

CLAIMS

1. An isolated anti-PD-L1 antibody or antigen-binding fragment thereof comprising a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region and/or the light chain variable region comprise a CDR sequence identical to that of an antibody defined by the following sequences ~~or obtained by 1-2 amino acid substitutions of the CDR sequence of the antibody defined by the following sequence:~~

(1) an amino acid sequence of a heavy chain variable region as shown in SEQ ID NO: 31; and/or

(2) an amino acid sequence of a light chain variable region as shown in SEQ ID NO:32.

~~2. The antibody or antigen-binding fragment thereof according to claim 1, wherein:~~

~~(1) for the heavy chain variable region, CDR1 comprises an amino acid sequence as shown in SEQ ID NO: 1, 7, 13, 19 or 25 or obtained by 1 or 2 amino acid substitutions of SEQ ID NO: 1, 7, 13, 19 or 25; CDR2 comprises an amino acid sequence as shown in SEQ ID NO: 2, 8, 14, 20 or 26 or obtained by 1 or 2 amino acid substitutions of SEQ ID NO: 2, 8, 14, 20 or 26; CDR3 comprises an amino acid sequence as shown in SEQ ID NO: 3, 9, 15, 21 or 27 or obtained by 1 or 2 amino acid substitutions of SEQ ID NO: 3, 9, 15, 21 or 27; and/or~~

~~(2) for the light chain variable region, CDR1 comprises an amino acid sequence as shown in SEQ ID NO: 4, 10, 16, 22 or 28 or obtained by 1 or 2 amino acid substitutions of SEQ ID NO: 4, 10, 16, 22 or 28; CDR2 comprises an amino acid sequence as shown in SEQ ID NO: 5, 11, 17, 23 or 29 or obtained by 1 or 2 amino acid substitutions of SEQ ID NO: 5, 11, 17, 23 or 29; CDR3 comprises an amino acid sequence as shown in SEQ ID NO: 6, 12, 18, 24 or 30 or obtained by 1 or 2 amino acid substitutions of SEQ ID NO: 6, 12, 18, 24 or 30.~~

~~23.~~ The antibody or antigen-binding fragment thereof according to claim ~~12~~, wherein:

(1) CDRs 1-3 of the heavy chain variable region comprise amino acid sequences of SEQ ID NOs: 1-3 ~~or obtained by 1 or 2 amino acid substitutions of SEQ ID NOs: 1-3~~, and/or the CDRs 1-

3 of the light chain variable region comprise amino acid sequences of SEQ ID NOs: 4-6 ~~or obtained by 1 or 2 amino acid substitutions of SEQ ID NOs: 4-6~~; or

(2) CDRs 1-3 of the heavy chain variable region comprise amino acid sequences of SEQ ID NOs: 7-9 ~~or obtained by 1 or 2 amino acid substitutions of SEQ ID NOs: 7-9~~, and/or CDRs 1-3 of the light chain variable region comprise amino acid sequences of SEQ ID NOs: 10-12 ~~or obtained by 1 or 2 amino acid substitutions of SEQ ID NOs: 10-12~~; or

(3) CDRs 1-3 of the heavy chain variable region comprise amino acid sequences of SEQ ID NOs: 13-15 ~~or obtained by 1 or 2 amino acid substitutions of SEQ ID NOs: 13-15~~, and/or CDRs 1-3 of the light chain variable region comprise amino acid sequences of SEQ ID NOs: 16-18 ~~or obtained by 1 or 2 amino acid substitutions of SEQ ID NOs: 16-18~~; or

(4) CDRs 1-3 of the heavy chain variable region comprise amino acid sequences of SEQ ID NOs: 19-21 ~~or obtained by 1 or 2 amino acid substitutions of SEQ ID NOs: 19-21~~, and/or CDRs 1-3 of the light chain variable region comprise amino acid sequences of SEQ ID NOs: 22-24 ~~or obtained by 1 or 2 amino acid substitutions of SEQ ID NOs: 22-24~~; or

(5) CDRs 1-3 of the heavy chain variable region comprise amino acid sequences of SEQ ID NOs: 25-27 ~~or obtained by 1 or 2 amino acid substitutions of SEQ ID NOs: 25-27~~, and/or CDRs 1-3 of the light chain variable region comprise amino acid sequences of SEQ ID NOs: 28-30 ~~or obtained by 1 or 2 amino acid substitutions of SEQ ID NOs: 28-30~~.

~~4. The antibody or antigen-binding fragment thereof according to any one of claims 1-3, wherein CDRs 1-3 of the heavy chain variable region comprise amino acid sequences of SEQ ID NOs: 1-3; and/or CDRs 1-3 of the light chain variable region comprise amino acid sequences of SEQ ID NOs: 4-6.~~

~~35.~~ The antibody or antigen-binding fragment thereof according to any one of claims 1-24, wherein:

(1) the heavy chain variable region comprises a sequence as shown in SEQ ID NO: 31, or comprising the same CDRs 1-3 as in SEQ ID NO: 31 and more than 80%, 85%, 90%, 95%, 96%,

97%, 98%, or 99% identical to SEQ ID NO: 31; and/or

(2) the light chain variable region comprises a sequence as shown in SEQ ID NO: 32, or comprising the same CDRs 1-3 as in SEQ ID NO: 32 and more than 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to SEQ ID NO: 32.

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46. The antibody or antigen-binding fragment thereof according to claim 35, wherein:

(1) the heavy chain variable region comprises an amino acid sequence as shown in SEQ ID NO: 31; and/or

(2) the light chain variable region comprises an amino acid sequence as shown in SEQ ID NO:32.

