replaced with a neutral amino acid such as alanine, to avoid the formation of disulfide-bridged IL-2 dimers. Thus, in certain embodiments the IL-2 or mutant IL-2 cytokine of the multispecific or multifunctional polypeptide according to the invention comprises an additional amino acid mutation at a position corresponding to residue 125 of human IL-2. In one embodiment said additional amino acid mutation is the amino acid substitution C125A.

In a specific embodiment the IL-2 cytokine of the multispecific or multifunctional polypeptide comprises the polypeptide sequence of SEQ ID NO: 7227

[APTSSSTKKTQLQLEHLLLDLQMILNGINN

YKNPKLTRMLTFKFYMPKKATELKHLQCLEEELKPLEEVLNLAQSKNFHL

RPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFAQSIISTLT]. In another

specific embodiment the IL-2 cytokine of the multispecific or multifunctional polypeptide comprises the polypeptide sequence of SEQ ID NO: 7228 [APASSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRMLTAKFAMPKKATELKHLQCLE EELKPLEEVLNGAQSKNFHL RPRDLISNIN

5 VIVLELKGSETTFMCEYADETATIVEFLNRWITFAQSIISTLT].

In another embodiment the cytokine of the multispecific or multifunctional polypeptide is IL-12. In a specific embodiment said IL-12 cytokine is a single chain IL-12 cytokine. In an even more specific embodiment the single chain IL-12 cytokine comprises the polypeptide sequence of SEQ ID NO: 7229

10 [IWELKKDVYVVELDWYPDAPGEMVVLTCDTPEEDGITWTLDQSSEVLGSGKTLTIQVK
EFGDAGQYTCHKGGEVLSHSLLLLHKKEDGIWSTDILKDQKEPKNKTFLRCEAKNYSGR
FTCWWTITISTDLTFSVKSSRGSSDPQGVTCGAATLSAERVGRDNKEYEYSVEQCEDSA
CPAAEESLPIEVMVDAVHKLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVEVSWEY
PDTWSTPHSYFSLTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSS
15 SWSEWASVPCSGGGGSGGGGSGGGGSRNLPVATPDPGMFPC LHHSQNLLRAVSNMLQ
KARQTLEFPCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNSRETSFITNGSCLASRK
TSFMMALCLSSIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQALNFN
SETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNAS]. In one embodiment,
the IL-12 cytokine can elicit one or more of the cellular responses selected from the group
20 consisting of: proliferation in a NK cell, differentiation in a NK cell, proliferation in a T cell, and
differentiation in a T cell.

In another embodiment the cytokine of the multispecific or multifunctional polypeptide is IL-10. In a specific embodiment said IL-10 cytokine is a single chain IL-10 cytokine. In an even more specific embodiment the single chain IL-10 cytokine comprises the polypeptide sequence of SEQ ID NO: 7230

25 [SPGQGTQSENSCTHFPGNLPNMLRDLRDAFSRVKTFQMKDQLDNLLLKESLLEDFKG
YLGCGALSEMIQFYLEEVMPPQAENQDPDIKAHVNSLGENLKTLLRLRLRRCHRFLPCENK
SKAVEQVKNAFNKLQEKGIYKAMSEFDIFINYIEAYMTMKIRNGGGGSGGGGSGGGGS
GGGGSSPGQGTQSENSCTHFPGNLPNMLRDLRDAFSRVKTFQMKDQLDNLLLKESLLE
30 DFKGYLGCGALSEMIQFYLEEVMPPQAENQDPDIKAHVNSLGENLKTLLRLRLRRCHRFLP

CENKSKAVEQVKNAFNKLQEKGIIYKAMSEFDIFINYIEAYMTMKIRN]. In another specific embodiment the IL-10 cytokine is a monomeric IL-10 cytokine. In a more specific embodiment the monomeric IL-10 cytokine comprises the polypeptide sequence of SEQ ID NO: 7231

5 [SPGQGTQSENSCTHFPGNLPNMLRDLRDAFSRVKTFQMKDQLDNLLLKESLLEDFKG
YLGCGALSEMIQFYLEEVMPPQAENQDPDIKAHVNSLGENLKTLLRLRLRRCHRFLPCENG
GGSGGKSKAVEQVKNAFNKLQEKGIIYKAMSEFDIFINYIEAYMTMKIRN]. In one
embodiment, the IL-10 cytokine can elicit one or more of the cellular responses selected from the
group consisting of: inhibition of cytokine secretion, inhibition of antigen presentation by
10 antigen presenting cells, reduction of oxygen radical release, and inhibition of T cell
proliferation. A multispecific or multifunctional polypeptide according to the invention wherein
the cytokine is IL-10 is particularly useful for downregulation of inflammation, e.g. in the
treatment of an inflammatory disorder.

In another embodiment, the cytokine of the multispecific or multifunctional polypeptide is
15 IL-15. In a specific embodiment said IL-15 cytokine is a mutant IL-15 cytokine having reduced
binding affinity to the α -subunit of the IL-15 receptor. Without wishing to be bound by theory, a
mutant IL-15 polypeptide with reduced binding to the α -subunit of the IL-15 receptor has a
reduced ability to bind to fibroblasts throughout the body, resulting in improved
pharmacokinetics and toxicity profile, compared to a wild-type IL-15 polypeptide. The use of an
20 cytokine with reduced toxicity, such as the described mutant IL-2 and mutant IL-15 effector
moieties, is particularly advantageous in a multispecific or multifunctional polypeptide according
to the invention, having a long serum half-life due to the presence of an Fc domain. In one
embodiment the mutant IL-15 cytokine of the multispecific or multifunctional polypeptide
according to the invention comprises at least one amino acid mutation that reduces or abolishes
25 the affinity of the mutant IL-15 cytokine to the α -subunit of the IL-15 receptor but
preserves the affinity of the mutant IL-15 cytokine to the intermediate-affinity IL-15/IL-2
receptor (consisting of the β - and γ -subunits of the IL-15/IL-2 receptor), compared to
the non-mutated IL-15 cytokine. In one embodiment the amino acid mutation is an amino acid
substitution. In a specific embodiment, the mutant IL-15 cytokine comprises an amino acid
30 substitution at the position corresponding to residue 53 of human IL-15. In a more specific

embodiment, the mutant IL-15 cytokine is human IL-15 comprising the amino acid substitution E53A. In one embodiment the mutant IL-15 cytokine additionally comprises an amino acid mutation at a position corresponding to position 79 of human IL-15, which eliminates the N-glycosylation site of IL-15. Particularly, said additional amino acid mutation is an amino acid substitution replacing an asparagine residue by an alanine residue. In an even more specific embodiment the IL-15 cytokine comprises the polypeptide sequence of SEQ ID NO: 7232 [NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLELQVISLASGDASIHDTVENLIILANNSLSSNGAVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS]. In one embodiment, the IL-15 cytokine can elicit one or more of the cellular responses selected from the group consisting of: proliferation in an activated T lymphocyte cell, differentiation in an activated T lymphocyte cell, cytotoxic T cell (CTL) activity, proliferation in an activated B cell, differentiation in an activated B cell, proliferation in a natural killer (NK) cell, differentiation in a NK cell, cytokine secretion by an activated T cell or an NK cell, and NK/lymphocyte activated killer (LAK) antitumor cytotoxicity.

Mutant cytokine molecules useful as effector moieties in the multispecific or multifunctional polypeptide can be prepared by deletion, substitution, insertion or modification using genetic or chemical methods well known in the art. Genetic methods may include site-specific mutagenesis of the encoding DNA sequence, PCR, gene synthesis, and the like. The correct nucleotide changes can be verified for example by sequencing. Substitution or insertion may involve natural as well as non-natural amino acid residues. Amino acid modification includes well known methods of chemical modification such as the addition or removal of glycosylation sites or carbohydrate attachments, and the like.

In one embodiment, the cytokine, particularly a single-chain cytokine, of the multispecific or multifunctional polypeptide is GM-CSF. In a specific embodiment, the GM-CSF cytokine can elicit proliferation and/or differentiation in a granulocyte, a monocyte or a dendritic cell. In one embodiment, the cytokine, particularly a single-chain cytokine, of the multispecific or multifunctional polypeptide is IFN- α . In a specific embodiment, the IFN- α cytokine can elicit one or more of the cellular responses selected from the group consisting of: inhibiting viral replication in a virus-infected cell, and upregulating the expression of major histocompatibility complex I (MHC I). In another specific embodiment, the IFN- α cytokine can inhibit proliferation

in a tumor cell. In one embodiment the cytokine, particularly a single-chain cytokine, of the multispecific or multifunctional polypeptide is IFN γ . In a specific embodiment, the IFN- γ cytokine can elicit one or more of the cellular responses selected from the group of: increased macrophage activity, increased expression of MHC molecules, and increased NK cell activity. In one embodiment the cytokine, particularly a single-chain cytokine, of the multispecific or multifunctional polypeptide is IL-7. In a specific embodiment, the IL-7 cytokine can elicit proliferation of T and/or B lymphocytes. In one embodiment, the cytokine, particularly a single-chain cytokine, of the multispecific or multifunctional polypeptide is IL-8. In a specific embodiment, the IL-8 cytokine can elicit chemotaxis in neutrophils. In one embodiment, the cytokine, particularly a single-chain cytokine, of the multispecific or multifunctional polypeptide, is MIP-1 α . In a specific embodiment, the MIP-1 α cytokine can elicit chemotaxis in monocytes and T lymphocyte cells. In one embodiment, the cytokine, particularly a single-chain cytokine, of the multispecific or multifunctional polypeptide is MIP-1 β . In a specific embodiment, the MIP-1 β cytokine can elicit chemotaxis in monocytes and T lymphocyte cells. In one embodiment, the cytokine, particularly a single-chain cytokine, of the multispecific or multifunctional polypeptide is TGF- β . In a specific embodiment, the TGF- β cytokine can elicit one or more of the cellular responses selected from the group consisting of: chemotaxis in monocytes, chemotaxis in macrophages, upregulation of IL-1 expression in activated macrophages, and upregulation of IgA expression in activated B cells.

In one embodiment, the multispecific or multifunctional polypeptide of the invention binds to an cytokine receptor with a dissociation constant (K_D) that is at least about 1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, 5, 5.5, 6, 6.5, 7, 7.5, 8, 8.5, 9, 9.5 or 10 times greater than that for a control cytokine. In another embodiment, the multispecific or multifunctional polypeptide binds to an cytokine receptor with a K_D that is at least 2, 3, 4, 5, 6, 7, 8, 9, or 10 times greater than that for a corresponding multispecific or multifunctional polypeptide comprising two or more effector moieties. In another embodiment, the multispecific or multifunctional polypeptide binds to an cytokine receptor with a dissociation constant K_D that is about 10 times greater than that for a corresponding the multispecific or multifunctional polypeptide comprising two or more cytokines.

In some embodiments, the multispecific molecules disclosed herein include a cytokine molecule. In embodiments, the cytokine molecule includes a full length, a fragment or a variant of a cytokine; a cytokine receptor domain, e.g., a cytokine receptor dimerizing domain; or an agonist of a cytokine receptor, e.g., an antibody molecule (e.g., an agonistic antibody) to a
 5 cytokine receptor.

In some embodiments the cytokine molecule is chosen from IL-2, IL-12, IL-15, IL-18, IL-7, IL-21, or interferon gamma, or a fragment or variant thereof, or a combination of any of the aforesaid cytokines. The cytokine molecule can be a monomer or a dimer. In embodiments, the cytokine molecule can further include a cytokine receptor dimerizing domain.

10 In other embodiments, the cytokine molecule is an agonist of a cytokine receptor, e.g., an antibody molecule (e.g., an agonistic antibody) to a cytokine receptor chosen from an IL-15Ra or IL-21R.

In one embodiment, the cytokine molecule is IL-15, e.g., human IL-15 (e.g., comprising the amino acid sequence:

15 NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCCKVTAMKCFLLLELQVISLES GDASIH
 DTVENLILANNSLSSNGNVTESGCKECEEELEEKNIKEFLQSFVHIVQMFINTS (SEQ ID
 NO: 7017), a fragment thereof, or an amino acid sequence substantially identical thereto (e.g.,
 95% to 99.9% identical thereto, or having at least one amino acid alteration, but not more than
 five, ten or fifteen alterations (e.g., substitutions, deletions, or insertions, e.g., conservative
 20 substitutions) to the amino acid sequence of SEQ ID NO: 7017.

In some embodiments, the cytokine molecule comprises a receptor dimerizing domain, e.g., an IL15Ralpha dimerizing domain. In one embodiment, the IL15Ralpha dimerizing domain comprises the amino acid sequence:

MAPRRARGCRTLGLPALLLLLLLLRPPATRGITCPPPMSVEHADIWVKSYSLYSRERYICN
 25 SGFKRKAGTSSLTECVL (SEQ ID NO: 7018), a fragment thereof, or an amino acid sequence
 substantially identical thereto (e.g., 95% to 99.9% identical thereto, or having at least one amino
 acid alteration, but not more than five, ten or fifteen alterations (e.g., substitutions, deletions, or
 insertions, e.g., conservative substitutions) to the amino acid sequence of SEQ ID NO: 7018. In
 some embodiments, the cytokine molecule (e.g., IL-15) and the receptor dimerizing domain
 30 (e.g., an IL15Ralpha dimerizing domain) of the multispecific molecule are covalently linked,

e.g., via a linker (e.g., a Gly-Ser linker, e.g., a linker comprising the amino acid sequence SGGSGGGGSGGGSGGGSLQ (SEQ ID NO: 7019). In other embodiments, the cytokine molecule (e.g., IL-15) and the receptor dimerizing domain (e.g., an IL15Alpha dimerizing domain) of the multispecific molecule are not covalently linked, e.g., are non-covalently associated.

In other embodiments, the cytokine molecule is IL-2, e.g., human IL-2 (e.g., comprising the amino acid sequence:

APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPKLTRMLTFKFYMPKKATELKHLQCL
EEELKPLEEVLNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNR

WITFCQSIISTLT (SEQ ID NO: 7020), a fragment thereof, or an amino acid sequence substantially identical thereto (e.g., 95% to 99.9% identical thereto, or having at least one amino acid alteration, but not more than five, ten or fifteen alterations (e.g., substitutions, deletions, or insertions, e.g., conservative substitutions) to the amino acid sequence of SEQ ID NO: 7020).

In other embodiments, the cytokine molecule is IL-18, e.g., human IL-18 (e.g., comprising the amino acid sequence:

YFGKLESKLSVIRNLNDQVLFDIQGNRPLFEDMTDSDCRDNAPRTIFIISMYKDSQPRGM
AVTISVKCEKISTLSCENKIISFKEMNPPDNIKDTKSDIIFQRSVPGHDNKMQFESSY
EGYFLACEKERDLFKLILKKEDELGDRSIMFTVQNED (SEQ ID NO: 7021), a fragment

thereof, or an amino acid sequence substantially identical thereto (e.g., 95% to 99.9% identical thereto, or having at least one amino acid alteration, but not more than five, ten or fifteen alterations (e.g., substitutions, deletions, or insertions, e.g., conservative substitutions) to the amino acid sequence of SEQ ID NO: 7021).

In other embodiments, the cytokine molecule is IL-21, e.g., human IL-21 (e.g., comprising the amino acid sequence:

QGQDRHMIRMRLIDIVDQLKNYVNDLVPEFLPAPEDVETNCEWSAFSCFQKAQLKSA
NTGNNERIINVSIKKLKRKPPSTNAGRQKHRLTCPSCDSYEKKPPKEFLERFKSLLQKMI
HQHLSSRTHGSEDS (SEQ ID NO: 7022), a fragment thereof, or an amino acid sequence

substantially identical thereto (e.g., 95% to 99.9% identical thereto, or having at least one amino acid alteration, but not more than five, ten or fifteen alterations (e.g., substitutions, deletions, or insertions, e.g., conservative substitutions) to the amino acid sequence of SEQ ID NO: 7022).

In yet other embodiments, the cytokine molecule is interferon gamma, e.g., human interferon gamma (e.g., comprising the amino acid sequence:

QDPYVKEAENLKKYFNAGHSDVADNGTLFLGILKNWKEESDRKIMQSQIVSFYFKLFK
NFKDDQSIQKSVETIKEDMNVKFFNSNKKKRDDFEKLTNYSVTDLNVQRKAIHELIQVM

5 AELSPAAKTGKRKRSQMLFRG (SEQ ID NO: 7023), a fragment thereof, or an amino acid sequence substantially identical thereto (e.g., 95% to 99.9% identical thereto, or having at least one amino acid alteration, but not more than five, ten or fifteen alterations (e.g., substitutions, deletions, or insertions, e.g., conservative substitutions) to the amino acid sequence of SEQ ID NO: 7023).

