

CLAIMS

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.