

CLAIMS

1. An isolated antibody or fragment thereof that binds to PD-L1, wherein the antibody or fragment thereof comprises
 - (i) a heavy chain CDR1, CDR2, and CDR3 sequence comprising SEQ ID NO: 81, 82, and 83, respectively, and a light chain CDR1, CDR2, and CDR3 sequence comprising SEQ ID NO: 84, 85, and 86, respectively;
 - (ii) a heavy chain CDR1, CDR2, and CDR3 sequence comprising SEQ ID NO: 93, 94, and 95, respectively, and a light chain CDR1, CDR2, and CDR3 sequence comprising SEQ ID NO: 96, 97, and 98, respectively;
 - (iii) a heavy chain CDR1, CDR2, and CDR3 sequence comprising SEQ ID NO: 99, 100, and 101, respectively, and a light chain CDR1, CDR2, and CDR3 sequence comprising SEQ ID NO: 102, 103, and 104, respectively;
 - (iv) a heavy chain CDR1, CDR2, and CDR3 sequence comprising SEQ ID NO: 111, 112, and 113, respectively, and a light chain CDR1, CDR2, and CDR3 sequence comprising SEQ ID NO: 114, 115, and 116, respectively;or
 - (v) a heavy chain CDR1, CDR2, and CDR3 sequence comprising SEQ ID NO: 123, 124, and 125, respectively, and a light chain CDR1, CDR2, and CDR3 sequence comprising SEQ ID NO: 126, 127, and 128, respectively.
2. The antibody or fragment of claim 1, wherein the antibody or fragment thereof comprises a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence according to SEQ ID NOs: 81, 82, and 83, respectively; and a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence according to SEQ ID NOs: 84, 85, and 86, respectively.
3. The antibody or fragment of claim 1, wherein the antibody or fragment thereof comprises a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence according to SEQ ID NOs: 93, 94, and 95, respectively; and a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence according to SEQ ID NOs: 96, 97, and 98, respectively.

4. The antibody or fragment of claim 1, wherein the antibody or fragment thereof comprises a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence according to SEQ ID NOs: 99, 100, and 101, respectively; and a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence according to SEQ ID NOs: 102, 103, and 104, respectively.
5. The antibody or fragment of claim 1, wherein the antibody or fragment thereof comprises a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence according to SEQ ID NOs: 111, 112, and 113, respectively; and a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence according to SEQ ID NOs: 114, 115, and 116, respectively.
6. The antibody or fragment of claim 1, wherein the antibody or fragment thereof comprises a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence according to SEQ ID NOs: 123, 124, and 125, respectively; and a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence according to SEQ ID NOs: 126, 127, and 128, respectively.
7. The isolated antibody or fragment thereof of any one of claims 1-6, wherein the antibody or fragment thereof is chimeric or humanized.
8. The isolated antibody or fragment thereof of claim 1, wherein the antibody or fragment thereof comprises:
 - (i) a heavy chain variable region having at least 80% homology to SEQ ID NO: 2 and a light chain variable region having at least 80% homology to SEQ ID NO: 4;
 - (ii) a heavy chain variable region having at least 80% homology to SEQ ID NO: 10 and a light chain variable region having at least 80% homology to SEQ ID NO: 12;
 - (iii) a heavy chain variable region having at least 80% homology to SEQ ID NO: 14 and a light chain variable region having at least 80% homology to SEQ ID NO: 16;

- (iv) a heavy chain variable region having at least 80% homology to SEQ ID NO: 22 and a light chain variable region having at least 80% homology to SEQ ID NO: 24;
- (v) a heavy chain variable region having at least 80% homology to SEQ ID NO: 30 and a light chain variable region having at least 80% homology to SEQ ID NO: 32;
- (vi) a heavy chain variable region having at least 80% homology to SEQ ID NO: 42 and a light chain variable region having at least 80% homology to SEQ ID NO: 44; or
- (vii) a heavy chain variable region having at least 80% homology to SEQ ID NO: 46 and a light chain variable region having at least 80% homology to SEQ ID NO: 48.