TGF-beta Inhibitors

The present disclosure further provides, *inter alia*, multispecific (e.g., bi-, tri-, quad-specific) or multifunctional molecules, that include, e.g., are engineered to contain, one or more cytokine inhibitor molecules, e.g., inhibitors of immunomodulatory (e.g., proinflammatory) cytokines and variants, e.g., functional variants, thereof. Accordingly, in some embodiments, the cytokine inhibitor molecule is a TGF-beta inhibitor. In some embodiments, the TGF-beta inhibitor binds to and inhibits TGF-beta, e.g., reduces the activity of TGF-beta. In some embodiments, the TGF-beta inhibitor inhibits (e.g., reduces the activity of) TGF-beta 1. In some embodiments, the TGF-beta inhibitor inhibits (e.g., reduces the activity of) TGF-beta 2. In some
15 embodiments, the TGF-beta inhibitor inhibits (e.g., reduces the activity of) TGF-beta 3. In some embodiments, the TGF-beta inhibitor inhibits (e.g., reduces the activity of) TGF-beta 1 and TGF-beta 3. In some embodiments, the TGF-beta inhibitor inhibits (e.g., reduces the activity of) TGF-beta 1, TGF-beta 2, and TGF-beta 3.

In some embodiments, the TGF-beta inhibitor comprises a portion of a TGF-beta receptor (e.g., an extracellular domain of a TGF-beta receptor) that is capable of inhibiting (e.g., reducing the activity of) TGF-beta, or functional fragment or variant thereof. In some embodiments, the TGF-beta inhibitor comprises a TGFBR1 polypeptide (e.g., an extracellular domain of TGFBR1 or functional variant thereof). In some embodiments, the TGF-beta inhibitor comprises a TGFBR2 polypeptide (e.g., an extracellular domain of TGFBR2 or functional variant thereof).

30 In some embodiments, the TGF-beta inhibitor comprises a TGFBR3 polypeptide (e.g., an

extracellular domain of TGFBR3 or functional variant thereof). In some embodiments, the TGF-beta inhibitor comprises a TGFBR1 polypeptide (e.g., an extracellular domain of TGFBR1 or functional variant thereof) and a TGFBR2 polypeptide (e.g., an extracellular domain of TGFBR2 or functional variant thereof). In some embodiments, the TGF-beta inhibitor comprises a

5 TGFBR1 polypeptide (e.g., an extracellular domain of TGFBR1 or functional variant thereof) and a TGFBR3 polypeptide (e.g., an extracellular domain of TGFBR3 or functional variant thereof). In some embodiments, the TGF-beta inhibitor comprises a TGFBR2 polypeptide (e.g., an extracellular domain of TGFBR2 or functional variant thereof) and a TGFBR3 polypeptide (e.g., an extracellular domain of TGFBR3 or functional variant thereof).

10 Exemplary TGF-beta receptor polypeptides that can be used as TGF-beta inhibitors have been disclosed in US8993524, US9676863, US8658135, US20150056199, US20070184052, and WO2017037634, all of which are herein incorporated by reference in their entirety.

In some embodiments, the TGF-beta inhibitor comprises an extracellular domain of TGFBR1 or a sequence substantially identical thereto (e.g., a sequence that is at least 80%, 85%,

15 90%, or 95% identical thereto). In some embodiments, the TGF-beta inhibitor comprises an extracellular domain of SEQ ID NO: 7257, or a sequence substantially identical thereto (e.g., a sequence that is at least 80%, 85%, 90%, or 95% identical thereto). In some embodiments, the TGF-beta inhibitor comprises an extracellular domain of SEQ ID NO: 7258, or a sequence substantially identical thereto (e.g., a sequence that is at least 80%, 85%, 90%, or 95% identical

20 thereto). In some embodiments, the TGF-beta inhibitor comprises an extracellular domain of SEQ ID NO: 7259, or a sequence substantially identical thereto (e.g., a sequence that is at least 80%, 85%, 90%, or 95% identical thereto). In some embodiments, the TGF-beta inhibitor comprises the amino acid sequence of SEQ ID NO: 7266, or a sequence substantially identical thereto (e.g., a sequence that is at least 80%, 85%, 90%, or 95% identical thereto). In some

25 embodiments, the TGF-beta inhibitor comprises the amino acid sequence of SEQ ID NO: 7267, or a sequence substantially identical thereto (e.g., a sequence that is at least 80%, 85%, 90%, or 95% identical thereto).

In some embodiments, the TGF-beta inhibitor comprises an extracellular domain of TGFBR2 or a sequence substantially identical thereto (e.g., a sequence that is at least 80%, 85%,

30 90%, or 95% identical thereto). In some embodiments, the TGF-beta inhibitor comprises an

extracellular domain of SEQ ID NO: 7260, or a sequence substantially identical thereto (e.g., a sequence that is at least 80%, 85%, 90%, or 95% identical thereto). In some embodiments, the TGF-beta inhibitor comprises an extracellular domain of SEQ ID NO: 7261, or a sequence substantially identical thereto (e.g., a sequence that is at least 80%, 85%, 90%, or 95% identical thereto). In some embodiments, the TGF-beta inhibitor comprises the amino acid sequence of SEQ ID NO: 7262, or a sequence substantially identical thereto (e.g., a sequence that is at least 80%, 85%, 90%, or 95% identical thereto). In some embodiments, the TGF-beta inhibitor comprises the amino acid sequence of SEQ ID NO: 7263, or a sequence substantially identical thereto (e.g., a sequence that is at least 80%, 85%, 90%, or 95% identical thereto). In some embodiments, the TGF-beta inhibitor comprises the amino acid sequence of SEQ ID NO: 7264, or a sequence substantially identical thereto (e.g., a sequence that is at least 80%, 85%, 90%, or 95% identical thereto). In some embodiments, the TGF-beta inhibitor comprises the amino acid sequence of SEQ ID NO: 7265, or a sequence substantially identical thereto (e.g., a sequence that is at least 80%, 85%, 90%, or 95% identical thereto).

In some embodiments, the TGF-beta inhibitor comprises an extracellular domain of TGFBR3 or a sequence substantially identical thereto (e.g., a sequence that is at least 80%, 85%, 90%, or 95% identical thereto). In some embodiments, the TGF-beta inhibitor comprises an extracellular domain of SEQ ID NO: 7268, or a sequence substantially identical thereto (e.g., a sequence that is at least 80%, 85%, 90%, or 95% identical thereto). In some embodiments, the TGF-beta inhibitor comprises an extracellular domain of SEQ ID NO: 7269, or a sequence substantially identical thereto (e.g., a sequence that is at least 80%, 85%, 90%, or 95% identical thereto). In some embodiments, the TGF-beta inhibitor comprises the amino acid sequence of SEQ ID NO: 7270, or a sequence substantially identical thereto (e.g., a sequence that is at least 80%, 85%, 90%, or 95% identical thereto).

In some embodiments, the TGF-beta inhibitor comprises no more than one TGF-beta receptor extracellular domain. In some embodiments, the TGF-beta inhibitor comprises two or more (e.g., two, three, four, five, or more) TGF-beta receptor extracellular domains, linked together, e.g., via a linker.

Table 16. Exemplary amino acid sequences of TGF-beta polypeptides or TGF-beta receptor polypeptides

SEQ ID NO	Description	Amino acid sequence
SEQ ID NO: 7254	Immature human TGF-beta 1 (P01137-1)	MPPSGLRLLLLLLPLLWLLVLTTPGRPAAGLSTCKTIDMELVKKRRIE AIRGQILSKLRLASPPSQGEVPPGPLPEAVLALYNSTRDRVAGESAEP EPEPEADYYAKEVTRVLMVETHNEIYDKFKQSTHSIYMFFNTSELRE AVPEPVLLSRAELRLLRLKLKVEQHVELYQKYSNNSWRYLNSRLLA PSDSPEWLSFDVTGVVRQWLSRGGEIEGFRLSAHCSCDSRDNTLQV DINGFTTGRRGDLATIHGMNRPFLLLMATPLERAQHLQSSRHRRAL DTNYCFSSTEKNCCVRQLYIDFRKDLGWKWIHEPKGYHANFCLGP CPYIWSLDTQYSKVLALYNQHNP GASAAPCCVPQALEPLPIVYYVG RKPKVEQLSNMIVRSCKCS
SEQ ID NO: 7271	Human TGF-beta 1 (P01137-1)	LSTCKTIDMELVKKRRIE AIRGQILSKLRLASPPSQGEVPPGPLPEAV LALYNSTRDRVAGESAEPEPEPEADYYAKEVTRVLMVETHNEIYDK FKQSTHSIYMFFNTSELREAVPEPVLLSRAELRLLRLKLKVEQHVEL YQKYSNNSWRYLNSRLLAPSDSPEWLSFDVTGVVRQWLSRGGEIE GFRLSAHCSCDSRDNTLQVDINGFTTGRRGDLATIHGMNRPFLLLM ATPLERAQHLQSSRHRRALDTNYCFSSTEKNCCVRQLYIDFRKDLG WKWIHEPKGYHANFCLGPCPYIWSLDTQYSKVLALYNQHNP GASA APCCVPQALEPLPIVYYVGRKPKVEQLSNMIVRSCKCS
SEQ ID NO: 7255	Immature human TGF-beta 2 (P61812-1)	MHYCVLSAFLILHLVTVALSLSTCSTLDMQDFMRKRIE AIRGQILSK LKLTSPPEDYPEPEEVPPEVISIYNSTRDLLQEKASRRAAACERERSD EEYYAKEVYKIDMPPFFPSENAIPPTFYRPFYFRIVRFDVSAMEKNAS NLVKAEFRVFRLQNP KARVPEQRIELYQILKSKDLTSPTQRYIDSKV VKTRAEGEWLSFDVTDVHEWLHHKDRNLGFKISLHCPCTFVPS NNYIIPNKSEELERFAGIDGTSTYTSQDQKTIKSTRKKNSGKTPHLL LMLPSYRLESQQTNRRKKRALDAAYCFRNVQDNCCLRPLYIDFKR DLGWKWIHEPKGYNANFCAGACPYLWSSDTQHSRVLSLYNTINPE ASASPCCVSQDLEPLTILYYIGKTPKIEQLSNMIVKSKCS
SEQ ID NO: 7272	Human TGF-beta 2 (P61812-1)	LSTCSTLDMQDFMRKRIE AIRGQILSKLKLTSPPEDYPEPEEVPPEVIS IYNSTRDLLQEKASRRAAACERERSDEEYYAKEVYKIDMPPFFPSEN AIPPTFYRPFYFRIVRFDVSAMEKNASNLVKAEFRVFRLQNP KARVPE QRIELYQILKSKDLTSPTQRYIDSKVVKTRAEGEWLSFDVTDVHE WLHHKDRNLGFKISLHCPCTFVPSNNYIIPNKSEELERFAGIDGTS TYTSQDQKTIKSTRKKNSGKTPHLLLMLPSYRLESQQTNRRKKRA LDAAYCFRNVQDNCCLRPLYIDFKRDLGWKWIHEPKGYNANFCAG ACPYLWSSDTQHSRVLSLYNTINPEASASPCCVSQDLEPLTILYYIGK TPKIEQLSNMIVKSKCS
SEQ ID NO: 7256	Immature human	MKMHLQRALVVLALLNFATVSLSLSTCTTLDFGHIKKRVEAIRGQ ILSKLRLTSPPEPTVMTHVPYQVLALYNSTRELLEEMHGEREEGCTQ ENTESEYYAKEIHKFDMIQGLAEHNELAVCPKGITSKVFRFNVSSVE

	TGF-beta 3 (P10600-1)	KNRTNLFRAEFRVLRVPNPSSKRNEQRIELFQILRPDEHIAKQRYIGG KNLPTRGTAEWLSFDVTDTVREWLLRRESNLGLEISIHCPCHTFQPN GDILENIHEVMEIKFKGVDNEDDHGRGDLGRLKKQKDDHNPPLIL MMIPPHRLDNPQGQGGQRKKRALDTNYCFRNLEENCCVRPLYIDFRQ DLGWKWWHEPKGYIANFCSGPCPYLRSADTTTHSTVLGLYNTLNPE ASASPCCVPQDLEPLTILYYVGRTPKVEQLSNMVMVKSCCKCS
SEQ ID NO: 7273	Human TGF-beta 3 (P10600-1)	LSTCTTLDFGHIKKRVEAIRGQILSKLRLTSPPEPTVMTHVPYQVL ALYNSTRELLEEMHGEREEGCTQENTESEYYAKEIHKFDMIQGLAE HNELAVCPKGITSKVFRFNVSSVEKNRTNLFRAEFRVLRVPNPSSKR NEQRIELFQILRPDEHIAKQRYIGGKNLPTRGTAEWLSFDVTDTVRE WLLRRESNLGLEISIHCPCHTFQPNGDILENIHEVMEIKFKGVDNED DHGRGDLGRLKKQKDDHNPPLILMMIPPHRLDNPQGQGGQRKKRAL DTNYCFRNLEENCCVRPLYIDFRQDLGWKWWHEPKGYIANFCSGP CPYLRSADTTTHSTVLGLYNTLNPEASASPCCVPQDLEPLTILYYVGR TPKVEQLSNMVMVKSCCKCS
SEQ ID NO: 7257	Immature human TGFBF1 isoform 1 (P36897-1)	MEAAVAAPRPRLLLLVLAAAAAAAALLPGATALQCFCHLCTKDN FTCVTDGLCFVSVTETTDKVIHNSMCIAEIDLIPDRPFVFCAPSSKTG SVTTTYCCNQDHCNKIELPTTVKSSPGLGPVELAAVIAGPVCFCISL MLMVYICHNRTVIHHRVPNEEDPSLDRPFISEGTTCLKDLIYDMMTSG SGSGLPLLVQRTIARTIVLQESIGKGRFGEVWRGKWRGEEVAVKIFS SREERSWFREAEIYQTVMLRHENILGFIAADNKDNGTWTQLWLVS DYEHEGSLFDYLNRYTVEGMIKLALSTASGLAHLHMEIVGTQGKP AIAHRDLKSKNILVKKNGTCCADLGLAVRHDSATDTIDIAPNHRVG TKRYMAPEVLDD SINMKHFESFKRADIYAMGLVFWEIARRCSIGGI HEDYQLPYDLPSPDPSVEEMRKVVCEQKLRPNIPNRWQSCEALR VMAKIMRECWYANGAARLTALRIKKTLSQLSQQEGIKM
SEQ ID NO: 7274	Human TGFBF1 isoform 1 (P36897-1)	LQCFCHLCTKDNFTCVTDGLCFVSVTETTDKVIHNSMCIAEIDLIPR DRPFVFCAPSSKTGSVTTTYCCNQDHCNKIELPTTVKSSPGLGPVELA AVIAGPVCFCISLMLMVYICHNRTVIHHRVPNEEDPSLDRPFISEGT TLKDLIYDMMTSGSGSGLPLLVQRTIARTIVLQESIGKGRFGEVWRG KWRGEEVAVKIFSSREERSWFREAEIYQTVMLRHENILGFIAADNK DNGTWTQLWLVS DYHEHGS LFDYLNRYTVEGMIKLALSTASGL AHLHMEIVGTQGKPAIAHRDLKSKNILVKKNGTCCADLGLAVRH DSATDTIDIAPNHRVGTKRYMAPEVLDD SINMKHFESFKRADIYAMG LVFWEIARRCSIGGIHEDYQLPYDLPSPDPSVEEMRKVVCEQKLRP NIPNRWQSCEALRVMAKIMRECWYANGAARLTALRIKKTLSQLSQ QEGIKM
SEQ ID NO: 7258	Immature human TGFBF1 isoform 2 (P36897-2)	MEAAVAAPRPRLLLLVLAAAAAAAALLPGATALQCFCHLCTKDN FTCVTDGLCFVSVTETTDKVIHNSMCIAEIDLIPDRPFVFCAPSSKTG SVTTTYCCNQDHCNKIELPTTGPFVSKSSPGLGPVELAAVIAGPVCF VCISLMLMVYICHNRTVIHHRVPNEEDPSLDRPFISEGTTCLKDLIYD MTTSGSGSGLPLLVQRTIARTIVLQESIGKGRFGEVWRGKWRGEEV AVKIFSSREERSWFREAEIYQTVMLRHENILGFIAADNKDNGTWTQ

