

CLAIMS

1. ~~An isolated antibody or fragment thereof that binds to PD-1, wherein the antibody or fragment thereof comprises a light chain CDR1 sequence having at least 80% homology to an amino acid sequence selected from the group consisting of SEQ ID NOs: 24, 34, 45, 55, 65, 75, 85, 95, 105, and 115; a light chain CDR2 sequence having at least 80% homology to an amino acid sequence selected from the group consisting of SEQ ID NOs: 25, 35, 46, 56, 66, 76, 86, 96, 106, and 116; a light chain CDR3 sequence having at least 80% homology to an amino acid sequence selected from the group consisting of SEQ ID NOs: 26, 36, 47, 57, 67, 77, 87, 97, 107, and 117; a heavy chain CDR1 sequence having at least 80% homology to an amino acid sequence selected from the group consisting of SEQ ID NOs: 19, 29, 40, 50, 60, 70, 80, 90, 100, and 110; a heavy chain CDR2 sequence having at least 80% homology to an amino acid sequence selected from the group consisting of SEQ ID NOs: 20, 30, 41, 51, 61, 71, 81, 91, 101, and 111; and a heavy chain CDR3 sequence having at least 80% homology to an amino acid sequence selected from the group consisting of SEQ ID NOs: 21, 31, 42, 52, 62, 72, 82, 92, 102, and 112.~~
2. ~~The antibody or fragment thereof of claim 1, wherein the antibody or fragment thereof comprises a light chain CDR1 consisting of an amino acid sequence selected from the group consisting of SEQ ID NOs: 24, 34, 45, 55, 65, 75, 85, 95, 105, and 115; a light chain CDR2 consisting of an amino acid sequence selected from the group consisting of SEQ ID NOs: 25, 35, 46, 66, 76, 86, 96, 106, and 116; a light chain CDR3 consisting of an amino acid sequences selected from the group consisting of SEQ ID NOs: 26, 36, 47, 57, 67, 77, 87, 97, 107, and 117; a heavy chain CDR1 consisting of an amino acid sequence selected from the group consisting of SEQ ID NOs: 19, 29, 40, 50, 60, 70, 80, 90, 100, and 110; a heavy chain CDR2 consisting of an amino acid sequence selected from the group consisting of SEQ ID NOs: 20, 30, 41, 51, 61, 71, 81, 91, 101, and 111; and a heavy chain CDR3 consisting of an amino acid sequence selected from the group consisting of SEQ ID NOs: 21, 31, 42, 52, 62, 72, 82, 92, 102, and 112.~~
3. ~~The antibody or fragment of claim 1, wherein the antibody or fragment thereof comprises a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence~~

~~having at least 80% homology to an amino acid sequence according to SEQ ID NOs: 24, 25, and 26, respectively; and a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence having at least 80% homology to an amino acid sequence according to SEQ ID NOs: 19, 20, and 21, respectively.~~

- ~~4. The antibody or fragment of claim 1, wherein the antibody or fragment thereof comprises a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence having at least 80% homology to an amino acid sequence according to SEQ ID NOs: 34, 35, and 36, respectively; and a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence having at least 80% homology to an amino acid sequence according to SEQ ID NOs: 29, 30, and 31, respectively.~~
- ~~5. The antibody or fragment of claim 1, wherein the antibody or fragment thereof comprises a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence having at least 80% homology to an amino acid sequence according to SEQ ID NOs: 45, 46, and 47, respectively; and a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence having at least 80% homology to an amino acid sequence according to SEQ ID NOs: 40, 41, and 42, respectively.~~
- ~~6. The antibody or fragment of claim 1, wherein the antibody or fragment thereof comprises a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence having at least 80% homology to an amino acid sequence according to SEQ ID NOs: 55, 56, and 57, respectively; and a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence having at least 80% homology to an amino acid sequence according to SEQ ID NOs: 50, 51, and 52, respectively.~~
- ~~7. The antibody or fragment of claim 1, wherein the antibody or fragment thereof comprises a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence having at least 80% homology to an amino acid sequence according to SEQ ID NOs: 65, 66, and 67, respectively; and a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence having at least 80% homology to an amino acid sequence according to SEQ ID NOs: 60, 61, and 62, respectively.~~

