CLAIMS

1. An antibody or antigen binding fragment thereof that binds to an epitope of PD-1 comprising amino acids at positions 128, 129, 130, 131 and 132 and at least one of amino acids at positions 35, 64, 82, 83 of SEQ ID NO: 24.

2. An antibody or antigen binding fragment thereof that binds to an epitope of human and murine PD-1, wherein the epitope comprises amino acids at positions 128, 129, 130, 131 and 132 of SEQ ID NO: 24.

3. The antibody or the antigen binding fragment thereof of claims 1 or 2, wherein the murine PD-1 is mouse or rat PD-1.

4. The antibody or the antigen binding fragment thereof of claims 1 to 3, wherein the antibody

a) binds to human PD-1 with a KD of 2.15E-10 M or less; and

b) binds to mouse PD-1 with a KD of 1.67E-08 M or less.

5. The antibody of any of claims 1 to 4, wherein the antibody exhibits at least one of the following properties:

a) binds to human PD-1 with a K_D of between 4.32E-10 M and 2.15E-10 M and to mouse PD-1 with a K_D of between 5.39E-08 M and 1.67E-08 M;

b) does not substantially bind to human CD28, CTLA-4;

c) increases T-cell proliferation;

d) increases interferon-gamma production; or

e) increases interleukin-2 secretion.

6. An antibody or an antigen binding fragment thereof, comprising an amino acid sequence that is at least 70%, 80%, 90% or 95% homologous to a sequence selected from a group consisting of SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8 and 9, wherein the antibody specifically binds to PD-1.

7. An antibody or an antigen binding fragment thereof, comprising an amino acid sequence selected from a group consisting of SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8 and 9, wherein the antibody specifically binds to PD-1.

8. An antibody, or an antigen-binding fragment thereof, comprising:

a) a variable region of a heavy chain having an amino acid sequence that is at least 70%, 80%, 90% or 95% homologous to a sequence selected from a group consisting of SEQ ID NOs: 1 and 2; and

b) a variable region of a light chain having an amino acid sequence that is at least 70%, 80%, 90% or 95% homologous to a sequence selected from a group consisting of SEQ ID NOs: 3, 4, 5, 6, 7, 8 and 9,

wherein the antibody specifically binds to PD-1.

9. An antibody or an antigen binding fragment thereof, comprising:

a) a variable region of a heavy chain having an amino acid sequence selected from the group consisting of SEQ ID NOs: 1 and 2; and

b) a variable region of a light chain having an amino acid sequence selected from the group consisting of SEQ ID NOs: 3, 4, 5, 6, 7, 8 and 9,

wherein the antibody specifically binds to PD-1.

10. An antibody or an antigen binding fragment thereof, comprising a complementarity-determining region (CDR) having an amino acid sequence selected from the group consisting of SEQ ID NOs: 10-23,

wherein the antibody specifically binds to PD-1.

11. An antibody, or antigen-binding fragment thereof, comprising:

a heavy chain variable region comprising CDR1, CDR2, and CDR3 sequences; and

a light chain variable region comprising CDR1, CDR2, and CDR3 sequences,

wherein the heavy chain variable region CDR3 sequence comprises a sequence selected from a group consisting of SEQ ID NOs: 12 and 13, and conservative modifications thereof,

wherein the antibody specifically binds to PD-1.

12. The antibody of claim 11, wherein the light chain variable region CDR3 sequence comprises an amino acid sequence selected from a group consisting of SEQ ID NOs: 20, 21, 22 and 23, and conservative modifications thereof.

13. The antibody of claim 11 or 12, wherein the heavy chain variable region CDR2 sequence comprises an amino acid sequence selected from a group consisting of amino acid sequences of SEQ ID NO: 11, and conservative modifications thereof.

14. The antibody of any of claims 11 to 13, wherein the light chain variable region CDR2 sequence comprises an amino acid sequence selected from a group consisting of amino acid sequences of SEQ ID NO: 19, and conservative modifications thereof.