		LWLVSDYHEHGSFLFDYLNRYTVTVEGMIKLALSTASGLAHLHMEI VGTQGKPAIAHRDLKSKNILVKKNGTCCIADLGLAVRHDSATDTIDI APNHRVGTKRYMAPEVLDDSI NMKHFESFKRADIYAMGLVFWEIA RRCSIGGIHEDYQLPYDLVPSDPSVEEMRKVVCEQKLRPNIPNRW QSCEALRVMAMIMRECWYANGAARLTALRIKKTLSQLSQQEGIKM
SEQ ID NO: 7275	Human TGFB1 isoform 2 (P36897-2)	LQCFCHLCTKDNFTCVTDGLCFVSVTETTDKVIHNSMCIAEIDLIPR DRPFVFCAPSSKTGSVTTTYCCNQDHCNKIELPTTGPFVSKSSPGLGP VELAAVIAGPVCFCISLMLMVYICHNRTVIHHRVPNEEDPSLDRPFI SEGTTCLKDLIYDMTTSGSGSGLPLL VQRTIARTIVLQESIGKGRFGEV WRGKWRGEEVAVKIFSSREERSWFREAEIYQTVMLRHENILGFIAA DNKDNGTWTQLWLVSDYHEHGSFLFDYLNRYTVTVEGMIKLALST ASGLAHLHMEIVGTQGKPAIAHRDLKSKNILVKKNGTCCIADLGLA VRHDSATDTIDIAPNHRVGTKRYMAPEVLDDSI NMKHFESFKRADI YAMGLVFWEIARRCSIGGIHEDYQLPYDLVPSDPSVEEMRKVVCE QKLRPNIPNRWQSCEALRVMAMIMRECWYANGAARLTALRIKKT LSQLSQQEGIKM
SEQ ID NO: 7259	Immature human TGFB1 isoform 3 (P36897-3)	MEAAVAAPRPRLLLLVLAAAAAAAALLPGATALQCFCHLCTKDN FTCVTDGLCFVSVTETTDKVIHNSMCIAEIDLIPRDRPFVFCAPSSKTG SVTTTYCCNQDHCNKIELPTTGLPLL VQRTIARTIVLQESIGKGRFGE VWRGKWRGEEVAVKIFSSREERSWFREAEIYQTVMLRHENILGFIA ADNKDNGTWTQLWLVSDYHEHGSFLFDYLNRYTVTVEGMIKLALS TASGLAHLHMEIVGTQGKPAIAHRDLKSKNILVKKNGTCCIADLGL AVRHDSATDTIDIAPNHRVGTKRYMAPEVLDDSI NMKHFESFKRAD IYAMGLVFWEIARRCSIGGIHEDYQLPYDLVPSDPSVEEMRKVVC EQKLRPNIPNRWQSCEALRVMAMIMRECWYANGAARLTALRIKKT LSQLSQQEGIKM
SEQ ID NO: 7276	Human TGFB1 isoform 3 (P36897-3)	LQCFCHLCTKDNFTCVTDGLCFVSVTETTDKVIHNSMCIAEIDLIPR DRPFVFCAPSSKTGSVTTTYCCNQDHCNKIELPTTGLPLL VQRTIARTI VLQESIGKGRFGEVWRGKWRGEEVAVKIFSSREERSWFREAEIYQTV MLRHENILGFIAADNKDNGTWTQLWLVSDYHEHGSFLFDYLNRYT VTVEGMIKLALSTASGLAHLHMEIVGTQGKPAIAHRDLKSKNILVK KNGTCCIADLGLAVRHDSATDTIDIAPNHRVGTKRYMAPEVLDDSI NMKHFESFKRADIYAMGLVFWEIARRCSIGGIHEDYQLPYDLVPS DPSVEEMRKVVCEQKLRPNIPNRWQSCEALRVMAMIMRECWYAN GAARLTALRIKKTLSQLSQQEGIKM
SEQ ID NO: 7266	Human TGFB1 fragment 1	LQCFCHLCTKDNFTCVTDGLCFVSVTETTDKVIHNSMCIAEIDLIPR DRPFVFCAPSSKTGSVTTTYCCNQDHCNKIELPTTVKSSPGLGPVEL
SEQ ID NO: 7267	Human TGFB1 fragment 2	ALQCFCHLCTKDNFTCVTDGLCFVSVTETTDKVIHNSMCIAEIDLIP RDRPFVFCAPSSKTGSVTTTYCCNQDHCNKIEL

SEQ ID NO: 7260	Immature human TGFB2 isoform B (short isoform) (P37173-1)	MGRGLLRGLWPLHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGAV KFPQLCKFCDVRFSTCDNQKSCMSNCSITSICEKPQEVCAVWRKN DENITLETVCHDPKLPYHDFILEDAAAPKIMKEKKKPGETFFMCSC SSDECNDNIIFSEEYNTSNPDLLLVIQVGTGISLLPPLGVAVISVIFCY RVNRQQKLSSTWETGKTRKLMFSEHCAILEDSDISSTCANNIN HNTELLPIELDTLVGKGRFAEVYKAKLKQNTSEQFETVAVKIFPYEE YASWKTEKDIFSDINLKHENILQFLTAERKTELKGQYWLITAFHAK GNLQEYLTRHVISWEDLRKLGLSSSLARGIAHLHSDHTPCGRPKMPIV HRDLKSSNILVKNDLTCCLCDFGLSLRLDPTLSVDDLANSQGQVGT ARYMAPEVLESRMNLENVESFKQTDVYSMALVLWEMTSRCNAVGE VKDYEPFPGSKVREHPCVESMKDNVLRDRGRPEIPSWLHNHQQIQM VCETLTECWDHDPEARLTAQCVAFERFSELEHLDRLSGRSCSEEKIPE DGS LN TTK
SEQ ID NO: 7277	Human TGFB2 isoform B (short isoform) (P37173-1)	TIPPHVQKSVNNDMIVTDNNGAVKFPQLCKFCDVRFSTCDNQKSC MSNCSITSICEKPQEVCAVWRKN DENITLETVCHDPKLPYHDFILE DAAPKIMKEKKKPGETFFMCSCSSDECNDNIIFSEEYNTSNPDLLL VIQVGTGISLLPPLGVAVISVIFCYRVNRQQKLSSTWETGKTRKLM EFSEHCAILEDSDISSTCANNINHNTELLPIELDTLVGKGRFAEVY KAKLKQNTSEQFETVAVKIFPYEEYASWKTEKDIFSDINLKHENILQ FLTAERKTELKGQYWLITAFHAKGNLQEYLTRHVISWEDLRKLGLS SLARGIAHLHSDHTPCGRPKMPIVHRDLKSSNILVKNDLTCCLCDFG LSLRLDPTLSVDDLANSQGQVGTARYMAPEVLESRMNLENVESFKQTD VYSMALVLWEMTSRCNAVGEVKDYEPFPGSKVREHPCVESMKD NVLRDRGRPEIPSWLHNHQQIQMVCETLTECWDHDPEARLTAQCV AFERFSELEHLDRLSGRSCSEEKIPEDGS LN TTK
SEQ ID NO: 7261	Immature human TGFB2 isoform A (long isoform) (P37173-2)	MGRGLLRGLWPLHIVLWTRIASTIPPHVQKSDVEMEAQKDEIICPSC NRTAHPLRHINNDMIVTDNNGAVKFPQLCKFCDVRFSTCDNQKSC MSNCSITSICEKPQEVCAVWRKN DENITLETVCHDPKLPYHDFILE DAAPKIMKEKKKPGETFFMCSCSSDECNDNIIFSEEYNTSNPDLLL VIQVGTGISLLPPLGVAVISVIFCYRVNRQQKLSSTWETGKTRKLM EFSEHCAILEDSDISSTCANNINHNTELLPIELDTLVGKGRFAEVY KAKLKQNTSEQFETVAVKIFPYEEYASWKTEKDIFSDINLKHENILQ FLTAERKTELKGQYWLITAFHAKGNLQEYLTRHVISWEDLRKLGLS SLARGIAHLHSDHTPCGRPKMPIVHRDLKSSNILVKNDLTCCLCDFG LSLRLDPTLSVDDLANSQGQVGTARYMAPEVLESRMNLENVESFKQTD VYSMALVLWEMTSRCNAVGEVKDYEPFPGSKVREHPCVESMKD NVLRDRGRPEIPSWLHNHQQIQMVCETLTECWDHDPEARLTAQCV AFERFSELEHLDRLSGRSCSEEKIPEDGS LN TTK
SEQ ID NO: 7278	Human TGFB2 isoform A (long	TIPPHVQKSDVEMEAQKDEIICPSCNRTAHPLRHINNDMIVTDNNGA VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICEKPQEVCAVWRK NDENITLETVCHDPKLPYHDFILEDAAAPKIMKEKKKPGETFFMCSC SSDECNDNIIFSEEYNTSNPDLLLVIQVGTGISLLPPLGVAVISVIFCY YRVNRQQKLSSTWETGKTRKLMFSEHCAILEDSDISSTCANNI

	isoform) (P37173-2)	NHNTPELLPIELDTLVGKGRFAEVYKAKLKQNTSEQFETVAVKIFPYE EYASWKTEKDIFSDINLKHENILQFLTAERKTEL GKQYWLITAFHA KGNLQEYLTRHVISWEDLRKLGSSSLARGIAHLHSDHTPCGRPKMPI VHRDLKSSNILVKNDLTCCLCDFGLSLRLDPTLSVDDLANSQVGT ARYMAPEVLES RMNLENVESFKQTDVYSMALVLWEMTSRCNAV G EVKDYEPFPGSKVREHPCVESMKDNVLRDRGRPEIPSWLNHQGIQ MVCETLTECWDHDPEARLTAQCVAERFSELEHLDRLSGRSCSEEKI PEDGSLNTTK
SEQ ID NO: 7262	Human TGFB2 fragment 1 (ECD of human TGFB2 isoform B)	TIPPHVQKSVNNDMIVTDNNGAVKFPQLCKFCDVRFSTCDNQKSC MSNCSITSICEKPQEVCAVWRKNDENITLETVCHDPKLPYHDFILE DAASPKCIMKEKKKPGETFFMCSCSSDECNDNIIFSEEYNTSNPD
SEQ ID NO: 7263	Human TGFB2 fragment 2	IPPHVQKSVNNDMIVTDNNGAVKFPQLCKFCDVRFSTCDNQKSCMS NCSITSICEKPQEVCAVWRKNDENITLETVCHDPKLPYHDFILEDA ASPKCIMKEKKKPGETFFMCSCSSDECNDNIIFSEEYNTSNPD
SEQ ID NO: 7264	Human TGFB2 fragment 3 (ECD of human TGFB2 isoform A)	TIPPHVQKSDVEMEAQKDEIICPCSNRTAHPLRHINNDMIVTDNNGA VKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICEKPQEVCAVWRK NDENITLETVCHDPKLPYHDFILEDAASPKCIMKEKKKPGETFFMC CSSDECNDNIIFSEEYNTSNPD
SEQ ID NO: 7265	Human TGFB2 fragment 4	QLCKFCDVRFSTCDNQKSCMSNCSITSICEKPQEVCAVWRKNDEN ITLETVCHDPKLPYHDFILEDAASPKCIMKEKKKPGETFFMCSCSSD ECNDNIIF
SEQ ID NO: 7268	Immature human TGFB3 isoform 1 (Q03167-1)	MTSHYVIAIFALMSSCLATAGPEPGALCELS PVSASHPVQALMESFT VLSGCASRGTTGLPQEVHVLNLRTAGQGPGQLQREVT LHLNPISSV HIIHKS VVFLNNSPHPLVWHLKTERLATGVSRLFLVSEGSVVQFSSA NFSLTAEETEERNFPHGNEHLLNWARKEYGAVTSFTELKIARNIYIKV GEDQVFPPKCNIGKNFLSLNYLAEYLQPKAAEGCVMSSQPQNEEVH IIEITPNSNPYSAFQVDITIDIRPSQEDLEVVKNLILKCKKSVNWVI KSFDVKGSLKIIAPNSIGFGKESERSMTMTKSIRDDIPSTQGNLVKW ALDNGYSPITSYTMAPVANRFHLRLNNAEEMGDEEVHTIPPELRIL LDPGALPALQNPPIRGGEGQNGGLPFPFDPISRRVWNEEGEDGLPRP KDPVIPS IQLFPGLEPEEVQGSVDIALSVKCDNEKMIVAVEKDSFQ ASGYSGMDVTLLDPTCKAKMNGTHFVLESPLNGCGTRPRWSALDG VVYYNSIVIQVPALGDSSGWP DGYEDLES GDNGFPGDMDEGDASLF TRPEIVVFNC SLQQVRNPSSFQE QPHGNITFNMELYNTDLFLVPSQG VFSVPENGHVYVEVSVTKAEQELGFAIQTCFISPYSNPDRMSHYTIE NICPKDES VKFYSPKRVHFPIQADMDKKRFSFVFKPVFNTSLLFLQ

		CELTLCTKMEKHPQKLPKCVPPDEACTSLDASIIWAMMQNKKTFTK PLAVIHHEAESKEKGPSMKEPNPISPPIFHGLDTLTVMGIAFAAFVIG ALLTGALWYIYSHTGETAGRQQVPTSPPASENSSAAHSIGSTQSTPC SSSSTA
SEQ ID NO: 7279	Human TGFBR3 isoform 1 (Q03167-1)	GPEPGALCELSPVASHPVQALMESFTVLSGCASRGTTGLPQEVHVL NLRTAGQGPGQLQREVTLHLNPISSVHHHKS VVFLNNSPHPLVWH LKTERLATGVSRLFLVSEGSVVQFSSANFSLTAETEERNFPHGNEHL LNWARKEYGAVTSFTELKIARNIYIKVGEDQVFPPKCNIGKNFLSLN YLAEYLQPKAAEGCVMSSQPQNEEVHIIELITPNSNPYSAFQVDITID IRPSQEDLEVVKNLILILKCKKSVNWVIKSFQVKGSLKIIAPNSIGFGK ESERSMTMTKSIRDDIPSTQGNLVKWALDNGYSPITSYTMAPVANR FHLRLNNAEEMGDEEVHTIPPELRILLDPGALPALQNPPIRGGEGQ NGGLPFPFPDISRRVWNEEGEDGLPRPKDPVIPSILFPLREPEEVQ GSVDIALSVKCDNEKMIVAVEKDSFQASGYSGMDVTLLDPTCKAK MNGTHFVLESPLNGCGTRPRWSALDGVVYYNSIVIQVPALGDSSG WPDGYEDLES GDNGFPGDMDEGDASLFT RPEIVVFNC SLQQVRNPS SFQEQPHGNITFNMELYNTDLFLVPSQGVFSVPENGHVYVEVSVTK AEQELGFAIQTCFISPYSNPDRMSHYTHIENICPKDES VKFYSPKRVHF PIPQADMDKKRFSFVKPVFNTSLLFLQCELTCTKMEKHPQKLPKC VPPDEACTSLDASIIWAMMQNKKTFTKPLAVIHHEAESKEKGPSMK EPNPISPPIFHGLDTLTVMGIAFAAFVIGALLTGALWYIYSHTGETAG RQQVPTSPPASENSSAAHSIGSTQSTPCSSSTA
SEQ ID NO: 7269	Immature human TGFBR3 isoform 2 (Q03167-2)	MTSHYVIAIFALMSSCLATAGPEPGALCELSPVASHPVQALMESFT VLSGCASRGTTGLPQEVHVLNLRTAGQGPGQLQREVTLHLNPISSV HHHKS VVFLNNSPHPLVWH LKTERLATGVSRLFLVSEGSVVQFSSA N FSLTAETEERNFPHGNEHL LNWARKEYGAVTSFTELKIARNIYIKV GEDQVFPPKCNIGKNFLSLNYLAEYLQPKAAEGCVMSSQPQNEEVH IELITPNSNPYSAFQVDITIDIRPSQEDLEVVKNLILILKCKKSVNWVI KSFQVKGSLKIIAPNSIGFGKESERSMTMTKSIRDDIPSTQGNLVKW ALDNGYSPITSYTMAPVANRFHLRLNNEEMGDEEVHTIPPELRILL DPGALPALQNPPIRGGEGQNGGLPFPFPDISRRVWNEEGEDGLPRPK DPVIPSILFPLREPEEVQGSVDIALSVKCDNEKMIVAVEKDSFQAS GYSGMDVTLLDPTCKAKMNGTHFVLESPLNGCGTRPRWSALDGV VYYNSIVIQVPALGDSSG WPDGYEDLES GDNGFPGDMDEGDASLFT RPEIVVFNC SLQQVRNPS SFQEQPHGNITFNMELYNTDLFLVPSQGV FSVPENGHVYVEVSVTKAEQELGFAIQTCFISPYSNPDRMSHYTHIEN ICPKDES VKFYSPKRVHFPIPQADMDKKRFSFVKPVFNTSLLFLQCE LTLCTKMEKHPQKLPKCVPPDEACTSLDASIIWAMMQNKKTFTKPL AVIHHEAESKEKGPSMKEPNPISPPIFHGLDTLTVMGIAFAAFVIGAL LTGALWYIYSHTGETAGRQQVPTSPPASENSSAAHSIGSTQSTPCSSS STA