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57. The antibody or antigen-binding fragment thereof according to claim 46, wherein:

(1) the heavy chain comprises an amino acid sequence as shown in SEQ ID NO: 33; and/or

(2) the light chain comprises an amino acid sequence as shown in SEQ ID NO: 34.

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68. The antibody or antigen-binding fragment thereof according to any one of claims 1-47, wherein the antibody is a monoclonal antibody, chimeric antibody, humanized antibody, bispecific antibody, multispecific antibody or Fab Fragment, F(ab') fragment, F(ab')₂ fragment, Fv fragment, dAb, Fd, single chain antibody (scFv).

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79. The antibody or antigen-binding fragment thereof according to any one of claims 1-68, wherein the antibody is a humanized monoclonal antibody.

8410. The antibody or antigen-binding fragment thereof according to any one of claims 1-4 and 6-79, further comprising a human or murine constant region.

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944. The antibody or antigen-binding fragment thereof according to claim 840, wherein the constant region is selected from IgG1, IgG2, IgG3, and IgG4.

1042. The antibody or antigen-binding fragment thereof according to claim 944, wherein the constant region is IgG1, IgG2A, or IgG2B.

1143. An isolated polynucleotide encoding the antibody or antigen-binding fragment thereof according to any one of claims 1-1042.

1244. A combination of an isolated polynucleotide comprising a polynucleotide encoding the heavy chain of the antibody or antigen-binding fragment thereof according to any one of claims 1-1042 and a polynucleotide encoding the light chain of the antibody or antigen-binding fragment thereof according to any one of claims 1-1042.

1345. A nucleic acid construct comprising the polynucleotide according to claim 1143.

1446. The nucleic acid construct of claim 1345, wherein the nucleic acid construct is a vector.

1547. A host cell comprising the nucleic acid construct of claim 1345 or the vector of claim 1546.

1648. The host cell of claim 1547, wherein the cell is a prokaryotic cell, eukaryotic cell, yeast cell, mammalian cell, E. coli cell or CHO cell, NS0 cell, Sp2/0 cell, BHK cell.

1749. An antibody-drug conjugate comprising the antibody or antigen-binding fragment thereof according to any one of claims 1-1042 and a drug toxin.

1820. The antibody-drug conjugate according to claim 1719, wherein the drug toxin is selected from chemicals, toxins, polypeptides, enzymes, isotopes, cytokines, antibodies, or other bioactive substances or a mixture thereof that can inhibit cell growth or kill cells directly, indirectly, or by activating the body's immune response to thereby treat tumors, preferably interleukins, tumor necrosis factors, chemokines, nanoparticles, MMAE, MMAF, DM1, DM4, calicheamicin, duocarmycin, and doxorubicin.

1924. A pharmaceutical composition comprising the antibody or antigen-binding fragment thereof according to any one of claims 1-1042 and/or the conjugate according to claim 1719 or 1920, and a pharmaceutically acceptable carrier.

2022. A method for the manufacture of an anti-PD-L1 antibody, comprising culturing the host cell according to claim 1517 or 1618 under a condition suitable for a vector encoding the anti-PD-L1 antibody or antigen-binding fragment to be expressed, and recovering the antibody or fragment.

~~23. A method for enhancing T cell function, comprising administering an effective amount of the pharmaceutical composition according to claim 21 to dysfunctional T cells.~~

~~24. A method for the treatment of T cell dysfunction, comprising administering a therapeutically effective amount of the pharmaceutical composition of claim 21 to a patient with T cell dysfunction, wherein the T cell dysfunction comprises infection and tumor immunization.~~

~~25. The method according to claim 24, wherein the tumor immunization is caused by a cancer selected from the group consisting of breast cancer, lung cancer, colon cancer, ovarian cancer, melanoma, bladder cancer, kidney cancer, liver cancer, salivary cancer, stomach cancer, glioma, thyroid cancer, thymic cancer, epithelial cancer, head and neck cancer, and gastric and pancreatic~~

cancer.

2126. Use of the antibody or antigen-binding fragment thereof according to any one of claims 1-~~10~~12, the polynucleotide according to claim 11~~13~~, the polynucleotide combination according to claim 12~~14~~, the nucleic acid construct according to claim 13~~15~~, the vector according to claim 14~~16~~, the antibody-drug conjugate according to claim 17~~19~~ or 18~~20~~, or the pharmaceutical composition according to claim 19~~21~~ for the manufacture of a medicament for use in the treatment or prevention of cancer.

2227. The use according to claim 2126, wherein the cancer is a solid tumor.

2328. The use according to claim 2227, wherein the solid tumor is lung cancer, colorectal cancer, breast cancer, ovarian cancer, melanoma, bladder cancer, urothelial cancer, kidney cancer, liver cancer, salivary cancer, stomach cancer, gliomas, thyroid cancer, thymic cancer, epithelial cancer, head and neck cancer, gastric cancer, pancreatic cancer, Merkel cell carcinoma.

2429. The use according to claim 2328, wherein the lung cancer is non-small cell lung cancer.

2530. The use according to claim 2329, wherein the breast cancer~~ovarian cancer~~ is triple negative breast cancer.

26. Use of the pharmaceutical composition according to claim 19 for the manufacture of a medicament for use in enhancing T cell function.

27. Use of the pharmaceutical composition according to claim 19 for the manufacture of a medicament for use in the treatment of T cell dysfunction, wherein the T cell dysfunction comprises

infection and tumor immunization.

28. The use according to claim 27, wherein the tumor immunization is caused by a cancer selected from the group consisting of breast cancer, lung cancer, colon cancer, ovarian cancer, melanoma, bladder cancer, kidney cancer, liver cancer, salivary cancer, stomach cancer, glioma, thyroid cancer, thymic cancer, epithelial cancer, head and neck cancer, and gastric and pancreatic cancer.