

Claims:

1. An antibody, or antigen binding fragment which is capable of binding to LAG-3, optionally isolated, having the amino acid sequences i) to vi):

- i) LC-CDR1: $X_1X_2SQSX_3X_4X_5X_6X_7X_8X_9X_{10}X_{11}X_{12}X_{13}$ (SEQ ID NO:53);
- ii) LC-CDR2: $X_{14}X_{15}SX_{16}RAX_{17}$ (SEQ ID NO:54);
- iii) LC-CDR3: $X_{18}QX_{19}X_{20}X_{21}X_{22}X_{23}X_{24}X_{25}X_{26}X_{27}$ (SEQ ID NO:55);
- iv) HC-CDR1: $X_{28}X_{29}X_{30}X_{31}X_{32}$ (SEQ ID NO:56);
- v) HC-CDR2: $X_{33}X_{34}X_{35}X_{36}X_{37}X_{38}X_{39}X_{40}X_{41}X_{42}YAX_{43}X_{44}X_{45}X_{46}G$ (SEQ ID NO:57);
- vi) HC-CDR3: one of TWFGELY (SEQ ID NO:41), PFGDFDY (SEQ ID NO:30), LPGWGAYAFDI (SEQ ID NO:33), DPDAANWGFLYYGMDV (SEQ ID NO:35) or ALADFWSGYYYYYYMDV (SEQ ID NO:38);

or a variant thereof in which one or two or three amino acids in one or more of the sequences (i) to (vi) are replaced with another amino acid, where $X_1 = R$ or T ; $X_2 = S, A$ or T ; $X_3 = L$ or V ; $X_4 = L$ or S ; $X_5 = H$ or S ; $X_6 = S, G$ or T ; $X_7 = N, F, Y, D$ or S ; $X_8 = G$ or L ; $X_9 = Y, A$ or D ; $X_{10} = \text{absent}$ or N ; $X_{11} = \text{absent}$ or Y ; $X_{12} = \text{absent}, L$ or F ; $X_{13} = \text{absent}$ or D ; $X_{14} = L, G$ or D ; $X_{15} = G$ or A ; $X_{16} = N$ or S ; $X_{17} = S, T$ or A ; $X_{18} = M$ or Q ; $X_{19} = A, Y$ or G ; $X_{20} = L, G$ or T ; $X_{21} = Q, P, S$ or H ; $X_{22} = T, S$ or W ; $X_{23} = P, I, R$ or L ; $X_{24} = Y, T, P$ or L ; $X_{25} = \text{absent}, T, I$ or G ; $X_{26} = \text{absent}, T$ or L ; $X_{27} = \text{absent}$ or T ; $X_{28} = S$ or E ; $X_{29} = Y$ or L ; $X_{30} = Y, G, A$ or S ; $X_{31} = M$ or I ; $X_{32} = H$ or S ; $X_{33} = I, G$ or V ; $X_{34} = I$ or F ; $X_{35} = N, S, I$ or D ; $X_{36} = P$ or Y ; $X_{37} = S, D, I$ or E ; $X_{38} = G, F$ or D ; $X_{39} = G$ or S ; $X_{40} = S, N, T$ or E ; $X_{41} = T, K$ or A ; $X_{42} = S, Y, N$ or I ; $X_{43} = Q$ or D ; $X_{44} = K$ or S ; $X_{45} = F$ or V ; and X_{46} is Q or K .

2. The antibody, or antigen binding fragment, of claim 1, wherein LC-CDR1 is one of RASQSVSSGYLA (SEQ ID NO:23), RSSQSLHSHNGYNYLD (SEQ ID NO:12), RASQSVSSSFLA (SEQ ID NO: 15), RASQSVSSSYLA (SEQ ID NO: 18), RSSQSLHSDGYNYFD (SEQ ID NO:20) or TTSQSVSSTSLD (SEQ ID NO:26).

3. The antibody, or antigen binding fragment, of claim 1 or claim 2, wherein LC-CDR2 is one of DASSRAT (SEQ ID NO:24), LGSNRAS (SEQ ID NO:13), GASSRAT (SEQ ID NO:16) or LGSNRAA (SEQ ID NO:21).

4. The antibody, or antigen binding fragment, of any one of claims 1 to 3, wherein LC-CDR3 is one of QQYGSSRPGLT (SEQ ID NO:25), MQALQTPYT (SEQ ID NO:14), QQYGPSIT (SEQ ID NO:17), QQYGSSPPIT (SEQ ID NO:19), MQGTHWPPT (SEQ ID NO:22) or QQYGSSLLT (SEQ ID NO:27).