SEQ ID NO: 7280	Human TGFB3 isoform 2 (Q03167-2)	GPEPGALCELSPVASHPVQALMESFTVLSGCASRGTTGLPQEVHVL NLRTAGQGPGQLQREVTLHLNPISSVHHHKSVVFLNLSHPLVWH LKTERLATGVSRFLVSEGSVVQFSSANFSLTAETEERNFPHGNEHL LNWARKEYGAVTSFTELKIARNIYIKVGEDQVFPPKCNIGKNFLSLN YLAEYLQPKAAEGCVMSSQPQNEEVHIIELITPNSNPYSAFQVDITID IRPSQEDLEVVKNLILILKCKSVNWVIKSFVDVKGSLKIIAPNSIGFGK ESERSMTMTKSIRDDIPSTQGNLVKWALDNGYSPITSYTMAPVANR FHLRLNNEEMGDDEEVHTIPPELRILLDPGALPALQNPPIRGGEGQN GGLPFPFPDISRRVWNEEGEDGLPRPKDPVIPSILFPGPREPEEVQG SVDIALSVKCDNEKMIVAVEKDSFQASGYSGMDVTLLDPTCKAKM NGTHFVLESPLNGCGTRPRWSALDGVVYYNSIVIQVPALGDSSGWP DGYEDLES GDNGFPGDMDEGDASLFTRPEIVVFNC SLQQVRNPSSF QEQPHGNITFNMELYN TDLFLVPSQGVFSVPENGHVYVEVSVTKAE QELGFAIQTCFISPYSNPDRMSHYTHIENICPKDES VKFYSPKRVHFPI PQADMDKKRFSFVFKPVFNTSLLFLQCELTLCTKMEKHQPQLPKCV PPDEACTSLDASIIWAMMQNKKTFTKPLAVIHHEAESKEKGPSMKE PNPISPPIFHGLDTLTVMGIAFAAFVIGALLTGALWYIYSHTGETAGR QQVPTSPPASENSSAAHSIGSTQSTPCSSSSTA
SEQ ID NO: 7270	Human TGFB3 fragment 1	GPEPGALCELSPVASHPVQALMESFTVLSGCASRGTTGLPQEVHVL NLRTAGQGPGQLQREVTLHLNPISSVHHHKSVVFLNLSHPLVWH LKTERLATGVSRFLVSEGSVVQFSSANFSLTAETEERNFPHGNEHL LNWARKEYGAVTSFTELKIARNIYIKVGEDQVFPPKCNIGKNFLSLN YLAEYLQPKAAEGCVMSSQPQNEEVHIIELITPNSNPYSAFQVDITID IRPSQEDLEVVKNLILILKCKSVNWVIKSFVDVKGSLKIIAPNSIGFGK ESERSMTMTKSIRDDIPSTQGNLVKWALDNGYSPITSYTMAPVANR FHLRLNNAEEMGDDEEVHTIPPELRILLDPGALPALQNPPIRGGEGQ NGGLPFPFPDISRRVWNEEGEDGLPRPKDPVIPSILFPGPREPEEVQ GSVDIALSVKCDNEKMIVAVEKDSFQASGYSGMDVTLLDPTCKAK MNGTHFVLESPLNGCGTRPRWSALDGVVYYNSIVIQVPALGDSSG WPDGYEDLES GDNGFPGDMDEGDASLFTRPEIVVFNC SLQQVRNPS SFQEQPHGNITFNMELYN TDLFLVPSQGVFSVPENGHVYVEVSVTK AEQELGFAIQTCFISPYSNPDRMSHYTHIENICPKDES VKFYSPKRVHF PIPQADMDKKRFSFVFKPVFNTSLLFLQCELTLCTKMEKHQPQLPKC VPPDEACTSLDASIIWAMMQNKKTFTKPLAVIHHEAESKEKGPSMK EPNPISPPIFHGLDTLTV
SEQ ID NO: 7281	hCH1- hFc_Hole- 3x4GS- TGFB2	ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALT SGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKV DKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEV TCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVV SVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVC TLPPSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTP PVLDS DGSFFLVSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS LSLSPGXGGGGSGGGSGGGGSIPPHVQKSVNNDMIVTDNNGAVK

		FPQLCKFCDVRFSTCDNQKSCMSNCSITSICEKPQEVCAVWRKND ENITLETVCHDPKLPYHDFILEDAAASPKCIMKEKKKPGETFFMCSCS SDECNDNIIFSEEYNTSNPD, wherein X is K or absent
SEQ ID NO: 7282	hCH1- hFc_Knob- 3x4GS- TGFbR2	ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALT SGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKV DKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEV TCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVV SVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVY TLPPCREEMTKNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSGDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS LSLSPGXGGGGSGGGSGGGGSIPPHVQKSVNNDMIVTDNNGAVK FPQLCKFCDVRFSTCDNQKSCMSNCSITSICEKPQEVCAVWRKND ENITLETVCHDPKLPYHDFILEDAAASPKCIMKEKKKPGETFFMCSCS SDECNDNIIFSEEYNTSNPD, wherein X is K or absent
SEQ ID NO: 7283	hFc_Hole- 3x4GS- TGFbR2	DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVS HEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQ DWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVCTLPSPREE MTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSGDG SFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGXG GGGSGGGSGGGGSIPPHVQKSVNNDMIVTDNNGAVKFPQLCKFC DVRFSTCDNQKSCMSNCSITSICEKPQEVCAVWRKNDENITLET VCHDPKLPYHDFILEDAAASPKCIMKEKKKPGETFFMCSCSSDECNDNI IFSEEYNTSNPD, wherein X is K or absent
SEQ ID NO: 7284	hFc_Knob- 3x4GS- TGFbR2	DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVS HEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQ DWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPCREE MTKNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSGDG SFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGX GGGSGGGSGGGGSIPPHVQKSVNNDMIVTDNNGAVKFPQLCKF CDVRFSTCDNQKSCMSNCSITSICEKPQEVCAVWRKNDENITLET VCHDPKLPYHDFILEDAAASPKCIMKEKKKPGETFFMCSCSSDECND NIIFSEEYNTSNPD, wherein X is K or absent
SEQ ID NO: 7285	TGFbR2- 3x4GS- hCH1- hFc_Hole	IPPHVQKSVNNDMIVTDNNGAVKFPQLCKFCDVRFSTCDNQKSCMS NCSITSICEKPQEVCAVWRKNDENITLETVCHDPKLPYHDFILEDAA ASPKCIMKEKKKPGETFFMCSCSSDECNDNIIFSEEYNTSNPDGGGG SGGGSGGGGSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEP VTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYIC NVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPK KDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPR EEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISK AKGQPREPQVCTLPSPREEEMTKNQVSLSCAVKGFYPSDIAVEWESN GQPENNYKTTPPVLDSGDGSFFLYSKLTVDKSRWQQGNVFSCSVMH EALHNHYTQKSLSLSPGX, wherein X is K or absent

SEQ ID NO: 7286	TGF β R2- 3x4GS- hCH1- hFc_Knob	IPPHVQKSVNNDMIVTDNNGAVKFPQLCKFCDVRFSTCDNQKSCMS NCSITSICEKPQEVCAVWRKNDENITLETVCHDPKLPYHDFILED ASPKCIMKEKKKPGETFFMCSCSSDECNDNIIFSEEYNTSNPDGGGG SGGGGSGGGGSGASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEP VTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYIC NVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKP KDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPR EEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISK AKGQPREPQVYTLPPCREEMTKNQVSLWCLVKGFYPSDIAVEWES NGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVM HEALHNHYTQKSLSLSPGX, wherein X is K or absent
SEQ ID NO: 7287	TGF β R2- 3x4GS- hCLIg_vl	IPPHVQKSVNNDMIVTDNNGAVKFPQLCKFCDVRFSTCDNQKSCMS NCSITSICEKPQEVCAVWRKNDENITLETVCHDPKLPYHDFILED ASPKCIMKEKKKPGETFFMCSCSSDECNDNIIFSEEYNTSNPDGGGG SGGGGSGGGGSGQPKANPTVTLFPPSSEELQANKATLVCLISDFYPG AVTVAWKADGSPVKAGVETTKPSKQSNKYYASSYLSLTPEQWKS HRSYSCQVTHEGSTVEKTVAPTECS
SEQ ID NO: 7288	TGF β R2- 3x4GS- hCLIg_vk	IPPHVQKSVNNDMIVTDNNGAVKFPQLCKFCDVRFSTCDNQKSCMS NCSITSICEKPQEVCAVWRKNDENITLETVCHDPKLPYHDFILED ASPKCIMKEKKKPGETFFMCSCSSDECNDNIIFSEEYNTSNPDGGGG SGGGGSGGGGSGRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPRE AKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEK HKVYACEVTHQGLSSPVTKSFNRGEC

Immune Cell Engagers

The immune cell engagers of the multispecific or multifunctional molecules disclosed herein can mediate binding to, and/or activation of, an immune cell, e.g., an immune effector cell. In some embodiments, the immune cell is chosen from a T cell, an NK cell, a B cell, a dendritic cell, or a macrophage cell engager, or a combination thereof. In some embodiments, the immune cell engager is chosen from one, two, three, or all of a T cell engager, NK cell engager, a B cell engager, a dendritic cell engager, or a macrophage cell engager, or a combination thereof. The immune cell engager can be an agonist of the immune system. In some embodiments, the immune cell engager can be an antibody molecule, a ligand molecule (e.g., a ligand that further comprises an immunoglobulin constant region, e.g., an Fc region), a small molecule, a nucleotide molecule.

Natural Killer Cell Engagers

Natural Killer (NK) cells recognize and destroy tumors and virus-infected cells in an antibody-independent manner. The regulation of NK cells is mediated by activating and inhibiting receptors on the NK cell surface. One family of activating receptors is the natural cytotoxicity receptors (NCRs) which include NKp30, NKp44 and NKp46. For example, the NCRs can initiate tumor targeting by recognition of heparan sulfate on cancer cells. NKG2D is a receptor that provides both stimulatory and costimulatory innate immune responses on activated killer (NK) cells, leading to cytotoxic activity. DNAM1 is a receptor involved in intercellular adhesion, lymphocyte signaling, cytotoxicity and lymphokine secretion mediated by cytotoxic T-lymphocyte (CTL) and NK cell. DAP10 (also known as HCST) is a transmembrane adapter protein which associates with KLRK1 to form an activation receptor KLRK1-HCST in lymphoid and myeloid cells; this receptor plays a major role in triggering cytotoxicity against target cells expressing cell surface ligands such as MHC class I chain-related MICA and MICB, and U(optionally L1)6-binding proteins (ULBPs); it KLRK1-HCST receptor plays a role in immune surveillance against tumors and is required for cytolysis of tumors cells; indeed, melanoma cells that do not express KLRK1 ligands escape from immune surveillance mediated by NK cells. CD16 is a receptor for the Fc region of IgG, which binds complexed or aggregated IgG and also monomeric IgG and thereby mediates antibody-dependent cellular cytotoxicity (ADCC) and other antibody-dependent responses, such as phagocytosis. Without wishing to be bound by theory, it is thought that NK cell engagers that bind, recruit, and/or activate receptors like those disclosed above (e.g., NKp30, NKp36, NKG2D, or CD16) may target immune system activity to a target cell, e.g., a cell comprising a TCRBV antigen (e.g., a TCRBV antigen corresponding to a biased TCRBV clonotype), e.g., promote cell death or lysis of a target cell.

The present disclosure provides, *inter alia*, multispecific (e.g., bi-, tri-, quad- specific) or multifunctional molecules, that are engineered to contain one or more NK cell engagers that mediate binding to and/or activation of an NK cell. Accordingly, in some embodiments, the NK cell engager is selected from an antigen binding domain or ligand that binds to (e.g., activates): NKp30, NKp40, NKp44, NKp46, NKG2D, DNAM1, DAP10, CD16 (e.g., CD16a, CD16b, or both), CRTAM, CD27, PSGL1, CD96, CD100 (SEMA4D), NKp80, CD244 (also known as

SLAMF4 or 2B4), SLAMF6, SLAMF7, KIR2DS2, KIR2DS4, KIR3DS1, KIR2DS3, KIR2DS5, KIR2DS1, CD94, NKG2C, NKG2E, or CD160.

In some embodiments, the NK cell engager is an antigen binding domain that binds to NKp30 (e.g., NKp30 present, e.g., expressed or displayed, on the surface of an NK cell) and comprises any CDR amino acid sequence, framework region (FWR) amino acid sequence, or variable region amino acid sequence disclosed in Tables 7-10. In some embodiments, the NK cell engager is an antigen binding domain that binds to NKp30 (e.g., NKp30 present, e.g., expressed or displayed, on the surface of an NK cell) and comprises any CDR amino acid sequence, framework region (FWR) amino acid sequence, or variable region amino acid sequence disclosed in U.S. Patent No. 6,979,546, U.S. Patent No. 9,447,185, PCT Application No. WO2015121383A1, PCT Application No. WO2016110468A1, PCT Application No. WO2004056392A1, or U.S. Application Publication No. US20070231322A1, the sequences of which are hereby incorporated by reference. In some embodiments, binding of the NK cell engager, e.g., antigen binding domain that binds to NKp30, to the NK cell activates the NK cell. An antigen binding domain that binds to NKp30 (e.g., NKp30 present, e.g., expressed or displayed, on the surface of an NK cell) may be said to target NKp30, the NK cell, or both.

In some embodiments, the antigen binding domain that binds to NKp30 comprises one or more CDRs (e.g., VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2, and/or VLCDR3) disclosed in Table 7, Table 18, or Table 8, or a sequence having at least 85%, 90%, 95%, or 99% identity thereto. In some embodiments, the antigen binding domain that binds to NKp30 comprises one or more framework regions (e.g., VHFWR1, VHFWR2, VHFWR3, VHFWR4, VLFWR1, VLFWR2, VLFWR3, and/or VLFWR4) disclosed in Table 7, Table 18, or Table 8, or a sequence having at least 85%, 90%, 95%, or 99% identity thereto. In some embodiments, the antigen binding domain that binds to NKp30 comprises a VH and/or a VL disclosed in Table 9, or a sequence having at least 85%, 90%, 95%, or 99% identity thereto. In some embodiments, any of the VH domains disclosed in Table 9 may be paired with any of the VL domains disclosed in Table 9 to form the antigen binding domain that binds to NKp30. In some embodiments, the antigen binding domain that binds to NKp30 comprises an amino acid sequence disclosed in Table 10, or a sequence having at least 85%, 90%, 95%, or 99% identity thereto.

In some embodiments, the antigen binding domain that binds to NKp30 comprises a VH comprising a heavy chain complementarity determining region 1 (VHCDR1), a VHCDR2, and a VHCDR3, and a VL comprising a light chain complementarity determining region 1 (VLCDR1), a VLCDR2, and a VLCDR3.

5 In some embodiments, the VHCDR1, VHCDR2, and VHCDR3 comprise the amino acid sequences of SEQ ID NOs: 7313, 6001, and 7315, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the VHCDR1, VHCDR2, and VHCDR3 comprise the amino acid sequences of SEQ ID NOs: 7313, 6001, and 6002, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some
10 embodiments, the VHCDR1, VHCDR2, and VHCDR3 comprise the amino acid sequences of SEQ ID NOs: 7313, 6008, and 6009, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the VHCDR1, VHCDR2, and VHCDR3 comprise the amino acid sequences of SEQ ID NOs: 7313, 7385, and 7315, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the
15 VHCDR1, VHCDR2, and VHCDR3 comprise the amino acid sequences of SEQ ID NOs: 7313, 7318, and 6009, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto).

