

CLAIMS:

1. An isolated antibody that specifically binds to human CTLA-4, comprising a heavy chain variable region and a light chain variable region wherein the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 8 and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 9.
2. The isolated antibody of claim 1, wherein antibody comprises a light chain comprising the amino acid sequence of SEQ ID NO: 27.
3. The isolated antibody of claim 1, wherein the heavy chain comprises the amino acid sequence of SEQ ID NO: 25; and the light chain comprises the amino acid sequence of SEQ ID NO: 27.
4. The isolated antibody of claim 1 or 2, wherein the antibody comprises a human IgG₁ heavy chain constant region that is a variant of a wild type human IgG heavy chain constant region, wherein the variant human IgG₁ heavy chain constant region binds to FcγRIIIA with a higher affinity than the wild type human IgG₁ heavy chain constant region binds to FcγRIIIA.
5. The isolated antibody of claim 4, wherein the amino acid sequence of the IgG₁ heavy chain constant region comprises S239D/A330L/I332E mutations, numbered according to the EU numbering system.
6. The isolated antibody of claim 5, wherein the antibody comprises a heavy chain constant region comprising the amino acid sequence of SEQ ID NO: 30.
7. The isolated antibody of any one of claims 1 or 4-6, wherein the antibody comprises a light chain constant region comprising the amino acid sequence of SEQ ID NO: 32.
8. The isolated antibody of any one of claims 1-7, wherein the antibody
 - (a) is a human antibody;
 - (b) is antagonistic to human CTLA-4;
 - (c) deactivates, reduces, or inhibits an activity of human CTLA-4;

- (d) inhibits binding of human CTLA-4 to human CD80 or human CD86; and/or
 - (e) induces IL-2 production by peripheral blood mononuclear cells (PBMCs) stimulated with staphylococcal enterotoxin A (SEA).
9. The isolated antibody of any one of claims 1-8 conjugated to a cytotoxic agent, cytostatic agent, toxin, radionuclide, or detectable label.
10. An isolated polynucleotide encoding:
- a) a heavy chain variable region and a light chain variable region of the antibody of any one of claims 1-8; or
 - b) a heavy chain and a light chain of the antibody of any one of claims 1-8.
11. A recombinant host cell comprising:
- a) the polynucleotide of claim 10;
 - b) a first polynucleotide encoding a heavy chain variable region of the antibody of any one of claims 1-8, and a second polynucleotide encoding a light chain variable region of the antibody of any one of claims 1-8; or
 - c) a first polynucleotide encoding a heavy chain of the antibody of any one of claims 1-8, and a second polynucleotide encoding a light chain of the antibody of any one of claims 1-8.
12. A method of producing an antibody that binds to human CTLA-4, the method comprising culturing the host cell of claim 11 so that the polynucleotide is expressed and the antibody is produced.
13. A pharmaceutical composition comprising the antibody of any one of claims 1-9, the polynucleotide of claim 10, or the recombinant host cell of claim 11, and a pharmaceutically acceptable carrier or excipient.
14. Use of the antibody of any one of claims 1-9 or the pharmaceutical composition of claim 13 in the manufacture of a medicament for
- a) increasing T-cell activation in response to an antigen in a subject; and/or
 - b) the treatment of cancer in a subject, wherein the cancer is selected from the group

consisting of HPV+ cancer, colorectal cancer, cervical cancer, endometrial cancer, pancreatic cancer, ovarian cancer and melanoma,
wherein the medicament is to be administered to the subject in an effective amount.

15. The use of claim 14, wherein the medicament is to be administered subcutaneously, intratumorally, or intravenously.

16. The use of claim 14 or claim 15, wherein the medicament is to be administered at a dose of 0.01 mg/kg, 0.03 mg/kg, 0.1 mg/kg, 0.3 mg/kg, 1 mg/kg, 3 mg/kg, 6 mg/kg, or 10 mg/kg.

17. The use of any one of claims 14-16, wherein the medicament is to be administered at an interval of once every two weeks, once every three weeks, once every four weeks, once every six weeks, or once every twelve weeks.

18. The use of any one of claims 14-17, wherein the medicament is to be conjointly administered with an additional therapeutic agent to the subject.

19. The use of claim 18, wherein the additional therapeutic agent is selected from the group consisting of a chemotherapeutic, a checkpoint targeting agent, an inhibitor of indoleamine-2,3-dioxygenase (IDO), and a vaccine.

20. The use of claim 19, wherein the checkpoint targeting agent is selected from the group consisting of an antagonist anti-PD-1 antibody, an antagonist anti-PD-L1 antibody, an antagonist anti-PD-L2 antibody, an antagonist anti-CTLA-4 antibody, an antagonist anti-TIM-3 antibody, an antagonist anti-LAG-3 antibody, an antagonist anti-CEACAM 1 antibody, an agonist anti-GITR antibody, an agonist anti-OX40 antibody, and an agonist anti-CD 137 antibody.

21. The antibody of any one of claims 1-9 or the pharmaceutical composition of claim 13 for use in therapy.