

Summary of the Invention

Aspects of the invention include isolated anti-PD-L1 antibodies, as well as compositions containing such antibodies, and methods of using the same in the treatment of diseases or conditions that are mediated by PD-L1 signaling.

In one aspect, the present invention provides an isolated anti-PD-L1 antibody, or an antigen-binding fragment thereof, comprising a heavy chain variable region (VH) and a light chain variable region (VL), wherein the antibody or antigen-binding fragment thereof comprises:

- (i) an HVR-H1 sequence having at least about 99% sequence identity to the sequence of GFSLTSYDIS (SEQ ID NO: 4);
- (ii) an HVR-H2 sequence having at least about 99% sequence identity to the sequence of VIWTGVGTN (SEQ ID NO: 5);
- (iii) an HVR-H3 sequence having at least about 99% sequence identity to the sequence of DPYYYGMDY (SEQ ID NO: 6);
- (iv) an HVR-L1 comprising at least about 99% sequence identity to the sequence of RASQDISIWLS (SEQ ID NO: 1);
- (v) an HVR-L2 comprising at least about 99% sequence identity to the sequence of KASNLHT (SEQ ID NO: 2); and
- 5 (vi) HVR-L3 comprising at least about 99% sequence identity to the sequence of LQSQSFPR (SEQ ID NO: 3).

In another aspect, the present invention provides an isolated anti-PD-L1 antibody or an antigen-binding fragment thereof, comprising a VH having at least 90% sequence identity to SEQ ID NO: 45 and a VL having at least about 90% sequence identity to SEQ ID NO: 46.

- 10 In yet another aspect, the present invention provides an isolated anti-PD-L1 antibody or antigen-binding fragment thereof, comprising a VH having at least 90% sequence identity to any one of SEQ ID NOS: 36, 37, 38, 39, 40, 41 or 42 and a VL having at least 90% sequence identity to any one of SEQ ID NOS: 43 or 44.

In yet another aspect, the present invention provides an isolated anti-PD-L1 antibody or an antigen-binding fragment thereof, made by the process of:

- (a) culturing a cell expressing an antibody comprising a heavy chain variable domain of any one of SEQ ID NOS: 36, 37, 38, 39, 40, 41 or 42, and a light chain variable domain of any one of SEQ ID NOS: 43 or 44; and
- 15 (b) isolating the antibody from the cell or from a cell culturing medium in which the cell is cultured.

In a further aspect, the present invention provides an IgM, IgA, IgG/IgM or IgG/IgA antibody or antigen-binding fragment thereof comprising a modified J-chain comprising an extraneous binding moiety, wherein the antibody, or antigen-binding fragment, binds to a cell surface protein, and wherein the extraneous binding moiety comprises an anti-PD-L1 antibody or antigen-binding fragment thereof as disclosed herein.

In yet another aspect, the present invention provides a polynucleotide encoding a heavy chain and/or a light chain of an antibody or antigen-binding fragment thereof as disclosed herein.

In yet another aspect, the present invention provides a vector comprising the polynucleotide as disclosed herein.

In yet another aspect, the present invention provides a recombinant host cell comprising the polynucleotide or the vector as disclosed herein.

In yet another aspect, the present invention provides a method of producing an isolated anti-PD-L1 antibody, the method comprising:

culturing the host cell as disclosed herein; and

isolating the anti-PD-L1 antibody.

In yet another aspect, the present invention provides use of the antibody or antigen-binding fragment thereof as disclosed herein in the preparation of a medicament to inhibit the growth of a tumor cell in a subject in need of treatment, thereby (i) inhibiting growth or proliferation of the tumor cell, or (ii) inducing death of the tumor cell.

In some examples, an isolated anti-PD-L1 antibody, or an antigen-binding fragment thereof, comprises a heavy chain variable region that comprises: (i) an HVR-H1 sequence having at least about 99% sequence identity to the sequence of GFSLTSYDIS (SEQ ID NO: 4); (ii) an HVR-H2 sequence having at least about 99% sequence identity to the sequence of VIWTGVGTN (SEQ ID NO: 5); and (iii) an HVR-H3 sequence having at least about 99% sequence identity to the sequence of DPYYYGMDY (SEQ ID NO: 6). In some examples, the HVR-H1 sequence comprises the sequence of GFSLTSYDIS (SEQ ID NO: 4); the HVR-H2 sequence comprises the sequence of VIWTGVGTN (SEQ ID NO: 5); and the HVR-H3 sequence comprises the sequence of DPYYYGMDY (SEQ ID NO: 6). In some examples, an isolated anti-PD-L1 antibody further comprises a light chain variable region comprising at least one HVR sequence selected from the group consisting of: (i) HVR-L1 comprising at least about 99% sequence identity to the sequence of RASQDISIWLS (SEQ ID NO: 1); (ii) HVR-L2 comprising at least about 99% sequence identity to the sequence of KASNLHT