In some embodiments, the VLCDR1, VLCDR2, and VLCDR3 comprise the amino acid sequences of SEQ ID NOs: 7326, 7327, and 7329, respectively (or a sequence having at least
20 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the VLCDR1, VLCDR2, and VLCDR3 comprise the amino acid sequences of SEQ ID NOs: 6063, 6064, and 7293, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the VLCDR1, VLCDR2, and VLCDR3 comprise the amino acid sequences of SEQ ID NOs: 6070, 6071, and 6072, respectively (or a sequence having at least 85%, 90%, 95%,
25 or 99% identity thereto). In some embodiments, the VLCDR1, VLCDR2, and VLCDR3 comprise the amino acid sequences of SEQ ID NOs: 6070, 6064, and 7321, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto).

In some embodiments, the VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2, and VLCDR3 comprise the amino acid sequences of SEQ ID NOs: 7313, 6001, 7315, 7326, 7327,
30 and 7329, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto).

In some embodiments, the VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2, and VLCDR3 comprise the amino acid sequences of SEQ ID NOs: 7313, 6001, 6002, 6063, 6064, and 7293, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2, and VLCDR3
5 comprise the amino acid sequences of SEQ ID NOs: 7313, 6008, 6009, 6070, 6071, and 6072, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2, and VLCDR3 comprise the amino acid sequences of SEQ ID NOs: 7313, 7385, 7315, 6070, 6064, and 7321, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some
10 embodiments, the VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2, and VLCDR3 comprise the amino acid sequences of SEQ ID NOs: 7313, 7318, 6009, 6070, 6064, and 7321, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto).

In some embodiments, the VH comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 7298 or 7300-7304 (or a sequence having at least 85%, 90%,
15 95%, or 99% identity thereto) and/or the VL comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 7299 or 7305-7309 (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the VH and VL comprise the amino acid sequences of SEQ ID NOs: 7302 and 7305, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the VH and VL comprise the amino
20 acid sequences of SEQ ID NOs: 7302 and 7309, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto).

In some embodiments, the VH comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 6121 or 6123-6128 (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto) and/or the VL comprises an amino acid sequence selected from the
25 group consisting of SEQ ID NOs: 7294 or 6137-6141 (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the VH comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 6122 or 6129-6134 (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto) and/or the VL comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 6136 or 6142-6147 (or a sequence having at
30 least 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the VH and VL comprise

the amino acid sequences of SEQ ID NOs: 7295 and 7296, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the VH and VL comprise the amino acid sequences of SEQ ID NOs: 7297 and 7296, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the VH and VL comprise
5 the amino acid sequences of SEQ ID NOs: 6122 and 6136, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto).

In some embodiments, the antigen binding domain that binds to NKp30 comprises the amino acid sequence of SEQ ID NO: 7310 (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the antigen binding domain that binds to NKp30
10 comprises the amino acid sequence of SEQ ID NO: 7311 (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the antigen binding domain that binds to NKp30 comprises the amino acid sequence of SEQ ID NO: 6187, 6188, 6189 or 6190 (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain
15 complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 6000 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 amino acid sequence of SEQ ID NO: 6001 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VHCDR3 amino acid sequence of SEQ ID NO: 6002 (or a sequence with no more than 1, 2, 3, or 4 mutations,
20 e.g., substitutions, additions, or deletions). In some embodiments, the NKp30 antigen binding domain comprises a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 6000, a VHCDR2 amino acid sequence of SEQ ID NO: 6001, and/or a VHCDR3 amino acid sequence of SEQ ID NO: 6002.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VL
25 comprising a light chain complementarity determining region 1 (VLCDR1) amino acid sequence of SEQ ID NO: 6063 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VLCDR2 amino acid sequence of SEQ ID NO: 6064 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VLCDR3 amino acid sequence of SEQ ID NO: 7293 (or a sequence with no more than 1, 2, 3, or
30 4 mutations, e.g., substitutions, additions, or deletions). In some embodiments, the antigen

binding domain that targets NKp30 comprises a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 6063, a VLCDR2 amino acid sequence of SEQ ID NO: 6064, and a VLCDR3 amino acid sequence of SEQ ID NO: 7293.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH
5 comprising a heavy chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 6000 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 amino acid sequence of SEQ ID NO: 6001 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VHCDR3 amino acid sequence of SEQ ID NO: 6002 (or a sequence with no more than
10 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and a VL comprising a light chain complementarity determining region 1 (VLCDR1) amino acid sequence of SEQ ID NO: 6063 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VLCDR2 amino acid sequence of SEQ ID NO: 6064 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VLCDR3 amino
15 acid sequence of SEQ ID NO: 7293 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions). In some embodiments, the NKp30 antigen binding domain comprises a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 6000, a VHCDR2 amino acid sequence of SEQ ID NO: 6001, and/or a VHCDR3 amino acid sequence of SEQ ID NO: 6002, and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 6063,
20 a VLCDR2 amino acid sequence of SEQ ID NO: 6064, and a VLCDR3 amino acid sequence of SEQ ID NO: 7293.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH
comprising a heavy chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 6007 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g.,
25 substitutions, additions, or deletions), a VHCDR2 amino acid sequence of SEQ ID NO: 6008 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VHCDR3 amino acid sequence of SEQ ID NO: 6009 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions). In some embodiments, the NKp30 antigen binding domain comprises a VH comprising a VHCDR1 amino acid sequence of

SEQ ID NO: 6007, a VHCDR2 amino acid sequence of SEQ ID NO: 6008, and/or a VHCDR3 amino acid sequence of SEQ ID NO: 6009.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a light chain complementarity determining region 1 (VLCDR1) amino acid sequence of SEQ ID NO: 6070 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VLCDR2 amino acid sequence of SEQ ID NO: 6071 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VLCDR3 amino acid sequence of SEQ ID NO: 6072 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions). In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 6070, a VLCDR2 amino acid sequence of SEQ ID NO: 6071, and a VLCDR3 amino acid sequence of SEQ ID NO: 6072.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 6007 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 amino acid sequence of SEQ ID NO: 6008 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VHCDR3 amino acid sequence of SEQ ID NO: 6009 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and a VL comprising a light chain complementarity determining region 1 (VLCDR1) amino acid sequence of SEQ ID NO: 6070 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VLCDR2 amino acid sequence of SEQ ID NO: 6071 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VLCDR3 amino acid sequence of SEQ ID NO: 6072 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions). In some embodiments, the NKp30 antigen binding domain comprises a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 6007, a VHCDR2 amino acid sequence of SEQ ID NO: 6008, and/or a VHCDR3 amino acid sequence of SEQ ID NO: 6009, and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 6070, a VLCDR2 amino acid sequence of SEQ ID NO: 6071, and a VLCDR3 amino acid sequence of SEQ ID NO: 6072.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6003, a VHFWR2 amino acid sequence of SEQ ID NO: 6004, a VHFWR3 amino acid sequence of SEQ ID NO: 6005, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6006.

5 In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6066, a VLFWR2 amino acid sequence of SEQ ID NO: 6067, a VLFWR3 amino acid sequence of SEQ ID NO: 7292, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6069.

10 In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6003, a VHFWR2 amino acid sequence of SEQ ID NO: 6004, a VHFWR3 amino acid sequence of SEQ ID NO: 6005, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6006, and a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6066, a VLFWR2 amino acid sequence of SEQ ID NO: 6067, a VLFWR3 amino acid sequence of SEQ ID NO: 7292, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6069.

15 In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a VHFWR1 amino acid sequence of SEQ ID NO: 6003 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6004 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6005 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 mutations, e.g., substitutions, additions, or deletions), and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6006.

20 In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a VLFWR1 amino acid sequence of SEQ ID NO: 6066 (or a sequence with no more than 1, 2, or 3 mutations, e.g., substitutions, additions, or deletions), a VLFWR2 amino acid sequence of SEQ ID NO: 6067 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), a VLFWR3 amino acid sequence of SEQ ID NO: 7292 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6069.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a VHFWR1 amino acid sequence of SEQ ID NO: 6003 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6004 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6005 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 mutations, e.g., substitutions, additions, or deletions), and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6006, and a VL comprising a VLFWR1 amino acid sequence of SEQ ID NO: 6066 (or a sequence with no more than 1, 2, or 3 mutations, e.g., substitutions, additions, or deletions), a VLFWR2 amino acid sequence of SEQ ID NO: 6067 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), a VLFWR3 amino acid sequence of SEQ ID NO: 7292 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6069.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6010, a VHFWR2 amino acid sequence of SEQ ID NO: 6011, a VHFWR3 amino acid sequence of SEQ ID NO: 6012, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6013.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6073, a VLFWR2 amino acid sequence of SEQ ID NO: 6074, a VLFWR3 amino acid sequence of SEQ ID NO: 6075, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6076.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6010, a VHFWR2 amino acid sequence of SEQ ID NO: 6011, a VHFWR3 amino acid sequence of SEQ ID NO: 6012, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6013, and a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6073, a VLFWR2 amino acid sequence of SEQ ID NO: 6074, a VLFWR3 amino acid sequence of SEQ ID NO: 6075, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6076.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a VHFWR1 amino acid sequence of SEQ ID NO: 6010 (or a sequence with no more

than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6011 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6012 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 mutations, e.g., substitutions, additions, or deletions), and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6013.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a VLFWR1 amino acid sequence of SEQ ID NO: 6073 (or a sequence with no more than 1, 2, or 3 mutations, e.g., substitutions, additions, or deletions), a VLFWR2 amino acid sequence of SEQ ID NO: 6074 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), a VLFWR3 amino acid sequence of SEQ ID NO: 6075 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6076.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a VHFWR1 amino acid sequence of SEQ ID NO: 6010 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6011 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6012 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 mutations, e.g., substitutions, additions, or deletions), and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6013, and a VL comprising a VLFWR1 amino acid sequence of SEQ ID NO: 6073 (or a sequence with no more than 1, 2, or 3 mutations, e.g., substitutions, additions, or deletions), a VLFWR2 amino acid sequence of SEQ ID NO: 6074 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), a VLFWR3 amino acid sequence of SEQ ID NO: 6075 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6076.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6014, a VHFWR2 amino acid sequence of SEQ ID NO: 6015, a VHFWR3 amino acid sequence of SEQ ID NO: 6016, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6017.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a VHFWR1 amino acid sequence of SEQ ID NO: 6014 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6015 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6016 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 mutations, e.g., substitutions, additions, or deletions), and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6017.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6077, a VLFWR2 amino acid sequence of SEQ ID NO: 6078, a VLFWR3 amino acid sequence of SEQ ID NO: 6079, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6080.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a VLFWR1 amino acid sequence of SEQ ID NO: 6077 (or a sequence with no more than 1, 2, or 3 mutations, e.g., substitutions, additions, or deletions), a VLFWR2 amino acid sequence of SEQ ID NO: 6078 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), a VLFWR3 amino acid sequence of SEQ ID NO: 6079 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6080.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6018, a VHFWR2 amino acid sequence of SEQ ID NO: 6019, a VHFWR3 amino acid sequence of SEQ ID NO: 6020, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6021.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a VHFWR1 amino acid sequence of SEQ ID NO: 6018 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6019 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6020 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10,

or 11 mutations, e.g., substitutions, additions, or deletions), and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6021.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6081, a VLFWR2 amino acid sequence of SEQ ID NO: 6082, a VLFWR3 amino acid sequence of SEQ ID NO: 6083, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6084.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a VLFWR1 amino acid sequence of SEQ ID NO: 6081 (or a sequence with no more than 1, 2, or 3 mutations, e.g., substitutions, additions, or deletions), a VLFWR2 amino acid sequence of SEQ ID NO: 6082 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), a VLFWR3 amino acid sequence of SEQ ID NO: 6083 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6084.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6022, a VHFWR2 amino acid sequence of SEQ ID NO: 6023, a VHFWR3 amino acid sequence of SEQ ID NO: 6024, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6025.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a VHFWR1 amino acid sequence of SEQ ID NO: 6022 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6023 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6024 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 mutations, e.g., substitutions, additions, or deletions), and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6025.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6085, a VLFWR2 amino acid sequence of SEQ ID NO: 6086, a VLFWR3 amino acid sequence of SEQ ID NO: 6087, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6088.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a VLFWR1 amino acid sequence of SEQ ID NO: 6085 (or a sequence with no more than 1, 2, or 3 mutations, e.g., substitutions, additions, or deletions), a VLFWR2 amino acid sequence of SEQ ID NO: 6086 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), a VLFWR3 amino acid sequence of SEQ ID NO: 6087 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6088.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6026, a VHFWR2 amino acid sequence of SEQ ID NO: 6027, a VHFWR3 amino acid sequence of SEQ ID NO: 6028, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6029.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a VHFWR1 amino acid sequence of SEQ ID NO: 6026 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6027 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6028 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 mutations, e.g., substitutions, additions, or deletions), and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6029.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6089, a VLFWR2 amino acid sequence of SEQ ID NO: 6090, a VLFWR3 amino acid sequence of SEQ ID NO: 6091, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6092.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a VLFWR1 amino acid sequence of SEQ ID NO: 6089 (or a sequence with no more than 1, 2, or 3 mutations, e.g., substitutions, additions, or deletions), a VLFWR2 amino acid sequence of SEQ ID NO: 6090 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), a VLFWR3 amino acid sequence of SEQ ID NO: 6091 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6092.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6030, a VHFWR2 amino acid sequence of SEQ ID NO: 6032, a VHFWR3 amino acid sequence of SEQ ID NO: 6033, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6034.

5 In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a VHFWR1 amino acid sequence of SEQ ID NO: 6030 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6032 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino
10 acid sequence of SEQ ID NO: 6033 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 mutations, e.g., substitutions, additions, or deletions), and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6034.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO:
15 6093, a VLFWR2 amino acid sequence of SEQ ID NO: 6094, a VLFWR3 amino acid sequence of SEQ ID NO: 6095, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6096.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a VLFWR1 amino acid sequence of SEQ ID NO: 6093 (or a sequence with no more than 1, 2, or 3 mutations, e.g., substitutions, additions, or deletions), a VLFWR2 amino acid
20 sequence of SEQ ID NO: 6094 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), a VLFWR3 amino acid sequence of SEQ ID NO: 6095 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6096.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO:
25 6035, a VHFWR2 amino acid sequence of SEQ ID NO: 6036, a VHFWR3 amino acid sequence of SEQ ID NO: 6037, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6038.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a VHFWR1 amino acid sequence of SEQ ID NO: 6035 (or a sequence with no more
30 than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a

VHFWR2 amino acid sequence of SEQ ID NO: 6036 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6037 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 mutations, e.g., substitutions, additions, or deletions), and/or a VHFWR4 amino acid
 5 sequence of SEQ ID NO: 6038.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6039, a VHFWR2 amino acid sequence of SEQ ID NO: 6040, a VHFWR3 amino acid sequence of SEQ ID NO: 6041, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6042.

