

ANTI-TCR ANTIBODY MOLECULES AND USES THEREOF

RELATED APPLICATIONS

This application claims priority to U.S. Provisional Application 62/808,784 filed on February 21, 2019 and U.S. Provisional Application 62/956,871 filed on January 3, 2020, the
5 entire contents of each of which are hereby incorporated by reference.

SEQUENCE LISTING

The instant application contains a Sequence Listing which has been submitted electronically in ASCII format and is hereby incorporated by reference in its entirety. Said
10 ASCII copy, created on February 17, 2020, is named E2070-7023WO_SL.txt and is 1,080,059 bytes in size.

BACKGROUND

T cell mediated antigen recognition depends on the interaction of the T-cell receptor
15 (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 fundamental property of an effective immune system. However, it is now understood that the immune repertoire can change greatly with the onset and progression of infectious diseases.
20 Thus, there exists a need in the art for improved strategies for treating infectious diseases by harnessing differences in the immune repertoire.

SUMMARY OF THE DISCLOSURE

Disclosed herein are, *inter alia*, methods of using antibodies directed to the variable chain
25 of the beta subunit of TCR (TCR β V) which bind and, *e.g.*, activate, T cells, *e.g.*, a subset of T cells, to treat infectious diseases. Generally, the invention features a method of expanding, *e.g.*, increasing the number of, a T cell population comprising a TCR β V molecule (*e.g.*, as described herein), the method comprising: contacting the T cell population with an antibody molecule, *e.g.*, humanized antibody molecule, which binds, *e.g.*, specifically binds, to a T cell receptor beta

variable chain (TCR β V) region (e.g., an anti-TCR β V antibody molecule), thereby expanding the T cell population. In some examples, the T cell population is obtained from or comprised in a subject, e.g., a subject having an infectious disease (e.g., as described herein). Without wishing to be bound by theory, in some examples, the TCR β V clonotype bound by the antibody molecule
5 does not have to be the particular TCR β V clonotype that is over-represented, e.g., that shows a higher level or activity, in the subject having the infectious disease.

Enumerated Examples

1. A method of expanding, e.g., increasing the number of, a T cell population comprising a TCR β V molecule (e.g., as described herein), the method comprising: contacting the T cell population with an antibody molecule, e.g., humanized antibody molecule, which binds, *e.g.*, specifically binds, to a T cell receptor beta variable chain (TCR β V) region, thereby expanding the T cell population, wherein the T cell population is obtained from or comprised in a subject having an infectious disease.
2. A method of treating a subject having an infectious disease, the method comprising administering an effective amount of an anti-TCR β V antibody molecule (e.g., a TCR β V agonist) to the subject, thereby treating the infectious disease.
3. A method of evaluating, e.g., identifying the level or activity of a TCR β V molecule in a subject having an infectious disease, the method comprising acquiring a status for the TCR β V molecule in the subject;
wherein the level or activity of the TCR β V molecule is higher (e.g., at least about 1.1, 1.2, 1.3, 1.4, 1.5, 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 200, 300, 400, 500, 600, 700, 800, 900, 1000, 5000, 10,000, or 100,000-fold higher) relative to the level or activity of the TCR β V molecule in a healthy subject (e.g., a subject that does not have the infectious disease).
4. A method of treating a subject having an infectious disease, the method comprising:
 - (i) acquiring a status for the TCR β V molecule in the subject; and

(ii) administering an effective amount of an anti-TCR β V antibody molecule (e.g., a TCR β V agonist) to the subject, thereby treating the infectious disease;

wherein the level or activity of the TCR β V molecule is higher (e.g., at least about 1.1, 1.2, 1.3, 1.4, 1.5, 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 200, 300, 400, 500, 600, 700, 800, 900, 1000, 5000, 10,000, or 100,000-fold higher) relative to the level or activity of the TCR β V molecule in a healthy subject (e.g., a subject that does not have the infectious disease).

5. A method of evaluating a subject for the presence of an infectious disease, the method comprising:

(i) acquiring a status for one or more TCR β V molecules in a biological sample from the subject and in a biological sample from a healthy subject (e.g., a subject that does not have the infectious disease); and

(ii) determining whether one or more of the TCR β V molecules exhibits an elevated level or activity in the subject relative to the healthy subject;

wherein an elevated level or activity in the subject relative to in the healthy subject is indicative of the presence of the infectious disease.

6. A method of treating a subject having an infectious disease, the method comprising:

(i) acquiring a status for one or more TCR β V molecules in a biological sample from the subject and in a biological sample from a healthy subject (e.g., a subject that does not have the infectious disease);

(ii) determining whether one or more of the TCR β V molecules exhibits an elevated level or activity in the subject relative to the healthy subject; and

(iii) if an elevated level or activity in the subject relative to in the healthy subject is determined, administering an effective amount of an anti-TCR β V antibody molecule (e.g., a TCR β V agonist) to the subject.

7. The method of any of the preceding examples, wherein the status is indicative of the subject having the infectious disease or a symptom thereof

8. The method of any of the preceding examples, wherein the status is indicative of responsiveness to a therapy, e.g., a TCR β V molecule.
9. The method of any of the preceding examples, wherein the status is determined, *e.g.*, measured, by an assay described herein.
10. The method of any of the preceding examples, wherein the acquiring comprises: isolating a biological sample from the subject, contacting the biological sample with an anti-TCR β V antibody molecule (e.g., the same anti-TCR β V antibody molecule or a different anti-TCR β V antibody molecule), and determining a level of T cell expansion in the biological sample, e.g., relative to the level of T cell expansion in a biological sample obtained from a healthy subject (e.g., a subject that does not have the infectious disease).
11. The method of example 10, further comprising administering expanded T cells from the biological sample to the subject.
12. The method of any of the preceding examples, wherein the acquiring comprises: isolating a biological sample from the subject, contacting the biological sample with an anti-TCR β V antibody molecule (e.g., the same anti-TCR β V antibody molecule or a different anti-TCR β V antibody molecule), and determining a level of T cell function (e.g., cytotoxic activity) in the biological sample, e.g., relative to the level of T cell expansion in a biological sample obtained from a healthy subject (e.g., a subject that does not have the infectious disease).
13. A method of identifying one or more TCR β V molecules associated with a disease, the method comprising:
 - (i) acquiring a status for a plurality of TCR β V molecules in a biological sample from a first subject having the disease and in a biological sample from a second subject not having the disease; and

(ii) determining whether one or more of the TCR β V molecules exhibits an elevated level or activity in the first subject relative to the second subject;

thereby identifying one or more TCR β V molecules associated with the disease.

14. The method of any of the preceding examples, wherein the infectious disease is selected from Epstein-Barr virus (EBV), influenza, human immunodeficiency virus (HIV), simian immunodeficiency virus (SIV), tuberculosis, malaria, or human cytomegalovirus (HCMV).

15. The method of any of the preceding examples, wherein the TCR β V is selected from TCR β V V5-6, TCR β V V6-5, TCR β V V7, TCR β V V9, TCR β V V10, TCR β V V12 (e.g., TCR β V V12-4), TCR β V V13, TCR β V V14, TCR β V V19, TCR β V V23-1, or a subfamily member thereof (e.g., as listed in Table 1 or Table 2).

16. The method of any of the preceding examples, wherein the anti-TCR β V antibody molecule induces expansion, e.g., increasing the number of, a T cell population comprising a TCR β V molecule (e.g., the TCR β V bound by the anti-TCR β V antibody molecule).

17. The method of example 16, wherein the T cell population comprises CD4 T cells, CD8 T cells, or CD3 T cells.

18. The method of example 16, wherein the T cell population derived from peripheral blood.

19. The method of any of the preceding examples, wherein the anti-TCR β V antibody molecule comprises:

(1) a heavy chain complementarity determining region (HC CDR1), a HC CDR2 and/or a HC CDR3 of SEQ ID NO: 3, SEQ ID NO: 4, and/or SEQ ID NO: 5; and/or

(2) a light chain complementarity determining region 1 (LC CDR1), a LC CDR2, and/or a LC CDR3 of SEQ ID NO: 6, SEQ ID NO: 7, and/or SEQ ID NO: 8.

20. The method of any of the preceding examples, wherein the anti-TCR β V antibody molecule comprises:

(1) a heavy chain complementarity determining region (HC CDR1), a HC CDR2 and/or a HC CDR3 of SEQ ID NO: 45, SEQ ID NO: 46, and/or SEQ ID NO: 47; and/or

(2) a light chain complementarity determining region 1 (LC CDR1), a LC CDR2, and/or a LC CDR3 of SEQ ID NO: 51, SEQ ID NO: 52, and/or SEQ ID NO: 53.

21. The method of any of the preceding examples, wherein the anti-TCR β V antibody molecule comprises:

(1) a heavy chain complementarity determining region (HC CDR1), a HC CDR2 and/or a HC CDR3 of SEQ ID NO: 48, SEQ ID NO: 49, and/or SEQ ID NO: 50; and/or

(2) a light chain complementarity determining region 1 (LC CDR1), a LC CDR2, and/or a LC CDR3 of SEQ ID NO: 54, SEQ ID NO: 55, and/or SEQ ID NO: 56.

22. The method of any of the preceding examples, wherein the anti-TCR β V antibody molecule comprises:

(1) a heavy chain complementarity determining region (HC CDR1), a HC CDR2 and/or a HC CDR3 of SEQ ID NO: 17, SEQ ID NO: 18, and/or SEQ ID NO: 19; and/or

(2) a light chain complementarity determining region 1 (LC CDR1), a LC CDR2, and/or a LC CDR3 of SEQ ID NO: 20, SEQ ID NO: 21, and/or SEQ ID NO: 22.

23. The method of any of the preceding examples, wherein the anti-TCR β V antibody molecule comprises:

(1) a heavy chain complementarity determining region (HC CDR1), a HC CDR2 and/or a HC CDR3 of SEQ ID NO: 57, SEQ ID NO: 58, and/or SEQ ID NO: 59; and/or

(2) a light chain complementarity determining region 1 (LC CDR1), a LC CDR2, and/or a LC CDR3 of SEQ ID NO: 63, SEQ ID NO: 64, and/or SEQ ID NO: 65.

24. The method of any of the preceding examples, wherein the anti-TCR β V antibody molecule comprises:

(1) a heavy chain complementarity determining region (HC CDR1), a HC CDR2 and/or a HC CDR3 of SEQ ID NO: 60, SEQ ID NO: 61, and/or SEQ ID NO: 62; and/or

(2) a light chain complementarity determining region 1 (LC CDR1), a LC CDR2, and/or a LC CDR3 of SEQ ID NO: 66, SEQ ID NO: 67, and/or SEQ ID NO: 68.

25. The method of any of the preceding examples, wherein the anti-TCR β V antibody molecule comprises a VH having at least 85% (e.g., at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) sequence identity to SEQ ID NO: 9.

26. The method of any of the preceding examples, wherein the anti-TCR β V antibody molecule comprises a VL having at least 85% (e.g., at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) sequence identity to SEQ ID NO: 10.

27. The method of any of the preceding examples, wherein the anti-TCR β V antibody molecule comprises a VH having at least 85% (e.g., at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) sequence identity to SEQ ID NO: 9 and a VL having at least X% sequence identity to SEQ ID NO: 10.

28. The method of any of the preceding examples, wherein the anti-TCR β V antibody molecule comprises a heavy chain having at least 85% (e.g., at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) sequence identity to SEQ ID NO: 69.

29. The method of any of the preceding examples, wherein the anti-TCR β V antibody molecule comprises a heavy chain having at least 85% (e.g., at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) sequence identity to SEQ ID NO: 70.

30. The method of any of the preceding examples, wherein the anti-TCR β V antibody molecule comprises a heavy chain having at least 85% (e.g., at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) sequence identity to SEQ ID NO: 71.

31. The method of any of the preceding examples, wherein the anti-TCR β V antibody molecule comprises a light chain having at least 85% (e.g., at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) sequence identity to SEQ ID NO: 72.

32. The method of any of the preceding examples, wherein the anti-TCR β V antibody molecule comprises a heavy chain having at least 85% (e.g., at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) sequence identity to SEQ ID NO: 69 and a light chain having at least 85% (e.g., at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) sequence identity to SEQ ID NO: 72.

33. The method of any of the preceding examples, wherein the anti-TCR β V antibody molecule comprises a heavy chain having at least 85% (e.g., at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) sequence identity to SEQ ID NO: 70 and a light chain having at least 85% (e.g., at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) sequence identity to SEQ ID NO: 72.

34. The method of any of the preceding examples, wherein the anti-TCR β V antibody molecule comprises a heavy chain having at least 85% (e.g., at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) sequence identity to SEQ ID NO: 71 and a light chain having at least 85% (e.g., at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) sequence identity to SEQ ID NO: 72.

35. The method of any of the preceding examples, wherein the anti-TCR β V antibody molecule is co-expressed with an IgJ chain (e.g., an IgJ chain comprising at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to SEQ ID NO: 76).

36. The method of any of the preceding examples, wherein the anti-TCR β V antibody molecule comprises a heavy chain having at least 85% (e.g., at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) sequence identity to SEQ ID NO: 69 and a light chain having at least 85% (e.g., at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) sequence identity to SEQ ID NO: 72; and wherein the anti-TCR β V antibody molecule is co-expressed with an IgJ chain (e.g., an IgJ chain comprising at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to SEQ ID NO: 76).

37. The method of any of the preceding examples, wherein the anti-TCR β V antibody molecule comprises a VH having at least 85% (e.g., at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) sequence identity to SEQ ID NO: 15.

38. The method of any of the preceding examples, wherein the anti-TCR β V antibody molecule comprises a VL having at least 85% (e.g., at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) sequence identity to SEQ ID NO: 16.

39. The method of any of the preceding examples, wherein the anti-TCR β V antibody molecule comprises a VH having at least 85% (e.g., at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) sequence identity to SEQ ID NO: 23.

40. The method of any of the preceding examples, wherein the anti-TCR β V antibody molecule comprises a VH having at least 85% (e.g., at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) sequence identity to SEQ ID NO: 24.

41. The method of any of the preceding examples, wherein the anti-TCR β V antibody molecule comprises a VH having at least 85% (e.g., at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) sequence identity to SEQ ID NO: 25.

42. The method of any of the preceding examples, wherein the anti-TCR β V antibody molecule comprises a VL having at least 85% (e.g., at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) sequence identity to SEQ ID NO: 26.

43. The method of any of the preceding examples, wherein the anti-TCR β V antibody molecule comprises a VL having at least 85% (e.g., at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) sequence identity to SEQ ID NO: 27.

44. The method of any of the preceding examples, wherein the anti-TCR β V antibody molecule comprises a VL having at least 85% (e.g., at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) sequence identity to SEQ ID NO: 28.
45. The method of any of the preceding examples, wherein the anti-TCR β V antibody molecule comprises a VL having at least 85% (e.g., at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) sequence identity to SEQ ID NO: 29.
46. The method of any of the preceding examples, wherein the anti-TCR β V antibody molecule comprises a VL having at least 85% (e.g., at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) sequence identity to SEQ ID NO: 30.
47. The method of any of the preceding examples, wherein the anti-TCR β V antibody molecule comprises a VH amino acid sequence as listed in Table 3 or Table 4, and/or a VL amino acid sequence as listed in Table 3 or Table 4.
48. The method of any of the preceding examples, wherein the anti-TCR β V antibody molecule selectively or preferentially expands $\alpha\beta$ T cells over $\gamma\delta$ T cells.
49. The method of any of the preceding examples, wherein the anti-TCR β V antibody molecule does not induce cytokine release syndrome (CRS).
50. The method of any of the preceding examples, wherein binding of the anti-TCR β V antibody molecule to the TCR β V region results in one, two, three, four, five, six, seven, eight, nine, ten or more (e.g., all) of the following:
- (i) reduced level, e.g., expression level, and/or activity of IL-1 β ;
 - (ii) reduced level, e.g., expression level, and/or activity of IL-6;
 - (iii) reduced level, e.g., expression level, and/or activity of TNF α ;
 - (iv) increased level, e.g., expression level, and/or activity of IL-2;
 - (v) a delay, e.g., at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more hours delay, in increased level, e.g., expression level, and/or activity of IL-2;

(vi) a delay, *e.g.*, at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 hours delay, in increased level, *e.g.*, expression level, and/or activity of IFN γ ;

(vii) reduced T cell proliferation kinetics; or

(viii) reduced cytokine storm, *e.g.*, cytokine release syndrome (CRS), *e.g.*, as measured by an assay of Example 3;

(ix) cell killing, *e.g.*, target cell killing,

(x) increased level, *e.g.*, expression level, and/or activity of IL-15; or

5 (xi) increased Natural Killer (NK) cell proliferation, *e.g.*, expansion, compared to an antibody that binds to: a CD3 molecule, *e.g.*, CD3 epsilon (CD3e) molecule; or a TCR alpha (TCR α) molecule, wherein the anti-TCR β V antibody molecule:

(1) does not bind to TCR β V12, TCR β V5-5*01 or TCR β V5-1*01;

(2) 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 murine mAb Antibody B; and/or

(3) binds to TCR β V5-5*01 TCR β V5-1*01 or 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.