8. ~~The antibody or fragment of claim 1, wherein the antibody or fragment thereof comprises a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence having at least 80% homology to an amino acid sequence according to SEQ ID NOs: 75, 76, and 77, respectively; and a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence having at least 80% homology to an amino acid sequence according to SEQ ID NOs: 70, 71, and 72, respectively.~~
9. ~~The antibody or fragment of claim 1, wherein the antibody or fragment thereof comprises a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence having at least 80% homology to an amino acid sequence according to SEQ ID NOs: 85, 86, and 87, respectively; and a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence having at least 80% homology to an amino acid sequence according to SEQ ID NOs: 80, 81, and 82, respectively.~~
10. ~~The antibody or fragment of claim 1, wherein the antibody or fragment thereof comprises a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence having at least 80% homology to an amino acid sequence according to SEQ ID NOs: 95, 96, and 97, respectively; and a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence having at least 80% homology to an amino acid sequence according to SEQ ID NOs: 90, 91, and 92, respectively.~~
11. ~~The antibody or fragment of claim 1, wherein the antibody or fragment thereof comprises a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence having at least 80% homology to an amino acid sequence according to SEQ ID NOs: 105, 106, and 107, respectively; and a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence having at least 80% homology to an amino acid sequence according to SEQ ID NOs: 100, 101, and 102, respectively.~~
12. ~~The antibody or fragment of claim 1, wherein the antibody or fragment thereof comprises a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence having at least 80% homology to an amino acid sequence according to SEQ ID NOs: 115, 116, and 117, respectively; and a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence having at least 80% homology to an amino acid sequence according to SEQ ID NOs: 110, 111, and 112, respectively.~~

13. ~~The isolated antibody or fragment thereof of any one of claims 1-12, wherein the antibody or fragment thereof is chimeric or humanized.~~
14. ~~An isolated antibody or fragment thereof that binds to PD-1, wherein the antibody or fragment thereof comprises a light chain variable region comprising an amino acid sequence having at least 80% homology to an amino acid sequence selected from the group consisting of SEQ ID NOs: 23, 33, 44, 54, 64, 74, 84, 94, 104, 114, 133, and 143; and a heavy chain variable region comprising an amino acid sequence having at least 80% homology to an amino acid sequence selected from the group consisting of SEQ ID NOs: 18, 28, 39, 49, 59, 69, 79, 89, 99, 109, 131, and 141.~~
15. ~~The isolated antibody or fragment thereof of claim 14, wherein the antibody or fragment thereof comprises a light chain variable region comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 23, 33, 44, 54, 64, 74, 84, 94, 104, 114, 133, and 143; and a heavy chain variable region comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 18, 28, 39, 49, 59, 69, 79, 89, 99, 109, 131, and 141.~~
16. ~~An isolated antibody or fragment thereof that binds to PD-1, wherein the antibody or fragment thereof comprises a light chain variable region according to SEQ ID NO: 133 or 152 and a heavy chain variable region according to SEQ ID NO: 131.~~
17. ~~An isolated antibody or fragment thereof that binds to PD-1, wherein the antibody or fragment thereof comprises a light chain variable region according to SEQ ID NO: 143 and a heavy chain variable region according to SEQ ID NO: 141.~~
18. ~~An isolated antibody or fragment thereof that binds to PD-1, wherein the antibody or fragment thereof comprises a light chain according to SEQ ID NO: 139 or 153 and a heavy chain according to SEQ ID NO: 135.~~
19. ~~An isolated antibody or fragment thereof that binds to PD-1, wherein the antibody or fragment thereof comprises a light chain according to SEQ ID NO: 139 or 153 and a heavy chain according to SEQ ID NO: 137.~~

20. ~~An isolated antibody or fragment thereof that binds to PD-1, wherein the antibody or fragment thereof comprises a light chain according to SEQ ID NO: 149 and a heavy chain according to SEQ ID NO: 145.~~
21. ~~An isolated antibody or fragment thereof that binds to PD-1, wherein the antibody or fragment thereof comprises a light chain according to SEQ ID NO: 149 and a heavy chain according to SEQ ID NO: 147.~~
22. ~~An isolated antibody or fragment thereof, wherein the antibody or fragment thereof binds to the same epitope as an antibody or fragment thereof according to any one of claims 1 to 21.~~
23. ~~An isolated antibody or fragment thereof, wherein the antibody or fragment thereof competes for binding to PD-1 with an antibody or fragment thereof of any one of claims 1 to 21, wherein the competition is measured by ELISA, flow cytometry, or surface plasmon resonance (SPR) assay.~~
24. ~~The isolated antibody or fragment thereof of any one of claims 1-21, 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.~~
25. ~~An antibody or fragment thereof according to any one of claims 1-21, wherein the antibody or fragment thereof is linked or conjugated to a therapeutic agent.~~
26. ~~The antibody or fragment thereof according to claim 25, wherein the therapeutic agent is a cytotoxic drug, a radioactive isotope, an immunomodulator, or an antibody.~~
27. ~~An isolated antibody or fragment thereof that binds to PD-1, wherein the antibody or fragment thereof has an affinity for PD-1 of about 1 nM to about 0.01 nM.~~
28. ~~The isolated antibody or fragment thereof according to claim 27, wherein the antibody or fragment thereof has an affinity for PD-1 of about 1 nM or less.~~