10 In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a VHFWR1 amino acid sequence of SEQ ID NO: 6039 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6040 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino
 15 acid sequence of SEQ ID NO: 6041 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 mutations, e.g., substitutions, additions, or deletions), and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6042.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6097, a VLFWR2 amino acid sequence of SEQ ID NO: 6098, a VLFWR3 amino acid sequence of SEQ ID NO: 6099, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6100.
 20

In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a VLFWR1 amino acid sequence of SEQ ID NO: 6097 (or a sequence with no more than 1, 2, or 3 mutations, e.g., substitutions, additions, or deletions), a VLFWR2 amino acid
 25 sequence of SEQ ID NO: 6098 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), a VLFWR3 amino acid sequence of SEQ ID NO: 6099 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6100.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH
 30 comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO:

6043, a VHFWR2 amino acid sequence of SEQ ID NO: 6044, a VHFWR3 amino acid sequence of SEQ ID NO: 6045, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6046.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a VHFWR1 amino acid sequence of SEQ ID NO: 6043 (or a sequence with no more
 5 than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6044 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6045 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 mutations, e.g., substitutions, additions, or deletions), and/or a VHFWR4 amino acid
 10 sequence of SEQ ID NO: 6046.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6101, a VLFWR2 amino acid sequence of SEQ ID NO: 6102, a VLFWR3 amino acid sequence of SEQ ID NO: 6103, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6104.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a VLFWR1 amino acid sequence of SEQ ID NO: 6101 (or a sequence with no more
 15 than 1, 2, or 3 mutations, e.g., substitutions, additions, or deletions), a VLFWR2 amino acid sequence of SEQ ID NO: 6102 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), a VLFWR3 amino acid sequence of SEQ ID NO: 6103 (or a sequence with
 20 no more than 1 mutation, e.g., substitution, addition, or deletion), and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6104.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6047, a VHFWR2 amino acid sequence of SEQ ID NO: 6048, a VHFWR3 amino acid sequence
 25 of SEQ ID NO: 6049, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6050.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a VHFWR1 amino acid sequence of SEQ ID NO: 6047 (or a sequence with no more
 than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a
 VHFWR2 amino acid sequence of SEQ ID NO: 6048 (or a sequence with no more than 1, 2, 3,
 30 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino

acid sequence of SEQ ID NO: 6049 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 mutations, e.g., substitutions, additions, or deletions), and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6050.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6105, a VLFWR2 amino acid sequence of SEQ ID NO: 6106, a VLFWR3 amino acid sequence of SEQ ID NO: 6107, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6108.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a VLFWR1 amino acid sequence of SEQ ID NO: 6105 (or a sequence with no more than 1, 2, or 3 mutations, e.g., substitutions, additions, or deletions), a VLFWR2 amino acid sequence of SEQ ID NO: 6106 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), a VLFWR3 amino acid sequence of SEQ ID NO: 6107 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6108.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6051, a VHFWR2 amino acid sequence of SEQ ID NO: 6052, a VHFWR3 amino acid sequence of SEQ ID NO: 6053, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6054.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a VHFWR1 amino acid sequence of SEQ ID NO: 6051 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6052 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6053 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 mutations, e.g., substitutions, additions, or deletions), and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6054.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6109, a VLFWR2 amino acid sequence of SEQ ID NO: 6110, a VLFWR3 amino acid sequence of SEQ ID NO: 6111, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6112.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a VLFWR1 amino acid sequence of SEQ ID NO: 6109 (or a sequence with no more than 1, 2, or 3 mutations, e.g., substitutions, additions, or deletions), a VLFWR2 amino acid sequence of SEQ ID NO: 6110 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), a VLFWR3 amino acid sequence of SEQ ID NO: 6111 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6112.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6055, a VHFWR2 amino acid sequence of SEQ ID NO: 6056, a VHFWR3 amino acid sequence of SEQ ID NO: 6057, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6058.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a VHFWR1 amino acid sequence of SEQ ID NO: 6055 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6056 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6057 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 mutations, e.g., substitutions, additions, or deletions), and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6058.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6113, a VLFWR2 amino acid sequence of SEQ ID NO: 6114, a VLFWR3 amino acid sequence of SEQ ID NO: 6115, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6116.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a VLFWR1 amino acid sequence of SEQ ID NO: 6113 (or a sequence with no more than 1, 2, or 3 mutations, e.g., substitutions, additions, or deletions), a VLFWR2 amino acid sequence of SEQ ID NO: 6114 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), a VLFWR3 amino acid sequence of SEQ ID NO: 6115 (or a sequence with

no more than 1 mutation, e.g., substitution, addition, or deletion), and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6116.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6059, a VHFWR2 amino acid sequence of SEQ ID NO: 6060, a VHFWR3 amino acid sequence of SEQ ID NO: 6061, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6062.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a VHFWR1 amino acid sequence of SEQ ID NO: 6059 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6060 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6061 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 mutations, e.g., substitutions, additions, or deletions), and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6062.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6117, a VLFWR2 amino acid sequence of SEQ ID NO: 6118, a VLFWR3 amino acid sequence of SEQ ID NO: 6119, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6120.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a VLFWR1 amino acid sequence of SEQ ID NO: 6117 (or a sequence with no more than 1, 2, or 3 mutations, e.g., substitutions, additions, or deletions), a VLFWR2 amino acid sequence of SEQ ID NO: 6118 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), a VLFWR3 amino acid sequence of SEQ ID NO: 6119 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6120.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising the amino acid sequence of SEQ ID NO: 6148 (or an amino acid sequence having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6148). In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising the amino acid sequence of SEQ ID NO: 6149 (or an amino acid sequence having at least about

77%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6149). In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising the amino acid sequence of SEQ ID NO: 6150 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6150). In some embodiments, antigen
5 binding domain that targets NKp30 comprises a VH comprising the amino acid sequence of SEQ ID NO: 6148. In some embodiments, antigen binding domain that targets NKp30 comprises a VH comprising the amino acid sequence of SEQ ID NO: 6149. In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising the amino acid sequence of SEQ ID NO: 6150.

10 In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising the amino acid sequence of SEQ ID NO: 6148, and a VL comprising the amino acid sequence of SEQ ID NO: 6150. In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising the amino acid sequence of SEQ ID NO: 6149, and a VL comprising the amino acid sequence of SEQ ID NO: 6150.

15 In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising the amino acid sequence of SEQ ID NO: 6151 (or an amino acid sequence having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6151). In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising
20 the amino acid sequence of SEQ ID NO: 6152 (or an amino acid sequence having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6152). In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising the amino acid sequence of SEQ ID NO: 6153 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6153). In some embodiments, antigen
25 binding domain that targets NKp30 comprises a VH comprising the amino acid sequence of SEQ ID NO: 6151. In some embodiments, antigen binding domain that targets NKp30 comprises a VH comprising the amino acid sequence of SEQ ID NO: 6152. In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising the amino acid sequence of SEQ ID NO: 6153.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising the amino acid sequence of SEQ ID NO: 6151, and a VL comprising the amino acid sequence of SEQ ID NO: 6153. In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising the amino acid sequence of SEQ ID NO: 6152, and a VL comprising the amino acid sequence of SEQ ID NO: 6153.

In some embodiments, the antigen binding domain that targets NKp30 comprises an scFv. In some embodiments, the scFv comprises an amino acid sequence selected from SEQ ID NOs: 6187-6190, or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity thereto.

Table 7. Exemplary heavy chain CDRs and FWRs of NKp30-targeting antigen binding domains

Ab ID	VHFWR1	VHCDR1	VHFWR2	VHCDR2	VHFWR3	VHCDR3	VHFWR4
9G1-HC	QIQLQES GPGLVKP SQSLSLTC SVTGFSIN (SEQ ID NO: 6003)	TGGYHW N (SEQ ID NO: 6000)	WIRQFPG KKLEWM G (SEQ ID NO: 6004)	YIYSSGST SYNPSLK S (SEQ ID NO: 6001)	RISITRDT SKNQFFL QLNSVTT EDTATYY CAR (SEQ ID NO: 6005)	GNWHYF DF (SEQ ID NO: 6002)	WGQGT M VTVSS (SEQ ID NO: 6006)
15H6-HC	QIQLQES GPGLVKP SQSLSLTC SVTGFSIN (SEQ ID NO: 6010)	TGGYHW N (SEQ ID NO: 6007)	WIRQFPG KKLEWM G (SEQ ID NO: 6011)	YIYSSGTT RYNPSLK S (SEQ ID NO: 6008)	RISITRDT SKNQFFL QLNSVTP EDTATYY CTR (SEQ ID NO: 6012)	GNWHYF DY (SEQ ID NO: 6009)	WGQGT L VAVSS (SEQ ID NO: 6013)
9G1-HC_1	QIQLQES GPGLVKP SETLSLTC TVSGFSIN (SEQ ID NO: 6014)	TGGYHW N (SEQ ID NO: 6000)	WIRQPAG KGLEWIG (SEQ ID NO: 6015)	YIYSSGST SYNPSLK S (SEQ ID NO: 6001)	RVTMSRD TSKNQFS LKLSSVT AADTAVY YCAR (SEQ ID NO: 6016)	GNWHYF DF (SEQ ID NO: 6002)	WGQGT M VTVSS (SEQ ID NO: 6017)
9G1-HC_2	QIQLQES GPGLVKP SQTLSTC TVSGFSIN (SEQ ID NO: 6018)	TGGYHW N (SEQ ID NO: 6000)	WIRQHPG KGLEWIG (SEQ ID NO: 6019)	YIYSSGST SYNPSLK S (SEQ ID NO: 6001)	LVTISRDT SKNQFSL KLSSVTA ADTAVYY CAR (SEQ ID NO: 6020)	GNWHYF DF (SEQ ID NO: 6002)	WGQGT M VTVSS (SEQ ID NO: 6021)
9G1-HC_3	EIQLLESG GGLVQPG GSLRLSC AVSGFSIN (SEQ ID NO: 6022)	TGGYHW N (SEQ ID NO: 6000)	WVRQAP GKLEW VG (SEQ ID NO: 6023)	YIYSSGST SYNPSLK S (SEQ ID NO: 6001)	RFTISRDT SKNTFY L QMNSLRA EDTAVYY CAR (SEQ ID NO: 6024)	GNWHYF DF (SEQ ID NO: 6002)	WGQGT M VTVSS (SEQ ID NO: 6025)

9G1-HC_4	QIQLVQS GAEVKKP GSSVKVS CKVSGFSI N (SEQ ID NO: 6026)	TGGYHW N (SEQ ID NO: 6000)	WVRQAP GQGLEW MG (SEQ ID NO: 6027)	YIYSSGST SYNPSLK S (SEQ ID NO: 6001)	RVTITRDT STNTFYM ELSSLRSE DTAVYYC AR (SEQ ID NO: 6028)	GNWHYF DF (SEQ ID NO: 6002)	WGQGT M VTVSS (SEQ ID NO: 6029)
9G1-HC_5	EIQLVESG GGLVQPG GSLRLSC AVSGFSIN (SEQ ID NO: 6030)	TGGYHW N (SEQ ID NO: 6000)	WVRQAP GKGLEW VG (SEQ ID NO: 6032)	YIYSSGST SYNPSLK S (SEQ ID NO: 6001)	RFTISRDT AKNSFY L QMNSLRA EDTAVYY CAR (SEQ ID NO: 6033)	GNWHYF DF (SEQ ID NO: 6002)	WGQGT M VTVSS (SEQ ID NO: 6034)
9G1-HC_6	QIQLVQS GAEVKKP GASVKVS CKVSGFSI N (SEQ ID NO: 6035)	TGGYHW N (SEQ ID NO: 6000)	WVRQAP GQGLEW MG (SEQ ID NO: 6036)	YIYSSGST SYNPSLK S (SEQ ID NO: 6001)	RVTMTRD TSTNTFY MELSSLR SEDTAVY YCAR (SEQ ID NO: 6037)	GNWHYF DF (SEQ ID NO: 6002)	WGQGT M VTVSS (SEQ ID NO: 6038)
15H6-HC_1	QIQLQES GPGLVKP SQTLSLTC TVSGFSIN (SEQ ID NO: 6039)	TGGYHW N (SEQ ID NO: 6007)	WIRQHPG KGLEWIG (SEQ ID NO: 6040)	YIYSSGTT RYNPSLK S (SEQ ID NO: 6008)	LVTISRDT SKNQFSL KLSSVTA ADTAVYY CAR (SEQ ID NO: 6041)	GNWHYF DY (SEQ ID NO: 6009)	WGQGT L VTVSS (SEQ ID NO: 6042)
15H6-HC_2	QIQLQES GPGLVKP SETLSLTC TVSGFSIN (SEQ ID NO: 6043)	TGGYHW N (SEQ ID NO: 6007)	WIRQPAG KGLEWIG (SEQ ID NO: 6044)	YIYSSGTT RYNPSLK S (SEQ ID NO: 6008)	RVTMSRD TSKNQFS LKLSSVT AADTAVY YCAR (SEQ ID NO: 6045)	GNWHYF DY (SEQ ID NO: 6009)	WGQGT L VTVSS (SEQ ID NO: 6046)
15H6-HC_3	EIQLLES G GGLVQPG GSLRLSC AVSGFSIN (SEQ ID NO: 6047)	TGGYHW N (SEQ ID NO: 6007)	WVRQAP GKGLEW VG (SEQ ID NO: 6048)	YIYSSGTT RYNPSLK S (SEQ ID NO: 6008)	RFTISRDT SKNTFY L QMNSLRA EDTAVYY CAR (SEQ ID NO: 6049)	GNWHYF DY (SEQ ID NO: 6009)	WGQGT L VTVSS (SEQ ID NO: 6050)
15H6-HC_4	QIQLVES GGGLVKP GGSLRLS CAVSGFSI N (SEQ ID NO: 6051)	TGGYHW N (SEQ ID NO: 6007)	WIRQAPG KGLEWV G (SEQ ID NO: 6052)	YIYSSGTT RYNPSLK S (SEQ ID NO: 6008)	RFTISRDT AKNSFY L QMNSLRA EDTAVYY CAR (SEQ ID NO: 6053)	GNWHYF DY (SEQ ID NO: 6009)	WGQGT L VTVSS (SEQ ID NO: 6054)
15H6-HC_5	QIQLVQS GAEVKKP GASVKVS CKVSGFSI	TGGYHW N (SEQ ID NO: 6007)	WVRQAP GQGLEW MG (SEQ ID NO: 6056)	YIYSSGTT RYNPSLK S (SEQ ID NO: 6008)	RVTMTRD TSTNTFY MELSSLR SEDTAVY YCAR	GNWHYF DY (SEQ ID NO: 6009)	WGQGT L VTVSS (SEQ ID NO: 6058)

	N (SEQ ID NO: 6055)				(SEQ ID NO: 6057)		
15H6-HC_6	EIQLVQS GAEVKKP GATVKIS CKVSGFSI N (SEQ ID NO: 6059)	TGGYHW N (SEQ ID NO: 6007)	WVQQAP GKGLEW MG (SEQ ID NO: 6060)	YIYSSGTT RYNPSLK S (SEQ ID NO: 6008)	RVTITRDT STNTFYM ELSSLRSE DTAVYYC AR (SEQ ID NO: 6061)	GNWHYF DY (SEQ ID NO: 6009)	WGQGT LVTSS (SEQ ID NO: 6062)

Table 18. Exemplary heavy chain CDRs and FWRs of NKp30-targeting antigen binding domains (according to the Kabat numbering scheme)

Ab ID	VHFWR1	VHCDR1	VHFWR2	VHCDR2	VHFWR3	VHCDR3	VHFWR4
9G1-HC	QIQLQESG PGLVKPSQ SLSLTCSV TGFSINTG (SEQ ID NO: 7317)	GYHWN (SEQ ID NO: 7313)	WIRQFPGK KLEWMG (SEQ ID NO: 6004)	YIYSSGST SYNPSLKS (SEQ ID NO: 6001)	RISITRDT SKNQFFLQ LNSVTTED TATYYCAR (SEQ ID NO: 6005)	GNWHYFDF (SEQ ID NO: 6002)	WGQGTMT VSS (SEQ ID NO: 6006)
15H6-HC	QIQLQESG PGLVKPSQ SLSLTCSV TGFSINTG (SEQ ID NO: 7317)	GYHWN (SEQ ID NO: 7313)	WIRQFPGK KLEWMG (SEQ ID NO: 6011)	YIYSSGTT RYNPSLKS (SEQ ID NO: 6008)	RISITRDT SKNQFFLQ LNSVTPED TATYYCTR (SEQ ID NO: 6012)	GNWHYFDY (SEQ ID NO: 6009)	WGQGTMT VSS (SEQ ID NO: 6013)
9G1-HC_1	QIQLQESG PGLVKPSE TLSLTCTV SGFSINTG (SEQ ID NO: 7371)	GYHWN (SEQ ID NO: 7313)	WIRQPAGK GLEWIG (SEQ ID NO: 6015)	YIYSSGST SYNPSLKS (SEQ ID NO: 6001)	RVTMSRDT SKNQFSLK LSSVTAAD TAVYYCAR (SEQ ID NO: 6016)	GNWHYFDF (SEQ ID NO: 6002)	WGQGTMT VSS (SEQ ID NO: 6017)
9G1-HC_2	QIQLQESG PGLVKPSQ TLSLTCTV SGFSINTG (SEQ ID NO: 7372)	GYHWN (SEQ ID NO: 7313)	WIRQHPGK GLEWIG (SEQ ID NO: 6019)	YIYSSGST SYNPSLKS (SEQ ID NO: 6001)	LVTISRDT SKNQFSLK LSSVTAAD TAVYYCAR (SEQ ID NO: 6020)	GNWHYFDF (SEQ ID NO: 6002)	WGQGTMT VSS (SEQ ID NO: 6021)
9G1-HC_3	EIQLLESG GGLVQPGG SLRLSCAV SGFSINTG (SEQ ID NO: 7373)	GYHWN (SEQ ID NO: 7313)	WVRQAPGK GLEWVG (SEQ ID NO: 6023)	YIYSSGST SYNPSLKS (SEQ ID NO: 6001)	RFTISRDT SKNTFYLQ MNSLRAED TAVYYCAR (SEQ ID NO: 6024)	GNWHYFDF (SEQ ID NO: 6002)	WGQGTMT VSS (SEQ ID NO: 6025)
9G1-HC_4	QIQLVQSG AEVKKPGS SVKVSKV SGFSINTG	GYHWN (SEQ ID NO: 7313)	WVRQAPGQ GLEWMG (SEQ ID NO: 6023)	YIYSSGST SYNPSLKS (SEQ ID NO: 6001)	RVTITRDT STNTFYME LSSLRSED TAVYYCAR	GNWHYFDF (SEQ ID NO: 6002)	WGQGTMT VSS (SEQ ID NO: 6029)

