

Claims:

1. An antibody, or antigen binding fragment, which is capable of binding to CTLA-4, having at least one light chain variable region incorporating the following CDRs:

5 LC-CDR1: RATQGISSWLA (SEQ ID NO:5)
 LC-CDR2: AASSLQS (SEQ ID NO:6)
 LC-CDR3: QQANTLPLFT (SEQ ID NO:7); and

having at least one heavy chain variable region incorporating the following CDRs:

10 HC-CDR1: SNTAAWN (SEQ ID NO:8)
 HC-CDR2: RTYYRSKWYSDYGLSVKS (SEQ ID NO:9)
 HC-CDR3: EGSGGTLIY (SEQ ID NO:10).

2. The antibody or antigen binding fragment of claim 1, comprising a light chain variable region sequence and a heavy chain variable region sequence, wherein:

15 the light chain variable region sequence has at least 70% sequence identity to the light chain sequence of SEQ ID NO:1 or 2; and
 the heavy chain variable region sequence has at least 70% sequence identity to the heavy chain sequence of SEQ ID NO:3 or 4.

20 3. The antibody, or antigen binding fragment, according to claim 1 or claim 2, wherein the antibody or antigen binding fragment does not bind to CD28.

4. The antibody, or antigen binding fragment, according to any one of claims 1 to 3, wherein the antibody or antigen binding fragment inhibits interaction between CTLA-4 and
 25 CD80, optionally human CTLA-4 and human CD80.

5. The antibody, or antigen binding fragment, according to any one of claims 1 to 4, wherein the antibody or antigen binding fragment inhibits interaction between CTLA-4 and CD86, optionally human CTLA-4 and human CD86.
 30

6. The antibody, or antigen binding fragment, of any one of claims 1 to 5, wherein the antibody is effective to restore T-cell function in T-cells exhibiting T-cell exhaustion or T-cell anergy.

35 7. An antibody or antigen binding fragment, optionally isolated, which is capable of binding to CTLA-4, which is a bispecific antibody or a bispecific antigen binding fragment comprising (i) an antigen binding fragment according to any one of claims 1 to 6, and (ii) an

antigen binding fragment or polypeptide which is capable of binding to a target protein other than CTLA-4.

8. The antibody, or antigen binding fragment, of claim 7, wherein the antigen binding fragment or polypeptide which is capable of binding to a target protein other than CTLA-4 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, LAG-3, 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.

9. A chimeric antigen receptor (CAR) comprising an antigen binding fragment according to any one of claims 1 to 8.

10. A cell comprising the CAR according to claim 9.

11. An *in vitro* complex, optionally isolated, comprising an antibody or antigen binding fragment according to any one of claims 1 to 8, a CAR according to claim 9 or a cell according to claim 10 bound to CTLA-4.

12. A composition comprising the antibody or antigen binding fragment according to any one of claims 1 to 8, the CAR according to claim 9, or the cell according to claim 10 and at least one pharmaceutically-acceptable carrier.

13. An isolated nucleic acid encoding the antibody or antigen binding fragment according to any one of claims 1 to 8, or the CAR according to claim 9.

14. A vector comprising the nucleic acid of claim 13.

15. A host cell comprising the vector of claim 14.

16. A method for making an antibody or antigen binding fragment according to any one of claims 1 to 8, a CAR according to claim 9, or a cell according to claim 10 comprising culturing the host cell of claim 15 under conditions suitable for the expression of a vector encoding the antibody, antigen binding fragment or CAR.

17. An antibody or antigen binding fragment according to any one of claims 1 to 8, a CAR according to claim 9, a cell according to claim 10 or a composition according to claim 12 for use in therapy, or in a method of medical treatment.

5 18. An antibody or antigen binding fragment according to any one of claims 1 to 8, a CAR according to claim 9, a cell according to claim 10 or a composition according to claim 12 for use in the treatment of a T-cell dysfunctional disorder, cancer or an infectious disease.

19. Use of an antibody or antigen binding fragment according to any one of claims 1 to 8,
10 a CAR according to claim 9, a cell according to claim 10 or a composition according to claim 12 in the manufacture of a medicament for use in the treatment of a T-cell dysfunctional disorder, cancer or an infectious disease.

20. A method of enhancing T-cell function, comprising administering an antibody or
15 antigen binding fragment according to any one of claims 1 to 8, a CAR according to claim 9, a cell according to claim 10 or a composition according to claim 12 to a dysfunctional T-cell *in vitro*.

20 21. A method comprising contacting, *in vitro*, a sample containing, or suspected to contain, CTLA-4 with an antibody or antigen binding fragment according to any one of claims 1 to 8, a CAR according to claim 9 or a cell according to claim 10 and detecting the formation of a complex of antibody or antigen binding fragment, CAR or cell and CTLA-4.

25 22. 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 or antigen binding fragment according to any one of claims 1 to 8, a CAR according to claim 9 or a cell according to claim 10 and detecting the formation of a complex of antibody, antigen binding fragment, CAR or cell and CTLA-4.

30

23. A method of selecting or stratifying a subject for treatment with CTLA-4 or CD86 or CD80 targeted agents, the method comprising contacting, *in vitro*, a sample from the subject with an antibody or antigen binding fragment according to any one of claims 1 to 8, a CAR according to claim 9 or a cell according to claim 10 and detecting the formation of a complex
35 of antibody, antigen binding fragment, CAR or cell and CTLA-4.

24. Use of an antibody or antigen binding fragment according to any one of claims 1 to 8, a CAR according to claim 9 or a cell according to claim 10 for the detection of CTLA-4 *in vitro*.

5 25. Use of an antibody or antigen binding fragment according to any one of claims 1 to 8, a CAR according to claim 9 or a cell according to claim 10 as an *in vitro* diagnostic agent.

26. A method for expanding a population of T cells, wherein T cells are contacted *in vitro* or *ex vivo* with an antibody or antigen binding fragment according to any one of claims 1 to 8, a CAR according to claim 9, a cell according to claim 10 or a composition according to claim 12.

27. An antibody or antigen binding fragment according to any one of claims 1 to 8, a CAR according to claim 9, a cell according to claim 10, or a composition according to claim 12 for use in a method of treatment of a subject having a T-cell dysfunctional disorder, wherein the method comprises culturing T cells obtained from a blood sample from a subject in the presence of an antibody or antigen binding fragment according to any one of claims 1 to 8, a CAR according to claim 9, a cell according to claim 10, or a composition according to claim 12 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.

28. A nucleic acid according to claim 13 or a vector according to claim 14 for use in a method of treating or preventing a cancer in a subject, the method comprising:

25 (a) isolating at least one cell from a subject;

(b) introducing into the at least one cell the nucleic acid according to claim 13 or the vector according to claim 14, thereby modifying the at least one cell, and;

(c) administering the modified at least one cell to a subject.

30 29. A kit of parts comprising a predetermined quantity of the antibody or antigen binding fragment according to any one of claims 1 to 8, the CAR according to claim 9, the cell according to claim 10 or claim 15, the composition according to claim 12, the nucleic acid according to claim 13, or the vector according to claim 14.