51. The method of any of the preceding examples, wherein binding of the anti-TCR β V antibody molecule to the TCR β V region results in expansion, *e.g.*, at least about 1.1-10 fold expansion (*e.g.*, at least about 1.1, 1.2, 1.3, 1.4, 1.5, 2, 3, 4, 5, 6, 7, 8, 9, or 10 fold expansion), of a population of memory T cells, *e.g.*, T effector memory (T_{EM}) cells, *e.g.*, T_{EM} cells expressing CD45RA (T_{EMRA}) cells, wherein the anti-TCR β V antibody molecule:

(1) does not bind to TCR β V12, TCR β V5-5*01 or TCR β V5-1*01;

(2) 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 murine mAb Antibody B; and/or

(3) binds to TCR β V5-5*01 TCR β V5-1*01 or 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.

52. The method of any of the preceding examples, wherein binding of the anti-TCR β V antibody molecule to a TCR β V region results in a reduction of at least 2, 5, 10, 20, 50, 100, or 200 fold, or at least 2-200 fold (*e.g.*, 5-150, 10-100, 20-50 fold) in the expression level and or activity of IL-1 β as measured by an assay of Example 3.

53. The method of any of the preceding examples, wherein binding of the anti-TCR β V antibody molecule to a TCR β V region results in a reduction of at least 2, 5, 10, 20, 50, 100, 200, 300, 400, 500, 600, 700, 800, 900, or 1000 fold, or at least 2-1000 fold (*e.g.*, 5-900, 10-800, 20-700, 50-600, 100-500, or 200-400 fold) in the expression level and or activity of IL-6 as measured by an assay of Example 3.

54. The method of any of the preceding examples, wherein binding of the anti-TCR β V antibody molecule to a TCR β V region results in a reduction of at least 2, 5, 10, 20, 50, 100, 200, 300, 400, 500, 600, 700, 800, 900, 1000, or 2000 fold, or at least 2-2000 fold (*e.g.*, 5-1000, 10-900, 20-800, 50-700, 100-600, 200-500, or 300-400 fold) in the expression level and or activity of TNF α as measured by an assay of Example 3.

55. The method of any of the preceding examples, wherein binding of the anti-TCR β V antibody molecule to a TCR β V region results in an increase of at least 2, 5, 10, 20, 50, 100, 200, 300, 400, 500, 600, 700, 800, 900, 1000, or 2000 fold, or at least 2-2000 fold (*e.g.*, 5-1000, 10-900, 20-800, 50-700, 100-600, 200-500, or 300-400 fold) in the expression level and or activity of IL-2 as measured by an assay of Example 3.

56. The method of any of the preceding examples, wherein the anti-TCR β V antibody molecule binds to one or more (*e.g.*, all) of the following TCR β V subfamilies:

(i) TCR β V6 subfamily comprising, *e.g.*, 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;

- (ii) TCR β V10 subfamily comprising, e.g., TCR β V10-1*01, TCR β V10-1*02, TCR β V10-3*01 or TCR β V10-2*01;
- (iii) TCR β V12 subfamily comprising, e.g., TCR β V12-4*01, TCR β V12-3*01, or TCR β V12-5*01;
- (iv) TCR β V5 subfamily comprising, e.g., TCR β V5-5*01, TCR β V5-6*01, TCR β V5-4*01, TCR β V5-8*01, or TCR β V5-1*01;
- (v) TCR β V7 subfamily comprising, e.g., 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;
- (vi) TCR β V11 subfamily comprising, e.g., TCR β V11-1*01, TCR β V11-2*01 or TCR β V11-3*01;
- (vii) TCR β V14 subfamily comprising, e.g., TCR β V14*01;
- (viii) TCR β V16 subfamily comprising, e.g., TCR β V16*01;
- (ix) TCR β V18 subfamily comprising, e.g., TCR β V18*01;
- (x) TCR β V9 subfamily comprising, e.g., TCR β V9*01 or TCR β V9*02;
- (xi) TCR β V13 subfamily comprising, e.g., TCR β V13*01;
- (xii) TCR β V4 subfamily comprising, e.g., TCR β V4-2*01, TCR β V4-3*01, or TCR β V4-1*01;
- (xiii) TCR β V3 subfamily comprising, e.g., TCR β V3-1*01;
- (xiv) TCR β V2 subfamily comprising, e.g., TCR β V2*01;
- (xv) TCR β V15 subfamily comprising, e.g., TCR β V15*01;
- (xvi) TCR β V30 subfamily comprising, e.g., TCR β V30*01, or TCR β V30*02;
- (xvii) TCR β V19 subfamily comprising, e.g., TCR β V19*01, or TCR β V19*02;
- (xviii) TCR β V27 subfamily comprising, e.g., TCR β V27*01;
- (xix) TCR β V28 subfamily comprising, e.g., TCR β V28*01;
- (xx) TCR β V24 subfamily comprising, e.g., TCR β V24-1*01;
- (xxi) TCR β V20 subfamily comprising, e.g., TCR β V20-1*01, or TCR β V20-1*02;
- (xxii) TCR β V25 subfamily comprising, e.g., TCR β V25-1*01;
- (xxiii) TCR β V29 subfamily comprising, e.g., TCR β V29-1*01; or
- (xxiv) TCR β V23 subfamily comprising, e.g., TCR β V23-1.

57. The method of any of the preceding examples, wherein the anti-TCR β V antibody molecule binds to one or more (*e.g.*, all) of the following TCR β V subfamilies:

- (i) TCR β V6 subfamily comprising, *e.g.*, TCR β V6-5*01;
- (ii) TCR β V10 subfamily comprising, *e.g.*, TCR β V10-1*01, TCR β V10-1*02, TCR β V10-3*01 or TCR β V10-2*01;
- (iii) TCR β V12 subfamily comprising, *e.g.*, TCR β V12-4*01, TCR β V12-3*01, or TCR β V12-5*01;
- (iv) TCR β V5 subfamily comprising, *e.g.*, TCR β V5-6*01;
- (v) TCR β V7 subfamily comprising, *e.g.*, 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;
- (vi) TCR β V14 subfamily comprising, *e.g.*, TCR β V14*01;
- (vii) TCR β V9 subfamily comprising, *e.g.*, TCR β V9*01 or TCR β V9*02;
- (viii) TCR β V13 subfamily comprising, *e.g.*, TCR β V13*01;
- (ix) TCR β V19 subfamily comprising, *e.g.*, TCR β V19*01, or TCR β V19*02; or
- (x) TCR β V23 subfamily comprising, *e.g.*, TCR β V23-1.

58. The method of any of the preceding examples, wherein the infectious disease is SIV and the anti-TCR β V antibody molecule binds to the TCR β V6 subfamily, *e.g.*, comprising TCR β V6-5*01.

59. The method of example 58, wherein the subject has a higher, *e.g.*, increased, level or activity of a TCR β V6 subfamily, *e.g.*, comprising TCR β V6-5*01.

60. The method of any of the preceding examples, wherein the infectious disease is HCMV and the anti-TCR β V antibody molecule binds to the TCR β V6 subfamily, *e.g.*, comprising TCR β V6-5*01.

61. The method of example 60, wherein the subject has a higher, *e.g.*, increased, level or activity of a TCR β V6 subfamily, *e.g.*, comprising TCR β V6-5*01.

62. The method of any of examples 58-61, wherein the anti-TCR β V antibody molecule comprises:

(1) a heavy chain complementarity determining region (HC CDR1), a HC CDR2 and/or a HC CDR3 of SEQ ID NO: 3, SEQ ID NO: 4, and/or SEQ ID NO: 5; and/or

(2) a light chain complementarity determining region 1 (LC CDR1), a LC CDR2, and/or a LC CDR3 of SEQ ID NO: 6, SEQ ID NO: 7, and/or SEQ ID NO: 8.

63. The method of any of examples 58-61, wherein the anti-TCR β V antibody molecule comprises:

(1) a heavy chain complementarity determining region (HC CDR1), a HC CDR2 and/or a HC CDR3 of SEQ ID NO: 45, SEQ ID NO: 46, and/or SEQ ID NO: 47; and/or

(2) a light chain complementarity determining region 1 (LC CDR1), a LC CDR2, and/or a LC CDR3 of SEQ ID NO: 51, SEQ ID NO: 52, and/or SEQ ID NO: 53.

64. The method of any of examples 58-61, wherein the anti-TCR β V antibody molecule comprises:

(1) a heavy chain complementarity determining region (HC CDR1), a HC CDR2 and/or a HC CDR3 of SEQ ID NO: 48, SEQ ID NO: 49, and/or SEQ ID NO: 50; and/or

(2) a light chain complementarity determining region 1 (LC CDR1), a LC CDR2, and/or a LC CDR3 of SEQ ID NO: 54, SEQ ID NO: 55, and/or SEQ ID NO: 56.

65. The method of any of examples 58-64, wherein the anti-TCR β V antibody molecule comprises a VH having at least 85% (e.g., at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) sequence identity to SEQ ID NO: 9.

66. The method of any of examples 58-65, wherein the anti-TCR β V antibody molecule comprises a VL having at least 85% (e.g., at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) sequence identity to SEQ ID NO: 10.

67. The method of any of examples 58-64, wherein the anti-TCR β V antibody molecule comprises a VH having at least 85% (e.g., at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) sequence identity to SEQ ID NO: 9 and a VL having at least X% sequence identity to SEQ ID NO: 10.

68. The method of any of examples 58-67, wherein the anti-TCR β V antibody molecule comprises a heavy chain having at least 85% (e.g., at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) sequence identity to SEQ ID NO: 69 and a light chain having at least 85% (e.g., at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) sequence identity to SEQ ID NO: 72.

69. The method of any of the preceding examples, wherein the infectious disease is EBV and the anti-TCR β V antibody molecule binds to the TCR β V10 subfamily, e.g., comprising TCR β V10-1*01, TCR β V10-1*02, TCR β V10-3*01 or TCR β V10-2*01.

70. The method of example 69, wherein the antigen is BZLF1(52-64).

71. The method of example 69 or 70, wherein the MHC restriction is HLA-B*3508.

72. The method of any of examples 69-71, wherein the subject has a higher, e.g., increased, level or activity of a TCR β V10 subfamily, e.g., comprising TCR β V10-1*01, TCR β V10-1*02, TCR β V10-3*01 or TCR β V10-2*01.

73. The method of any of the preceding examples, wherein the infectious disease is malaria and the anti-TCR β V antibody molecule binds to the TCR β V12 subfamily, e.g., comprising TCR β V12-4*01, TCR β V12-3*01, or TCR β V12-5*01.

74. The method of example 73, wherein the subject has a higher, e.g., increased, level or activity of a TCR β V12 subfamily, e.g., comprising TCR β V12-4*01, TCR β V12-3*01, or TCR β V12-5*01.

75. The method of any of the preceding examples, wherein the infectious disease is tuberculosis and the anti-TCR β V antibody molecule binds to the TCR β V12 subfamily, e.g., comprising TCR β V12-4*01, TCR β V12-3*01, or TCR β V12-5*01.

76. The method of example 75, wherein the subject has a higher, e.g., increased, level or activity of a TCR β V12 subfamily, e.g., comprising TCR β V12-4*01, TCR β V12-3*01, or TCR β V12-5*01.

77. The method of any of the preceding examples, wherein the infectious disease is HCMV and the anti-TCR β V antibody molecule binds to the TCR β V12 subfamily, e.g., comprising TCR β V12-4*01.

78. The method of example 77, wherein the subject has a higher, e.g., increased, level or activity of a TCR β V12 subfamily, e.g., comprising TCR β V12-4*01.

79. The method of any of examples 73-78, wherein the anti-TCR β V antibody molecule comprises:

(1) a heavy chain complementarity determining region (HC CDR1), a HC CDR2 and/or a HC CDR3 of SEQ ID NO: 17, SEQ ID NO: 18, and/or SEQ ID NO: 19; and/or

(2) a light chain complementarity determining region 1 (LC CDR1), a LC CDR2, and/or a LC CDR3 of SEQ ID NO: 20, SEQ ID NO: 21, and/or SEQ ID NO: 22.

80. The method of any of examples 73-78, wherein the anti-TCR β V antibody molecule comprises:

(1) a heavy chain complementarity determining region (HC CDR1), a HC CDR2 and/or a HC CDR3 of SEQ ID NO: 57, SEQ ID NO: 58, and/or SEQ ID NO: 59; and/or

(2) a light chain complementarity determining region 1 (LC CDR1), a LC CDR2, and/or a LC CDR3 of SEQ ID NO: 63, SEQ ID NO: 64, and/or SEQ ID NO: 65.

81. The method of any of examples 73-78, wherein the anti-TCR β V antibody molecule comprises:

(1) a heavy chain complementarity determining region (HC CDR1), a HC CDR2 and/or a HC CDR3 of SEQ ID NO: 60, SEQ ID NO: 61, and/or SEQ ID NO: 62; and/or

(2) a light chain complementarity determining region 1 (LC CDR1), a LC CDR2, and/or a LC CDR3 of SEQ ID NO: 66, SEQ ID NO: 67, and/or SEQ ID NO: 68.

82. The method of any of examples 73-81, wherein the anti-TCR β V antibody molecule comprises a VH having at least 85% (e.g., at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) sequence identity to SEQ ID NO: 15.

83. The method of any of examples 73-82, wherein the anti-TCR β V antibody molecule comprises a VL having at least 85% (e.g., at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) sequence identity to SEQ ID NO: 16,

optionally wherein the anti-TCR β V antibody molecule comprises a VH having at least 85% (e.g., at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) sequence identity to SEQ ID NO: 15 and a VL having at least 85% (e.g., at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) sequence identity to SEQ ID NO: 16.

84. The method of any of examples 73-81, wherein the anti-TCR β V antibody molecule comprises a VH having at least 85% (e.g., at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) sequence identity to SEQ ID NO: 23.

85. The method of any of examples 73-81, wherein the anti-TCR β V antibody molecule comprises a VH having at least 85% (e.g., at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) sequence identity to SEQ ID NO: 24.

86. The method of any of examples 73-81, wherein the anti-TCR β V antibody molecule comprises a VH having at least 85% (e.g., at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) sequence identity to SEQ ID NO: 25.

87. The method of any of examples 73-86, wherein the anti-TCR β V antibody molecule comprises a VL having at least 85% (e.g., at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) sequence identity to SEQ ID NO: 26.
88. The method of any of examples 73-86, wherein the anti-TCR β V antibody molecule comprises a VL having at least 85% (e.g., at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) sequence identity to SEQ ID NO: 27.
89. The method of any of examples 73-86, wherein the anti-TCR β V antibody molecule comprises a VL having at least 85% (e.g., at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) sequence identity to SEQ ID NO: 28.
90. The method of any of examples 73-86, wherein the anti-TCR β V antibody molecule comprises a VL having at least 85% (e.g., at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) sequence identity to SEQ ID NO: 29.
91. The method of any of examples 73-86, wherein the anti-TCR β V antibody molecule comprises a VL having at least 85% (e.g., at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) sequence identity to SEQ ID NO: 30.
92. The method of any of the preceding examples, wherein the infectious disease is HIV and the anti-TCR β V antibody molecule binds to the TCR β V5 subfamily, e.g., comprising TCR β V5-6*01.
93. The method of example 92, wherein the antigen is Gag p17 (77-85).
94. The method of example 92 or 93, wherein the MHC restriction is HLA-B*0801.
95. The method of any of examples 92-94, wherein the subject has a higher, e.g., increased, level or activity of a TCR β V5 subfamily, e.g., comprising TCR β V5-6*01.