	(SEQ ID NO: 7374)		NO: 6027)	NO: 6001)	(SEQ ID NO: 6028)		
9G1-HC_5	EIQLVESG GGLVQPGG SLRLSCAV SGFSINTG (SEQ ID NO: 7375)	GYHWN (SEQ ID NO: 7313)	WVRQAPGK GLEWVG (SEQ ID NO: 6032)	YIYSSGST SYNPSLKS (SEQ ID NO: 6001)	RFTISRDT AKNSFYLQ MNSLRAED TAVYYCAR (SEQ ID NO: 6033)	GNWHYFDF (SEQ ID NO: 6002)	WGQGTMTV VSS (SEQ ID NO: 6034)
9G1-HC_6	QIQLVQSG AEVKKPGA SVKVSCKV SGFSINTG (SEQ ID NO: 7376)	GYHWN (SEQ ID NO: 7313)	WVRQAPGQ GLEWMG (SEQ ID NO: 6036)	YIYSSGST SYNPSLKS (SEQ ID NO: 6001)	RVTMTRDT STNTFYME LSSLRSED TAVYYCAR (SEQ ID NO: 6037)	GNWHYFDF (SEQ ID NO: 6002)	WGQGTMTV VSS (SEQ ID NO: 6038)
15H6-HC_1	QIQLQESG PGLVKPSQ TLSLTCTV SGFSINTG (SEQ ID NO: 7372)	GYHWN (SEQ ID NO: 7313)	WIRQHPGK GLEWIG (SEQ ID NO: 6040)	YIYSSGTT RYNPSLKS (SEQ ID NO: 6008)	LVTISRDT SKNQFSLK LSSVTAAD TAVYYCAR (SEQ ID NO: 6041)	GNWHYFDY (SEQ ID NO: 6009)	WGQGTMTV VSS (SEQ ID NO: 6042)
15H6-HC_2	QIQLQESG PGLVKPSE TLSLTCTV SGFSINTG (SEQ ID NO: 7371)	GYHWN (SEQ ID NO: 7313)	WIRQPAGK GLEWIG (SEQ ID NO: 6044)	YIYSSGTT RYNPSLKS (SEQ ID NO: 6008)	RVTMSRDT SKNQFSLK LSSVTAAD TAVYYCAR (SEQ ID NO: 6045)	GNWHYFDY (SEQ ID NO: 6009)	WGQGTMTV VSS (SEQ ID NO: 6046)
15H6-HC_3	EIQLLES GGLVQPGG SLRLSCAV SGFSINTG (SEQ ID NO: 7373)	GYHWN (SEQ ID NO: 7313)	WVRQAPGK GLEWVG (SEQ ID NO: 6048)	YIYSSGTT RYNPSLKS (SEQ ID NO: 6008)	RFTISRDT SKNTFYLQ MNSLRAED TAVYYCAR (SEQ ID NO: 6049)	GNWHYFDY (SEQ ID NO: 6009)	WGQGTMTV VSS (SEQ ID NO: 6050)
15H6-HC_4	QIQLVESG GGLVKPGG SLRLSCAV SGFSINTG (SEQ ID NO: 7377)	GYHWN (SEQ ID NO: 7313)	WIRQAPGK GLEWVG (SEQ ID NO: 6052)	YIYSSGTT RYNPSLKS (SEQ ID NO: 6008)	RFTISRDT AKNSFYLQ MNSLRAED TAVYYCAR (SEQ ID NO: 6053)	GNWHYFDY (SEQ ID NO: 6009)	WGQGTMTV VSS (SEQ ID NO: 6054)
15H6-HC_5	QIQLVQSG AEVKKPGA SVKVSCKV SGFSINTG (SEQ ID NO: 7376)	GYHWN (SEQ ID NO: 7313)	WVRQAPGQ GLEWMG (SEQ ID NO: 6056)	YIYSSGTT RYNPSLKS (SEQ ID NO: 6008)	RVTMTRDT STNTFYME LSSLRSED TAVYYCAR (SEQ ID NO: 6057)	GNWHYFDY (SEQ ID NO: 6009)	WGQGTMTV VSS (SEQ ID NO: 6058)
15H6-HC_6	EIQLVQSG AEVKKPGA TVKISCKV	GYHWN (SEQ ID	WVQAPGK GLEWMG (SEQ ID	YIYSSGTT RYNPSLKS (SEQ ID	RVTITRDT STNTFYME LSSLRSED	GNWHYFDY (SEQ ID	WGQGTMTV VSS (SEQ

DEMANDE OU BREVET VOLUMINEUX

LA PRÉSENTE PARTIE DE CETTE DEMANDE OU CE BREVET COMPREND PLUS D'UN TOME.

CECI EST LE TOME 1 DE 2
CONTENANT LES PAGES 1 À 292

NOTE : Pour les tomes additionels, veuillez contacter le Bureau canadien des brevets

JUMBO APPLICATIONS/PATENTS

THIS SECTION OF THE APPLICATION/PATENT CONTAINS MORE THAN ONE VOLUME

THIS IS VOLUME 1 OF 2
CONTAINING PAGES 1 TO 292

NOTE: For additional volumes, please contact the Canadian Patent Office

NOM DU FICHIER / FILE NAME :

NOTE POUR LE TOME / VOLUME NOTE:

We claim:

1. A multifunctional molecule, comprising:

(i) a first antigen binding domain that binds to, e.g., selectively binds to, T cell receptor variable beta (TCRBV), e.g., a TCRBV antigen,

5 and

(ii) one, two, or all of:

(a) an immune cell engager chosen from an NK cell engager, a T cell engager, a B cell engager, a dendritic cell engager, or a macrophage cell engager;

(b) a cytokine molecule or cytokine inhibitor molecule; and

10 (c) a death receptor signal engager.

2. A multifunctional molecule, comprising:

(i) a first antigen binding domain that binds to, e.g., selectively binds to, T cell receptor variable beta (TCRBV), e.g., a TCRBV antigen, and

15 (ii) an NK cell engager, e.g., an anti-NKp30, anti-NKp46, anti-NKG2D, or anti-CD16 antibody molecule.

3. The multifunctional molecule of claim 2, wherein the NK cell engager comprises an anti-NKp30 antibody molecule.

20

4. The multifunctional molecule of claim 2, wherein the NK cell engager comprises an anti-NKp46 antibody molecule.

5. A multifunctional molecule, comprising:

25 (i) a first antigen binding domain that binds to, e.g., selectively binds to, T cell receptor variable beta (TCRBV), e.g., a TCRBV antigen, and

(ii) a death receptor signal engager.

6. A multifunctional molecule, comprising:

(i) a first antigen binding domain that binds to, e.g., selectively binds to, T cell receptor variable beta (TCRBV), e.g., a TCRBV antigen, and
(ii) a cytokine inhibitor molecule.

5 7. A nucleic acid molecule encoding the multifunctional molecule of any one of claims 1-
6.

8. A vector, e.g., an expression vector, comprising the nucleic acid molecules of claim 7.

10 9. A host cell comprising the nucleic acid molecule of claim 7 or the vector of claim 8.

10. A method of making, e.g., producing, the multifunctional molecule or antibody molecule of any one of claims 1-6, comprising culturing the host cell of claim 9, under suitable conditions, e.g., conditions suitable for gene expression and/or homo- or heterodimerization.

15 11. A pharmaceutical composition comprising the multifunctional molecule of any one of claims 1-6 and a pharmaceutically acceptable carrier, excipient, or stabilizer.

20 12. A method of treating a TCR bias, comprising administering to a subject in need thereof the multifunctional molecule of any one of claims 1-6, wherein the multifunctional molecule is administered in an amount effective to treat the TCR bias.

25 13. A method of treating an autoimmune disease (e.g., an autoimmune disease associated with a TCR bias), comprising administering to a subject in need thereof the multifunctional molecule of any one of claims 1-6, wherein the multifunctional molecule is administered in an amount effective to treat the autoimmune disease.

14. A method of treating a TCR bias, comprising:

responsive to determining that a subject has a TCR bias, administering to a subject in need thereof the multifunctional molecule of any one of claims 1-6, wherein the multifunctional molecule is administered in an amount effective to treat the TCR bias.

5 15. A method of treating an autoimmune disease (e.g., an autoimmune disease associated with a TCR bias), comprising:

responsive to determining that a subject has an autoimmune disease (e.g., an autoimmune disease associated with a TCR bias), administering to a subject in need thereof the multifunctional molecule of any one of claims 1-6, wherein the multifunctional molecule is
10 administered in an amount effective to treat the autoimmune disease (e.g., an autoimmune disease associated with a TCR bias).

16. A method of identifying a subject in need of treatment for cancer using a multifunctional molecule of any of claims 1-6, comprising determining (e.g., directly
15 determining or indirectly determining, e.g., obtaining information regarding) whether a subject has a TCR bias (e.g., a biased TCRBV clonotype) and/or an autoimmune disease associated with said bias, wherein:

responsive to determining that the subject has a TCR bias (e.g., a biased TCRBV clonotype) and/or an autoimmune disease associated with said bias, identifying the subject as a
20 candidate for treatment using a multifunctional molecule comprising an antigen binding domain that binds to the TCRBV antigen, and optionally not as a candidate for treatment using a multifunctional molecule comprising an antigen binding domain that does not bind to the TCRBV antigen (e.g., that binds to a different TCRBV antigen).

25 17. A method of evaluating a subject in need of treatment for a TCR bias (e.g., a biased TCRBV clonotype) and/or an autoimmune disease associated with said bias, comprising determining (e.g., directly determining or indirectly determining, e.g., obtaining information regarding) whether a subject has a TCR bias.

18. A method of treating an autoimmune disease (e.g., an autoimmune disease associated with a TCR bias), in a subject in need thereof, comprising administering to said subject an effective amount, *e.g.*, a therapeutically effective amount, of an antibody molecule which binds (e.g., specifically binds) to a T cell receptor beta variable region (TCR β V) (“anti-TCR β V antibody molecule”), thereby treating the disorder.

19. A method of depleting a population of T cells in a subject having an autoimmune disorder (e.g., an autoimmune disease associated with a TCR bias), comprising, contacting the T cell population with an effective amount of an antibody molecule which binds (e.g., specifically binds) to a T cell receptor beta variable region (TCR β V) (“anti-TCR β V antibody molecule”).

20. The method of claim 19, wherein the contacting occurs in vivo or in vitro.

21. The method of any one of claims 18-20, wherein the anti-TCR β V antibody molecule:

(i) is not an antibody molecule disclosed in US Patent 5,861,155;

(ii) binds to TCR β V12 with an affinity and/or binding specificity that is less than (*e.g.*, less than about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90% or about 2-, 5-, or 10- fold) the affinity and/or binding specificity of the 16G8 murine antibody or a humanized version thereof as described in US Patent 5,861,155;

(iii) binds to TCR β V12 with an affinity and/or binding specificity that is greater than (*e.g.*, greater than about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90% or about 2-, 5-, or 10- fold) the affinity and/or binding specificity of the 16G8 murine antibody or a humanized version thereof as described in US Patent 5,861,155;

(iii) binds to TCR β V5-5*01 or TCR β V5-1*01 with an affinity and/or binding specificity that is greater than (*e.g.*, greater than about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90% or about 2-, 5-, or 10- fold) the affinity and/or binding specificity of the TM23 murine antibody or a humanized version thereof as described in US Patent 5,861,155 or

(iv) binds to TCR β V5-5*01 or TCR β V5-1*01 with an affinity and/or binding specificity that is greater than (*e.g.*, greater than about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90% or

about 2-, 5-, or 10- fold) the affinity and/or binding specificity of the TM23 murine antibody or a humanized version thereof as described in US Patent 5,861,155.

22. The method of any one of claims 18-21, wherein the anti-TCR β V antibody molecule
5 comprises an Fc region, e.g., an Fc region having effector function, e.g., antibody dependent cell-mediated cytotoxicity (ADCC), Antibody-dependent cellular phagocytosis (ADCP) and/or complement dependent cytotoxicity (CDC).

23. The method of any claim 22, wherein the anti-TCR β V antibody molecule comprises
10 an Fc region with enhanced effector function, e.g., as compared to a wildtype Fc region.

24. The method of any one of claims 18-23, wherein the anti-TCR β V antibody molecule comprises a human IgG1 region or a human IgG4 region.

15

VH		Framework 1															CDR 1																			
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35
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SEQ ID NO: 9		Q	V	Q	L	V	Q	S	G	A	E	V	K	K	P	G	S	S	V	K	V	S	C	K	A	S	G	Y	S	F	T	T	Y	Y	I	H
		Framework 2															CDR 2																			
		36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	52a	53	54	55	56	57	58	59	60	61	62	63	64	65				
SEQ ID NO: 1		W	V	K	Q	R	P	G	Q	G	L	E	W	I	G	W	F	F	P	G	S	G	N	I	K	Y	N	E	K	F	K	G				
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		66	67	68	69	70	71	72	73	74	75	76	77	78	79	80	81	82	82a	82b	82c	83	84	85	86	87	88	89	90	91	92	93	94			
SEQ ID NO: 1		K	A	T	L	T	A	D	T	S	S	T	A	Y	M	Q	L	S	S	L	T	S	E	E	S	A	V	Y	F	C	A	G				
SEQ ID NO: 9		R	V	T	I	T	A	D	I	S	T	S	T	A	Y	M	E	L	S	S	L	R	S	E	D	T	A	V	Y	C	A	G				
		CDR 3															Framework 4																			
		95	96	97	98	99	100	100a	100b	101	102	103	104	105	106	107	108	109	110	111	112	113														
SEQ ID NO: 1		S	Y	Y	S	Y	D	V	L	D	Y	W	G	H	G	T	T	L	T	V	S	S														
SEQ ID NO: 9		S	Y	Y	S	Y	D	V	L	D	Y	W	G	Q	G	T	T	V	T	V	S	S														

FIG. 1A

VL	Framework 1																																		CDR 1																																	
SEQ ID NO: 2	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34																																		
	D	I	L	M	T	Q	S	Q	K	F	M	S	T	S	L	G	D	R	V	S	V	S	C	K	A	S	Q	N	V	G	I	N	V	V																																		
SEQ ID NO: 10	D	I	Q	M	T	Q	S	P	S	F	L	S	A	S	V	G	D	R	V	T	I	T	C	K	A	S	Q	N	V	G	I	N	V	V																																		
SEQ ID NO: 11	D	I	Q	M	T	Q	S	P	S	S	L	S	A	S	V	G	D	R	V	T	I	T	C	K	A	S	Q	N	V	G	I	N	V	V																																		
	Framework 2																																		CDR 2																																	
SEQ ID NO: 2	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56																																														
	W	H	Q	Q	K	P	G	Q	S	P	K	A	L	I	Y	S	S	S	H	R	Y	S																																														
SEQ ID NO: 10	W	H	Q	Q	K	P	G	K	A	P	K	A	L	I	Y	S	S	S	H	R	Y	S																																														
SEQ ID NO: 11	W	H	Q	Q	K	P	G	K	V	P	K	A	L	I	Y	S	S	S	H	R	Y	S																																														
	Framework 3																																																																			
SEQ ID NO: 2	57	58	59	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80	81	82	83	84	85	86	87	88																																				
	G	V	P	D	R	F	T	G	S	G	S	G	T	D	F	T	L	T	I	N	N	V	Q	S	E	D	L	A	E	Y	F	C																																				
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	CDR 3																																		Framework 4																																	
SEQ ID NO: 2	89	90	91	92	93	94	95	96	97	98	99	100	101	102	103	104	105	106	107																																																	
	Q	Q	F	K	S	Y	P	L	T	F	G	A	G	T	K	L	E	L	K																																																	
SEQ ID NO: 10	Q	Q	F	K	S	Y	P	L	T	F	G	Q	G	T	K	L	E	I	K																																																	
SEQ ID NO: 11	Q	Q	F	K	S	Y	P	L	T	F	G	Q	G	T	K	L	E	I	K																																																	

