

There remains a need to provide alternative antibodies that bind human PD-L1 and neutralize the PD-L1 interactions with PD-1 and B7-1. In particular, there remains a need to provide PD-L1 antibodies that bind with more favorable attributes, such as better association rates. Faster association to the target can translate into better *in vivo* activity for a therapeutic antibody. Also, there remains a need to provide PD-L1 antibodies that better enhance the T cell response to a tumor, as measured by influence on tumor size, by the level of infiltration of CD3-positive T cells, and by the percentage of T cells that are CD8-positive in *in vivo* models.

Summary

In one aspect of the present disclosure, there is provided an antibody that binds human PD-L1 (SEQ ID NO: 1), comprising a light chain (LC) and a heavy chain (HC), wherein the light chain comprises a light chain variable region (LCVR) and the heavy chain comprises a heavy chain variable region (HCVR), and wherein the LCVR comprises light chain complementarity determining regions LCDR1, LCDR2, and LCDR3 consisting of the amino acid sequences SGSSSNIGSNTVN (SEQ ID NO: 5), YGNSNRPS (SEQ ID NO: 6), and QSYDSSLGSGSV (SEQ ID NO: 7), respectively, and wherein the HCVR comprises heavy chain complementarity determining regions HCDR1, HCDR2, and HCDR3 consisting of the amino acid sequences KASGGTFSSYAIS (SEQ ID NO: 2), GIPIFGTANYAQKFQG (SEQ ID NO: 3), and ARSPDYSPYYYYGMDV (SEQ ID NO: 4), respectively.

In another aspect of the present disclosure, there is provided an antibody, comprising a light chain (LC) and a heavy chain (HC), wherein the light chain comprises a light chain variable region (LCVR) and the heavy chain comprises a heavy chain variable region (HCVR), wherein the LCVR has the amino acid sequence given in SEQ ID NO: 9, and the HCVR has the amino acid sequence given in SEQ ID NO: 8.

In a further aspect of the present disclosure, there is provided a mammalian cell comprising a DNA molecule comprising a polynucleotide sequence encoding a polypeptide having an amino acid sequence of SEQ ID NO: 11 and a polynucleotide sequence encoding a polypeptide having an amino acid sequence of SEQ ID NO: 10,

wherein the cell is capable of expressing an antibody comprising a light chain having an amino acid sequence of SEQ ID NO: 11 and a heavy chain having an amino acid sequence of SEQ ID NO: 10.

5 In another aspect of the present disclosure, there is provided a process for producing an antibody comprising a light chain having an amino acid sequence of SEQ ID NO: 11 and a heavy chain having an amino acid sequence of SEQ ID NO: 10, comprising cultivating the mammalian cell of Claim 7 under conditions such that the antibody is expressed, and recovering the expressed antibody.

10 In a further aspect of the present disclosure, there is provided an antibody produced by the process disclosed herein.

In another aspect of the present disclosure, there is provided a pharmaceutical composition, comprising the antibody disclosed herein, and an acceptable carrier, diluent, or excipient.

15 In a further aspect of the present disclosure, there is provided a use of the antibody disclosed herein in the manufacture of a medicament for treating cancer, wherein said medicament is to be administered to a patient in need thereof.

In another aspect of the present disclosure, there is provided the antibody disclosed herein, for use in therapy.

20 In a further aspect of the present disclosure, there is provided the antibody disclosed herein, for use in the treatment of cancer.

In another aspect of the present disclosure, there is provided the antibody disclosed herein, for use in the treatment of cancer, wherein said antibody is to be administered in simultaneous, separate, or sequential combination with one or more anti-tumor agents.

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Description

Certain antibodies of the present invention mediate enhanced T cell response to a tumor as measured by tumor size compared to certain prior art antibodies in established and non-established tumor models. Certain antibodies of the present invention mediate enhanced T cell response to a tumor as measured by CD3-positive T cell infiltration compared to certain prior art antibodies in a model.