96. The method of any of the preceding examples, wherein the infectious disease is EBV and the anti-TCR β V antibody molecule binds to the TCR β V7 subfamily, e.g., comprising 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.

97. The method of example 96, wherein the antigen is EBNA3(339-347).

98. The method of example 96 or 97, wherein the MHC restriction is HLA-B*0801.

99. The method of any of examples 96-98, wherein the subject has a higher, e.g., increased, level or activity of a TCR β V7 subfamily, e.g., comprising 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.

100. The method of any of the preceding examples, wherein the infectious disease is SIV and the anti-TCR β V antibody molecule binds to the TCR β V14 subfamily, e.g., comprising TCR β V14*01.

101. The method of example 100, wherein the subject has a higher, e.g., increased, level or activity of a TCR β V14 subfamily, e.g., comprising TCR β V14*01.

102. The method of any of the preceding examples, wherein the infectious disease is EBV and the anti-TCR β V antibody molecule binds to the TCR β V9 subfamily, e.g., comprising TCR β V9*01 or TCR β V9*02.

103. The method of example 102, wherein the antigen is EBNA1(407-417).

104. The method of example 102 or 103, wherein the MHC restriction is HLA-B*3508 or HLA-B*3501.

105. The method of any of examples 102-104, wherein the subject has a higher, e.g., increased, level or activity of a TCR β V9 subfamily, e.g., comprising TCR β V9*01 or TCR β V9*02.

106. The method of any of the preceding examples, wherein the infectious disease is SIV and the anti-TCR β V antibody molecule binds to the TCR β V13 subfamily, e.g., comprising TCR β V13*01.

107. The method of example 106, wherein the subject has a higher, e.g., increased, level or activity of a TCR β V13 subfamily, e.g., comprising TCR β V13*01.

108. The method of any of the preceding examples, wherein the infectious disease is influenza and the anti-TCR β V antibody molecule binds to the TCR β V19 subfamily, e.g., comprising TCR β V19*01, or TCR β V19*02.

109. The method of example 108, wherein the antigen is Matrix protein (58-66).

110. The method of example 108 or 109, wherein the MHC restriction is HLA-A2.

111. The method of any of examples 108-110, wherein the subject has a higher, e.g., increased, level or activity of a TCR β V19 subfamily, e.g., comprising TCR β V19*01, or TCR β V19*02.

112. The method of any of the preceding examples, wherein the infectious disease is HIV and the anti-TCR β V antibody molecule binds to the TCR β V19 subfamily, e.g., comprising TCR β V19*01, or TCR β V19*02.

113. The method of example 112, wherein the subject has a higher, e.g., increased, level or activity of a TCR β V19 subfamily, e.g., comprising TCR β V19*01, or TCR β V19*02.

114. The method of any of the preceding examples, wherein the infectious disease is HIV and the anti-TCR β V antibody molecule binds to the TCR β V23 subfamily, *e.g.*, comprising TCR β V23-1.

115. The method of example 114, wherein the subject has a higher, *e.g.*, increased, level or activity of a TCR β V23 subfamily, *e.g.*, comprising TCR β V23-1.

116. The method of any of the preceding examples, wherein the anti-TCR β V antibody molecule:

(i) binds specifically to an epitope on TCR β V, *e.g.*, the same or similar epitope as the epitope recognized by an anti-TCR β V antibody molecule as described herein, *e.g.*, a second anti-TCR β V antibody molecule;

(ii) shows the same or similar binding affinity or specificity, or both, as an anti-TCR β V antibody molecule as described herein, *e.g.*, a second anti-TCR β V antibody molecule;

(iii) inhibits, *e.g.*, competitively inhibits, the binding of an anti-TCR β V antibody molecule as described herein, *e.g.*, a second anti-TCR β V antibody molecule;

(iv) binds the same or an overlapping epitope with an anti-TCR β V antibody molecule as described herein, *e.g.*, a second anti-TCR β V antibody molecule; or

(v) competes for binding, and/or binds the same epitope, with an anti-TCR β V antibody molecule as described herein, *e.g.*, a second anti-TCR β V antibody molecule,

117. The method of any of the preceding examples, wherein the anti-TCR β V antibody molecule comprises an antigen binding domain comprising:

(i) a heavy chain complementarity determining region 1 (HC CDR1), a heavy chain complementarity determining region 2 (HC CDR2) and/or a heavy chain complementarity determining region 3 (HC CDR3) of SEQ ID NO: 1 or SEQ ID NO: 9; or

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

118. The method of any of the preceding examples, wherein the anti-TCR β V antibody molecule comprises an antigen binding domain comprising a light chain variable region (VL) comprising one, two or all (*e.g.*, three) of a LC CDR1, a LC CDR2 and a LC CDR3 of SEQ ID NO: 2, SEQ ID NO: 10, or SEQ ID NO: 11.

119. The method of any of the preceding examples, wherein the anti-TCR β V antibody molecule comprises an antigen binding domain comprising a heavy chain variable region (VH) comprising one, two or all (*e.g.*, three) of a HC CDR1, a HC CDR2 and a HC CDR3 of SEQ ID NO:1 or SEQ ID NO: 9.

120. The method of any of the preceding examples, wherein the anti-TCR β V antibody molecule comprises an antigen binding domain comprising:

(i) a VL comprising: a LC CDR1 amino acid sequence of SEQ ID NO: 6 (or an amino acid sequence with not more than 1, 2, 3 or 4 modifications, *e.g.*, substitutions, additions or deletions thereof), a LC CDR2 amino acid sequence of SEQ ID NO:7 (or an amino acid sequence with not more than 1, 2, 3 or 4 modifications, *e.g.*, substitutions, additions or deletions thereof), and/or a LC CDR3 amino acid sequence of SEQ ID NO:8 (or an amino acid sequence with not more than 1, 2, 3 or 4 modifications, *e.g.*, substitutions, additions or deletions thereof); and/or

(ii) a VH comprising: a HC CDR1 amino acid sequence of SEQ ID NO: 3 (or an amino acid sequence with not more than 1, 2, 3 or 4 modifications, *e.g.*, substitutions, additions or deletions thereof), a HC CDR2 amino acid sequence of SEQ ID NO:4 (or an amino acid sequence with not more than 1, 2, 3 or 4 modifications, *e.g.*, substitutions, additions or deletions thereof), and/or a HC CDR3 amino acid sequence of SEQ ID NO:5 (or an amino acid sequence with not more than 1, 2, 3 or 4 modifications, *e.g.*, substitutions, additions or deletions thereof).

121. The method of any of the preceding examples, wherein the anti-TCR β V antibody molecule comprises an antigen binding domain comprising:

a variable heavy chain (VH) of SEQ ID NO: 9, or a sequence having at least about 85%, 90%, 95%, or 99% sequence identity thereto; and/or

a variable light chain (VL) of SEQ ID NO: 10 or SEQ ID NO: 11, or a sequence having at least about 85%, 90%, 95%, or 99% sequence identity thereto.

122. The method of any of the preceding examples, wherein the anti-TCR β V antibody molecule comprises an antigen binding domain comprising the VH amino acid sequence of SEQ ID NO: 9 and the VL amino acid sequence of SEQ ID NO: 10.

123. The method of any of the preceding examples, wherein the anti-TCR β V antibody molecule comprises an antigen binding domain comprising the VH amino acid sequence of SEQ ID NO: 9 and the VL amino acid sequence of SEQ ID NO: 11.

124. The method of any of the preceding examples, wherein the anti-TCR β V antibody molecule comprises an antigen binding domain comprising a single chain Fv (scFv) or a Fab.

125. The method of any of the preceding examples, wherein the anti-TCR β V antibody molecule binds to a conformational or a linear epitope on the T cell.

126. The method of any of the preceding examples, wherein the anti-TCR β V antibody molecule is a full antibody (*e.g.*, an antibody that includes at least one, and preferably two, complete heavy chains, and at least one, and preferably two, complete light chains), or 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).

127. The method of example 126, wherein the anti-TCR β V antibody molecule comprises a heavy chain constant region chosen from IgG1, IgG2, IgG3, or IgG4, or a fragment thereof.

128. The method of example 126 or 127, wherein the anti-TCR β V antibody molecule comprises a light chain constant region chosen from the light chain constant regions of kappa or lambda, or a fragment thereof.

129. A method of making, *e.g.*, producing or manufacturing, the anti-TCR β V antibody molecule of the method of any of the preceding examples, comprising culturing a host cell comprising a nucleic acid encoding the anti-TCR β V antibody molecule, under suitable conditions, *e.g.*, conditions suitable expression of the anti- TCR β V antibody molecule.

130. A pharmaceutical composition comprising the anti-TCR β V antibody molecule of the method of any of the preceding examples, and a pharmaceutically acceptable carrier, excipient, or stabilizer.

131. The method of any of examples 1-128, wherein the expansion occurs *in vivo* or *ex vivo* (*e.g.*, *in vitro*).

132. The method of any of examples 1-128 or 131, wherein the T cell population comprises a T cell, a Natural Killer cell, a B cell, or a myeloid cell.

133. The method of any of examples 1-128, 131, or 132, wherein the T cell population comprises a CD4 T cell, a CD8 T cell, *e.g.*, an effector T cell or a memory T cell (*e.g.*, a memory effector T cell (*e.g.*, T_{EM} cell, *e.g.*, T_{EMRA} cell), or a combination thereof.

134. The method of any of examples 1-128 or 131-133, wherein the T cell population is obtained from a healthy subject.

135. The method of any of examples 1-128 or 131-134, wherein the T cell population is obtained from a subject (*e.g.*, from an apheresis sample from the subject) having a disease, *e.g.*, an infectious disease, *e.g.*, as described herein.

136. The method of any of examples 1-128 or 131-135, wherein the method results in an expansion of at least 1.1-10 fold (*e.g.*, at least 1.1, 1.2, 1.3, 1.4, 1.5, 2, 3, 4, 5, 6, 7, 8, 9, or 10 fold expansion).

137. The method of any of examples 1-128 or 131-136, further comprising contacting the population of cells with an agent that promotes, e.g., increases, immune cell (e.g., T cell) expansion.

138. The method of any of examples 1-128 or 131-137, further comprising contacting the population of cells with an additional therapeutic agent.

139. The method of example 138, wherein the additional therapeutic agent targets the infectious disease.

140. The method of any of examples 1-128 or 131-139, further comprising contacting the population of cells with a non-dividing population of cells, e.g., feeder cells, e.g., irradiated allogenic human PBMCs.

141. The method of any of examples 1-128 or 131-140, wherein the population of cells is expanded in an appropriate media (e.g., media described herein) that includes one or more cytokines, e.g., IL-2, IL-7, IL-15, or a combination thereof.

142. The method of any of examples 1-128 or 131-141, wherein the population of cells is expanded for a period of at least about 4 hours, 6 hours, 10 hours, 12 hours, 15 hours, 18 hours, 20 hours, or 22 hours, or for at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 or 21 days, or for at least about 1 week, 2 weeks, 3 weeks, 4 weeks, 5 weeks, 6 weeks, 7 weeks or 8 weeks.

143. The method of any of examples 1-128 or 131-142, wherein expansion of the population of T cells is compared to expansion of a similar population of cells with an antibody that binds to: a CD3 molecule, e.g., CD3 epsilon (CD3e) molecule; or a TCR alpha (TCR α) molecule.

144. The method of any of examples 1-128 or 131-143, wherein expansion of the population of T cells is compared to expansion of a similar population of cells not contacted with the anti-TCR β V antibody molecule.

145. The method of any of examples 1-128 or 131-144, wherein expansion of the population of T cells, e.g., memory effector T cells, *e.g.*, T_{EM} cells, *e.g.*, T_{EMRA} cells, is compared to expansion of a similar population of cells with an antibody that binds to: a CD3 molecule, *e.g.*, CD3 epsilon (CD3e) molecule; or a TCR alpha (TCR α) molecule.

146. The method of any of examples 1-128 or 131-145, wherein the population of expanded T cells, e.g., expanded T effector memory cells, comprises cells which:

- (i) have a detectable level of CD45RA, *e.g.*, express or re-express CD45RA;
- (ii) have low or no expression of CCR7; and/or
- (iii) have a detectable level of CD95, *e.g.*, express CD95,
e.g., a population of CD45RA+, CCR7-, CD95+ T cells, optionally wherein the T cells comprise CD3+, CD4+ or CD8+ T cells.

147. The method of any of examples 1-128 or 131-146, wherein the antibody molecule, e.g., humanized antibody molecule, which binds, *e.g.*, specifically binds, to the TCR β V region (the anti-TCR β V antibody molecule) is chosen from:

(A) a humanized antibody molecule which binds, *e.g.*, specifically binds, to a T cell receptor beta variable chain (TCR β V) region chosen from TCR β V V5-6, TCR β V V6-5, TCR β V V7, TCR β V V9, TCR β V V10, TCR β V V12 (*e.g.*, TCR β V V12-4), TCR β V V13, TCR β V V14, TCR β V V19, TCR β V V23-1, or a subfamily member thereof (*e.g.*, as listed in Table 1 or Table 2);

(B) a humanized antibody molecule which:

- (i) binds specifically to an epitope on TCR β V, *e.g.*, the same or similar epitope as the epitope recognized by a second anti-TCR β V antibody molecule;
- (ii) shows the same or similar binding affinity or specificity, or both, as a second anti-TCR β V antibody molecule;

(iii) inhibits, *e.g.*, competitively inhibits, the binding of a second anti-TCR β V antibody molecule;

(iv) binds the same or an overlapping epitope with an anti-TCR β V antibody molecule as a second anti-TCR β V antibody molecule; or

(v) competes for binding, and/or binds the same epitope, with a second anti-TCR β V antibody molecule,

wherein the second anti-TCR β V antibody molecule comprises an antigen binding domain comprising:

(1) a heavy chain complementarity determining region (HC CDR1), a HC CDR2 and/or a HC CDR3 of SEQ ID NO: 3, SEQ ID NO: 4, and/or SEQ ID NO: 5, and/or

(2) a light chain complementarity determining region 1 (LC CDR1), a LC CDR2, and/or a LC CDR3 of SEQ ID NO: 6, SEQ ID NO: 7, and/or SEQ ID NO: 8;

(1) a heavy chain complementarity determining region (HC CDR1), a HC CDR2 and/or a HC CDR3 of SEQ ID NO: 45, SEQ ID NO: 46, and/or SEQ ID NO: 47, and/or

(2) a light chain complementarity determining region 1 (LC CDR1), a LC CDR2, and/or a LC CDR3 of SEQ ID NO: 51, SEQ ID NO: 52, and/or SEQ ID NO: 53;

(1) a heavy chain complementarity determining region (HC CDR1), a HC CDR2 and/or a HC CDR3 of SEQ ID NO: 48, SEQ ID NO: 49, and/or SEQ ID NO: 50, and/or

(2) a light chain complementarity determining region 1 (LC CDR1), a LC CDR2, and/or a LC CDR3 of SEQ ID NO: 54, SEQ ID NO: 55, and/or SEQ ID NO: 56;

(1) a heavy chain complementarity determining region (HC CDR1), a HC CDR2 and/or a HC CDR3 of SEQ ID NO: 17, SEQ ID NO: 18, and/or SEQ ID NO: 19, and/or

(2) a light chain complementarity determining region 1 (LC CDR1), a LC CDR2, and/or a LC CDR3 of SEQ ID NO: 20, SEQ ID NO: 21, and/or SEQ ID NO: 22;

(1) a heavy chain complementarity determining region (HC CDR1), a HC CDR2 and/or a HC CDR3 of SEQ ID NO: 57, SEQ ID NO: 58, and/or SEQ ID NO: 59, and/or