(SEQ ID NO: 2); and (iii) HVR-L3 comprising at least about 99% sequence identity to the sequence of LQSQSFPR (SEQ ID NO: 3). In certain examples, the light chain variable region comprises all of said HVR-L1, HVR-L2, and HVR-L3 sequences.

5 In some examples, an anti-DP-L1 antibody, or antigen-binding fragment thereof, comprises: (i) an HVR-L1 that comprises the sequence of RASQDISIWLS (SEQ ID NO: 1); (ii) an HVR-L2 that comprises the sequence of KASNLHT (SEQ ID NO: 2); and (iii) an HVR-L3 that comprises the sequence of LQSQSFPR (SEQ ID NO: 3). In some examples, the antibody, or antigen-binding fragment, comprises: (i) an HVR-L1 that comprises the sequence of RASQDISIWLS (SEQ ID NO: 1); (ii) an HVR-L2 that comprises the sequence of
10 KASNLHT (SEQ ID NO: 2); and (iii) an HVR-L3 that comprises the sequence of LQSQSFPR (SEQ ID NO: 3).

In some examples, the antibody, or antigen-binding fragment, is a monoclonal antibody. In some examples, the antibody is a chimeric, humanized, or human antibody. In some examples, the heavy chain variable region comprises a framework sequence. In some
15 examples, at least a portion of the framework sequence comprises a human framework sequence. In some examples, at least a portion of the framework sequence

comprises a human consensus framework sequence. In some examples, the framework sequence comprises a framework region 1 (FR1) sequence selected from the group consisting of: SEQ ID NOS: 7, 8, 9, 10 and 11. In some examples, the framework sequence comprises a framework region 2 (FR2) sequence selected from the group consisting of: SEQ ID NOS: 12, 13, 14, 15 and 16. In some examples, the framework sequence comprises a framework region 3 (FR3) sequence selected from the group consisting of: SEQ ID NOS: 17, 18, 19, 20, 21, 22, 23 and 24. In some examples, the framework sequence comprises a framework region 4 (FR4) sequence selected from the group consisting of: SEQ ID NOS: 25 and 26. In some examples, the framework sequence comprises an FR1 sequence selected from the group consisting of: SEQ ID NOS: 7, 8, 9, 10 and 11; an FR2 sequence selected from the group consisting of: SEQ ID NOS: 12, 13, 14, 15 and 16; an FR3 sequence selected from the group consisting of: SEQ ID NOS: 17, 18, 19, 20, 21, 22, 23 and 24; and an FR4 sequence selected from the group consisting of: SEQ ID NOS: 25 and 26.

In some examples, the light chain variable region comprises a framework sequence. In some examples, at least a portion of the framework sequence comprises a human framework sequence. In some examples, at least a portion of the framework sequence comprises a human consensus framework sequence. In some examples, the framework sequence comprises a framework region 1 (FR1) sequence selected from the group consisting of: SEQ ID NOS: 27, 28 and 29. In some examples, the framework sequence comprises a framework region 2 (FR2) sequence selected from the group consisting of: SEQ ID NOS: 30 and 31. In some examples, the framework sequence comprises a framework region 3 (FR3) sequence selected from the group consisting of: SEQ ID NOS: 32 and 33. In some examples, the framework sequence comprises a framework region 4 (FR4) sequence selected from the group consisting of: SEQ ID NOS: 34 and 35. In some examples, the framework region comprises: an FR1 sequence selected from the group consisting of: SEQ ID NOS: 27, 28 and 29; an FR2 sequence selected from the group consisting of: SEQ ID NOS: 30 and 31; an FR3 sequence selected from the group consisting of: SEQ ID NOS: 32 and 33; and an FR4 sequence selected from the group consisting of: SEQ ID NOS: 34 and 35.