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Accordingly, in some embodiments the present invention provides an antibody that binds human PD-L1 (SEQ ID NO: 1), comprising a light chain (LC) and a heavy chain (HC), wherein the light chain comprises a light chain variable region (LCVR) and the heavy chain comprises a heavy chain variable region (HCVR), and wherein the LCVR
5 comprises light chain complementarity determining regions LCDR1, LCDR2, and LCDR3 consisting of the amino acid sequences SGSSSNIGSNTVN (SEQ ID NO: 5), YGNSNRPS (SEQ ID NO: 6), and QSYDSSLGSGSV (SEQ ID NO: 7), respectively, and wherein the HCVR comprises heavy chain complementarity determining regions HCDR1, HCDR2, and HCDR3 consisting of the amino acid sequences
10 KASGGTFSSY AIS (SEQ ID NO: 2), GIPIFGTANYAQKFQG (SEQ ID NO: 3), and ARSPDYSPYYYYGMDV (SEQ ID NO: 4), respectively.

In some embodiments, the present invention provides an antibody, comprising a light chain (LC) and a heavy chain (HC), wherein the light chain comprises a light chain variable region (LCVR) and the heavy chain comprises a heavy chain variable region
15 (HCVR), wherein the LCVR has the amino acid sequence given in SEQ ID NO: 9, and the HCVR has the amino acid sequence given in SEQ ID NO: 8.

6. The antibody of any one of Claims 1-5, wherein the antibody is glycosylated.
7. A mammalian cell comprising a DNA molecule comprising a polynucleotide sequence encoding a polypeptide having an amino acid sequence of SEQ ID NO: 11 and a polynucleotide sequence encoding a polypeptide having an amino acid sequence of SEQ ID NO: 10, wherein the cell is capable of expressing an antibody comprising a light chain having an amino acid sequence of SEQ ID NO: 11 and a heavy chain having an amino acid sequence of SEQ ID NO: 10.
8. A process for producing an antibody comprising a light chain having an amino acid sequence of SEQ ID NO: 11 and a heavy chain having an amino acid sequence of SEQ ID NO: 10, comprising cultivating the mammalian cell of Claim 7 under conditions such that the antibody is expressed, and recovering the expressed antibody.
9. An antibody produced by the process of Claim 8.
10. A pharmaceutical composition, comprising the antibody of any one of Claims 1-6 or 9, and an acceptable carrier, diluent, or excipient.
11. Use of the antibody of any one of Claims 1-6 or 9 in the manufacture of a medicament for treating cancer, wherein said medicament is to be administered to a patient in need thereof.
12. The use of Claim 11, wherein the cancer is melanoma, lung cancer, head and neck cancer, colorectal cancer, pancreatic cancer, gastric cancer, kidney cancer, bladder cancer, prostate cancer, breast cancer, ovarian cancer, esophageal cancer, soft tissue sarcoma, or hepatocellular carcinoma.
13. The use of Claim 11 or 12, wherein said medicament is to be further administered in simultaneous, separate, or sequential combination with one or more anti-tumor agents.
14. The antibody of any one of Claims 1-6 or 9, for use in therapy.
15. The antibody of any one of Claims 1-6 or 9, for use in the treatment of cancer.

- 5 16. The antibody for use of Claim 15, wherein the cancer is melanoma, lung cancer, head and neck cancer, colorectal cancer, pancreatic cancer, gastric cancer, kidney cancer, bladder cancer, prostate cancer, breast cancer, ovarian cancer, esophageal cancer, soft tissue sarcoma, or hepatocellular carcinoma.
17. The antibody of any one of Claims 1-6 or 9, for use in the treatment of cancer, wherein said antibody is to be administered in simultaneous, separate, or sequential combination with one or more anti-tumor agents.
- 10 18. The antibody for use of Claim 17, wherein the cancer is melanoma, lung cancer, head and neck cancer, colorectal cancer, pancreatic cancer, gastric cancer, kidney cancer, bladder cancer, prostate cancer, breast cancer, ovarian cancer, esophageal cancer, soft tissue sarcoma, or hepatocellular carcinoma.