(2) a light chain complementarity determining region 1 (LC CDR1), a LC CDR2, and/or a LC CDR3 of SEQ ID NO: 63, SEQ ID NO: 64, and/or SEQ ID NO: 65;

(1) a heavy chain complementarity determining region (HC CDR1), a HC CDR2 and/or a HC CDR3 of SEQ ID NO: 60, SEQ ID NO: 61, and/or SEQ ID NO: 62, and/or

(2) a light chain complementarity determining region 1 (LC CDR1), a LC CDR2, and/or a LC CDR3 of SEQ ID NO: 66, SEQ ID NO: 67, and/or SEQ ID NO: 68; or

(1) a heavy chain complementarity determining region (HC CDR1), a HC CDR2 and/or a HC CDR3 of SEQ ID NO: 15, SEQ ID NO: 23, SEQ ID NO: 24, or SEQ ID NO: 25, and/or

(2) a light chain complementarity determining region 1 (LC CDR1), a LC CDR2, and/or a 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; or

(C) a humanized antibody molecule which binds, *e.g.*, specifically binds, to a T cell receptor beta variable chain (TCR β V) region, wherein the anti-TCR β V antibody molecule comprises an antigen binding domain comprising:

(1) a heavy chain complementarity determining region (HC CDR1), a HC CDR2 and/or a HC CDR3 of SEQ ID NO: 3, SEQ ID NO: 4, and/or SEQ ID NO: 5, and/or

(2) a light chain complementarity determining region 1 (LC CDR1), a LC CDR2, and/or a LC CDR3 of SEQ ID NO: 6, SEQ ID NO: 7, and/or SEQ ID NO: 8;

(1) a heavy chain complementarity determining region (HC CDR1), a HC CDR2 and/or a HC CDR3 of SEQ ID NO: 45, SEQ ID NO: 46, and/or SEQ ID NO: 47, and/or

(2) a light chain complementarity determining region 1 (LC CDR1), a LC CDR2, and/or a LC CDR3 of SEQ ID NO: 51, SEQ ID NO: 52, and/or SEQ ID NO: 53;

(1) a heavy chain complementarity determining region (HC CDR1), a HC CDR2 and/or a HC CDR3 of SEQ ID NO: 48, SEQ ID NO: 49, and/or SEQ ID NO: 50, and/or

(2) a light chain complementarity determining region 1 (LC CDR1), a LC CDR2, and/or a LC CDR3 of SEQ ID NO: 54, SEQ ID NO: 55, and/or SEQ ID NO: 56;

(1) a heavy chain complementarity determining region (HC CDR1), a HC CDR2 and/or a HC CDR3 of SEQ ID NO: 17, SEQ ID NO: 18, and/or SEQ ID NO: 19, and/or

(2) a light chain complementarity determining region 1 (LC CDR1), a LC CDR2, and/or a LC CDR3 of SEQ ID NO: 20, SEQ ID NO: 21, and/or SEQ ID NO: 22;

(1) a heavy chain complementarity determining region (HC CDR1), a HC CDR2 and/or a HC CDR3 of SEQ ID NO: 57, SEQ ID NO: 58, and/or SEQ ID NO: 59, and/or

(2) a light chain complementarity determining region 1 (LC CDR1), a LC CDR2, and/or a LC CDR3 of SEQ ID NO: 63, SEQ ID NO: 64, and/or SEQ ID NO: 65;

(1) a heavy chain complementarity determining region (HC CDR1), a HC CDR2 and/or a HC CDR3 of SEQ ID NO: 60, SEQ ID NO: 61, and/or SEQ ID NO: 62, and/or

(2) a light chain complementarity determining region 1 (LC CDR1), a LC CDR2, and/or a LC CDR3 of SEQ ID NO: 66, SEQ ID NO: 67, and/or SEQ ID NO: 68; or

(i) a heavy chain complementarity determining region (HC CDR1), a HC CDR2 and/or a HC CDR3 of SEQ ID NO: 15, SEQ ID NO: 23, SEQ ID NO: 24, or SEQ ID NO: 25; and/or

(ii) a light chain complementarity determining region 1 (LC CDR1), a LC CDR2, and/or a 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.

148. The method of any of examples 1-128 or 131-147, wherein the anti-TCR β V antibody molecule comprises an antigen binding domain comprising a light chain variable region (VL) comprising one, two or all of a LC CDR1, a LC CDR2 and a 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.

149. The method of any of examples 1-128 or 131-148, wherein the anti-TCR β V antibody molecule comprises an antigen binding domain comprising a heavy chain variable region (VH)

comprising one, two or all of a HC CDR1, a HC CDR2 and a HC CDR3 of SEQ ID NO: 15, SEQ ID NO: 23, SEQ ID NO: 24, or SEQ ID NO: 25.

150. The method of any of examples 1-128 or 131-149, wherein the anti-TCR β V antibody molecule comprises an antigen binding domain comprising:

(i) a VL comprising: a LC CDR1 amino acid sequence of SEQ ID NO: 20 (or an amino acid sequence with not more than 1, 2, 3 or 4 modifications, *e.g.*, substitutions, additions or deletions thereof), a LC CDR2 amino acid sequence of SEQ ID NO:21 (or an amino acid sequence with not more than 1, 2, 3 or 4 modifications, *e.g.*, substitutions, additions or deletions thereof), and/or a LC CDR3 amino acid sequence of SEQ ID NO:22 (or an amino acid sequence with not more than 1, 2, 3 or 4 modifications, *e.g.*, substitutions, additions or deletions thereof); and/or

(ii) a VH comprising: a HC CDR1 amino acid sequence of SEQ ID NO: 17 (or an amino acid sequence with not more than 1, 2, 3 or 4 modifications, *e.g.*, substitutions, additions or deletions thereof), a HC CDR2 amino acid sequence of SEQ ID NO:18 (or an amino acid sequence with not more than 1, 2, 3 or 4 modifications, *e.g.*, substitutions, additions or deletions thereof), and/or a HC CDR3 amino acid sequence of SEQ ID NO:19 (or an amino acid sequence with not more than 1, 2, 3 or 4 modifications, *e.g.*, substitutions, additions or deletions thereof).

151. The method of any of examples 1-128 or 131-150, wherein the anti-TCR β V antibody molecule comprises an antigen binding domain comprising:

a variable heavy chain (VH) of SEQ ID NO: 23, SEQ ID NO: 24, or SEQ ID NO: 25, or a sequence having at least about 85%, 90%, 95%, or 99% sequence identity thereto; and/or

a variable light chain (VL) of SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO: 29, or SEQ ID NO: 30, or a sequence having at least about 85%, 90%, 95%, or 99% sequence identity thereto.

152. The method of any of examples 1-128 or 131-151, wherein the anti-TCR β V antibody molecule comprises a light chain comprising a framework region, *e.g.*, framework region 1 (FR1), comprising one, two or all (*e.g.*, three) of:

(i) an Aspartic Acid at position 1, *e.g.*, a substitution at position 1 according to Kabat numbering, *e.g.*, a Alanine to Aspartic Acid substitution; or

(ii) an Asparagine at position 2, *e.g.*, a substitution at position 2 according to Kabat numbering, *e.g.*, a Isoleucine to Asparagine, a Serine to Asparagine, or a Tyrosine to Asparagine substitution; or

(iii) a Leucine at position 4, *e.g.*, a substitution at position 4 according to Kabat numbering, *e.g.*, a Methionine to Leucine substitution,

wherein the substitution is relative to a human germline light chain framework region sequence.

153. The method of any of examples 1-128 or 131-153, wherein the anti-TCR β V antibody molecule comprises a light chain comprising a framework region, *e.g.*, framework region 3 (FR3), comprising one, two or all (*e.g.*, three) of:

(i) a Glycine at position 66, *e.g.*, a substitution at position 66 according to Kabat numbering, *e.g.*, a Lysine to Glycine, or a Serine to Glycine substitution; or

(ii) an Asparagine at position 69, *e.g.*, a substitution at position 69 according to Kabat numbering, *e.g.*, a Threonine to Asparagine substitution; or

(iii) a Tyrosine at position 71, *e.g.*, a substitution at position 71 according to Kabat numbering, *e.g.*, a Phenylalanine to Tyrosine, or Alanine to Tyrosine substitution,

wherein the substitution is relative to a human germline light chain framework region sequence.

154. The method of any of examples 1-128 or 131-153, wherein the method results in expansion of, *e.g.*, selective or preferential expansion of, T cells expressing a T cell receptor (TCR) comprising a TCR alpha and/or TCR beta molecule, *e.g.*, TCR alpha-beta T cells ($\alpha\beta$ T cells).

5 155. The method of any of examples 1-128 or 131-154, wherein the method results in expansion of $\alpha\beta$ T cells over expansion of T cells expressing a TCR comprising a TCR gamma and/or TCR delta molecule, *e.g.*, TCR gamma-delta T cells ($\gamma\delta$ T cells).

10 In some examples, the anti-TCR β V antibody molecules disclosed herein result in lesser or no production of cytokines associated with cytokine release syndrome (CRS), *e.g.*, IL-6, IL-

1beta and TNF alpha; and enhanced and/or delayed production of IL-2 and IFNg. In some examples, the anti-TCRβV antibodies disclosed herein result in expansion of an immune cell, e.g., a T cell, or a subset of memory effector T cells known as T_{EMRA}), an NK cell, or other immune cells (e.g., as described herein). Also provided herein are methods of making said anti-TCRβV antibody molecules, and methods of using said anti-TCRβV antibody molecules including, methods of using an anti-TCRβV antibody molecule for expanding an immune cell or an immune cell population. This disclosure further provides multispecific molecules, e.g., bispecific molecules, comprising said anti-TCRβV antibody molecules. In some examples, compositions comprising anti-TCRβV antibody molecules of the present disclosure, can be used, e.g., to activate and/or redirect T cells to treat an infectious disease. In some examples, compositions comprising anti-TCRβV antibody molecules as disclosed herein limit the unwanted side-effects of CRS, e.g., CRS associated with anti-CD3e targeting.

Accordingly, provided herein are, anti-TCRβV antibody molecules, multispecific or multifunctional molecules (e.g., multispecific or multifunctional antibody molecules) (also referred to herein as a “composition”) that comprise anti-TCRβV antibody molecules, nucleic acids encoding the same, methods of producing the aforesaid molecules, pharmaceutical compositions comprising aforesaid molecules, and methods of treating a disease or disorder, e.g., an infectious disease, e.g., as described herein, using the aforesaid molecules. The antibody molecules and pharmaceutical compositions disclosed herein can be used (alone or in combination with other agents or therapeutic modalities) to treat, prevent and/or diagnose disorders and conditions, e.g., an infectious disease, e.g., as described herein.

In one aspect, the disclosure provides a composition comprising a multispecific molecule, wherein the multispecific molecule comprises:

- (1) an anti-TCRβV moiety, and
- an infectious disease-targeting moiety.

In one aspect, the disclosure provides a recombinant polynucleotide comprising a sequence encoding the multispecific molecule of the composition as described herein.

In one aspect, the disclosure provides a medicament comprising the composition as described herein, and a pharmaceutically acceptable carrier, excipient, or stabilizer.

In one aspect, the disclosure provides a use of a pharmaceutical composition comprising the composition as described herein in the manufacture of a medicament for treating an infectious
5 disease in a subject in need thereof.

In one aspect, the disclosure provides a composition as described herein for use in therapy.

In one example, the disclosure provides a non-murine, *e.g.*, human or humanized antibody molecule, which binds, *e.g.*, specifically binds, to a T cell receptor beta variable
10 (TCR β V) region. In some examples, binding of the anti-TCR β V antibody molecule to a TCR β V region results in one, two, three, four, five, six, seven, eight, nine, ten or more (*e.g.*, all) of the following:

- (i) reduced level, *e.g.*, expression level, and/or activity of IL-1 β ;
- (ii) reduced level, *e.g.*, expression level, and/or activity of IL-6;
- 15 (iii) reduced level, *e.g.*, expression level, and/or activity of TNF α ;
- (iv) increased level, *e.g.*, expression level, and/or activity of IL-2;
- (v) a delay, *e.g.*, at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more hours delay, in increased level, *e.g.*, expression level, and/or activity of IL-2;
- (vi) a delay, *e.g.*, at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 hours delay, in increased level, *e.g.*,
20 expression level, and/or activity of IFN γ ;
- (vii) reduced T cell proliferation kinetics;
- (viii) reduced cytokine storm, *e.g.*, cytokine release syndrome (CRS), *e.g.*, as measured by an assay of Example 3;
- (ix) cell killing, *e.g.*, target cell killing;
- 25 (x) increased level, *e.g.*, expression level, and/or activity of IL-15; or
- (xi) increased Natural Killer (NK) cell proliferation, *e.g.*, expansion.

In some examples, any one or all of (i)-(xi) or any combination thereof resulting from an anti-TCR β V antibody molecule disclosed herein is compared to an antibody that binds to: a CD3 molecule, *e.g.*, CD3 epsilon (CD3e) molecule; or a TCR alpha (TCR α) molecule.

5 In some examples, binding of the anti-TCR β V antibody molecule to a TCR β V region results in secretion, *e.g.*, production of perforin and/or Granzyme B.

In another example, the disclosure provides a non-murine, *e.g.*, human or humanized antibody molecule, which binds, *e.g.*, specifically binds, to a T cell receptor beta variable (TCR β V) region. In some examples, binding of the anti-TCR β V antibody molecule results in
10 expansion, *e.g.*, at least about 1.1-50 fold expansion (*e.g.*, at least about 1.5-40 fold, 2-35 fold, 3-30 fold, 5-25 fold, 8-20 fold, or 10-15 fold expansion), of a population of memory T cells, *e.g.*, T effector memory (T_{EM}) cells, *e.g.*, T_{EM} cells expressing CD45RA (T_{EMRA}) cells, *e.g.*, CD4+ or CD8+ T_{EMRA} cells. In some examples, the expansion is at least about 1.1-10 fold expansion (*e.g.*, at least about 1.1, 1.2, 1.3, 1.4, 1.5, 2, 3, 4, 5, 6, 7, 8, 9, or 10 fold expansion).

15 In some examples, expansion of the population of memory effector T cells, *e.g.*, T_{EM} cells, *e.g.*, T_{EMRA} cells, *e.g.*, CD4+ or CD8+ T_{EMRA} cells, is compared to expansion of a similar population of cells with an antibody that binds to: a CD3 molecule, *e.g.*, CD3 epsilon (CD3e) molecule; or a TCR alpha (TCR α) molecule.

In some examples, the population of expanded T effector memory cells comprises cells T
20 cells, *e.g.*, CD3+, CD8+ or CD4+ T cells. In some examples, the population of expanded T effector memory cells comprises CD3+ and CD8+ T cells. In some examples, the population of expanded T effector memory cells comprises CD3+ and CD4+ T cells.

In some examples, the population of expanded T effector memory (T_{EM}) cells comprises
25 cells T cells, *e.g.*, CD3+, CD8+ or CD4+ T cells, which express or re-express, CD45RA, *e.g.*, CD45RA+. In some examples, the population comprises T_{EM} cells expressing CD45RA, *e.g.*, T_{EMRA} cells. In some examples, expression of CD45RA on T_{EMRA} cells, *e.g.*, CD4+ or CD8+ T_{EMRA} cells, can be detected by a method disclosed herein, *e.g.*, flow cytometry.

In some examples, T_{EMRA} cells have low or no expression of CCR7, *e.g.*, CCR7- or CCR7 low. In some examples, expression of CCR7 on T_{EMRA} cells cannot be detected by a
30 method disclosed herein, *e.g.*, flow cytometry.

In some examples, T_{EMRA} cells express CD95, *e.g.*, CD95+. In some examples, expression of CD95 on T_{EMRA} cells can be detected by a method disclosed herein, *e.g.*, flow cytometry.

5 In some examples, T_{EMRA} cells express CD45RA, *e.g.*, CD45RA+, have low or no expression of CCR7, *e.g.*, CCR7- or CCR7 low, and express CD95, *e.g.*, CD95+. In some examples T_{EMRA} cells can be identified as CD45RA+, CCR7- and CD95+ cells. In some examples, T_{EMRA} cells comprise CD3+, CD4+ or CD8+ T cells (*e.g.*, CD3+ T cells, CD3+ CD8+ T cells, or CD3+ CD4+ T cells).