5. The antibody, or antigen binding fragment, of any one of claims 1 to 4, wherein HC-CDR1 is one of ELSMH (SEQ ID NO:39), SYMH (SEQ ID NO:28), SYGMH (SEQ ID NO:31), SYAMH (SEQ ID NO:34) or SYAIS (SEQ ID NO:36).

6. The antibody, or antigen binding fragment, of any one of claims 1 to 5, wherein HC-CDR2 is one of GFDPEDGETIYAQKFQG (SEQ ID NO:40), IINPSGGSTSYAQKFQG (SEQ ID NO:29) VISYDGSNKYYADSVKG (SEQ ID NO:32) or GIPIFGTANYAQKFQG (SEQ ID NO:37).

7. The antibody, or antigen binding fragment, of any one of claims 1 to 6, having at least one light chain variable region incorporating the following CDRs:

LC-CDR1: $X_1X_2SQSX_3X_4X_5X_6X_7X_8X_9X_{10}X_{11}X_{12}X_{13}$ (SEQ ID NO:53)

LC-CDR2: $X_{14}X_{15}SX_{16}RAX_{17}$ (SEQ ID NO:54)

LC-CDR3: $Xi_8QX_{19}X_{20}X_{21}X_{22}X_{23}X_{24}X_{25}X_{26}X_{27}$ (SEQ ID NO:55);

where $X_1 = R$ or T ; $X_2 = S$, A or T ; $X_3 = L$ or V ; $X_4 = L$ or S ; $X_5 = H$ or S ; $X_6 = S$, G or T ; $X_7 = N$, F , Y , D or S ; $X_8 = G$ or L ; $X_9 = Y$, A or D ; $X_{10} =$ absent or N ; $X_{11} =$ absent or Y ; $X_{12} =$ absent, L or F ; $X_{13} =$ absent or D ; $X_{14} = L$, G or D ; $X_{15} = G$ or A ; $X_{16} = N$ or S ; $X_{17} = S$, T or A ; $X_{18} = M$ or Q ; $X_{19} = A$, Y or G ; $X_{20} = L$, G or T ; $X_{21} = Q$, P , S or H ; $X_{22} = T$, S or W ; $X_{23} = P$, I , R or L ; $X_{24} = Y$, T , P or L ; $X_{25} =$ absent, T , I or G ; $X_{26} =$ absent, T or L ; and $X_{27} =$ absent or T .

8. The antibody, or antigen binding fragment, of any one of claims 1 to 7, having at least one light chain variable region incorporating the following CDRs:

LC-CDR1: RASQSVSSGYLA (SEQ ID NO:23)

LC-CDR2: DASSRAT (SEQ ID NO:24)

LC-CDR3: QQYGSSRPGLT (SEQ ID NO:25).

9. The antibody, or antigen binding fragment, of any one of claims 1 to 8, having at least one heavy chain variable region incorporating the following CDRs:

HC-CDR1: $X_{28}X_{29}X_{30}X_{31}X_{32}$ (SEQ ID NO:56);

HC-CDR2: $X_{33}X_{34}X_{35}X_{36}X_{37}X_{38}X_{39}X_{40}X_{41}X_{42}YAX_{43}X_{44}X_{45}X_{46}G$ (SEQ ID NO:57);

HC-CDR3: one of TWFGELY (SEQ ID NO:41), PFGDFDY (SEQ ID NO:30), LPGWGAYAFDI (SEQ ID NO:33), DPDAANWGFLLYYGMDV (SEQ ID NO:35) or ALADFWSGYYYYYYMDV (SEQ ID NO:38);

where X_{28} = S or E; X_{29} = Y or L; X_{30} = Y, G, A or S; X_{31} = M or I; X_{32} = H or S; X_{33} = I, G or V; X_{34} = I or F; X_{35} = N, S, I or D; X_{36} = P or Y; X_{37} = S, D, I or E; X_{38} = G, F or D; X_{39} = G or S; X_{40} = S, N, T or E; X_{41} = T, K or A; X_{42} = S, Y, N or I; X_{43} = Q or D; X_{44} = K or S; X_{45} = F or V; and X_{46} is Q or K.

10. The antibody, or antigen binding fragment, of any one of claims 1 to 9, having at least one heavy chain variable region incorporating the following CDRs:

HC-CDR1: ELSMH (SEQ ID NO:39)

HC-CDR2: GFDPEDGETIYAQKFQG (SEQ ID NO:40)

HC-CDR3: TWFGELY (SEQ ID NO:41).