In some examples, an isolated anti-PD-L1 antibody, or an antigen-binding fragment thereof, comprises a heavy chain variable domain having at least about 90% sequence identity to SEQ ID NO: 45 and/or a light chain variable domain having at least about 90% sequence identity to SEQ ID NO: 46. In some examples, an isolated anti-PD-L1 antibody, or antigen-

binding fragment thereof, comprises a heavy chain variable domain comprising SEQ ID NO: 45 and/or a light chain variable domain comprising SEQ ID NO: 46.

In some examples, the antibody is a monoclonal antibody. In some examples, the antibody is a chimeric, humanized or human antibody.

5 In some examples, an isolated anti-PD-L1 antibody, or antigen-binding fragment thereof, comprises a heavy chain variable domain having at least 90% sequence identity to any one of SEQ ID NOS: 36, 37, 38, 39, 40, 41 or 42 and/or a light chain variable domain having at least 90% sequence identity to any one of SEQ ID NOS: 43 or 44. In some examples, an isolated anti-PD-L1 antibody, or antigen-binding fragment thereof, comprising a heavy chain
10 variable domain comprising any one of SEQ ID NOS: 36, 37, 38, 39, 40, 41 or 42 and/or a light chain variable domain comprising any one of SEQ ID NOS: 43 or 44. In some examples, an antibody: (i) binds substantially to the same epitope as an anti-PD-L1 antibody comprising a heavy chain variable domain of any one of SEQ ID NOS: 36, 37, 38, 39, 40, 41 or 42, and a light chain variable domain of any one of SEQ ID NOS: 43 or 44; or (ii) competes for binding
15 to the same epitope as an anti-PD-L1 antibody comprising a heavy chain variable domain of any one of SEQ ID NOS: 36, 37, 38, 39, 40, 41 or 42, and a light chain variable domain of any one of SEQ ID NOS: 43 or 44. In some examples, an anti-PD-L1 antibody, or an antigen-binding fragment thereof, made by the process of: (a) culturing a cell expressing an antibody comprising a heavy chain variable domain of any one of SEQ ID NOS: 36, 37, 38, 39, 40, 41
20 or 42, and a light chain variable domain of any one of SEQ ID NOS: 43 or 44; and (b) isolating the antibody from the cell or from a cell culturing medium in which the cell is cultured. In some examples, the antibody is a monoclonal antibody. In some examples, the antibody is a chimeric, humanized or human antibody.

In some examples, an antibody or antigen-binding fragment is monospecific. In some
25 examples, an antibody or antigen-binding fragment is bispecific. In some examples, the antibody or antigen-binding fragment binds to a PD-L1 protein and a cell surface protein. In some examples, the cell surface protein is selected from the group consisting of: CD20, EGFR, HER2, CTLA-4, TIM3, LAG3, VISTA and TIGIT. In some examples, the antibody or antigen-binding fragment is multispecific. In some examples, the antibody or antigen-binding
30 fragment binds to a PD-L1 protein and one or more cell surface proteins. In some examples, the cell surface proteins are selected from the group consisting of: CD20, EGFR, HER2, CTLA-4, TIM3, LAG3, VISTA and TIGIT.

In some examples, an antigen-binding fragment is selected from the group consisting of: Fab, Fab', F(ab)₂, F(ab')₂, Fv, scFv, and single domain antibody. In some examples, an antibody comprises a kappa light chain or a lambda light chain. In some examples, an antibody is an IgG, IgM, IgA, IgD, or IgE isotype. In some examples, an antibody is an IgG isotype, and the antibody is a subclass selected from the group consisting of: IgG1, IgG2, IgG3 and IgG4. In some examples, an antibody is an IgM isotype. In some examples, an antibody comprises a J-chain. In some examples, an antibody is an IgA isotype, and wherein the antibody is a subclass selected from the group consisting of: IgA1 and IgA2. In some examples, the antibody comprises a J-chain. In some examples, an antibody is an IgG/IgM or an IgG/IgA hybrid antibody comprising a J-chain. In some examples, a J-chain is a modified J-chain comprising an extraneous binding moiety. In some examples, the extraneous binding moiety is selected from the group consisting of: antibodies, antigen-binding fragments of antibodies, antibody-drug conjugates, antibody-like molecules, antigen-binding fragments of antibody-like molecules, soluble and membrane-bound proteins, ligands, and receptors. In some examples, the extraneous moiety is an antigen-binding fragment of an antibody, and is selected from the group consisting of: Fab, Fab', F(ab)₂, F(ab')₂, Fv, scFv, and single domain antibody. In some examples, the antigen-binding fragment is an scFv.