10 In some examples, binding of the anti-TCR β V antibody molecule to a TCR β V region results in one, two, three, four, five, six, seven, eight, nine, ten or more (*e.g.*, all) of the following:

- (i) reduced level, *e.g.*, expression level, and/or activity of IL-1 β ;
- (ii) reduced level, *e.g.*, expression level, and/or activity of IL-6;
- 15 (iii) reduced level, *e.g.*, expression level, and/or activity of TNF α ;
- (iv) increased level, *e.g.*, expression level, and/or activity of IL-2;
- (v) a delay, *e.g.*, at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more hours delay, in increased level, *e.g.*, expression level, and/or activity of IL-2;
- (vi) a delay, *e.g.*, at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 hours delay, in increased level, *e.g.*,
20 expression level, and/or activity of IFN γ ;
- (vii) reduced T cell proliferation kinetics;
- (viii) reduced cytokine storm, *e.g.*, cytokine release syndrome (CRS), *e.g.*, as measured by an assay of Example 3;
- (ix) cell killing, *e.g.*, target cell killing;
- 25 (x) increased level, *e.g.*, expression level, and/or activity of IL-15; or
- (xi) increased Natural Killer (NK) cell proliferation, *e.g.*, expansion, compared to an antibody that binds to: a CD3 molecule, *e.g.*, CD3 epsilon (CD3e) molecule; or a TCR alpha (TCR α) molecule.

In some examples of any of the compositions disclosed herein, binding of the anti-TCR β V antibody molecule to a TCR β V region results in a reduction of at least 2, 5, 10, 20, 50, 100, or 200 fold, or at least 2-200 fold (*e.g.*, 5-150, 10-100, 20-50 fold) in the expression level and or activity of IL-1 β as measured by an assay of Example 3.

5 In some examples of any of the compositions disclosed herein, binding of the anti-TCR β V antibody molecule to a TCR β V region results in a reduction of at least 2, 5, 10, 20, 50, 100, 200, 300, 400, 500, 600, 700, 800, 900, or 1000 fold, or at least 2-1000 fold (*e.g.*, 5-900, 10-800, 20-700, 50-600, 100-500, or 200-400 fold) in the expression level and or activity of IL-6 as measured by an assay of Example 3.

10 In some examples of any of the compositions disclosed herein, binding of the anti-TCR β V antibody molecule to a TCR β V region results in a reduction of at least 2, 5, 10, 20, 50, 100, 200, 300, 400, 500, 600, 700, 800, 900, 1000, or 2000 fold, or at least 2-2000 fold (*e.g.*, 5-1000, 10-900, 20-800, 50-700, 100-600, 200-500, or 300-400 fold) in the expression level and or activity of TNF α as measured by an assay of Example 3.

15 In some examples of any of the compositions disclosed herein, binding of the anti-TCR β V antibody molecule to a TCR β V region results in an increase of at least 2, 5, 10, 20, 50, 100, 200, 300, 400, 500, 600, 700, 800, 900, 1000, or 2000 fold, or at least 2-2000 fold (*e.g.*, 5-1000, 10-900, 20-800, 50-700, 100-600, 200-500, or 300-400 fold) in the expression level and or activity of IL-2 as measured by an assay of Example 3.

20 In some examples of any of the compositions disclosed herein, binding of the anti-TCR β V antibody molecule to a TCR β V region results in an increase of at least 2, 5, 10, 20, 50, 100, 200, 300, 400, 500, 600, 700, 800, 900, 1000, or 2000 fold, or at least 2-2000 fold (*e.g.*, 5-1000, 10-900, 20-800, 50-700, 100-600, 200-500, or 300-400 fold) in the expression level and or activity of IL-15.

25 In some examples of any of the compositions disclosed herein, binding of the anti-TCR β V antibody molecule results in proliferation, *e.g.*, expansion, *e.g.*, at least about 1.1-50 fold expansion (*e.g.*, at least about 1.5-40 fold, 2-35 fold, 3-30 fold, 5-25 fold, 8-20 fold, or 10-15 fold expansion), of a population of Natural Killer (NK) cells. In some examples, the expansion of NK cells is at least about 1.1-30 fold expansion (*e.g.*, at least about 1.1, 1.2, 1.3, 1.4, 1.5, 2, 3, 4,
30 5, 6, 7, 8, 9, 10, 15, 20, 25, or at least about 1.1-5, 5-10, 10-15, 15-20, 20-25, or 25-30 fold

expansion). In some examples, the expansion of NK cells by, e.g., binding of, the anti-TCR β V antibody molecule is compared to expansion of an otherwise similar population not contacted with the anti-TCR β V antibody molecule.

In some examples of any of the compositions disclosed herein, binding of the anti-TCR β V antibody molecule results in cell killing, e.g., target cell killing. In some examples, binding of the anti-TCR β V antibody molecule results in cell killing in vitro or in vivo.

In some examples of any of the compositions disclosed herein, binding of the anti-TCR β V antibody molecule to a TCR β V region results in an increase or decrease of at least 2, 5, 10, 20, 50, 100, 200, 300, 400, 500, 600, 700, 800, 900, 1000, or 2000 fold, or at least 2-2000 fold (e.g., 5-1000, 10-900, 20-800, 50-700, 100-600, 200-500, or 300-400 fold) of any of the activities described herein compared the activity of Antibody B or murine Antibody C, or a humanized version thereof (e.g., humanized mAb Antibody B-H.1 to B-H.6) as described in US Patent 5,861,155.

In an example, provided herein is an antibody molecule which binds, e.g., specifically binds, to a T cell receptor beta variable chain (TCR β V) region (an anti-TCR β V antibody molecule), wherein the anti-TCR β V antibody molecule:

(i) binds specifically to an epitope on TCR β V, e.g., the same or similar epitope as the epitope recognized by an anti-TCR β V antibody molecule as described herein, e.g., a second anti-

TCR β V antibody molecule;

(ii) shows the same or similar binding affinity or specificity, or both, as an anti-TCR β V antibody molecule as described herein, e.g., a second anti-TCR β V antibody molecule;

(iii) inhibits, e.g., competitively inhibits, the binding of an anti-TCR β V antibody molecule as described herein, e.g., a second anti-TCR β V antibody molecule;

(iv) binds the same or an overlapping epitope with an anti-TCR β V antibody molecule as described herein, e.g., a second anti-TCR β V antibody molecule; or

(v) competes for binding, and/or binds the same epitope, with an anti-TCR β V antibody molecule as described herein, e.g., a second anti-TCR β V antibody molecule,

In some examples, the second anti-TCR β V antibody molecule comprises an antigen binding domain chosen from Table 3 or Table 4, or a sequence substantially identical thereto. In

some examples, the second anti-TCR β V antibody molecule comprises an antigen binding domain, comprising:

a heavy chain complementarity determining region 1 (HC CDR1), a heavy chain complementarity determining region 2 (HC CDR2) and/or a heavy chain complementarity determining region 3 (HC CDR3) of SEQ ID NO: 1 or SEQ ID NO: 9; and/or a light chain complementarity determining region 1 (LC CDR1), a light chain complementarity determining region 2 (LC CDR2), and/or a light chain complementarity determining region 3 (LC CDR3) of SEQ ID NO: 2, SEQ ID NO: 10 or SEQ ID NO: 11.

In some examples of any of the compositions disclosed herein, binding of the anti-TCR β V antibody molecule to a TCR β V region results in a change in any (e.g., one, two, three, four or all) of (i)-(v) that is different, e.g., an increase or decrease, of at least 2, 5, 10, 20, 50, 100-fold, compared the activity of Antibody B or murine Antibody C or a humanized version thereof (e.g., humanized mAb Antibody B-H.1 to B-H.6) as described in US Patent 5,861,155.

In some examples of any of the compositions disclosed herein, the anti-TCR β V antibody molecule binds to a TCRBV family (e.g., gene family), e.g., a TCRBV gene family comprising subfamilies, e.g., as described herein. In some examples, the TCRBV family, e.g., 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 v, 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 or a TCR β V29 subfamily.

In some examples, the anti-TCR β V antibody binds to a TCR β V6 subfamily chosen from: 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 examples the TCR β V6 subfamily comprises TCR β V6-5*01.

In some examples, the anti-TCR β V antibody binds to a TCR β V10 subfamily chosen from: TCR β V10-1*01, TCR β V10-1*02, TCR β V10-3*01 or TCR β V10-2*01.

In some examples, the anti-TCR β V antibody binds to a TCR β V12 subfamily chosen from: TCR β V12-4*01, TCR β V12-3*01 or TCR β V12-5*01.

In some examples of any of the compositions disclosed herein, 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 murine mAb Antibody B or a humanized version thereof (e.g., humanized mAb Antibody B-H.1 to B-H.6) as described in US Patent 5,861,155.

In some examples of any of the compositions disclosed herein, 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 murine mAb Antibody B or a humanized version thereof (e.g., humanized mAb Antibody B-H.1 to B-H.6) as described in US Patent 5,861,155.

In some examples of any of the compositions disclosed herein, 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 murine mAb Antibody B or a humanized version thereof (e.g., humanized mAb Antibody B-H.1 to B-H.6) as described in US Patent 5,861,155.

In some examples of any of the compositions disclosed herein, the anti-TCR β V antibody molecule does not comprise the CDRs of the murine mAb Antibody B.

In some examples of any of the compositions disclosed herein, the anti-TCR β V antibody binds to a TCR β V5 subfamily 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.

In some examples of any of the compositions disclosed herein, the anti-TCR β V antibody binds to a TCR β V5 subfamily 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.

In some examples of any of the compositions disclosed herein, 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 examples of any of the compositions disclosed herein, 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 examples of any of the compositions disclosed herein, 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.

In some examples of any of the compositions disclosed herein, the anti-TCR β V antibody molecule does not comprise the CDRs of murine Antibody C.

In some examples of any of the compositions disclosed herein, the anti-TCR β V antibody molecule binds to one or more (e.g., all) of the following TCR β V subfamilies:

- (i) TCR β V6, e.g., 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;
- (ii) TCR β V10, e.g., TCR β V10-1*01, TCR β V10-1*02, TCR β V10-3*01 or TCR β V10-2*01;
- (iii) TCR β V12, e.g., TCR β V12-4*01, TCR β V12-3*01, or TCR β V12-5*01; or
- (iv) TCR β V5, e.g., 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.

In some examples, the anti-TCR β V antibody molecule binds to TCR β V6, *e.g.*, 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 examples, the anti-TCR β V antibody molecule binds to TCR β V6-5*01.

5 In some examples, the anti-TCR β V antibody molecule does not bind to TCR β V12.

In some examples, the anti-TCR β V antibody molecule does not bind to TCR β V5-5*01 or TCR β V5-1*01.

10 In another example, provided herein is a method of expanding, *e.g.*, increasing the number of, an immune cell population comprising, contacting the immune cell population with an antibody molecule, *e.g.*, humanized antibody molecule, which binds, *e.g.*, specifically binds, to a T cell receptor beta variable chain (TCR β V) region (*e.g.*, anti-TCR β V antibody molecule described herein or a multispecific molecule comprising an anti-TCR β V antibody molecule described herein), thereby expanding the immune cell population.

15 In some examples, the expansion occurs *in vivo* or *ex vivo* (*e.g.*, *in vitro*).

In some examples, the immune cell population comprises a T cell, a Natural Killer cell, a B cell, an antigen presenting cell, or a myeloid cell (*e.g.*, a monocyte, a macrophage, a neutrophil or a granulocyte).

20 In some examples, the immune cell population comprises a T cell, *e.g.*, a CD4+ T cell, a CD8+ T cell, a TCR alpha-beta T cell, or a TCR gamma-delta T cell. In some examples, a T cell comprises a memory T cell (*e.g.*, a central memory T cell, or an effector memory T cell (*e.g.*, a T_{EMRA}) or an effector T cell.

In some examples, the immune cell population is obtained from a healthy subject.

25 In some examples, the immune cell population is obtained from a subject (*e.g.*, from an apheresis sample from the subject) having a disease, *e.g.*, infectious disease, *e.g.*, as described herein. In some examples, the immune cell population obtained from a subject having a disease, *e.g.*, an infectious disease, comprises a T cell, a Natural Killer cell, a B cell, or a myeloid cell.

In some examples, the method results in an expansion of at least 1.1-10 fold (*e.g.*, at least 1.1, 1.2, 1.3, 1.4, 1.5, 2, 3, 4, 5, 6, 7, 8, 9, or 10 fold expansion).

In some examples, the method further comprises contacting the population of cells with an agent that promotes, e.g., increases, immune cell expansion. In some examples, the agent includes an immune checkpoint inhibitor, e.g., as described herein. In some examples, the agent includes a 4-1BB (CD127) agonist, e.g., an anti-4-1BB antibody.

5 In some examples, the method further comprises comprising contacting the population of cells with a non-dividing population of cells, e.g., feeder cells, e.g., irradiated allogenic human PBMCs.

In some examples, an expansion method described herein comprises expanding the cells for a period of at least about 4 hours, 6 hours, 10 hours, 12 hours, 15 hours, 18 hours, 20 hours,
10 or 22 hours, or for at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 or 21 days, or for at least about 1 week, 2 weeks, 3 weeks, 4 weeks, 5 weeks, 6 weeks, 7 weeks or 8 weeks.

In some examples, expansion of the population of immune cells, is compared to expansion of a similar population of cells with an antibody that binds to: a CD3 molecule, e.g.,
15 CD3 epsilon (CD3e) molecule; or a TCR alpha (TCR α) molecule.

In some examples, expansion of the population of immune cells, is compared to expansion of a similar population of cells not contacted with the anti-TCR β V antibody molecule.

In some examples, expansion of the population of memory effector T cells, e.g., T_{EM} cells, e.g., T_{EMRA} cells, is compared to expansion of a similar population of cells with an
20 antibody that binds to: a CD3 molecule, e.g., CD3 epsilon (CD3e) molecule; or a TCR alpha (TCR α) molecule.

In some examples, the method results in expansion of, e.g., selective or preferential expansion of, T cells expressing a T cell receptor (TCR) comprising a TCR alpha and/or TCR beta molecule, e.g., TCR alpha-beta T cells ($\alpha\beta$ T cells).

25 In some examples, the method results in expansion of $\alpha\beta$ T cells over expansion of T cells expressing a TCR comprising a TCR gamma and/or TCR delta molecule, e.g., TCR gamma-delta T cells ($\gamma\delta$ T cells). In some examples, expansion of $\alpha\beta$ T cells over $\gamma\delta$ T cells results in reduced production of cytokines associated with CRS. In some examples, expansion of $\alpha\beta$ T cells over $\gamma\delta$ T cells results in immune cells that have reduced capacity to, e.g., are less prone to, induce CRS
30 upon administration into a subject.

In some examples, an immune cell population (e.g., T cells (e.g., T_{EMRA} cells or TILs) or NK cells) cultured in the presence of, e.g., expanded with, an anti- TCR β V antibody disclosed herein does not induce CRS when administered into a subject, e.g., a subject having a disease or condition as described herein.

