

CDR2 sequence that is selected from the group consisting of SEQ ID NOs: 29-32, and a CDR3 sequence that is selected from the group consisting of SEQ ID NOs: 19-22; and

(b) expressing the altered antibody sequence as a protein.

In another aspect, the present disclosure refers to a method for preparing an anti-CTLA-4 antibody or an antigen-binding fragment thereof comprising:

(a) providing:

(i) a heavy chain variable region antibody sequence comprising a CDR1 sequence of SEQ ID NO: 36, a CDR2 sequence of SEQ ID NO: 28; and a CDR3 sequence of SEQ ID NO: 18; and/or

(ii) a light chain variable region antibody sequence comprising a CDR1 sequence of SEQ ID NO: 41, a CDR2 sequence of SEQ ID NO: 32, and a CDR3 sequence of SEQ ID NO: 22; and

(b) expressing the ~~altered~~ antibody sequence as a protein.

In another aspect, the present disclosure refers to the antibody or antigen binding fragment thereof as disclosed herein for use as a medicament.

The disclosure also provides a method of modulating an immune response in a subject comprising administering to the subject the antibody, or antigen binding fragment of any one of said antibodies in this disclosure.

In another example, the present disclosure refers to use of the antibody or the antigen binding fragment thereof as disclosed herein in the manufacture of a medicament for the treatment or prophylaxis of an immune disorder or cancer.

In another aspect, the present disclosure refers to use of the antibody or the antigen binding fragment thereof as disclosed herein in the manufacture of a medicament for the treatment of ~~an immune disorder or~~ cancer.

The disclosure also provides a method of inhibiting growth of tumor cells in a subject, comprising administering to the subject a therapeutically effective amount of said antibody, or said antigen-binding fragment to inhibit growth of the tumor cells.

In another aspect, the present disclosure refers to use of the antibody or the antigen binding fragment thereof as disclosed herein in the manufacture of a medicament for inhibiting growth of tumor cells.

Wherein, the disclosure provides the method, wherein the tumor cells are of a cancer selected from a group consisting of melanoma, renal cancer, prostate cancer, breast cancer, colon cancer, lung cancer, bone cancer, pancreatic cancer, skin cancer, cancer of the head or neck, cutaneous or intraocular malignant melanoma, uterine cancer, ovarian cancer, and rectal cancer.

Wherein, the disclosure provides the method, wherein the antibody is a chimeric antibody, humanized antibody, human antibody or rat antibody.

The features and advantages of this disclosure

The inventors have generated humanized antibodies against CTLA-4

Claims

1. An antibody or antigen binding fragment thereof, comprising
a light chain variable region comprising a light chain complementary-determining region 1 (LCDR1) defined by SEQ ID NO: 41, LCDR2 defined by SEQ ID NO: 32, and LCDR3 defined by SEQ ID NO: 22, and
a heavy chain variable region comprising a heavy chain complementary determining region 1 (HCDR1) defined by SEQ ID NO: 36, HCDR2 defined by SEQ ID NO: 28, and HCDR3 defined by SEQ ID NO: 18; and
wherein the antibody or the antigen binding fragment specifically binds to CTLA-4.
2. The antibody or an antigen binding fragment thereof according to claim 1, comprising an amino acid sequence that is at least 90% or 95% homologous to SEQ ID NO: 7 or 14.
3. The antibody or antigen binding fragment thereof according to claim 1 or 2, wherein the light chain variable region has the amino acid sequence of SEQ ID NO: 14.
4. The antibody or antigen binding fragment thereof according to any one of claims 1-3, wherein the heavy chain variable region has the amino acid sequence of SEQ ID NO: 7.
5. The antibody or antigen binding fragment thereof according to claim 4, wherein the light chain variable region has the amino acid sequence of SEQ ID NO: 14 and the heavy chain variable region has the amino acid sequence of SEQ ID NO: 7.
6. The antibody or the antigen binding-fragment thereof according to any one of claims 1-5, wherein the antibody inhibits CTLA-4 binding to CD80 or CD86.
7. The antibody or the antigen binding-fragment thereof according to any one of claims 1-6, wherein binding epitope of antibody or antigen binding-fragment comprises N145, polysaccharide on N145, or P138 of CTLA-4.

8. The antibody or an antigen binding fragment thereof according to any one of claims 1-7, wherein the antibody or the antigen binding-fragment
 - a) binds to human CTLA-4 with a K_D of $4.77E-10$ M or less; and
 - b) binds to mouse CTLA-4 with a K_D of $1.39E-09$ M or less.
9. The antibody or the antigen binding fragment thereof according to any one of claims 1-8, wherein the antibody is chimeric, humanized, fully human, or rat antibody.
10. A nucleic acid molecule encoding the antibody or the antigen binding fragment thereof according to any one of claims 1 to 9.
11. A cloning or expression vector comprising the nucleic acid molecule of claim 10.
12. A host cell comprising one or more expression vectors of claim 11.
13. A process for the production of the antibody of any one of claims 1-9, comprising culturing the host cell of claim 12 and isolating the antibody.
14. A transgenic rat comprising human immunoglobulin heavy and light chain transgenes, wherein the rat expresses the antibody of any one of claims 1-9.
15. A pharmaceutical composition comprising the antibody or the antigen binding fragment thereof according to any one of claims 1 to 9, and one or more of a pharmaceutically acceptable excipient, a diluent and a carrier.
16. An immunoconjugate comprising the antibody or the antigen binding fragment thereof according to any one of claims 1-9, linked to a therapeutic agent.
17. A method for preparing an anti-CTLA-4 antibody or an antigen-binding fragment thereof comprising:

(a) providing:

(i) a heavy chain variable region antibody sequence comprising a CDR1 sequence of SEQ ID NO: 36, a CDR2 sequence of SEQ ID NO: 28; and a CDR3 sequence of SEQ ID NO: 18; and ~~for~~

(ii) a light chain variable region antibody sequence comprising a CDR1 sequence of SEQ ID NO: 41, a CDR2 sequence of SEQ ID NO: 32, and a CDR3 sequence of SEQ ID NO: 22; and

(b) expressing the ~~altered~~ antibody sequence as a protein.

18. The antibody or antigen binding fragment thereof according to any one of claims 1 to 9 for use as a medicament.

19. Use of the antibody or the antigen binding fragment thereof according to any one of claims 1 to 9 in the manufacture of a medicament for the treatment of ~~an immune disorder or~~ cancer.

20. Use of the antibody or the antigen binding fragment thereof according to any one of claims 1 to 9 in the manufacture of a medicament for inhibiting growth of tumor cells.

21. The use of claim 20, wherein the tumor cells are of a cancer selected from a group consisting of melanoma, renal cancer, prostate cancer, breast cancer, colon cancer, lung cancer, bone cancer, pancreatic cancer, skin cancer, cancer of the head or neck, cutaneous or intraocular malignant melanoma, uterine cancer, ovarian cancer, and rectal cancer.