In some examples, the extraneous binding moiety affects a T-cell signaling pathway. In some examples, the extraneous binding moiety antagonizes a T-cell inhibitory signaling pathway. In some examples, the extraneous binding moiety binds to a cell surface protein selected from the group consisting of: CTLA-4, PD-1, TIM3, LAG3, BTLA, VISTA and TIGIT. In some examples, the extraneous binding moiety binds to an albumin protein, or a fragment of an albumin protein. In some examples, the extraneous binding moiety comprises an albumin-binding peptide. In some examples, the extraneous binding moiety comprises an albumin-binding antibody fragment. In some examples, the albumin-binding antibody fragment is selected from the group consisting of: Fab, scFv, VHH, scFab and dAb. In some examples, the extraneous binding moiety comprises an FcRn-binding peptide. In some examples, the extraneous binding moiety comprises an FcRn-binding antibody fragment. In some examples, the FcRn-binding antibody fragment is selected from the group consisting of: Fab, scFv, VHH, scFab and dAb. In some examples, the extraneous binding moiety comprises an Fc domain.

Examples of the disclosure include an IgM, IgA, IgG/IgM or IgG/IgA antibody, or antigen-binding fragment, comprising a modified J-chain comprising an extraneous binding

moiety, wherein the antibody binds to a cell surface protein, and wherein the extraneous binding moiety comprises an anti-PD-L1 antibody, or an antigen-binding fragment, as described herein. In some examples, the cell surface protein is selected from the group consisting of: CD20, EGFR, HER2, CTLA-4, PD-1, TIM3, LAG3, BTLA, VISTA and TIGIT.

5 In some examples, the extraneous binding moiety binds to an effector cell. In some examples, the effector cell is selected from the group consisting of: T-cells, natural killer (NK) cells, macrophages and neutrophils. In some examples, the effector cell is a T-cell. In some examples, the extraneous binding moiety binds to a CD3 protein (e.g., a CD3 ϵ protein) on the T-cell. In some examples, the effector cell is an NK cell. In some examples, the extraneous
10 binding moiety binds to a target on the NK cell selected from the group consisting of: CD16, CD64 and NKG2D. In some examples, the effector cell is a macrophage. In some examples, the extraneous binding moiety binds to a CD14 on the macrophage. In some examples, the effector cell is a neutrophil. In some examples, the extraneous binding moiety binds to CD16b or CD177 on the neutrophil.

15 In some examples, an antibody, or antigen-binding fragment, is a PD-L1 antagonist. In some examples, an antibody, or antigen-binding fragment, antagonizes a PD-L1 signaling pathway. In some examples, an antibody, or antigen-binding fragment, antagonizes an interaction between a PD-L1 protein and a PD-1 protein. In some examples, an antibody, or antigen-binding fragment, inhibits binding between a PD-L1 protein and a PD-1 protein. In
20 some examples, an antibody, or antigen-binding fragment, blocks binding between a PD-L1 protein and a PD-1 protein. In some examples, an antibody, or an antigen-binding fragment, binds to a PD-L1 protein and inhibits one or more functions of a PD-1 protein.

Examples of the disclosure include a polynucleotide encoding a heavy chain and/or a light chain of an antibody as described herein. Examples of the disclosure include a vector
25 comprising a polynucleotide as described herein. Examples of the disclosure include a host cell comprising a vector as described herein. In some examples, the host cell is a prokaryotic cell. In some examples, the host cell is a eukaryotic cell.

Examples of the disclosure include kits that comprise an anti-PD-L1 antibody as described herein.

30 Examples of the disclosure include methods of producing an isolated anti-PD-L1 antibody, the method comprising: transfecting a host cell with a nucleic acid comprising a polynucleotide encoding a heavy chain and/or a light chain of an anti-PD-L1 antibody as

described herein; culturing the host cell under suitable conditions for producing the anti-PD-L1 antibody; and isolating the anti-PD-L1 antibody.