29. — ~~The isolated antibody or fragment thereof according to claim 27, wherein the antibody or fragment thereof has an affinity for PD-1 of about 0.1 nM or less.~~
30. — ~~An isolated antibody or fragment thereof that binds to PD-1, wherein the antibody has a binding EC₅₀ of about 5 ng/mL to about 1000 ng/mL.~~
31. — ~~An isolated antibody or fragment thereof that binds to PD-1, wherein the antibody blocks binding of PD-1 to PD-L1.~~
32. — ~~An isolated antibody or fragment thereof of claim 31, wherein the antibody or fragment thereof blocks the binding of PD-1 to PD-L1 or PD-L2 at an IC₅₀ of about 5 ng/mL to about 1000 ng/mL.~~
33. — ~~An isolated antibody or fragment thereof that binds to PD-1, wherein the antibody or fragment increases T cell activation as measured by inflammatory cytokine production.~~
34. — ~~The isolated antibody or fragment thereof according to claim 28, wherein the antibody or fragment thereof increases T cell production of IL-2 and IFN γ .~~
35. — ~~An isolated antibody or fragment thereof that binds to PD-1, wherein the antibody or fragment thereof is produced by a hybridoma selected from the group consisting of 10D1, 4C10, 7D3, 13F1, 15H5, 14A6, 22A5, 6E1, 5A8, 7A4, and/or 7A4D.~~
36. — ~~A composition comprising the antibody or fragment thereof according to any one of claims 1-35 and a pharmaceutically acceptable carrier.~~
37. — ~~An isolated polynucleotide encoding the antibody or fragment thereof according to any one of claims 1-35.~~
38. — ~~An expression vector comprising the isolated polynucleotide according to claim 37.~~
39. — ~~A host cell comprising the expression vector according to claim 38.~~

40. — ~~An isolated hybridoma cell line selected from the group consisting of 10D1, 4C10, 7D3, 13F1, 15H5, 14A6, 22A5, 6E1, 5A8, 7A4 and 7A4D.~~
41. — ~~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 1-35.~~
42. — ~~A method for reducing tumors or inhibiting the growth of tumor cells in a subject, the method comprising administering to the subject a therapeutically effective amount of the isolated antibody or fragment thereof according to any one of claims 1-35.~~
43. — ~~A method for treating a cancer in a subject in need thereof, the method comprising administering a therapeutically effective amount of the isolated antibody or fragment thereof according to any one of claims 1-35 to the subject.~~
44. — ~~The method according to claim 43, 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.~~
45. — ~~A method for treating an infectious disease in a subject in need thereof, the method comprising administering a therapeutically effective amount of the isolated antibody or fragment thereof according to any one of claims 1-35 to the subject.~~
46. — ~~The method according to claim 45, 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.~~
1. An isolated antibody or fragment thereof that binds to PD-1, wherein the antibody or fragment thereof comprises

- (i) a light chain CDR1, CDR2, and CDR3 sequence comprising SEQ ID NO: 34, 35, and 36, respectively, and a heavy chain CDR1, CDR2, and CDR3 sequence comprising SEQ ID NO: 29, 30, and 31, respectively;
 - (ii) a light chain CDR1, CDR2, and CDR3 sequence comprising SEQ ID NO: 55, 56, and 57, respectively, and a heavy chain CDR1, CDR2, and CDR3 sequence comprising SEQ ID NO: 50, 51, and 52, respectively;
 - (iii) a light chain CDR1, CDR2, and CDR3 sequence comprising SEQ ID NO: 65, 66, and 67, respectively, and a heavy chain CDR1, CDR2, and CDR3 sequence comprising SEQ ID NO: 60, 61, and 62, respectively;
 - (iv) a light chain CDR1, CDR2, and CDR3 sequence comprising SEQ ID NO: 105, 106, and 107, respectively, and a heavy chain CDR1, CDR2, and CDR3 sequence comprising SEQ ID NO: 100, 101, and 102, respectively; or
 - (v) a light chain CDR1, CDR2, and CDR3 sequence comprising SEQ ID NO: 115, 116, and 117, respectively, and a heavy chain CDR1, CDR2, and CDR3 sequence comprising SEQ ID NO: 110, 111, and 112, respectively.
2. The antibody or fragment of claim 1, wherein the antibody or fragment thereof comprises a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence according to SEQ ID NOs: 34, 35, and 36, respectively; and a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence according to SEQ ID NOs: 29, 30, and 31, respectively.
3. The antibody or fragment of claim 1, wherein the antibody or fragment thereof comprises a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence according to SEQ ID NOs: 55, 56, and 57, respectively; and a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence according to SEQ ID NOs: 50, 51, and 52, respectively.
4. The antibody or fragment of claim 1, wherein the antibody or fragment thereof comprises a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence according to SEQ ID NOs: 65, 66, and 67, respectively; and a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence according to SEQ ID NOs: 60, 61, and 62, respectively.