11. The antibody, or antigen binding fragment, according to any one of claims 1 to 10, that specifically binds to human, rhesus macaque or murine LAG-3.

12. The antibody, or antigen binding fragment, according to any one of claims 1 to 11, that inhibits interaction between LAG-3 and MHC class II, optionally human LAG-3 and human MHC class II.

13. The antibody, or antigen binding fragment, of any one of claims 1 to 12, wherein the antibody is effective to restore T-cell function in T-cells exhibiting T-cell exhaustion or T-cell anergy.

14. An isolated light chain variable region polypeptide comprising the following CDRs:

LC-CDR1: $X_1X_2SQSX_3X_4X_5X_6X_7X_8X_9X_{10}X_{11}X_{12}X_{13}$ (SEQ ID NO:53)

LC-CDR2: $X_{14}X_{15}SX_{16}RAX_{17}$ (SEQ ID NO:54)

LC-CDR3: $X_{18}QX_{19}X_{20}X_{21}X_{22}X_{23}X_{24}X_{25}X_{26}X_{27}$ (SEQ ID NO:55);

where X_1 = R or T; X_2 = S, A or T; X_3 = L or V; X_4 = L or S; X_5 = H or S; X_6 = S, G or T; X_7 = N, F, Y, D or S; X_8 = G or L; X_9 = Y, A or D; X_{10} = absent or N; X_{11} = absent or Y; X_{12} = absent, L or F; X_{13} = absent or D; X_{14} = L, G or D; X_{15} = G or A; X_{16} = N or S; X_{17} = S, T or A; X_{18} = M or Q; X_{19} = A, Y or G; X_{20} = L, G or T; X_{21} = Q, P, S or H; X_{22} = T, S or W; X_{23} = P, I, R or L; X_{24} = Y, T, P or L; X_{25} = absent, T, I or G; X_{26} = absent, T or L; and X_{27} = absent or T.

15. The isolated light chain variable region polypeptide of claim 14, wherein LC-CDR1 is one of RASQSVSSGYLA (SEQ ID NO:23), RSSQSLLHSNGYNYLD (SEQ ID NO:12), RASQSVSSSFLA (SEQ ID NO: 15), RASQSVSSSYLA (SEQ ID NO: 18), RSSQSLLHSDGYNYFD (SEQ ID NO:20) or TTSQSVSSTSLD (SEQ ID NO:26).

16. The isolated light chain variable region polypeptide of claim 14 or claim 15, wherein LC-CDR2 is one of DASSRAT (SEQ ID NO:24), LGSNRAS (SEQ ID NO:13), GASSRAT (SEQ ID NO:16) or LGSNRAA (SEQ ID NO:21).
17. The isolated light chain variable region polypeptide of any one of claims 14 to claim 25, wherein LC-CDR3 is one of QQYGSSRPGLT (SEQ ID NO:25), MQALQTPYT (SEQ ID NO:14), QQYGPSIT (SEQ ID NO:17), QQYGSSPPIT (SEQ ID NO:19), MQGTHWPPT (SEQ ID NO:22) or QQYGSSLLT (SEQ ID NO:27).
18. An isolated light chain variable region polypeptide comprising an amino acid sequence having at least 85% sequence identity to the light chain sequence: SEQ ID NO:1, 2, 3, 4, 5 or 6 (Figure 1).
19. An isolated heavy chain variable region polypeptide comprising the following CDRs:
 HC-CDR1: X₂₈X₂₉X₃₀X₃₁X₃₂ (SEQ ID NO:56);
 HC-CDR2:: X₃₃X₃₄X₃₅X₃₆X₃₇X₃₈X₃₉X₄₀X₄₁X₄₂YAX₄₃X₄₄X₄₅X₄₆G (SEQ ID NO:57);
 HC-CDR3: one of TWFGELY (SEQ ID NO:41), PFGDFDY (SEQ ID NO:30), LPGWGAYAFDI (SEQ ID NO:33), DPDAANWGFLLYYGMDV (SEQ ID NO:35), ALADFWSGYYYYYYMDV (SEQ ID NO:38);
- where X₂₈ = S or E; X₂₉ = Y or L; X₃₀ = Y, G, A or S; X₃₁ = M or I; X₃₂ = H or S; X₃₃ = I, G or V; X₃₄ = I or F; X₃₅ = N, S, I or D; X₃₆ = P or Y; X₃₇ = S, D, I or E; X₃₈ = G, F or D; X₃₉ = G or S; X₄₀ = S, N, T or E; X₄₁ = T, K or A; X₄₂ = S, Y, N or I; X₄₃ = Q or D; X₄₄ = K or S; X₄₅ = F or V; and X₄₆ is Q or K.
20. The isolated heavy chain variable region polypeptide of claim 19, wherein HC-CDR1 is one of ELSMH (SEQ ID NO:39), SYMH (SEQ ID NO:28), SYGMH (SEQ ID NO:31), SYAMH (SEQ ID NO:34) or SYAIS (SEQ ID NO:36).
21. The isolated heavy chain variable region polypeptide of claim 19 or claim 20, wherein HC-CDR2 is one of GFDPEDGETIYAQKFQG (SEQ ID NO:40), IINPSGGSTSYAQKFQG (SEQ ID NO:29) VISYDGSNKYYADSVKG (SEQ ID NO:32) or GIPIFGTANYAQKFQG (SEQ ID NO:37).

