

CLAIMS

1. An isolated human monoclonal antibody or antigen-binding fragment thereof that binds specifically to human programmed death-1 (PD-1) protein, wherein the antibody or antigen-binding fragment thereof comprises three heavy chain complementarity determining regions (CDRs) (HCDR1, HCDR2 and HCDR3) contained within a heavy chain variable region (HCVR) sequence of SEQ ID NO:162; and three light chain CDRs (LCDR1, LCDR2 and LCDR3) contained within a light chain variable region (LCVR) sequence of SEQ ID NO:170.
2. The isolated antibody or antigen-binding fragment thereof of claim 1, comprising:
 - (a) a HCDR1 domain having an amino acid sequence of SEQ ID NO:164;
 - (b) a HCDR2 domain having an amino acid sequence of SEQ ID NO:166;
 - (c) a HCDR3 domain having an amino acid sequence of SEQ ID NO:168;
 - (d) a LCDR1 domain having an amino acid sequence of SEQ ID NO:172;
 - (e) a LCDR2 domain having an amino acid sequence of SEQ ID NO:174; and
 - (f) a LCDR3 domain having an amino acid sequence of SEQ ID NO:176.
3. The isolated antibody or antigen-binding fragment thereof of claim 2, wherein the antibody or antigen-binding fragment thereof comprises a HCVR/LCVR amino acid sequence pair of SEQ ID NO:162/170.
4. The isolated antibody or antigen-binding fragment thereof of claim 2, wherein the antibody or antigen-binding fragment thereof has one or more of the following properties:
 - (a) blocks human PD-1 protein binding to PD-L1 with an IC_{50} of less than 3 nM as measured in a competition sandwich ELISA assay at 25° C.;
 - (b) binds monomeric human PD-1 with a binding dissociation equilibrium constant (K_D) of less than about 50 nM as measured in a surface plasmon resonance assay at 37° C.;
 - (c) binds monomeric human PD-1 with a K_D less than about 12 nM in a surface plasmon resonance assay at 25° C.;
 - (d) binds monomeric cynomolgus PD-1 with a K_D less than about 8.5 nM in a surface plasmon resonance assay at 25° C.;

- (e) binds monomeric human PD-1 with a dissociative half-life ($t_{1/2}$) of greater than about 6.3 minutes as measured in a surface plasmon resonance assay at 25° C.; and
 - (f) binds monomeric human PD-1 with a dissociative half-life ($t_{1/2}$) of greater than about 0.9 minutes as measured in a surface plasmon resonance assay at 37° C.
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- 5. The isolated antibody or antigen-binding fragment of claim 4, wherein the antibody or antigen-binding fragment thereof comprises a heavy chain and a light chain, wherein the heavy chain comprises an amino acid sequence of SEQ ID NO:330.
 - 6. The isolated antibody or antigen-binding fragment of claim 4, wherein the antibody or antigen-binding fragment thereof comprises a heavy chain and a light chain, wherein the light chain comprises an amino acid sequence of SEQ ID NO:331.
 - 7. The isolated antibody or antigen-binding fragment of claim 6, wherein the antibody or antigen-binding fragment thereof comprises a heavy chain/light chain amino acid sequence pair of SEQ ID NO:330/331.
 - 8. A pharmaceutical composition comprising an isolated human monoclonal antibody or antigen-binding fragment thereof that binds PD-1 according to claim 1, and a pharmaceutically acceptable carrier or diluent.
 - 9. An isolated human monoclonal antibody or antigen-binding fragment thereof that binds specifically to human programmed death-1 (PD-1) protein, wherein the antibody or antigen-binding fragment thereof comprises a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO: 162, and a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO: 170.
 - 10. An isolated human monoclonal antibody or antigen-binding fragment thereof that binds specifically to human programmed death-1 (PD-1) protein, wherein the antibody or antigen-binding fragment thereof comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 330, and a light chain comprising the amino acid sequence of SEQ ID NO: 331.