9. The isolated antibody or fragment thereof of claim 8, wherein the antibody or fragment thereof comprises

- (i) a heavy chain variable region comprising SEQ ID NO: 2 and a light chain variable region comprising SEQ ID NO: 4;
- (ii) a heavy chain variable region comprising SEQ ID NO: 10 and a light chain variable region comprising SEQ ID NO: 12;
- (iii) a heavy chain variable region comprising SEQ ID NO: 14 and a light chain variable region comprising SEQ ID NO: 16;
- (iv) a heavy chain variable region comprising SEQ ID NO: 22 and a light chain variable region comprising SEQ ID NO: 24;
- (v) a heavy chain variable region comprising SEQ ID NO: 30 and a light chain variable region comprising SEQ ID NO: 32;
- (vi) (xi) a heavy chain variable region comprising SEQ ID NO: 42 and a light chain variable region comprising SEQ ID NO: 44; or
- (vii) (xii) a heavy chain variable region comprising SEQ ID NO: 46 and a light chain variable region comprising SEQ ID NO: 48.

10. The isolated antibody or fragment thereof of claim 1, wherein the antibody or fragment thereof comprises a heavy chain variable region according to SEQ ID NO: 42 and a light chain variable region according to SEQ ID NO: 44.

11. The isolated antibody or fragment thereof of claim 1, wherein the antibody or fragment thereof comprises a heavy chain variable region according to SEQ ID NO: 46 and a light chain variable region according to SEQ ID NO: 48.
12. The isolated antibody or fragment thereof of claim 1, wherein the antibody or fragment thereof comprises a heavy chain having at least 80% homology to SEQ ID NO: 70 and a light chain having at least 80% homology to SEQ ID NO: 74.
13. The isolated antibody or fragment thereof of claim 1, wherein the antibody or fragment thereof comprises a heavy chain having at least 80% homology to SEQ ID NO: 72 and a light chain having at least 80% homology to SEQ ID NO: 74.
14. The isolated antibody or fragment thereof of claim 1, wherein the antibody or fragment thereof comprises a heavy chain having at least 80% homology to SEQ ID NO: 76 and a light chain having at least 80% homology to SEQ ID NO: 80.
15. The isolated antibody or fragment thereof of claim 1, wherein the antibody or fragment thereof comprises a heavy chain having at least 80% homology to SEQ ID NO: 78 and a light chain having at least 80% homology to SEQ ID NO: 80.
16. The isolated antibody or fragment thereof of claim 1, wherein the antibody comprises
 - (i) a heavy chain according to SEQ ID NO: 70 and a light chain according to SEQ ID NO: 74;
 - (ii) a heavy chain according to SEQ ID NO: 72 and a light chain according to SEQ ID NO: 74;
 - (iii) a heavy chain according to SEQ ID NO: 76 and a light chain according to SEQ ID NO: 80; or
 - (iv) a heavy chain according to SEQ ID NO: 78 and a light chain according to SEQ ID NO: 80.
17. The isolated antibody or fragment thereof of any one of claims 1-16, wherein the antibody or fragment thereof is selected from the group consisting of a monoclonal antibody, an scFv, a Fab fragment, an Fab' fragment, and an F(ab)' fragment.

18. An antibody or fragment thereof according to any one of claims 1-16, wherein the antibody or fragment thereof is linked or conjugated to a therapeutic agent.
19. The antibody or fragment thereof according to claim 18, wherein the therapeutic agent is a cytotoxic drug, a radioactive isotope, an immunomodulator, or an antibody.
20. The isolated antibody or fragment thereof according to any one of claims 1-16, wherein the antibody or fragment thereof has an affinity for PD-L1 of about 10 nM to about 0.01 nM.
21. The isolated antibody or fragment thereof according to claim 20, wherein the antibody or fragment thereof has an affinity for PD-L1 of about 10 nM or less.
22. The isolated antibody or fragment thereof according to claim 20, wherein the antibody or fragment thereof has an affinity for PD-L1 of about 1.0 nM or less.
23. The isolated antibody or fragment thereof according to any one of claims 1-16, wherein the antibody has a binding EC₅₀ of about 5 ng/mL to about 1000 ng/mL.
24. The isolated antibody or fragment thereof according to any one of claims 1-16, wherein the antibody blocks binding of PD-L1 to PD-1.
25. The isolated antibody or fragment thereof of claim 24, wherein the antibody or fragment thereof blocks the binding of PD-L1 to PD-1 at an IC₅₀ of about 5 ng/mL to about 1000 ng/mL.
26. The isolated antibody or fragment thereof according to any one of claims 1-16, wherein the antibody or fragment increases T cell activation as measured by inflammatory cytokine production.
27. The isolated antibody or fragment thereof according to claim 26, wherein the antibody or fragment thereof increases T cell production of IL-2 and IFN γ .