22. An isolated heavy chain variable region polypeptide comprising an amino acid sequence having at least 85% sequence identity to the heavy chain sequence of SEQ ID NO:7, 8, 9, 10 or 11 (Figure 2).

23. An isolated light chain variable region polypeptide of any one of claims 14 to 18 in combination with a heavy chain variable region polypeptide according to any one of claims 28 to 31.

24. An antibody or antigen binding fragment which is capable of binding to LAG-3, comprising a heavy chain and a light chain variable region sequence, wherein:

the light chain comprises a LC-CDR1, LC-CDR2, LC-CDR3, having at least 85% overall sequence identity to LC-CDR1: one of $X_1X_2SQSX_3X_4X_5X_6X_7X_8X_9X_{10}X_{11}X_{12}X_{13}$ (SEQ ID NO:53), RASQSVSSGYLA (SEQ ID NO:23), RSSQSLLHSNGYNYLD (SEQ ID NO:12), RASQSVSSSFLA (SEQ ID NO: 15), RASQSVSSSYLA (SEQ ID NO: 18), RSSQSLLHSDGYNYFD (SEQ ID NO:20) or TTSQSVSSTSLD (SEQ ID NO:26), LC-CDR2: one of $X_{i4}X_{i5}SX_{i6}RAX_{i7}$ (SEQ ID NO:54), DASSRAT (SEQ ID NO:24), LGSNRAS (SEQ ID NO:13), GASSRAT (SEQ ID NO:16), or LGSNRAA (SEQ ID NO:21), LC-CDR3: one of $X_{i8}QX_{19}X_{20}X_{21}X_{22}X_{23}X_{24}X_{25}X_{26}X_{27}$ (SEQ ID NO:55), QQYGSSRPGLT (SEQ ID NO:25), MQALQTPYT (SEQ ID NO:14), QQYGPSIT (SEQ ID NO:17), QQYGSSPPIT (SEQ ID NO:19), MQGTHWPPT (SEQ ID NO:22), or QQYGSSLLT (SEQ ID NO:27), respectively, where $X_1 = R$ or T ; $X_2 = S$, A or T ; $X_3 = L$ or V ; $X_4 = L$ or S ; $X_5 = H$ or S ; $X_6 = S$, G or T ; $X_7 = N$, F , Y , D or S ; $X_8 = G$ or L ; $X_9 = Y$, A or D ; $X_{10} = \text{absent}$ or N ; $X_{11} = \text{absent}$ or Y ; $X_{12} = \text{absent}$, L or F ; $X_{13} = \text{absent}$ or D ; $X_{14} = L$, G or D ; $X_{15} = G$ or A ; $X_{16} = N$ or S ; $X_{17} = S$, T or A ; $X_{18} = M$ or Q ; $X_{19} = A$, Y or G ; $X_{20} = L$, G or T ; $X_{21} = Q$, P , S or H ; $X_{22} = T$, S or W ; $X_{23} = P$, I , R or L ; $X_{24} = Y$, T , P or L ; $X_{25} = \text{absent}$, T , I or G ; $X_{26} = \text{absent}$, T or L ; and $X_{27} = \text{absent}$ or T , and;