FIG. 1B

VH	Framework 1																								CDR 1										
SEQ ID NO: 15	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35
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SEQ ID NO: 23	Q	V	Q	L	V	E	S	G	G	G	V	V	Q	P	G	R	S	L	R	L	S	C	A	A	S	G	F	T	F	S	N	F	G	M	H
SEQ ID NO: 24	E	V	Q	L	V	E	S	G	G	G	L	V	Q	P	G	G	S	L	R	L	S	C	A	A	S	G	F	T	F	S	N	F	G	M	H
SEQ ID NO: 24	E	V	Q	L	V	E	S	G	G	G	L	V	Q	P	G	G	S	L	R	L	S	C	A	A	S	G	F	T	F	S	N	F	G	M	H
Framework 2																								CDR 2											
SEQ ID NO: 15	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	52a	53	54	55	56	57	58	59	60	61	62	63	64	65				
SEQ ID NO: 25	W	V	R	Q	A	P	D	K	G	L	E	W	V	A	Y	I	S	S	G	S	S	T	I	Y	Y	A	D	T	L	K	G				
SEQ ID NO: 23	W	V	R	Q	A	P	G	K	G	L	E	W	V	A	Y	I	S	S	G	S	S	T	I	Y	Y	A	D	T	L	K	G				
SEQ ID NO: 24	W	V	R	Q	A	P	G	K	G	L	E	W	V	S	Y	I	S	S	G	S	S	T	I	Y	Y	A	D	T	L	K	G				
SEQ ID NO: 24	W	V	R	Q	A	P	G	K	G	L	E	W	V	S	Y	I	S	S	G	S	S	T	I	Y	Y	A	D	T	L	K	G				
Framework 3																																			
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SEQ ID NO: 24	R	F	T	I	S	R	D	N	A	K	N	S	L	Y	L	Q	M	N	S	L	R	A	E	D	T	A	V	Y	Y	C	A	R			
SEQ ID NO: 24	R	F	T	I	S	R	D	N	S	K	N	T	L	Y	L	Q	M	N	S	L	R	A	E	D	T	A	V	Y	Y	C	A	R			
CDR 3																								Framework 4											
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SEQ ID NO: 25	R	G	E	G	A	M	D	Y	W	G	Q	G	T	S	V	T	V	S	S																
SEQ ID NO: 23	R	G	E	G	A	M	D	Y	W	G	Q	G	T	T	V	T	V	S	S																
SEQ ID NO: 24	R	G	E	G	A	M	D	Y	W	G	Q	G	T	T	V	T	V	S	S																
SEQ ID NO: 24	R	G	E	G	A	M	D	Y	W	G	Q	G	T	T	V	T	V	S	S																

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FIG. 2A

4/8

VL		Framework 1																				CDR 1													
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34
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SEQ ID NO: 26	D	N	Q	L	T	Q	S	P	S	F	L	S	A	S	V	G	D	R	V	T	I	T	C	R	A	S	S	S	V	-	N	Y	I	Y	
SEQ ID NO: 27	D	N	Q	L	T	Q	S	P	S	S	L	S	A	S	V	G	D	R	V	T	I	T	C	R	A	S	S	S	V	-	N	Y	I	Y	
SEQ ID NO: 28	E	N	V	L	T	Q	S	P	A	T	L	S	V	S	P	G	E	R	A	T	L	S	C	R	A	S	S	S	V	-	N	Y	I	Y	
SEQ ID NO: 29	Q	N	V	L	T	Q	P	P	S	-	A	S	G	T	P	G	Q	R	V	T	I	S	C	R	A	S	S	S	V	-	N	Y	I	Y	
SEQ ID NO: 30	S	N	E	L	T	Q	P	P	S	-	V	S	V	S	P	G	Q	T	A	R	I	T	C	R	A	S	S	S	V	-	N	Y	I	Y	

		Framework 2																			CDR 2									
		35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56							
SEQ ID NO: 16	W	Y	Q	Q	K	S	D	A	S	P	K	L	W	I	Y	Y	Y	T	S	N	L	A	P							
SEQ ID NO: 26	W	Y	Q	Q	K	P	G	K	A	P	K	L	L	I	Y	Y	Y	T	S	N	L	A	P							
SEQ ID NO: 27	W	Y	Q	Q	K	P	G	K	A	P	K	L	L	I	Y	Y	Y	T	S	N	L	A	P							
SEQ ID NO: 28	W	Y	Q	Q	K	P	G	Q	A	P	R	L	L	I	Y	Y	Y	T	S	N	L	A	P							
SEQ ID NO: 29	W	Y	Q	Q	L	P	G	T	A	P	K	L	L	I	Y	Y	Y	T	S	N	L	A	P							
SEQ ID NO: 30	W	Y	Q	Q	K	S	G	Q	A	P	V	L	V	I	Y	Y	Y	T	S	N	L	A	P							

FIG. 2B

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Framework 3	
SEQ ID NO: 16	57 58 59 60 61 62 63 64 65 66 67 68 69 70 71 72 73 74 75 76 77 78 79 80 81 82 83 84 85 86 87 88
SEQ ID NO: 26	G V P T R F S G S G S G N S Y S L T I S S M E G E D A A T Y Y C
SEQ ID NO: 27	G V P S R F S G S G N E Y T L T I S S L Q P E D F A T Y Y C
SEQ ID NO: 28	G V P S R F S G S G N D Y T L T I S S L Q P E D F A T Y Y C
SEQ ID NO: 29	G I P A R F S G S G N E Y T L T I S S L Q S E D F A V Y Y C
SEQ ID NO: 29	G V P D R F S G S G N S Y T L A I S S G L R S E D A D Y Y C
SEQ ID NO: 30	G I P E R F S G S G N M Y T L T I S S G A Q V E D A D Y Y C
CDR 3	
Framework 4	
SEQ ID NO: 16	89 90 91 92 93 94 95 96 97 98 99 100 101 102 103 104 105 106 107
SEQ ID NO: 26	Q Q F T S S P F T F G S G T K L E I K
SEQ ID NO: 27	Q Q F T S S P F T F G Q G T K L E I K
SEQ ID NO: 28	Q Q F T S S P F T F G Q G T K L E I K
SEQ ID NO: 29	Q Q F T S S P F T F G Q G T K L E I K
SEQ ID NO: 30	Q Q F T S S P F T F G T G T K V T V L

FIG. 2B
(Continued)

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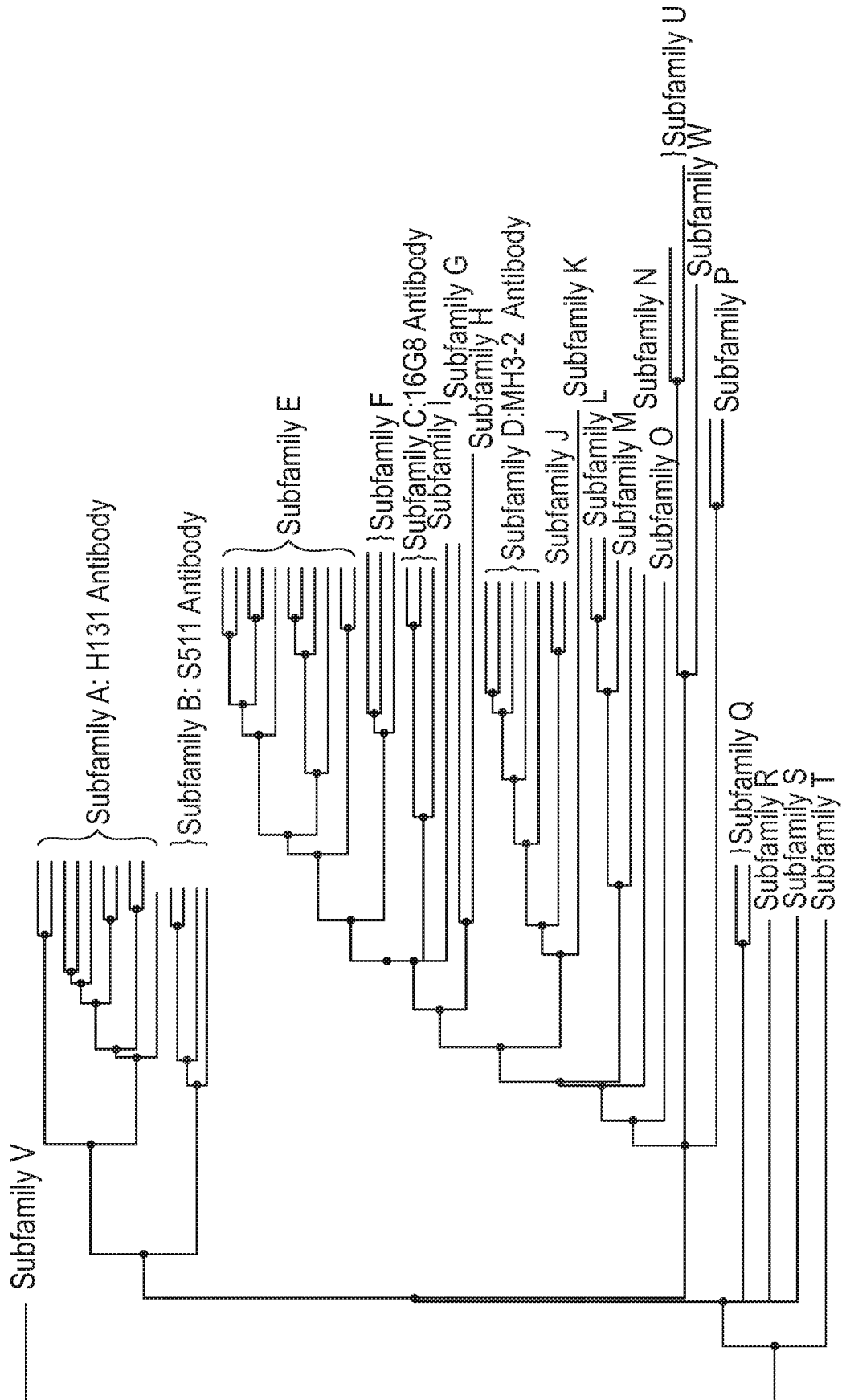


FIG. 3

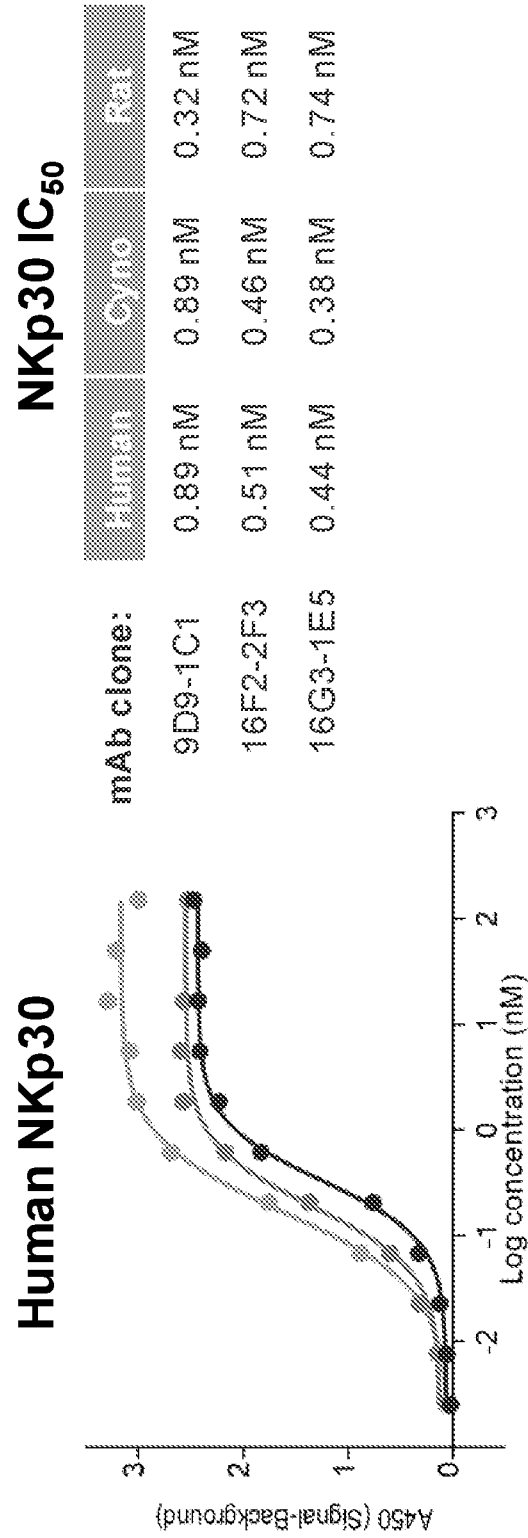


FIG. 4

Activation of NK92 cells by NK p30 Ab

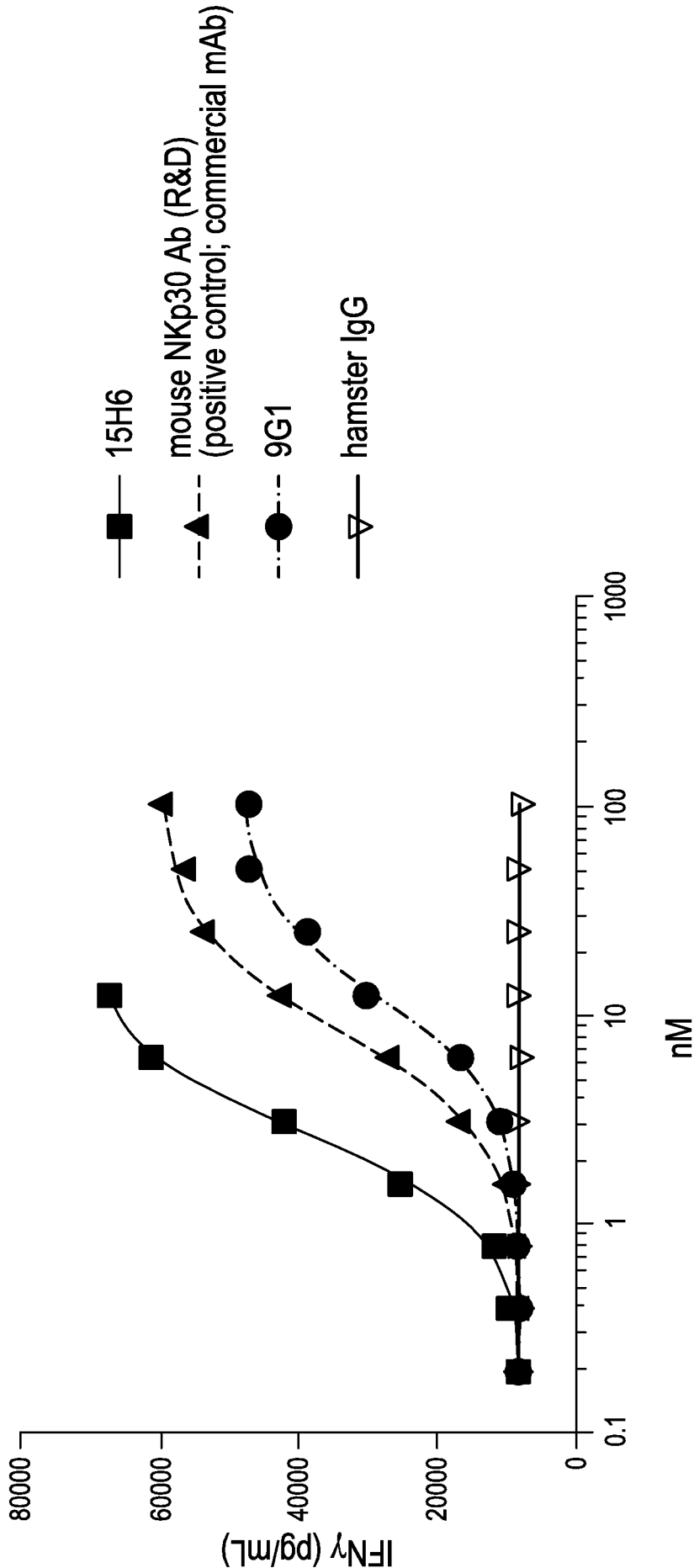


FIG. 5