

What is claimed is:

1. An antibody or antigen-binding fragment thereof that binds specifically to cytotoxic T-lymphocyte-associated protein 4 (CTLA-4), wherein the antibody or antigen-binding fragment thereof comprises three heavy chain complementarity determining regions (CDRs) (HCDR1, HCDR2 and HCDR3) contained within a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO: 194; and three light chain CDRs (LCDR1, LCDR2 and LCDR3) contained within a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO: 202.
2. The antibody or antigen-binding fragment of claim 1, wherein the antibody or antigen-binding fragment comprises HCDR1-HCDR2-HCDR3-LCDR1-LCDR2-LCDR3 consisting of amino acid sequences of SEQ ID NOs: 196, 198, 200, 204, 206 and 208 respectively.
3. The antibody or antigen-binding fragment of claim 2, wherein the antibody or antigen-binding fragment thereof comprises a HCVR/LCVR amino acid sequence pair of SEQ ID NOs: 194/202.
4. The antibody or antigen-binding fragment thereof of any one of claims 1 – 3, wherein the antibody or antigen-binding fragment thereof is a monoclonal antibody.
5. The antibody or antigen-binding fragment thereof of any one of claims 1 – 4, wherein the antibody or antigen-binding fragment thereof is a fully human antibody.
6. The antibody or antigen-binding fragment thereof of any one of claims 1 – 5, wherein the antibody or antigen-binding fragment thereof comprises a human IgG1 heavy chain constant region.
7. The antibody of any one of claims 1 – 6 comprising a heavy chain and a light chain, wherein the heavy chain comprises an amino acid sequence of SEQ ID NO: 509.
8. The antibody of any one of claims 1 – 6 comprising a heavy chain and a light chain, wherein the light chain comprises an amino acid sequence of SEQ ID NO: 510.

9. The antibody of any one of claims 1 – 6 comprising a heavy chain and a light chain, wherein the heavy chain comprises an amino acid sequence of SEQ ID NO: 509 and the light chain comprises an amino acid sequence of SEQ ID NO: 510.

10. A pharmaceutical composition comprising an isolated antibody or antigen-binding fragment thereof of any one of claims 1 – 9 and a pharmaceutically acceptable carrier or diluent.

11. An isolated polynucleotide molecule comprising a polynucleotide sequence that encodes a HCVR of an antibody as set forth in any one of claims 1 – 9, and an isolated polynucleotide molecule comprising a polynucleotide sequence that encodes a LCVR of an antibody as set forth in any one of claims 1 – 9.

12. A vector comprising the polynucleotide molecules of claim 11.

13. A host cell expressing the vector of claim 12.

14. A host cell comprising the polynucleotide molecules of claim 11.

15. A method of producing an anti-CTLA-4 antibody or antigen-binding fragment thereof, comprising growing the host cell of claim 13 or 14 under conditions permitting production of the antibody or fragment, and recovering the antibody or fragment so produced.

16. The method of claim 15, further comprising formulating the antibody or antigen-binding fragment thereof as a pharmaceutical composition comprising an acceptable carrier.

17. Use of an antibody or antigen-binding fragment thereof of any one of claims 1-9 in the manufacture of a medicament for inhibiting growth of a tumor or a tumor cell in a subject.

18. The use of claim 17, wherein the tumor is a primary or a recurrent tumor.

19. The use of claim 17, wherein the tumor is an established tumor.

20. The use of any one of claims 17-19, wherein the tumor is present in a subject with a disease or disorder selected from the group consisting of blood cancer, brain cancer, renal cell cancer, ovarian cancer, bladder cancer, prostate cancer, breast cancer, hepatic cell carcinoma, bone cancer, colon cancer, non-small-cell lung cancer, squamous cell carcinoma of head and neck, colorectal cancer, mesothelioma, B cell lymphoma, and melanoma.

21. The use of any one of claims 17-20, wherein the medicament is to be administered as an initial dose followed by one or more secondary doses, wherein each secondary dose is to be administered 1 to 12 weeks after the immediately preceding dose.

22. The use of any one of claims 17-21, wherein the medicament is to be administered at a dose of 25 – 600mg.

23. The use of any one of claims 17-22, wherein the medicament is to be administered to the subject in combination with a second therapeutic agent or radiation.

24. The use of claim 23, wherein the second therapeutic agent is selected from the group consisting of a PD-1 inhibitor, an antibody to a tumor specific antigen, an antibody to a virally-infected-cell antigen, a PD-L1 inhibitor, a CD20 inhibitor, a bispecific antibody against CD20 and CD3, a VEGF antagonist, a chemotherapeutic agent, a cytotoxic agent, ~~radiation, a NSAID, or a corticosteroid, and any other therapy useful for ameliorating at least one symptom associated with the disease or disorder.~~

25. The use of claim 24, wherein the second therapeutic agent is a PD-1 inhibitor.

26. The use of claim 25, wherein the PD-1 inhibitor is cemiplimab, nivolumab or pembrolizumab.

27. The use of claim 26, wherein the PD-1 inhibitor is to be administered at a dose of 1, 3 or 10 mg/kg of the subject's body weight.

28. The use of claim 26, wherein the PD-1 inhibitor is to be administered at a dose of 50 – 1200mg.

29. The ~~use~~method of any one of claims 17-28, wherein the medicament is to be administered subcutaneously, intravenously, intradermally, intraperitoneally, orally, intramuscularly or intracranially.

30. The use of any one of claims 25-29, wherein the tumor is non-small cell lung cancer (NSCLC).

31. The use of claim 30, wherein the PD-1 inhibitor is cemiplimab.

32. The use of claim 30 or 31, wherein the NSCLC is advanced or metastatic NSCLC.