15. The antibody of any of claims 11 to 14, wherein the heavy chain variable region CDR1 sequence comprises an amino acid sequence selected from a group consisting of amino acid sequences of SEQ ID NO: 10, and conservative modifications thereof.

16. The antibody of any of claims 11 to 15, wherein the light chain variable region CDR1 sequence comprises an amino acid sequence selected from a group consisting of amino acid sequences of SEQ ID NOs: 14, 15, 16, 17 and 18, and conservative modifications thereof

17. The antibody of any one of claims 1 to 16, wherein the antibody is chimeric or humanized or human antibody.

18. The antibody of any one of claim 6 to 17, wherein the antibody exhibits at least one of the following properties:

a) binds to human PD-1 with a KD of 2.15E-10 M or less and to mouse PD-1 with a KD of 1.67E-08 M or less;

b) does not substantially bind to human CD28, CTLA-4;

c) increases T-cell proliferation;

d) increases interferon-gamma production; or

e) increases interleukin-2 secretion.

19. A nucleic acid molecule encoding the antibody or the antigen binding fragment of anyone of claims 1 to 18.

20. A cloning or expression vector comprising the nucleic acid molecule of claim 19.

21. A host cell comprising one or more cloning or expression vectors of claim 20.

22. A process for the production of the antibody of any one of claims 1 to 18, comprising culturing the host cell of claim 21 and isolating the antibody.

23. The process of claims 22, wherein the antibody is prepared through immunization in SD rat with human PD-1 extracellular domain and mouse PD-1 extracellular domain.

24. A transgenic rat comprising human immunoglobulin heavy and light chain transgenes, wherein the mouse expresses the antibody of any one of claims 1 to 18.

25. A hybridoma prepared from the rat of claim 24, wherein the hybridoma produces said antibody.

26. A pharmaceutical composition comprising the antibody, or the antigen binding fragment of any one of claims 1 to 18, and one or more of a pharmaceutically acceptable excipient, diluent or carrier.

27. An immunoconjugate comprising the antibody, or antigen-binding fragment thereof, according to any one of claims 1 to 18, linked to a therapeutic agent.

28. A pharmaceutical composition comprising the immunoconjugate of claim 27 and a pharmaceutically acceptable excipient, diluent or carrier.

29. A method for preparing an anti-PD-1 antibody or an antigen-binding fragment thereof comprising:

(a) providing:

(i) a heavy chain variable region antibody sequence comprising a CDR1 sequence that is selected from a group consisting of SEQ ID NO: 10, a CDR2 sequence that is selected from a group consisting of SEQ ID NO: 11; and a CDR3 sequence that is selected from the group consisting of SEQ ID NOs: 12 and 13; and/or

(ii) a light chain variable region antibody sequence comprising a CDR1 sequence that is selected from the group consisting of SEQ ID NOs: 14, 15, 16, 17 and 18, a CDR2 sequence that is selected from the group consisting of SEQ ID NO: 19, and a CDR3 sequence that is selected from the group consisting of 30 SEQ ID NOs: 20, 21, 22 and 23; and

(b) expressing the altered antibody sequence as a protein.

30. Use of the antibody, or antigen binding fragment of any one of claims 1 to 18 in the manufacture of a medicament for modulating an immune response in a subject, wherein the medicament is to be administered to the subject.

31. The use of the antibody any one of claims 1 to 18 in the manufacture of a medicament for the treatment or prophylaxis of an immune disorder or cancer.

32. Use of a therapeutically effective amount of the antibody, or the antigen-binding fragment of any one of claims 1-17 in the manufacture of a medicament for inhibiting growth of tumor cells in a subject, wherein the medicament is to be administered to the subject.

33. The use of claim 32, wherein the tumor cells are of a cancer selected from a group consisting of melanoma, renal cancer, prostate cancer, breast cancer, colon cancer, lung cancer, bone cancer, pancreatic cancer, skin cancer, cancer of the head or neck, cutaneous or intraocular malignant melanoma, uterine cancer, ovarian cancer, and rectal cancer.

34. The use of any one of claims 32 or 33, wherein the antibody is a chimeric antibody or humanized antibody.