5

Alternatively or in combination with any of the examples disclosed herein, provided herein is an anti-TCR β V antibody molecule which:

- (i) binds specifically to an epitope on TCR β V, *e.g.*, the same or similar epitope as the epitope recognized by an anti-TCR β V antibody molecule as described herein, *e.g.*, a second anti-TCR β V antibody molecule;
- (ii) shows the same or similar binding affinity or specificity, or both, as an anti-TCR β V antibody molecule as described herein, *e.g.*, a second anti-TCR β V antibody molecule;
- (iii) inhibits, *e.g.*, competitively inhibits, the binding of an anti-TCR β V antibody molecule as described herein, *e.g.*, a second anti-TCR β V antibody molecule;
- (iv) binds the same or an overlapping epitope with an anti-TCR β V antibody molecule as described herein, *e.g.*, a second anti-TCR β V antibody molecule; or
- (v) competes for binding, and/or binds the same epitope, with an anti-TCR β V antibody molecule as described herein, *e.g.*, a second anti-TCR β V antibody molecule,

In some examples, the second anti-TCR β V antibody molecule comprises an antigen binding domain chosen from Table 3 or Table 4, or a sequence substantially identical thereto. In some examples, the second anti-TCR β V antibody molecule comprises an antigen binding domain, comprising:

a heavy chain complementarity determining region 1 (HC CDR1), a heavy chain complementarity determining region 2 (HC CDR2) and/or a heavy chain complementarity determining region 3 (HC CDR3) of SEQ ID NO: 1 or SEQ ID NO: 9; and/or a light chain complementarity determining region 1 (LC CDR1), a light chain complementarity determining region 2 (LC CDR2), and/or a light chain complementarity determining region 3 (LC CDR3) of SEQ ID NO: 2, SEQ ID NO: 10, or SEQ ID NO: 11.

In another example, the disclosure provides a multispecific molecule, *e.g.*, a bispecific molecule, comprising the anti-TCR β V antibody molecule disclosed herein.

In some examples, the multispecific molecule further comprises: an infectious disease-targeting moiety, a cytokine molecule, an immune cell engager, *e.g.*, a second immune cell
5 engager, and/or a stromal modifying moiety.

In yet another example, disclosed herein is a multispecific molecule, *e.g.*, a bispecific molecule, comprising:

- (i) a first moiety comprising a first immune cell engager comprising an anti-TCR β V
10 antibody molecule disclosed herein; and
- (ii) a second moiety comprising one or more of: an infectious disease-targeting moiety; a second immune cell engager; a cytokine molecule or a stromal modifying moiety.

In some examples of any of the compositions disclosed herein, the anti-TCR β V antibody molecule comprises an antigen binding domain comprising:

- (i) a heavy chain complementarity determining region 1 (HC CDR1), a heavy chain complementarity determining region 2 (HC CDR2) and/or a heavy chain complementarity determining region 3 (HC CDR3) of SEQ ID NO: 1 or SEQ ID NO: 9; or
15
- (ii) a light chain complementarity determining region 1 (LC CDR1), a light chain complementarity determining region 2 (LC CDR2), and/or a light chain complementarity
20 determining region 3 (LC CDR3) of SEQ ID NO: 2, SEQ ID NO: 10, or SEQ ID NO: 11.

In some examples of any of the compositions disclosed herein, the anti-TCR β V antibody molecule comprises an antigen binding domain comprising a light chain variable region (VL) comprising one, two or all (*e.g.*, three) of a LC CDR1, a LC CDR2 and a LC CDR3 of SEQ ID NO: 2, SEQ ID NO: 10, or SEQ ID NO: 11.

In some examples of any of the compositions disclosed herein, the anti-TCR β V antibody molecule comprises an antigen binding domain comprising a heavy chain variable region (VH) comprising one, two or all (*e.g.*, three) of a HC CDR1, a HC CDR2 and a HC CDR3 of SEQ ID NO:1 or SEQ ID NO: 9.
25

In some examples of any of the compositions disclosed herein, the anti-TCR β V antibody molecule comprises an antigen binding domain comprising:

(i) a VL comprising: a LC CDR1 amino acid sequence of SEQ ID NO: 6 (or an amino acid sequence with not more than 1, 2, 3 or 4 modifications, *e.g.*, substitutions, additions or deletions thereof), a LC CDR2 amino acid sequence of SEQ ID NO:7 (or an amino acid sequence with not more than 1, 2, 3 or 4 modifications, *e.g.*, substitutions, additions or deletions thereof), and/or a LC CDR3 amino acid sequence of SEQ ID NO:8 (or an amino acid sequence with not more than 1, 2, 3 or 4 modifications, *e.g.*, substitutions, additions or deletions thereof); and/or

(ii) a VH comprising: a HC CDR1 amino acid sequence of SEQ ID NO: 3 (or an amino acid sequence with not more than 1, 2, 3 or 4 modifications, *e.g.*, substitutions, additions or deletions thereof), a HC CDR2 amino acid sequence of SEQ ID NO: 4 (or an amino acid sequence with not more than 1, 2, 3 or 4 modifications, *e.g.*, substitutions, additions or deletions thereof), and/or a HC CDR3 amino acid sequence of SEQ ID NO: 5 (or an amino acid sequence with not more than 1, 2, 3 or 4 modifications, *e.g.*, substitutions, additions or deletions thereof).

In some examples of any of the compositions disclosed herein, the anti-TCR β V antibody molecule comprises an antigen binding domain comprising:

a variable heavy chain (VH) of SEQ ID NO: 9, or a sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto; and/or

a variable light chain (VL) of SEQ ID NO: 10 or SEQ ID NO: 11, or a sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto.

In some examples of any of the compositions disclosed herein, the anti-TCR β V antibody molecule comprises an antigen binding domain comprising the VH amino acid sequence of SEQ ID NO: 9 and the VL amino acid sequence of SEQ ID NO: 10.

In some examples of any of the compositions disclosed herein, the anti-TCR β V antibody molecule comprises an antigen binding domain comprising the VH amino acid sequence of SEQ ID NO: 9 and the VL amino acid sequence of SEQ ID NO: 11.

In some examples of any of the compositions disclosed herein, the anti-TCR β V antibody molecule comprises a heavy chain comprising a framework region, *e.g.*, framework region 3

(FR3), comprising one or both of: (i) a Threonine at position 73, *e.g.*, a substitution at position 73 according to Kabat numbering, *e.g.*, a Glutamic Acid to Threonine substitution; or (ii) a Glycine at position, *e.g.*, a substitution at position 94 according to Kabat numbering, *e.g.*, a Arginine to Glycine substitution. In some examples, the substitution is relative to a human germline heavy chain framework region sequence.

In some examples of any of the compositions disclosed herein, the anti-TCR β V antibody molecule comprises a light chain comprising a framework region, *e.g.*, 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. In some examples, the substitution is relative to a human germline light chain framework region sequence.

In some examples of any of the compositions disclosed herein, the anti-TCR β V antibody molecule comprises a light chain comprising a framework region, *e.g.*, framework region 2 (FR2), comprising one or both of: (i) a Histidine at position 36, *e.g.*, a substitution at position 36 according to Kabat numbering, *e.g.*, a Tyrosine to Histidine substitution; or (ii) an Alanine at position 46, *e.g.*, a substitution at position 46 according to Kabat numbering, *e.g.*, a Arginine to Alanine substitution. In some examples, the substitution is relative to a human germline light chain framework region sequence.

In some examples of any of the compositions disclosed herein, the anti-TCR β V antibody molecule comprises a light chain comprising a framework region, *e.g.*, 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. In some examples, the substitution is relative to a human germline light chain framework region sequence.

In some examples of any of the compositions disclosed herein, the anti-TCR β V antibody molecule binds to TCR β V6, *e.g.*, 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 examples the anti-TCR β V antibody molecule binds to TCR β V6-5*01.

In some examples, TCR β V6, *e.g.*, 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, is recognized, *e.g.*, bound, by SEQ ID NO: 1 and/or SEQ ID NO: 2. In some examples, TCR β V6, *e.g.*, 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, is recognized, *e.g.*, bound, by SEQ ID NO: 9 and/or SEQ ID NO: 10. In some examples, TCR β V6, *e.g.*, 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, is recognized, *e.g.*, bound, by SEQ ID NO: 9 and/or SEQ ID NO: 11. In some examples, TCR β V6-5*01 is recognized, *e.g.*, bound by SEQ ID NO: 9 and/or SEQ ID NO: 10, or a sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto. In some examples, TCR β V6-5*01 is recognized, *e.g.*, bound by SEQ ID NO: 9 and/or SEQ ID NO: 11, or a sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto.

In some examples of any of the compositions disclosed herein, the anti-TCR β V antibody molecule comprises an antigen binding domain comprising:

- (i) a heavy chain complementarity determining region (HC CDR1), a HC CDR2 and/or a HC CDR3 of SEQ ID NO: 15, SEQ ID NO: 23, SEQ ID NO: 24, or SEQ ID NO: 25; and/or
- (ii) a light chain complementarity determining region 1 (LC CDR1), a LC CDR2, and/or a 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.

In some examples of any of the compositions disclosed herein, the anti-TCR β V antibody molecule comprises an antigen binding domain comprising a light chain variable region (VL) comprising one, two or all of a LC CDR1, a LC CDR2 and a 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.

In some examples of any of the compositions disclosed herein, the anti-TCR β V antibody molecule comprises an antigen binding domain comprising a heavy chain variable region (VH) comprising one, two or all of a HC CDR1, a HC CDR2 and a HC CDR3 of SEQ ID NO: 15, SEQ ID NO: 23, SEQ ID NO: 24, or SEQ ID NO: 25.

In some examples of any of the compositions disclosed herein, the anti-TCR β V antibody molecule comprises an antigen binding domain comprising:

- (i) a VL comprising: a LC CDR1 amino acid sequence of SEQ ID NO: 20 (or an amino acid sequence with not more than 1, 2, 3 or 4 modifications, *e.g.*, substitutions, additions or

deletions thereof), a LC CDR2 amino acid sequence of SEQ ID NO:21 (or an amino acid sequence with not more than 1, 2, 3 or 4 modifications, *e.g.*, substitutions, additions or deletions thereof), and/or a LC CDR3 amino acid sequence of SEQ ID NO:22 (or an amino acid sequence with not more than 1, 2, 3 or 4 modifications, *e.g.*, substitutions, additions or deletions thereof);

and/or

(ii) a VH comprising: a HC CDR1 amino acid sequence of SEQ ID NO: 17 (or an amino acid sequence with not more than 1, 2, 3 or 4 modifications, *e.g.*, substitutions, additions or deletions thereof), a HC CDR2 amino acid sequence of SEQ ID NO:18 (or an amino acid sequence with not more than 1, 2, 3 or 4 modifications, *e.g.*, substitutions, additions or deletions thereof), and/or a HC CDR3 amino acid sequence of SEQ ID NO:19 (or an amino acid sequence with not more than 1, 2, 3 or 4 modifications, *e.g.*, substitutions, additions or deletions thereof).

In some examples of any of the compositions disclosed herein, the anti-TCR β V antibody molecule comprises an antigen binding domain comprising:

a variable heavy chain (VH) of SEQ ID NO: 23, SEQ ID NO: 24 or SEQ ID NO: 25, or a sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto; and/or

a variable light chain (VL) of SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO: 29, or SEQ ID NO: 30, or a sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto.

In some examples of any of the compositions disclosed herein, the anti-TCR β V antibody molecule comprises a light chain comprising a framework region, *e.g.*, framework region 1 (FR1), comprising one, two or all (*e.g.*, three) of: (i) an Aspartic Acid at position 1, *e.g.*, a substitution at position 1 according to Kabat numbering, *e.g.*, a Alanine to Aspartic Acid substitution; or (ii) an Asparagine at position 2, *e.g.*, a substitution at position 2 according to Kabat numbering, *e.g.*, a Isoleucine to Asparagine substitution, a Serine to Asparagine substitution, or a Tyrosine to Asparagine substitution; or (iii) a Leucine at position 4, *e.g.*, a substitution at position 4 according to Kabat numbering, *e.g.*, a Methionine to Leucine substitution. In some examples, the substitution is relative to a human germline light chain framework region sequence.

In some examples of any of the compositions disclosed herein, the anti-TCR β V antibody molecule comprises a light chain comprising a framework region, *e.g.*, framework region 3 (FR3), comprising one, two or all (*e.g.*, three) of: (i) a Glycine as 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; or (ii) an Asparagine at position 69, *e.g.*, a substitution at position 69 according to Kabat numbering, *e.g.*, a Threonine to Asparagine substitution; or (iii) 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 examples, the substitution is relative to a human germline light chain framework region sequence.

In some examples of any of the compositions disclosed herein, the anti-TCR β V antibody molecule binds to TCR β V12, *e.g.*, TCR β V12-4*01, TCR β V12-3*01, or TCR β V12-5*01. In some examples the anti-TCR β V antibody molecule binds to TCR β V12-4*01 or TCR β V12-3*01.

In some examples, TCR β V12, *e.g.*, TCR β V12-4*01, TCR β V12-3*01, or TCR β V12-5*01 is recognized, *e.g.*, bound, by SEQ ID NO: 15 and/or SEQ ID NO: 16. In some examples, TCR β V12, *e.g.*, TCR β V12-4*01, TCR β V12-3*01, or TCR β V12-5*01, is recognized, *e.g.*, bound, by any one of SEQ ID NOs 23-25, and/or any one of SEQ ID NO: 26-30A, or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto. In some examples TCR β V12-4*01 is recognized, *e.g.*, bound, by any one of SEQ ID NOs 23-25, and/or any one of SEQ ID NO: 26-30, or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto. In some examples TCR β V12-3*01 is recognized, *e.g.*, bound, by any one of SEQ ID NOs 23-25, and/or any one of SEQ ID NO: 26-30, or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto.

In some examples of any of the compositions disclosed herein, the anti-TCR β V antibody molecule comprises the anti-TCR β V antibody molecule comprises an antigen binding domain comprising a single chain Fv (scFv) or a Fab.

In some examples of any of the compositions disclosed herein, the anti-TCR β V antibody molecule comprises binds to a conformational or a linear epitope on the T cell.

In some examples of any of the compositions disclosed herein, the anti-TCR β V antibody molecule is a full antibody (*e.g.*, an antibody that includes at least one, and preferably two, complete heavy chains, and at least one, and preferably two, complete light chains), or 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 examples of any of the compositions disclosed herein, the anti-TCR β V antibody molecule comprises the anti-TCR β V antibody molecule comprises a heavy chain constant region chosen from IgG1, IgG2, IgG3, or IgG4, or a fragment thereof.

In some examples of any of the compositions disclosed herein, the anti-TCR β V antibody molecule comprises a light chain constant region chosen from the light chain constant regions of kappa or lambda, or a fragment thereof.

In some examples, the anti-TCR β V antibody molecule in a multispecific molecule disclosed herein is a first immune cell engager moiety. In some examples, 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 murine mAb Antibody B or a humanized version thereof (*e.g.*, humanized mAb Antibody B-H.1 to B-H.6) as described in US Patent 5,861,155. In some examples, 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 murine mAb Antibody B or a humanized version thereof (*e.g.*, humanized mAb Antibody B-H.1 to B-H.6) as described in US Patent 5,861,155. In some examples, 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 murine mAb Antibody B or a humanized version thereof (e.g., humanized mAb Antibody B-H.1 to B-H.6) as described in US Patent 5,861,155. In some examples, the anti-TCR β V antibody molecule does not comprise the CDRs of the murine mAb Antibody B.

5 In some examples, the anti-TCR β V antibody molecule in a multispecific molecule disclosed herein is a first immune cell engager moiety. In some examples, 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
10 US Patent 5,861,155. In some examples, 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
15 as described in US Patent 5,861,155. In some examples, 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
20 C or a humanized version thereof as described in US Patent 5,861,155. In some examples, the anti-TCR β V antibody molecule does not comprise the CDRs of murine Antibody C.

 In some examples, the multispecific molecule further comprises a second immune cell engager moiety. In some examples, the first and/or second immune cell engager binds to and
25 activates an immune cell, *e.g.*, an effector cell. In some examples, the first and/or second immune cell engager binds to, but does not activate, an immune cell, *e.g.*, an effector cell. In some examples, the second immune cell engager is chosen from an NK cell engager, a T cell engager, a B cell engager, a dendritic cell engager, or a macrophage cell engager, or a combination thereof. In some examples, the second immune cell engager comprises a T cell

engager which binds to CD3, TCR α , TCR γ , TCR ζ , ICOS, CD28, CD27, HVEM, LIGHT, CD40, 4-1BB, OX40, DR3, GITR, CD30, TIM1, SLAM, CD2, or CD226.