5 Examples of the disclosure include methods of inhibiting one or more functions of a PD-1 protein, the methods comprising contacting the PD-L1 protein with an antibody as described herein. In some examples, a method is carried out in vitro. In some examples, a method is carried out in vivo in a mammalian subject.

10 Examples of the disclosure include a method of inhibiting the growth of a tumor cell that expresses PD-L1, the method comprising administering an antibody as described herein to a subject having the tumor cell, thereby (i) inhibiting growth or proliferation of the tumor cell, or (ii) inducing death of the tumor cell.

Examples of the disclosure include a pharmaceutical composition comprising an antibody as described herein and a pharmaceutically-acceptable carrier.

15 Examples of the disclosure include a method of treating a subject having cancer, the method comprising administering an effective amount of a pharmaceutical composition as described herein to the subject. Examples of the disclosure include use of an antibody as described herein in the preparation of a medicament for treating cancer. In some examples, the cancer is a hematologic cancer or an epithelial cancer. In some examples, the hematologic cancer is a leukemia, lymphoma, myeloma, or myelodysplastic syndrome. In some examples, the leukemia is an acute myeloid leukemia, acute lymphoblastic leukemia, chronic myelogenous leukemia, or chronic lymphocytic leukemia. In some examples, the lymphoma is Hodgkin's lymphoma or non-Hodgkin's lymphoma. In some examples, the epithelial cancer is non-small-cell lung, urinary bladder, renal, liver, colorectal, ovarian, gastric, esophageal, pancreatic, thyroid, breast, or nasopharyngeal cancer. In some examples, the breast cancer is hormone receptor negative or triple negative breast cancer. In some examples, the cancer is melanoma. In some examples, the cancer is glioblastoma.

25 In some examples, a pharmaceutical composition or medicament further comprises an effective amount of a second therapeutic agent.

30 Examples of the disclosure include methods of screening a sample to determine the presence of a PD-L1 polypeptide in the sample, the methods comprising: contacting the sample with an anti-PD-L1 antibody described herein; and determining whether the anti-PD-L1 antibody binds to a PD-L1 polypeptide in the sample, wherein the presence of such binding is indicative of the presence of the PD-L1 polypeptide in the sample. In some examples, an

anti-PD-L1 antibody is detectably labeled, and determining whether the anti-PD-L1 antibody binds to the PD-L1 polypeptide comprises detecting the detectable label.

Brief Description of the Drawings

5 **FIG. 1** is a schematic representation of an indirect ELISA assay.

FIG. 2 is a schematic representation of a flow cytometry assay that was used to determine reactivity and specificity of anti-human PD-L1 antibodies.

FIG. 3, Panel A is a graph showing activity of three hybridoma supernatants in the indirect ELISA along with positive and negative control antibodies. Panel B is a graph
10 showing example data from FACS screening of hybridoma supernatants along with positive and negative controls.

FIG. 4 is a schematic representation of a PD-1/PD-L1 blockade assay based on NFAT-driven expression of luciferase on a Jurkat-based reporter cell line that overexpresses PD-1 and is suppressed in the presence of CHO cells over-expressing the PD-L1 antigen.

15 **FIG. 5**, Panel A is a graph showing example data from screening of hybridoma supernatants in a PD-1/PD-L1 blockade assay. Panel B is a schematic depiction of the hybridoma screening strategy and results.

FIG. 6, Panel A is a bar graph showing the distribution of NGS-derived sequences from 3C5-2G12 light chains. Panel B is a bar graph showing the distribution of NGS-derived
20 sequences from 3C5-2G12 heavy chains. Not all heavy chains were expressed at the same level.

FIG. 7 is an image of a Coomassie stained hybrid gel (left) and western blot with anti-J chain antibody. The images show formation of fully assembled IgM pentamer as well as incorporation of J-chain.

25 **FIG. 8** is a graph showing PD-L1 blockade data from the 3C5.2G12 IgM, 3C5.2G12 IgM + J chain, and 3C5.2G12 IgG antibody formats.

FIG. 9, Panel A is a graph showing 3C5.2G12 cross reactivity with Cyno PD-L1. Panel B is a graph showing lack of 3C5.2G12 cross reactivity with mouse PD-L1. Panel C is a graph showing lack of 3C5.2G12 cross reactivity with human PD-L2.