the heavy chain comprises a HC-CDR1, HC-CDR2, HC-CDR3, having at least 85% overall sequence identity to HC-CDR1 : one of $X_{28}X_{29}X_{30}X_{31}X_{32}$ (SEQ ID NO:56), ELSMH (SEQ ID NO:39), SYMH (SEQ ID NO:28), SYGMH (SEQ ID NO:31), SYAMH (SEQ ID NO:34), or SYAIS (SEQ ID NO:36), HC-CDR2: one of $X_{33}X_{34}X_{35}X_{36}X_{37}X_{38}X_{39}X_{40}X_{41}X_{42}YAX_{43}X_{44}X_{45}X_{46}G$ (SEQ ID NO:57), GFDPEDGETIYAQKFQG (SEQ ID NO:40), IINPSGGSTSYAQKFQG (SEQ ID NO:29) VISYDGSNKYYADSVKG (SEQ ID NO:32), or GIPIFGTANYAQKFQG (SEQ ID NO:37), HC-CDR3: one of TWFGELY (SEQ ID NO:41), PFGDFDY (SEQ ID NO:30), LPGWGAYAFDI (SEQ ID NO:33), DPDAANWGFLYYGMDV (SEQ ID NO:35), or ALADFWSGYYYYYYMDV (SEQ ID NO:38), respectively, where $X_{28} = S$ or E ; $X_{29} = Y$ or L ; $X_{30} = Y$, G , A or S ; $X_{31} = M$ or I ; $X_{32} = H$ or S ; $X_{33} = I$, G or V ; $X_{34} = I$ or F ; $X_{35} = N$, S , I or D ; $X_{36} = P$ or Y ; $X_{37} = S$, D , I or E ; $X_{38} = G$, F or D ;

X_{39} = G or S; X_{40} = S, N, T or E; X_{41} = T, K or A; X_{42} = S, Y, N or I; X_{43} = Q or D; X_{44} = K or S; X_{45} = F or V; and X_{46} is Q or K.

25. An antibody or antigen binding fragment which is capable of binding to LAG-3, optionally isolated, comprising a heavy chain and a light chain variable region sequence, wherein:

the light chain sequence has at least 85% sequence identity to the light chain sequence: SEQ ID NO:1, 2, 3, 4, 5 or 6 (Figure 1), and;

the heavy chain sequence has at least 85% sequence identity to the heavy chain sequence of SEQ ID NO:7, 8, 9, 10 or 11 (Figure 2).

26. An antibody or antigen binding fragment, optionally isolated, which is capable of binding to LAG-3, which is a bispecific antibody or a bispecific antigen binding fragment comprising (i) an antigen binding fragment or polypeptide according to any one of claims 1 to 34, and (ii) an antigen binding fragment or polypeptide which is capable of binding to a target protein other than LAG-3.

27. The antibody, or antigen binding fragment, of claim 26, wherein the antigen binding fragment or polypeptide which is capable of binding to a target protein other than LAG-3 is capable of binding to one of PD-1, PD-L1, CD27, CD28, ICOS, CD40, CD122, OX43, 4-1BB, GITR, B7-H3, B7-H4, BTLA, CTLA-4, A2AR, VISTA, TIM-3, KIR, HER-2, HER-3, EGFR, EpCAM, CD30, CD33, CD38, CD20, CD24, CD90, CD15, CD52, CA-125, CD34, CA-15-3, CA-19-9, CEA, CD99, CD117, CD31, CD44, CD123, CD133, ABCB5 and CD45.

28. A chimeric antigen receptor (CAR) comprising an antigen binding fragment according to any one of claims 1 to 27.

29. A cell comprising the CAR according to claim 28.

30. An in vitro complex, optionally isolated, comprising an antibody, antigen binding fragment, polypeptide, CAR or cell according to any one of claims 1 to 29 bound to LAG-3.

31. A composition comprising the antibody, or antigen binding fragment, polypeptide, CAR or cell of any one of claims 1 to 28 and at least one pharmaceutically-acceptable carrier.

32. An isolated nucleic acid encoding the antibody, or antigen binding fragment, polypeptide or CAR of any of one of claims 1 to 28.
33. A vector comprising the nucleic acid of claim 32.
34. A host cell comprising the vector of claim 33.
35. A method for making an antibody, antigen binding fragment, polypeptide or CAR of any of one of claims 1 to 28 comprising culturing the host cell of claim 43 under conditions suitable for the expression of a vector encoding the antibody, or antigen binding fragment, polypeptide or CAR, and recovering the antibody, or antigen binding fragment, polypeptide or CAR.
36. An antibody, antigen binding fragment, polypeptide, CAR, cell or composition according to any one of claims 1 to 29 or 31 for use in therapy, or in a method of medical treatment.
37. An antibody, antigen binding fragment, polypeptide, CAR, cell or composition according to any one of claims 1 to 29 or 31 for use in the treatment of a T-cell dysfunctional disorder.
38. An antibody, antigen binding fragment, polypeptide, CAR, cell or composition according to any one of claims 1 to 29 or 31 for use in the treatment of cancer.
39. An antibody, antigen binding fragment, polypeptide, CAR, cell or composition according to any one of claims 1 to 29 or 31 for use in the treatment of an infectious disease.
40. Use of an antibody, antigen binding fragment, polypeptide, CAR, cell or composition according to any one of claims 1 to 29 or 31 in the manufacture of a medicament for use in the treatment of a T-cell dysfunctional disorder.
41. Use of an antibody, antigen binding fragment, polypeptide, CAR, cell or composition according to any one of claims 1 to 29 or 31 in the manufacture of a medicament for use in the treatment of cancer.