5. The antibody or fragment of claim 1, wherein the antibody or fragment thereof comprises a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence according to SEQ ID NOs: 105, 106, and 107, respectively; and a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence according to SEQ ID NOs: 100, 101, and 102, respectively.
6. The antibody or fragment of claim 1, wherein the antibody or fragment thereof comprises a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence according to SEQ ID NOs: 115, 116, and 117, respectively; and a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence according to SEQ ID NOs: 110, 111, and 112, respectively.
7. The isolated antibody or fragment thereof of claim 1, wherein the antibody or fragment thereof is chimeric or humanized.
8. The isolated antibody or fragment of claim 1, wherein the antibody or fragment thereof comprises:
- (i) a light chain variable region comprising SEQ ID NO: 33 and a heavy chain variable region comprising SEQ ID NO: 28;
 - (ii) a light chain variable region comprising SEQ ID NO: 54 and a heavy chain variable region comprising SEQ ID NO: 49;
 - (iii) a light chain variable region comprising SEQ ID NO: 64 and a heavy chain variable region comprising SEQ ID NO: 59;
 - (iv) a light chain variable region comprising SEQ ID NO: 104 and a heavy chain variable region comprising SEQ ID NO: 99;
 - (v) a light chain variable region comprising SEQ ID NO: 114 and a heavy chain variable region comprising SEQ ID NO: 109;
 - (vi) a light chain variable region comprising SEQ ID NO: 143 and a heavy chain variable region comprising SEQ ID NO: 141; or
 - (vii) a light chain variable region comprising SEQ ID NO: 152 and a heavy chain variable region comprising SEQ ID NO: 131.

9. The isolated antibody or fragment of claim 1, wherein the antibody or fragment thereof comprises a light chain variable region according to SEQ ID NO: 133 or 152 and a heavy chain variable region according to SEQ ID NO: 131.
10. The isolated antibody or fragment of claim 1, wherein the antibody or fragment thereof comprises a light chain variable region according to SEQ ID NO: 143 and a heavy chain variable region according to SEQ ID NO: 141.
11. The isolated antibody or fragment thereof of claim 1, 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.
12. An antibody or fragment thereof according to claim 1, wherein the antibody or fragment thereof is linked or conjugated to a therapeutic agent.
13. The antibody or fragment thereof according to claim 12, wherein the therapeutic agent is a cytotoxic drug, a radioactive isotope, an immunomodulator, or an antibody.
14. The isolated antibody or fragment thereof according to claim 1, wherein the antibody or fragment thereof has an affinity for PD-1 of about 1 nM to about 0.01 nM.
15. The isolated antibody or fragment thereof according to claim 14, wherein the antibody or fragment thereof has an affinity for PD-1 of about 1 nM or less.
16. The isolated antibody or fragment thereof according to claim 14, wherein the antibody or fragment thereof has an affinity for PD-1 of about 0.1 nM or less.
17. The isolated antibody or fragment thereof according to claim 1, wherein the antibody has a binding EC50 of about 5 ng/mL to about 1000 ng/mL.
18. The isolated antibody or fragment thereof of claim 1, wherein the antibody blocks binding of PD-1 to PD-L1.

19. An isolated antibody or fragment thereof of claim 18, wherein the antibody or fragment thereof blocks the binding of PD-1 to PD-L1 or PD-L2 at an IC50 of about 5 ng/mL to about 1000 ng/mL.
20. The isolated antibody or fragment thereof of claim 1, wherein the antibody or fragment increases T cell activation as measured by inflammatory cytokine production.
21. The isolated antibody or fragment thereof according to claim 20, wherein the antibody or fragment thereof increases T cell production of IL-2 and IFN γ .
22. A composition comprising the antibody or fragment thereof according to claim 1 and a pharmaceutically acceptable carrier.
23. An isolated polynucleotide encoding the antibody or fragment thereof according to claim 1.
24. An expression vector comprising the isolated polynucleotide according to claim 23.
25. A host cell comprising the expression vector according to claim 24.
26. A method for increasing T cell activation, the method comprising contacting T cells with an antibody or fragment thereof according to claim 1.