In some examples, a multispecific molecule disclosed herein comprises an infectious
5 disease-targeting moiety. In some example, the infectious disease-targeting moiety comprises an antibody molecule (*e.g.*, Fab or scFv), a receptor molecule (*e.g.*, a receptor, a receptor fragment or functional variant thereof), or a ligand molecule (*e.g.*, a ligand, a ligand fragment or functional variant thereof), or a combination thereof, that binds to an antigen from an infectious agent, *e.g.*, a bacteria (*e.g.*, *Mycobacterium tuberculosis*), virus (*e.g.*, Epstein-Barr virus (EBV), influenza
10 virus, human immunodeficiency virus (HIV), simian immunodeficiency virus (SIV), human cytomegalovirus (HCMV)), or eukaryotic infectious agent (*e.g.*, a malaria parasite). In some examples, the infectious disease-targeting moiety binds to an antigen present on an infectious agent, *e.g.*, a bacteria (*e.g.*, *Mycobacterium tuberculosis*), virus (*e.g.*, Epstein-Barr virus (EBV), influenza virus, human immunodeficiency virus (HIV), simian immunodeficiency virus (SIV),
15 human cytomegalovirus (HCMV)), or eukaryotic infectious agent (*e.g.*, a malaria parasite).

In some examples, the infectious disease-targeting antibody molecule binds to a conformational or a linear epitope on an antigen from an infectious agent, *e.g.*, as described herein.

In some examples of any of the compositions or methods disclosed herein, the infectious
20 disease-targeting moiety is an antigen, *e.g.*, an infectious disease antigen, *e.g.*, an antigen from a bacterium (*e.g.*, *Mycobacterium tuberculosis*), virus (*e.g.*, Epstein-Barr virus (EBV), influenza virus, human immunodeficiency virus (HIV), simian immunodeficiency virus (SIV), human cytomegalovirus (HCMV)), or eukaryotic infectious agent (*e.g.*, a malaria parasite).

In some examples of any of the compositions or methods disclosed herein, the infectious
25 disease-targeting moiety binds to an antigen chosen from: EBNA3 (*e.g.*, 339-347), EBNA1 (*e.g.*, 407-417), BZLF1 (*e.g.*, 52-64), matrix protein (*e.g.*, influenza virus matrix protein, *e.g.*, 58-66), HIV Gag (*e.g.*, HIV Gag p17, *e.g.*, 77-85), HIV Env, HIV p24 capsid, SIV Tat (*e.g.*, 28-35), SIV Gag (*e.g.*, 181-189), or HCMV pp65 (*e.g.*, 495-503).

In some examples of any of the compositions or methods disclosed herein, the infectious
30 disease includes but not limited to: Epstein-Barr virus (EBV), influenza, human

immunodeficiency virus (HIV), simian immunodeficiency virus (SIV), tuberculosis, malaria, or human cytomegalovirus (HCMV).

In some examples, a multispecific molecule disclosed herein further comprises a cytokine molecule, e.g., one or two cytokine molecules. In some examples, the cytokine molecule is
5 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, variant or combination thereof. In some examples, is a monomer or a dimer. In some examples, the cytokine molecule further comprises a receptor dimerizing domain, e.g., an IL15Ralpha dimerizing domain. In some examples, the cytokine molecule (e.g., IL-15) and the receptor
10 dimerizing domain (e.g., an IL15Ralpha dimerizing domain) are not covalently linked, e.g., are non-covalently associated.

In some examples, a multispecific molecule disclosed herein comprises:

(i) an anti-TCR β V antibody molecule (e.g., an anti-TCR β V antibody molecule as described herein); and

15 (ii) an infectious disease-targeting antibody molecule (e.g., an antibody molecule that binds to an antigen as described herein, e.g., chosen from one or more of EBNA3 (e.g., 339-347), EBNA1 (e.g., 407-417), BZLF1 (e.g., 52-64), matrix protein (e.g., influenza virus matrix protein, e.g., 58-66), HIV Gag (e.g., HIV Gag p17, e.g., 77-85), HIV Env, HIV p24 capsid, SIV Tat (e.g., 28-35), SIV Gag (e.g., 181-189), or HCMV pp65 (e.g., 495-503)).

20 In some examples, a multispecific molecule disclosed herein further comprises an immunoglobulin constant region (e.g., Fc region) chosen from the heavy chain constant regions of IgG1, IgG2, and IgG4, more particularly, the heavy chain constant region of human IgG1, IgG2 or IgG4. In some examples, the immunoglobulin constant region (e.g., an Fc region) is linked, e.g., covalently linked to, one or more of an infectious disease-targeting moiety (e.g.,
25 which can bind to one or more of EBNA3 (e.g., 339-347), EBNA1 (e.g., 407-417), BZLF1 (e.g., 52-64), matrix protein (e.g., influenza virus matrix protein, e.g., 58-66), HIV Gag (e.g., HIV Gag p17, e.g., 77-85), HIV Env, HIV p24 capsid, SIV Tat (e.g., 28-35), SIV Gag (e.g., 181-189), or HCMV pp65 (e.g., 495-503)), the immune cell engager, the cytokine molecule, or the stromal modifying moiety. In some examples, an interface of a first and second immunoglobulin chain
30 constant regions (e.g., Fc region) is altered, e.g., mutated, to increase or decrease dimerization,

e.g., relative to a non-engineered interface. In some examples, the dimerization of the immunoglobulin chain constant region (*e.g.*, Fc region) is enhanced by providing an Fc interface of a first and a second Fc region with one or more of: a paired cavity-protuberance (“knob-in-a hole”), an electrostatic interaction, or a strand-exchange, such that a greater ratio of

heteromultimer:homomultimer forms, *e.g.*, relative to a non-engineered interface. In some examples,

In some examples, a multispecific molecule disclosed herein further comprises a linker, *e.g.*, a linker described herein, optionally wherein the linker is selected 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.

In some examples, the multispecific molecule comprises at least two non-contiguous polypeptide chains.

In some examples, the multispecific molecule comprises the following configuration:

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

wherein:

(1) 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

(2) A, B, C, and D are independently absent; (i) an antigen binding domain that preferentially binds to a first immune cell engager comprising an anti-TCRβV antibody molecule disclosed herein; (ii) an infectious disease-targeting moiety (*e.g.*, as described herein), (iii) a second 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; (iv) a cytokine molecule; 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 preferentially binds to a TCRβV region disclosed herein, and

any of the remaining A, B, C, and D is absent or comprises one of a infectious disease-targeting moiety, a second immune cell engager, a cytokine molecule, or a stromal modifying moiety.

In some examples, 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. In some examples, 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. In some examples, 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.

In some examples, the multispecific molecule further comprises a linker, *e.g.*, a linker between one or more of: the antigen binding domain of an anti-TCR β V antibody molecule disclosed herein and the infectious disease-targeting moiety; the antigen binding domain of an anti-TCR β V antibody molecule disclosed herein and the second immune cell engager, the antigen binding domain of an anti-TCR β V antibody molecule disclosed herein and the cytokine molecule, the antigen binding domain of an anti-TCR β V antibody molecule disclosed herein and the stromal modifying moiety, the second immune cell engager and the cytokine molecule, the second immune cell engager and the stromal modifying moiety, the cytokine molecule and the stromal modifying moiety, the antigen binding domain of an anti-TCR β V antibody molecule disclosed herein and the dimerization module, the second immune cell engager and the dimerization module, the cytokine molecule and the dimerization module, the stromal modifying moiety and the dimerization module, the infectious disease-targeting moiety and the dimerization module, the infectious disease-targeting moiety and the cytokine molecule, the infectious disease-targeting moiety and the second immune cell engager, or the infectious disease-targeting moiety and the antigen binding domain of an anti-TCR β V antibody molecule disclosed herein.

In some examples, 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. In some examples, the linker is a peptide linker. In some examples, the peptide linker comprises Gly and Ser. In some examples, the peptide linker comprises an amino acid sequence chosen from SEQ ID NOs: 3460-3463 or 3467-3470.

In another example, the disclosure provides an isolated nucleic acid molecule comprising a nucleotide sequence encoding an anti-TCR β V antibody molecule disclosed herein, or a nucleotide sequence having at least 75%, 80%, 85%, 90%, 95%, or 99% identity thereto.

5 In another example, the disclosure provides an isolated nucleic acid molecule comprising a nucleotide sequence encoding a multispecific molecule disclosed herein, or a nucleotide sequence having at least 75%, 80%, 85%, 90%, 95%, or 99% identity thereto.

10 In another example, the disclosure provides a method of making, *e.g.*, producing, an anti-TCR β V antibody molecule, a multispecific molecule described herein, comprising culturing a host cell described herein, under suitable conditions. In some examples of a method of making a multispecific molecule, the conditions comprise, *e.g.*, conditions suitable for gene expression and/or homo- or heterodimerization.

15 In another example, the disclosure provides a pharmaceutical composition comprising an anti-TCR β V antibody molecule, or a multispecific molecule described herein, and a pharmaceutically acceptable carrier, excipient, or stabilizer.

20 In an example, provided herein is a method of treating a disease *e.g.*, an infectious disease, in a subject comprising administering to the subject an effective amount, *e.g.*, a therapeutically effective amount, of an anti-TCR β V antibody molecule or a multispecific molecule comprising an anti-TCR β V antibody molecule disclosed herein, thereby treating the disease.

25 In a related example, provided herein is a composition comprising an anti-TCR β V antibody molecule or a multispecific molecule comprising an anti-TCR β V antibody molecule disclosed herein, for use in the treatment of a disease, *e.g.*, an infectious disease, in a subject.

In some examples, the method further comprises administering a second agent, *e.g.*, therapeutic agent, *e.g.*, as described herein. In some examples, second agent comprises a therapeutic agent. In some examples, therapeutic agent is a biologic agent.

In another example, provided herein is a method of targeting, *e.g.*, directing or re-directing, a therapy, *e.g.*, treatment, to a T cell, *e.g.*, in a subject, *e.g.*, having a disease, *e.g.*, an infectious disease, comprising administering an effective amount of: (i) an anti-TCR β V antibody disclosed herein; and (ii) the therapy, *e.g.*, an infectious disease-targeting therapy (*e.g.*, an antibody that binds to an antigen as described herein), *e.g.*, as described herein, thereby targeting the T cell.

In some examples, (i) and (ii) are conjugated, *e.g.*, linked.

In some examples, (i) and (ii) are administered simultaneously or concurrently.

In some examples, the method results in: reduced cytokine release syndrome (CRS) (*e.g.*, lesser duration of CRS or no CRS), or a reduced severity of CRS (*e.g.*, absence of severe CRS, *e.g.*, CRS grade 4 or 5) compared to administration of (ii) alone. In some examples, CRS is assessed by an assay of Example 3.

In yet another example, the disclosure provides, a method of targeting a T cell, *e.g.*, in a subject having a disease, *e.g.*, an infectious disease, with an anti-TCR β V antibody disclosed herein or a multispecific molecule comprising an anti-TCR β V antibody disclosed herein.

In another example, the disclosure provides a method of treating, *e.g.*, preventing or reducing, cytokine release syndrome (CRS) in a subject, *e.g.*, CRS associated with a treatment, *e.g.*, a previously administered treatment, comprising administering to the subject an effective amount of an anti-TCR β V antibody disclosed herein or a multispecific molecule comprising an anti-TCR β V antibody disclosed herein, wherein, the subject has a disease, *e.g.*, an infectious disease, thereby treating, *e.g.*, preventing or reducing, CRS in the subject

In a related example, the disclosure provides a composition comprising an anti-TCR β V antibody disclosed herein or a multispecific molecule comprising an anti-TCR β V antibody disclosed herein, for use in the treatment, *e.g.*, prevention or reduction, of cytokine release syndrome (CRS) in a subject, *e.g.*, CRS associated with a treatment, *e.g.*, a previously administered treatment, comprising administering to the subject an effective amount of the anti-TCR β V antibody, wherein the subject has a disease, *e.g.*, an infectious disease.

In some examples of a method or composition for use disclosed herein, the anti-TCR β V antibody is administered concurrently with or after the administration of the treatment associated with CRS.

5 In some examples of any of the methods disclosed herein, the anti-TCR β V antibody molecule comprises an antigen binding domain comprising:

(i) a heavy chain complementarity determining region 1 (HC CDR1), a heavy chain complementarity determining region 2 (HC CDR2) and/or a heavy chain complementarity determining region 3 (HC CDR3) of SEQ ID NO: 1 or SEQ ID NO: 9; or

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

In some examples of any of the methods disclosed herein, the anti-TCR β V antibody molecule comprises an antigen binding domain comprising a light chain variable region (VL) comprising one, two or all (*e.g.*, three) of a LC CDR1, a LC CDR2 and a LC CDR3 of SEQ ID NO: 2, SEQ ID NO: 10, or SEQ ID NO: 11.

In some examples of any of the methods disclosed herein, the anti-TCR β V antibody molecule comprises an antigen binding domain comprising a heavy chain variable region (VH) comprising one, two or all (*e.g.*, three) of a HC CDR1, a HC CDR2 and a HC CDR3 of SEQ ID NO: 1 or SEQ ID NO: 9.

In some examples of any of the methods disclosed herein, the anti-TCR β V antibody molecule comprises an antigen binding domain comprising:

(i) a VL comprising: a LC CDR1 amino acid sequence of SEQ ID NO: 6 (or an amino acid sequence with not more than 1, 2, 3 or 4 modifications, *e.g.*, substitutions, additions or deletions thereof), a LC CDR2 amino acid sequence of SEQ ID NO: 7 (or an amino acid sequence with not more than 1, 2, 3 or 4 modifications, *e.g.*, substitutions, additions or deletions thereof), and/or a LC CDR3 amino acid sequence of SEQ ID NO: 8 (or an amino acid sequence with not more than 1, 2, 3 or 4 modifications, *e.g.*, substitutions, additions or deletions thereof); and/or

(ii) a VH comprising: a HC CDR1 amino acid sequence of SEQ ID NO: 3 (or an amino acid sequence with not more than 1, 2, 3 or 4 modifications, *e.g.*, substitutions, additions or deletions thereof), a HC CDR2 amino acid sequence of SEQ ID NO: 4 (or an amino acid sequence with not more than 1, 2, 3 or 4 modifications, *e.g.*, substitutions, additions or deletions thereof), and/or a HC CDR3 amino acid sequence of SEQ ID NO: 5 (or an amino acid sequence with not more than 1, 2, 3 or 4 modifications, *e.g.*, substitutions, additions or deletions thereof).

In some examples of any of the methods disclosed herein, the anti-TCR β V antibody molecule comprises an antigen binding domain comprising:

a variable heavy chain (VH) of SEQ ID NO: 9, or a sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto; and/or

a variable light chain (VL) of SEQ ID NO: 10 or SEQ ID NO: 11, or a sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto.

In some examples of any of the methods disclosed herein, the anti-TCR β V antibody molecule comprises an antigen binding domain comprising the VH amino acid sequence of SEQ ID NO: 9 and the VL amino acid sequence of SEQ ID NO: 10.

In some examples of any of the methods disclosed herein, the anti-TCR β V antibody molecule comprises an antigen binding domain comprising the VH amino acid sequence of SEQ ID NO: 9 and the VL amino acid sequence of SEQ ID NO: 11.

In some examples of any of the methods disclosed herein, the anti-TCR β V antibody molecule comprises a heavy chain comprising a framework region, *e.g.*, framework region 3 (FR3), comprising one or both of: (i) a Threonine at position 73, *e.g.*, a substitution at position 73 according to Kabat numbering, *e.g.*, a Glutamic Acid to Threonine substitution; or (ii) a Glycine at position, *e.g.*, a substitution at position 94 according to Kabat numbering, *e.g.*, a Arginine to Glycine substitution. In some examples, the substitution is relative to a human germline heavy chain framework region sequence.

In some examples of any of the methods disclosed herein, the anti-TCR β V antibody molecule comprises a light chain comprising a framework region, *e.g.*, 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. In some examples, the substitution is relative to a human germline light chain framework region sequence.

In some examples of any of the methods disclosed herein, the anti-TCR β V antibody molecule comprises a light chain comprising a framework region, *e.g.*, framework region 2 (FR2), comprising one or both of: (i) a Histidine at position 36, *e.g.*, a substitution at position 36 according to Kabat numbering, *e.g.*, a Tyrosine to Histidine substitution; or (ii) an Alanine at position 46, *e.g.*, a substitution at position 46 according to Kabat numbering, *e.g.*, a Arginine to Alanine substitution. In some examples, the substitution is relative to a human germline light chain framework region sequence.