28. An isolated antibody or fragment thereof that binds to PD-L1, wherein the antibody or fragment thereof is produced by a hybridoma selected from the group consisting of 13C5, 5G11, 8C6, 4D1, or 8H4.
29. A composition comprising the antibody or fragment thereof according to any one of claims 1-28 and a pharmaceutically acceptable carrier.
30. An isolated polynucleotide encoding the antibody or fragment thereof according to any one of claims 1-28.
31. An expression vector comprising the isolated polynucleotide according to claim 30.
32. A host cell comprising the expression vector according to claim 31.
33. An isolated hybridoma cell line selected from the group consisting of 13C5, 5G11, 8C6, 4D1, or 8H4.
34. A method for increasing T cell activation, the method comprising contacting T cells with an antibody or fragment thereof according to any one of claims 1-28.
35. The isolated antibody or fragment thereof according to any one of claims 1-28 for use in the reduction of tumors or inhibition of the growth of tumor cells in a subject.
36. The isolated antibody or fragment thereof according to any one of claims 1-28 for use in the treatment of a cancer in a subject.
37. The isolated antibody or fragment thereof according to claim 36, wherein the cancer is selected from the group consisting of lymphoma, leukemia, melanoma, glioma, breast cancer, lung cancer, colon cancer, bone cancer, ovarian cancer, bladder cancer, kidney cancer, liver cancer, stomach cancer, rectal cancer, testicular cancer, salivary cancer, thyroid cancer, thymic cancer, epithelial cancer, head or neck cancer, gastric cancer, pancreatic cancer, or a combination thereof.

38. The isolated antibody or fragment thereof according to any one of claims 1-28 for use in the treatment of an infectious disease in a subject.
39. The isolated antibody or fragment thereof according to claim 38, wherein the infectious disease is selected from the group consisting of candidiasis, candidemia, aspergillosis, streptococcal pneumonia, streptococcal skin and oropharyngeal conditions, gram negative sepsis, tuberculosis, mononucleosis, influenza, respiratory illness caused by Respiratory Syncytial Virus, malaria, schistosomiasis, and trypanosomiasis.
40. Use of the isolated antibody or fragment thereof according to any one of claims 1-28 in the manufacture of a medicament for the reduction of tumors or inhibition of the growth of tumor cells in a subject.
41. Use of the isolated antibody or fragment thereof according to any one of claims 1-28 in the manufacture of a medicament for the treatment of cancer in a subject.
42. The use according to claim 41, wherein the cancer is selected from the group consisting of lymphoma, leukemia, melanoma, glioma, breast cancer, lung cancer, colon cancer, bone cancer, ovarian cancer, bladder cancer, kidney cancer, liver cancer, stomach cancer, rectal cancer, testicular cancer, salivary cancer, thyroid cancer, thymic cancer, epithelial cancer, head or neck cancer, gastric cancer, pancreatic cancer, or a combination thereof.
43. Use of the isolated antibody or fragment thereof according to any one of claims 1-28 in the manufacture of a medicament for the treatment of an infectious disease in a subject.
44. The use according to claim 43, wherein the infectious disease is selected from the group consisting of candidiasis, candidemia, aspergillosis, streptococcal pneumonia, streptococcal skin and oropharyngeal conditions, gram negative sepsis, tuberculosis, mononucleosis, influenza, respiratory illness caused by Respiratory Syncytial Virus, malaria, schistosomiasis, and trypanosomiasis.