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Claims:

1. An isolated anti-PD-L1 antibody, or an antigen-binding fragment thereof, comprising a heavy chain variable region (VH) and a light chain variable region (VL), wherein the antibody or antigen-binding fragment thereof comprises:

- (i) an HVR-H1 sequence having at least about 99% sequence identity to the sequence of GFSLTSYDIS (SEQ ID NO: 4);
- (ii) an HVR-H2 sequence having at least about 99% sequence identity to the sequence of VIWTGVGTN (SEQ ID NO: 5);
- (iii) an HVR-H3 sequence having at least about 99% sequence identity to the sequence of DPYYYGMDY (SEQ ID NO: 6);
- (iv) an HVR-L1 comprising at least about 99% sequence identity to the sequence of RASQDISIWLS (SEQ ID NO: 1);
- (v) an HVR-L2 comprising at least about 99% sequence identity to the sequence of KASNLHT (SEQ ID NO: 2); and
- (vi) HVR-L3 comprising at least about 99% sequence identity to the sequence of LQSQSFRT (SEQ ID NO: 3).

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

- (i) the HVR-H1 sequence comprises the sequence of GFSLTSYDIS (SEQ ID NO: 4);
- (ii) the HVR-H2 sequence comprises the sequence of VIWTGVGTN (SEQ ID NO: 5);
- (iii) the HVR-H3 sequence comprises the sequence of DPYYYGMDY (SEQ ID NO: 6);
- (iv) the HVR-L1 comprises the sequence of RASQDISIWLS (SEQ ID NO: 1);
- (v) the HVR-L2 comprises the sequence of KASNLHT (SEQ ID NO: 2); and
- (vi) the HVR-L3 comprises the sequence of LQSQSFRT (SEQ ID NO: 3).

3. The antibody or antigen-binding fragment thereof of claim 1 or claim 2 wherein the VH comprises the amino acid sequence SEQ ID NO: 45 and the VL comprises the amino acid sequence SEQ ID NO: 46.

4. An isolated anti-PD-L1 antibody or an antigen-binding fragment thereof, comprising a VH having at least 90% sequence identity to SEQ ID NO: 45 and a VL having at least about 90% sequence identity to SEQ ID NO: 46.
5. The antibody or antigen-binding fragment thereof according to any one of claims 1 to 4, which is a chimeric antibody or a humanized antibody.
6. An isolated anti-PD-L1 antibody or antigen-binding fragment thereof, comprising a VH having at least 90% sequence identity to any one of SEQ ID NOS: 36, 37, 38, 39, 40, 41 or 42 and a VL having at least 90% sequence identity to any one of SEQ ID NOS: 43 or 44.
7. The antibody or antigen-binding fragment thereof of claim 6, wherein the VH comprises SEQ ID NOS: 36, 37, 38, 39, 40, 41 or 42 and the VL comprises SEQ ID NOS: 43 or 44.
8. An isolated anti-PD-L1 antibody or an antigen-binding fragment thereof, made by the process of:
 - (a) culturing a cell expressing an antibody comprising a heavy chain variable domain of any one of SEQ ID NOS: 36, 37, 38, 39, 40, 41 or 42, and a light chain variable domain of any one of SEQ ID NOS: 43 or 44; and
 - (b) isolating the antibody from the cell or from a cell culturing medium in which the cell is cultured.
9. The antibody or antigen-binding fragment thereof according to any one of claims 1 to 8, which is monospecific.
10. The antibody or antigen-binding fragment thereof according to any one of claims 1-8, which is multispecific.
11. The antibody or antigen-binding fragment thereof according to claim 10, which is bispecific.

12. The antibody or antigen-binding fragment thereof according to claim 10 or claim 11, which binds to a PD-L1 protein and a cell surface protein.
13. The antibody or antigen-binding fragment thereof according to claim 12, wherein the cell surface protein is selected from the group consisting of: CD20, EGFR, HER2, CTLA-4, TIM3, LAG3, VISTA and TIGIT.
14. The antibody or antigen-binding fragment thereof according to any one of claims 1-13, wherein the antigen-binding fragment is selected from the group consisting of: Fab, Fab', F(ab)₂, F(ab')₂, Fv, scFv, and single domain antibody.
15. The antibody or antigen-binding fragment thereof according to any one of claims 1-14, wherein the antibody comprises a kappa light chain constant region or a lambda light chain constant region.
16. The antibody or antigen-binding fragment thereof according to any one of claims 1-15, wherein the antibody is an IgG, IgM, IgA, IgD, or IgE isotype.
17. The antibody or antigen-binding fragment thereof according to claim 16, wherein the antibody is an IgG isotype, and wherein the antibody is a subclass selected from the group consisting of: IgG1, IgG2, IgG3 and IgG4.
18. The antibody or antigen-binding fragment thereof according to claim 16, wherein the antibody is an IgM isotype.
19. The antibody or antigen-binding fragment thereof according to claim 16, wherein the antibody is an IgA isotype, and wherein the antibody is a subclass selected from the group consisting of: IgA1 and IgA2.
20. The antibody or antigen-binding fragment thereof according to claim 18 or claim 19, wherein the antibody further comprises a J-chain.