In some examples of any of the methods disclosed herein, the anti-TCR β V antibody molecule comprises a light chain comprising a framework region, *e.g.*, 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. In some examples, the substitution is relative to a human germline light chain framework region sequence.

In some examples of any of the methods disclosed herein, the anti-TCR β V antibody molecule binds to TCR β V6, *e.g.*, 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 examples the anti-TCR β V antibody molecule binds to TCR β V6-5*01.

In some examples, TCR β V6, *e.g.*, 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, is recognized, *e.g.*, bound, by SEQ ID NO: 1 and/or SEQ ID NO: 2. In some examples, TCR β V6, *e.g.*, 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, is recognized, *e.g.*, bound, by SEQ ID NO: 9 and/or SEQ ID NO: 10. In some examples, TCR β V6, *e.g.*, 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, is recognized, *e.g.*, bound, by SEQ ID NO: 9 and/or SEQ ID NO: 11. In some examples, TCR β V6-5*01 is recognized, *e.g.*, bound by SEQ ID NO: 9 and/or SEQ ID NO: 10, or a sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto. In some examples, TCR β V6-5*01 is recognized, *e.g.*, bound by SEQ ID NO: 9 and/or SEQ ID NO: 11, or a sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto.

In some examples of any of the methods disclosed herein, the anti-TCR β V antibody molecule comprises an antigen binding domain comprising:

- 5 (i) a heavy chain complementarity determining region (HC CDR1), a HC CDR2 and/or a HC CDR3 of SEQ ID NO: 15, SEQ ID NO: 23, SEQ ID NO: 24, or SEQ ID NO: 25; and/or
- (ii) a light chain complementarity determining region 1 (LC CDR1), a LC CDR2, and/or a 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.

10 In some examples of any of the methods disclosed herein, the anti-TCR β V antibody molecule comprises an antigen binding domain comprising a light chain variable region (VL) comprising one, two or all of a LC CDR1, a LC CDR2 and a 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.

15 In some examples of any of the methods disclosed herein, the anti-TCR β V antibody molecule comprises an antigen binding domain comprising a heavy chain variable region (VH) comprising one, two or all of a HC CDR1, a HC CDR2 and a HC CDR3 of SEQ ID NO: 15, SEQ ID NO: 23, SEQ ID NO: 24, or SEQ ID NO: 25.

In some examples of any of the methods disclosed herein, the anti-TCR β V antibody molecule comprises an antigen binding domain comprising:

- 20 (i) a VL comprising: a LC CDR1 amino acid sequence of SEQ ID NO: 20 (or an amino acid sequence with not more than 1, 2, 3 or 4 modifications, *e.g.*, substitutions, additions or deletions thereof), a LC CDR2 amino acid sequence of SEQ ID NO:21 (or an amino acid sequence with not more than 1, 2, 3 or 4 modifications, *e.g.*, substitutions, additions or deletions thereof), and/or a LC CDR3 amino acid sequence of SEQ ID NO: 22 (or an amino acid sequence with not more than 1, 2, 3 or 4 modifications, *e.g.*, substitutions, additions or deletions thereof);
- 25 and/or

(ii) a VH comprising: a HC CDR1 amino acid sequence of SEQ ID NO: 17 (or an amino acid sequence with not more than 1, 2, 3 or 4 modifications, *e.g.*, substitutions, additions or deletions thereof), a HC CDR2 amino acid sequence of SEQ ID NO:18 (or an amino acid sequence with not more than 1, 2, 3 or 4 modifications, *e.g.*, substitutions, additions or deletions

thereof), and/or a HC CDR3 amino acid sequence of SEQ ID NO:19 (or an amino acid sequence with not more than 1, 2, 3 or 4 modifications, *e.g.*, substitutions, additions or deletions thereof). In some examples of any of the compositions disclosed herein, the anti-TCR β V antibody molecule comprises an antigen binding domain comprising:

5 a variable heavy chain (VH) of SEQ ID NO: 23, SEQ ID NO: 24, or SEQ ID NO: 25, or a sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto; and/or

a variable light chain (VL) of SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO: 29, or SEQ ID NO:30, or a sequence having at least about 75%, 80%, 85%, 90%, 95%, or
10 99% sequence identity thereto.

In some examples of any of the methods disclosed herein, the anti-TCR β V antibody molecule comprises a light chain comprising a framework region, *e.g.*, framework region 1 (FR1), comprising one, two or all (*e.g.*, three) of: (i) an Aspartic Acid at position 1, *e.g.*, a substitution at position 1 according to Kabat numbering, *e.g.*, a Alanine to Aspartic Acid
15 substitution; or (ii) an Asparagine at position 2, *e.g.*, a substitution at position 2 according to Kabat numbering, *e.g.*, a Isoleucine to Asparagine substitution, a Serine to Asparagine substitution, or a Tyrosine to Asparagine substitution; or (iii) a Leucine at position 4, *e.g.*, a substitution at position 4 according to Kabat numbering, *e.g.*, a Methionine to Leucine substitution. In some examples, the substitution is relative to a human germline light chain
20 framework region sequence.

In some examples of any of the methods disclosed herein, the anti-TCR β V antibody molecule comprises a light chain comprising a framework region, *e.g.*, framework region 3 (FR3), comprising one, two or all (*e.g.*, three) of: (i) a Glycine as position 66, *e.g.*, a substitution at position 66 according to Kabat numbering, *e.g.*, a Lysine to Glycine substitution, or a Serine to
25 Glycine substitution; or (ii) an Asparagine at position 69, *e.g.*, a substitution at position 69 according to Kabat numbering, *e.g.*, a Threonine to Asparagine substitution; or (iii) 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 examples, the substitution is relative to a human germline light chain framework region
30 sequence.

In some examples of any of the methods disclosed herein, the anti-TCR β V antibody molecule binds to TCR β V12, *e.g.*, TCR β V12-4*01, TCR β V12-3*01, or TCR β V12-5*01. In some examples the anti-TCR β V antibody molecule binds to TCR β V12-4*01 or TCR β V12-3*01.

In some examples, TCR β V12, *e.g.*, TCR β V12-4*01, TCR β V12-3*01, or TCR β V12-5*01 is recognized, *e.g.*, bound, by SEQ ID NO: 15 and/or SEQ ID NO: 16. In some examples, TCR β V12, *e.g.*, TCR β V12-4*01, TCR β V12-3*01, or TCR β V12-5*01, is recognized, *e.g.*, bound, by any one of SEQ ID NOs 23-25, and/or any one of SEQ ID NO: 26-30A, or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto. In some examples TCR β V12-4*01 is recognized, *e.g.*, bound, by any one of SEQ ID NOs 23-25, and/or any one of SEQ ID NO: 26-30, or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto. In some examples TCR β V12-3*01 is recognized, *e.g.*, bound, by any one of SEQ ID NOs 23-25, and/or any one of SEQ ID NO: 26-30, or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto.

In some examples of any of the methods disclosed herein, the anti-TCR β V antibody molecule comprises the anti-TCR β V antibody molecule comprises an antigen binding domain comprising a single chain Fv (scFv) or a Fab.

In some examples of any of the methods disclosed herein, the anti-TCR β V antibody molecule comprises binds to a conformational or a linear epitope on the T cell.

In some examples of any of the methods disclosed herein, the anti-TCR β V antibody molecule is a full antibody (*e.g.*, an antibody that includes at least one, and preferably two, complete heavy chains, and at least one, and preferably two, complete light chains), or 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 examples of any of the methods disclosed herein, the anti-TCR β V antibody molecule comprises the anti-TCR β V antibody molecule comprises a heavy chain constant region chosen from IgG1, IgG2, IgG3, or IgG4, or a fragment thereof.

In some examples of any of the methods disclosed herein, the anti-TCR β V antibody molecule comprises a light chain constant region chosen from the light chain constant regions of kappa or lambda, or a fragment thereof.

5 In some examples of any of the methods disclosed herein, 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 murine mAb Antibody B or a humanized version thereof (e.g., humanized mAb Antibody B-H.1 to B-H.6) as
10 described in US Patent 5,861,155.

 In some examples of any of the methods disclosed herein, 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 murine mAb Antibody B or a humanized
15 version thereof (e.g., humanized mAb Antibody B-H.1 to B-H.6) as described in US Patent 5,861,155.

In some examples of any of the methods disclosed herein, 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 murine mAb Antibody B or a humanized version thereof (e.g., humanized mAb Antibody B-H.1 to B-H.6) as described in US Patent 5,861,155.

In some examples of any of the methods disclosed herein, the anti-TCR β V antibody molecule does not comprise the CDRs of the murine mAb Antibody B.

In some examples of any of the methods disclosed herein, 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 examples of any of the methods disclosed herein, 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 examples of any of the methods disclosed herein, 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.

In some examples of any of the methods disclosed herein, the anti-TCR β V antibody molecule does not comprise the CDRs of murine Antibody C.

In some examples of a method or composition for use disclosed herein, the disease is an infectious disease chosen from: Epstein-Barr virus (EBV), influenza, human immunodeficiency virus (HIV), simian immunodeficiency virus (SIV), tuberculosis, malaria, or human cytomegalovirus (HCMV), or a combination thereof.

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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;
5 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;
10 Subfamily T: TCR β V24; Subfamily U: TCR β V20; Subfamily V: TCR β V25; and Subfamily

CLAIMS

What is claimed is:

1. A composition comprising a multispecific molecule, wherein the multispecific molecule comprises:
 - (1) an anti-TCR β V moiety, and
 - (2) an infectious disease-targeting moiety.
2. The composition of claim 1, wherein the infectious disease-targeting moiety binds to an antigen, and wherein the antigen is from an infectious agent or is presented on a surface of a cell infected by the infectious agent.
3. The composition of claim 1 or 2, wherein the infectious agent comprises a bacterium, a virus or a eukaryotic infectious agent.
4. The composition of any one of claims 1-3, wherein the bacterium comprises a mycobacterium tuberculosis.
5. The composition of any one of claims 1-3, wherein the virus comprises an Epstein-Barr virus (EBV), an influenza virus, a human immunodeficiency virus (HIV), a hepatitis virus, a herpes virus, an adenovirus, a flavivirus, a echovirus, a rhinovirus, a coxsackie virus, a cornovirus, a respiratory syncytial virus, a mumps virus, a rotavirus, a measles virus, a rubella virus, a parvovirus, a vaccinia virus, a HTLV virus, a dengue virus, a papillomavirus, a molluscum virus, a poliovirus, a rabies virus, a JC virus, a arboviral encephalitis virus, a simian immunodeficiency virus (SIV) or a human cytomegalovirus (HCMV).
6. The composition of any one of claims 1-3, wherein the eukaryotic infectious agent comprises a fungus or a parasite.
7. The composition of any one of claims 1-3, wherein the antigen comprises EBNA3, EBNA1, BZLF1, amatrix protein, HIV Gag, HIV Env, HIV p24 capsid, SIV Tat, SIV Gag, or HCMV pp65.
8. The composition of any one of claims 1-7, wherein the antigen comprises a protein, a polypeptide, a peptide, a nucleic acid, a sugar, a small molecule, a lipid, or any combination thereof.

9. The composition of any one of claims 1-8, wherein the infectious disease-targeting moiety comprises an antibody molecule, a receptor molecule, or a ligand molecule.
10. The composition of any one of claims 1-9, wherein the infectious disease-targeting moiety binds to a conformational or a linear epitope of the antigen.
11. The composition of any one of claims 1-10, wherein the anti-TCR β V moiety is a full-length antibody, a Fab, a F(ab')₂, an Fv, a single chain Fv, a single domain antibody, a half arm antibody, a diabody (dAb), a bivalent antibody, a monovalent antibody, a bispecific antibody or fragment thereof, or a camelid antibody.
12. The composition of any one of claims 1-11, wherein the TCR β V is selected from the group consisting of 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, and a TCR β V26 subfamily.
13. The composition of any one of claims 1-12, wherein the anti-TCR β V moiety comprises a murine, human, or humanized antibody or a fragment thereof.
14. The composition of claim 13, wherein the humanized antibody comprises a heavy chain variable (VH) domain comprises as amino acid sequence with at least 80% sequence identity to a sequence selected from the group consisting of SEQ ID NOs: 1310-1312.
15. The composition of claim 13, wherein the humanized antibody comprises a light chain variable (VL) domain comprises as amino acid sequence with at least 80% sequence identity to a sequence selected from the group consisting of SEQ ID NOs: 1313-1314.
16. The composition of any one of claims 1-13, wherein the anti-TCR β V moiety comprises an amino acid sequence with at least 80% sequence identity to a sequence selected from the group consisting of SEQ ID NOs: 1309, 1326-1342 and 1344.
17. The composition of any one of claims 1-13, wherein the anti-TCR β V moiety comprises:

- (i) a VH comprising a heavy chain complementarity determining region 1 (HC CDR1) of any one of the sequences selected from the group consisting of SEQ ID NOs: 1102, 1105, 3474, 1120, 1123, 1125, 1141, 1144, 1163, 1166, 1185, 1188, 1190, 1208, 1211, 1213, 1229, 1232, 1234, 1248, 1251, 1253, 1268, 1271, and 1273; a heavy chain complementarity determining region 2 (HC CDR2) of any one of the sequences selected from the group consisting of SEQ ID NOs: 1103, 1106, 1121, 1124, 1142, 1145, 1164, 1167, 1186, 1189, 1209, 1212, 1230, 1233, 1230, 1249, 1252, 1269, 1272, and 1269; and a heavy chain complementarity determining region 3 (HC CDR3) of any one of the sequences selected from the group consisting of SEQ ID NOs: 1104, 1122, 1143, 1165, 1187, 1210, 1231, 1250, and 1270; and/or
- (ii) a VL comprising a light chain complementarity determining region 1 (LC CDR1) of any one of the sequences selected from the group consisting of SEQ ID NOs: 1107, 1110, 1126, 1147, 1168, 3476, 1191, 1194, 1214, 1217, 1235, 1238, 1254, 1257, and 1275; a light chain complementarity determining region 2 (LC CDR2) of any one of the sequences selected from the group consisting of SEQ ID NOs: 1108, 1127, 1148, 1169, 1192, 1215, 1236, 1255, and 1276; and a light chain complementarity determining region 3 (LC CDR3) of any one of the sequences selected from the group consisting of SEQ ID NOs: 1109, 1128, 1149, 1170, 1193, 1216, 1237, 1256, and 1277.
18. The composition of claim 17, wherein the anti-TCR β V moiety comprises:
- (i) a VH comprising an amino acid sequence with at least 95% sequence identity to SEQ ID NOs: 1112-1116, 1130-1135, 1152-1157, 1172-1177, 1196-1202, 1219-1223, 1240-1243, 1259-1263, 1274, and 1283-1287; and/or
- (ii) a VL comprising an amino acid sequence with at least 95% sequence identity to SEQ ID Nos: 1111, 1117-1119, 1129, 1136-1140, 1151, 1158-1162, 1171, 1178-1184, 1195, 1203-1207, 1218, 1224-1227, 1239, 1244-1247, 1258, 1264-1267, and 1278-1282.
19. The composition of any one of claims 1-18, wherein the multispecific molecule further comprises a cytokine molecule, an immune cell engager, or a stromal modifying moiety.
20. A recombinant polynucleotide comprising a sequence encoding the multispecific molecule of the composition of any one of claims 1-19.

21. A medicament comprising the composition of any one of claims 1-19, and a pharmaceutically acceptable carrier, excipient, or stabilizer.
22. Use of a pharmaceutical composition comprising the composition of any one of claims 1-19 in the manufacture of a medicament for treating an infectious disease in a subject in need thereof.
23. The use of claim 22, wherein the infectious disease is selected from Epstein-Barr vims (EBV), influenza, human immunodeficiency vims (HIV), simian immunodeficiency vims (SIV), tuberculosis, malaria, or human cytomegalovims (HCMV), or a combination thereof.
24. The composition of any one of claims 1-19 for use in therapy.