42. Use of an antibody, antigen binding fragment, polypeptide, CAR, cell or composition according to any one of claims 1 to 29 or 31 in the manufacture of a medicament for use in the treatment of an infectious disease.
43. A method, in vitro or in vivo, of enhancing T-cell function comprising administering an antibody, antigen binding fragment, polypeptide, CAR, cell or composition according to any one of claims 1 to 29 or 31 to a dysfunctional T-cell.
44. A method of treating a T-cell dysfunctional disorder comprising administering an antibody, antigen binding fragment, polypeptide, CAR, cell or composition according to any one of claims 1 to 29 or 31 to a patient suffering from a T-cell dysfunctional disorder.
45. A method of treating cancer comprising administering an antibody, antigen binding fragment, polypeptide, CAR, cell or composition according to any one of claims 1 to 29 or 31 to a patient suffering from a cancer.
46. A method of treating an infectious disease comprising administering an antibody, antigen binding fragment, polypeptide, CAR, cell or composition according to any one of claims 1 to 29 or 31 to a patient suffering from an infectious disease.
47. A method comprising contacting a sample containing, or suspected to contain, LAG-3 with an antibody, antigen binding fragment, CAR or cell according to any one of claims 1 to 38 and detecting the formation of a complex of antibody, antigen binding fragment, CAR or cell, and LAG-3.
48. A method of diagnosing a disease or condition in a subject, the method comprising contacting, in vitro, a sample from the subject with an antibody, antigen binding fragment, CAR or cell according to any one of claims 1 to 29 and detecting the formation of a complex of antibody, or antigen binding fragment, CAR or cell and LAG-3.
49. A method of selecting or stratifying a subject for treatment with LAG-3 or MHC class II targeted agents, the method comprising contacting, in vitro, a sample from the subject with an antibody, antigen binding fragment, CAR or cell according to any one of claims 1 to 29 and detecting the formation of a complex of antibody, or antigen binding fragment, CAR or cell and LAG-3.

50. Use of an antibody, antigen binding fragment, CAR or cell according to any one of claims 1 to 29 for the detection of LAG-3 in vitro.
51. Use of an antibody, antigen binding fragment, CAR or cell according to any one of claims 1 to 29 as an in vitro diagnostic agent.
52. A method for expanding a population of T cells, wherein T cells are contacted in vitro or ex vivo with an antibody, antigen binding fragment, polypeptide, CAR, cell or composition according to any one of claims 1 to 29 or 31.
53. A method of treatment of a subject having a T-cell dysfunctional disorder, the method comprising culturing T cells obtained from a blood sample from a subject in the presence of an antibody, antigen binding fragment, polypeptide, CAR, cell or composition according to any one of claims 1 to 29 or 31 so as to expand the T cell population, collecting expanded T cells, and administering the expanded T cells to a subject in need of treatment.
54. A method of treating or preventing a cancer in a subject, comprising:
- (a) isolating at least one cell from a subject;
 - (b) modifying the at least one cell to express or comprise the antibody, antigen binding fragment, polypeptide, CAR, nucleic acid or vector according to any one of claims 1 to 28, 32 or 33, and;
 - (c) administering the modified at least one cell to a subject.
55. A method of treating or preventing a cancer in a subject, comprising:
- (a) isolating at least one cell from a subject;
 - (b) introducing into the at least one cell the nucleic acid according to claim 32 or the vector according to claim 33, thereby modifying the at least one cell, and;
 - (c) administering the modified at least one cell to a subject.
56. A kit of parts comprising a predetermined quantity of the antibody, antigen binding fragment, polypeptide, CAR, composition, nucleic acid, vector or cell according to any one of claims 1 to 29, or 31 to 34.