

Claims

1. An isolated antibody that specifically binds PD-1 or an antigen binding fragment thereof, comprising a heavy chain complementarity determining region 1 (HCDR1), a HCDR2, a HCDR3, a light chain complementarity determining region 1 (LCDR1), a LCDR2 and a LCDR3 of SEQ ID NOs: 2, 165, 4, 166, 6 and 7, respectively.
2. The antibody or the antigen binding fragment thereof of claim 1, wherein the antibody or the antigen binding fragment thereof has one, two, three, four or five of the following properties: a) does not block PD-L1 binding to PD-1; wherein lack of blocking is measured by inability of the antibody to inhibit clustering of PD-L1 expressing and PD-1 expressing cells as described in Example 1; b) binds PD-1 with an equilibrium dissociation constant (K_D) of about 5×10^{-8} M or less, wherein the K_D is measured using a ProteOn XPR36 system at +25° C.; c) binds PD-1 with an association constant (k_a) of about 3×10^4 l/Ms or more, wherein the k_a is measured using a ProteOn XPR36 system at +25° C.; d) binds PD-1 with a dissociation constant (k_d) of about 3×10^{-3} l/s or less, wherein the k_d is measured using a ProteOn XPR36 system at +25° C.; or e) inhibits proliferation of antigen specific T cells; wherein proliferation is assessed in a CMV-PBMC assay measured by inhibition of cell proliferation upon treatment of CMV-reactive donors' PBMC with CMV peptide mix.
3. The antibody or the antigen binding fragment thereof of claim 2, comprising the HCDR2 of SEQ ID NOs: 3, 145, 146 or 147 and/or the LCDR1 of SEQ ID NOs: 5, 148 or 149.
4. The antibody or the antigen binding fragment thereof of claim 3, comprising the HCDR1, the HCDR2, the HCDR3, the LCDR1, the LCDR2 and the LCDR3 of a) SEQ ID NOs: 2, 3, 4, 5, 6 and 7, respectively; b) SEQ ID NOs: 2, 145, 4, 5, 6, and 7, respectively; c) SEQ ID NOs: 2, 146, 4, 5, 6, and 7, respectively; d) SEQ ID NOs: 2, 147, 4, 5, 6, and 7, respectively; e) SEQ ID NOs: 2, 3, 4, 148, 6 and 7, respectively; f) SEQ ID NOs: 2, 3, 4, 149, 6 and 7, respectively; g) SEQ ID NOs: 2, 145, 4, 148, 6 and 7, respectively; h) SEQ ID NOs: 2, 146, 4, 148, 6 and 7, respectively; i) SEQ ID NOs: 2, 147, 4, 148, 6 and 7, respectively; j) SEQ ID NOs: 2, 145, 4, 149, 6 and 7, respectively; k) SEQ ID NOs: 2, 146, 4, 149, 6 and 7, respectively; or l) SEQ ID NOs: 2, 147, 4, 149, 6 and 7, respectively.
5. The antibody or the antigen binding fragment thereof of claim 4, comprising a) a heavy chain variable region (VH) framework derived from IGHV7-4-1*1 (SEQ ID NO: 125); b) a light chain variable region (VL) framework derived from IGKV3D-20*1 (SEQ ID NO: 126); or c) the VH framework derived from IGHV7-4-1*1 (SEQ ID NO: 125) and the VL framework derived from IGKV3D-20*1 (SEQ ID NO: 126).
6. The antibody or the antigen binding fragment thereof of claim 5, comprising a) a heavy chain variable region (VH) of SEQ ID NO: 118; b) a light chain variable region (VL) of SEQ ID NO: 119; or c) the VH and the VL of SEQ ID NOs: 118 and 119, respectively.
7. The antibody or the antigen binding fragment thereof of claim 6, comprising the VH of SEQ ID NO: 10 and the VL of SEQ ID NO: 16.
8. The antibody or the antigen binding fragment thereof of claim 1, comprising a) the HCDR1, the HCDR2, the HCDR3, the LCDR1, the LCDR2 and the LCDR3 of SEQ ID NOs: 2, 3, 4, 5, 6 and 7, respectively; b) the VH of SEQ ID NO: 10 and the VL of SEQ ID NO: 16; and/or c) a heavy chain (HC) of SEQ ID NO: 22 and a light chain (LC) of SEQ ID NO: 28.
9. The antibody or the antigen binding fragment thereof of claim 1, wherein the antibody or the

antigen binding fragment thereof is an agonist of PD-1 or mediates antibody-dependent cell cytotoxicity (ADCC) of PD-1 expressing cells, or both.

10. The antibody or the antigen binding fragment thereof of claim 9, wherein the PD-1 expressing cells are activated memory T cells, T follicular helper cells (T_{FH}) or T peripheral helper cells (T_{PH}), or any combination thereof.

11. The antibody or the antigen binding fragment thereof of claim 10, wherein the antibody or the antigen binding fragment thereof is an IgG1, an IgG2, and IgG3 or an IgG4 isotype.

12. The antibody or the antigen binding fragment thereof of claim 11, wherein the antibody or the antigen binding fragment thereof comprises at least one mutation in the antibody Fc that modulates binding of the antibody to an Fc receptor (FcR).

13. The antibody or the antigen binding fragment thereof of claim 12, wherein the at least one mutation in the antibody Fc, using residue numbering according to the EU index, comprises: a) a S267E mutation in the antibody Fc region; b) a S267D mutation in the antibody Fc region; c) a S267E/I332E mutation in the antibody Fc region; d) a S267E/L328F mutation in the antibody Fc region; e) a G236D/S267E mutation in the antibody Fc region; f) a P238D mutation in the antibody Fc region; or g) a P238D/E233D/G237D/H268D/P271G/A330R mutation in the antibody Fc region.

14. The antibody or the antigen binding fragment thereof of claim 7, wherein the antibody comprises the HC of SEQ ID NO: 22 and the LC of SEQ ID NO: 28.

15. The antibody or the antigen binding fragment thereof of claim 14, wherein the antibody VH and the antibody VL or the antibody HC and the antibody LC are encoded by a polynucleotide comprising the polynucleotide sequence of SEQ ID NOs: 13 and 19, respectively.

16. The antibody or the antigen binding fragment thereof of claim 1, wherein the antibody or the antigen binding fragment thereof has a biantennary glycan structure with a fucose content of about between 1% to about 15%.

17. A pharmaceutical composition comprising the antibody or the antigen binding fragment thereof of claim 1.

18. A kit comprising the antibody or the antigen binding fragment thereof of claim 1.

19. An immunoconjugate comprising the antibody or the antigen binding fragment of claim 7 conjugated to a heterologous molecule.