21. The antibody or antigen-binding fragment thereof according to any one of claims 1-15, wherein the antibody is an IgG/IgM or an IgG/IgA hybrid antibody comprising a J-chain.
22. The antibody or antigen-binding fragment thereof according to claim 20 or claim 21, wherein the J-chain is a modified J-chain comprising an extraneous binding moiety selected from the group consisting of: antibodies, antigen-binding fragments of antibodies, antibody-drug conjugates, antibody-like molecules, antigen-binding fragments of antibody-like molecules, soluble and membrane-bound proteins, ligands, and receptors.
23. The antibody or antigen-binding fragment thereof according to claim 22, wherein the extraneous binding moiety is an antigen-binding fragment of an antibody, and is selected from the group consisting of: Fab, Fab', F(ab)₂, F(ab')₂, Fv, scFv, and single domain antibody.
24. The antibody or antigen-binding fragment thereof according to claim 22 or claim 23, where the extraneous binding moiety antagonizes a T-cell inhibitory signaling pathway.
25. The antibody or antigen-binding fragment thereof according to claim 24, wherein the extraneous binding moiety binds to a cell surface protein selected from the group consisting of: CTLA-4, TIM3, LAG3, BTLA, VISTA and TIGIT.
26. The antibody or antigen-binding fragment thereof according to claim 22 or claim 23, wherein the extraneous binding moiety comprises an albumin protein, a fragment of an albumin protein, an albumin-binding peptide, an albumin-binding antibody fragment, an FcRn-binding peptide, an FcRn-binding antibody fragment or an Fc domain.
27. The antibody or antigen-binding fragment thereof according to 22 or claim 23, wherein the extraneous binding moiety binds to an effector cell.
28. The antibody or antigen-binding fragment thereof according to claim 27, wherein the effector cell is selected from the group consisting of: T-cells, natural killer (NK) cells, macrophages and neutrophils.

29. The antibody or antigen-binding fragment thereof according to claim 28, wherein the effector cell is a T-cell, and wherein the extraneous binding moiety binds to a CD3 on the T-cell.
30. An IgM, IgA, IgG/IgM or IgG/IgA antibody or antigen-binding fragment thereof comprising a modified J-chain comprising an extraneous binding moiety, wherein the antibody, or antigen-binding fragment, binds to a cell surface protein, and wherein the extraneous binding moiety comprises an anti-PD-L1 antibody or antigen-binding fragment thereof according to any one of claims 1-8.
31. The antibody or antigen-binding fragment thereof according to claim 30, wherein the cell surface protein is selected from the group consisting of: CD20, EGFR, HER2, CTLA-4, TIM3, LAG3, VISTA and TIGIT.
32. The antibody or antigen-binding fragment thereof according to any one of claims 1-31, wherein the antibody or antigen-binding fragment thereof antagonizes the interaction between a PD-L1 protein and a PD-1 protein.
33. A polynucleotide encoding a heavy chain and/or a light chain of an antibody or antigen-binding fragment thereof according to any one of the preceding claims.
34. A vector comprising the polynucleotide of claim 33.
35. A recombinant host cell comprising the polynucleotide of claim 33 or the vector of claim 34.
36. A method of producing an isolated anti-PD-L1 antibody, the method comprising:
culturing the host cell of claim 35; and
isolating the anti-PD-L1 antibody.
37. Use of the antibody or antigen-binding fragment thereof of any one of claims 1 to 32 in the preparation of a medicament to inhibit the growth of a tumor cell in a subject in need of

treatment, thereby (i) inhibiting growth or proliferation of the tumor cell, or (ii) inducing death of the tumor cell.