tissues and cell types, including antigen-presenting cells of the immune system, and are upregulated on many types of tumor cells. Upregulation of PD-L1 within the tumor microenvironment is a proposed mechanism of tumors to subvert protective anti-tumor immune responses by the host. Antibodies directed at PD-1 that block the interaction of the receptor with either of its ligands result in inhibition of negative signaling. In vitro inhibition of the PD-1 mediated checkpoint signal has been demonstrated to result in prolonged antigen-specific T cell activation. In vivo PD-1 blockade has been shown to enhance anti-tumor immune responses in both syngeneic mouse tumor models and in human clinical trials.

[0008] Anti-tumor immune responses in patients with solid tumors have been enhanced by anti-PD-1 treatment. There are two approved and marketed antagonistic anti-PD-1 monoclonal antibodies: nivolumab (OPDIVO®) and pembrolizumab (KEYTRUDA®), with approvals in the US and the European Union to treat diseases such as unresectable or metastatic melanoma and metastatic non-small cell lung cancer. Treatment of patients with these agents has resulted in anti-tumor responses as measured by improvement in either progression free survival and/or overall survival.

[0009] The recent failure of OPDIVO® to slow progression of advanced lung cancer in a treatment-naïve patient population in a clinical trial comparing OPDIVO® with conventional chemotherapy highlights the need for alternative approaches and additional cancer treatments to complement existing therapeutic standards of care.

5. SUMMARY

[0009a] In one aspect, provided herein is an anti-human PD-1 antibody, wherein the antibody comprises (i) a V_H chain comprising three CDRs; and (ii) a V_L chain comprising three CDRs, wherein:

V_H CDR#1 is GYTFTHYGMN (SEQ ID NO:11);
V_H CDR#2 is WVNTYTGEPTYADDFKG (SEQ ID NO:12);
V_H CDR#3 is EGEGLGFGD (SEQ ID NO:13);
V_L CDR#1 is RSSQSIVHSHGDTYLE (SEQ ID NO:14);
V_L CDR#2 is KVSNRFS (SEQ ID NO:15); and
V_L CDR#3 is FQGSHIPVT (SEQ ID NO:16).

[0009b] In one aspect, provided herein is one or more nucleic acids comprising nucleotide sequences encoding the anti-human PD-1 antibody.

[0009c] In one aspect, provided herein is one or more vectors comprising the one or more nucleic acids as described herein.

[0009d] In one aspect, provided herein is a host cell transformed with the one or more vectors as described herein, wherein the host cell is: a) prokaryotic; or b) eukaryotic, optionally wherein the host cell is a mammalian host cell.

[0009e] In one aspect, provided herein is a method of producing an anti-human PD-1 antibody, comprising: (a) culturing the host cell of claim 12 and (b) recovering the anti-human PD-1 antibody.

[0010] The present disclosure provides anti-PD-1 antibodies and binding fragments thereof that specifically bind to PD-1. The amino acid sequences of exemplary CDRs, as well as the amino acid sequence of the V_H and V_L regions of the heavy and light chains of exemplary anti-PD-1 antibodies are provided in the Detailed Description below. Antibodies provided herein interfere with the interaction of the PD-1 receptor with either of its ligands (PD-L1, SEQ ID NO:3; PD-L2, SEQ ID NO:4), resulting in inhibition of negative signaling and upregulation of the adaptive immune response.

[0011] The anti-PD-1 antibodies may include modifications and/or mutations that alter the properties of the antibodies, such as increase half-life, increase or decrease ADCC, etc., as is known in the art.

[0012] Nucleic acids comprising nucleotide sequences encoding the anti-PD-1 antibodies of the disclosure are provided herein, as are vectors comprising nucleic acids. Additionally, prokaryotic and eukaryotic host cells transformed with a vector comprising a nucleotide sequence encoding a

WHAT IS CLAIMED IS:

1. An anti-human PD-1 antibody, wherein the antibody comprises (i) a V_H chain comprising three CDRs; and (ii) a V_L chain comprising three CDRs, wherein:

   V_H CDR#1 is GYTFTHYGMN (SEQ ID NO:11);

   V_H CDR#2 is WVNTYTGEPTYADDFKG (SEQ ID NO:12);

   V_H CDR#3 is EGEGLGFGD (SEQ ID NO:13);

   V_L CDR#1 is RSSQSIVHSHGDTYLE (SEQ ID NO:14);

   V_L CDR#2 is KVSNRFS (SEQ ID NO:15); and

   V_L CDR#3 is FQGSHIPVT (SEQ ID NO:16).

2. The anti-human PD-1 antibody of claim 1, which is humanized.

3. The anti-human PD-1 antibody of claim 2, which comprises a V_H chain corresponding in sequence to SEQ ID NO:36; and a V_L chain corresponding in sequence to SEQ ID NO:42.

4. The anti-human PD-1 antibody of claim 3 which is an IgG_1 and comprises a variant CH2 domain having amino acid substitutions L234A and L235A.

5. The anti-human PD-1 antibody of claim 3, which is an IgG_4 and comprises a variant Fc region having an amino acid substitution S228P.

6. The anti-human PD-1 antibody of claim 3 which is an IgG and comprises a kappa light constant region.

7. The anti-human PD-1 antibody of claim 3 which comprises a heavy chain corresponding in sequence to SEQ ID NO:51 or SEQ ID NO:52, and a light chain corresponding in sequence to SEQ ID NO:61.

8. The anti-human PD-1 antibody of claim 1, which is an IgG antibody consisting of heavy chains each consisting of the amino acid sequence of SEQ ID NO:51 and light chains each consisting of the amino acid sequence of SEQ ID NO:61.

9. The anti-human PD-1 antibody of claim 1, which is an IgG antibody consisting of heavy chains each consisting of the amino acid sequence of SEQ ID NO:52 and light chains each consisting of the amino acid sequence of SEQ ID NO:61.

10. One or more nucleic acids comprising nucleotide sequences encoding the anti-human PD-1 antibody of any one of claims 1 to 9.

11. One or more vectors comprising the one or more nucleic acids of claim 10.

12. A host cell transformed with the one or more vectors of claim 11, wherein the host cell is:

    a) prokaryotic; or

    b) eukaryotic, optionally wherein the host cell is a mammalian host cell.

13. A method of producing an anti-human PD-1 antibody, comprising: (a) culturing the host cell of claim 12 and (b) recovering the anti-human PD-1 antibody.