

WHAT IS CLAIMED IS:

1. An isolated antibody that specifically binds to PD-L1, wherein the antibody binds to an epitope comprising amino acid residues 279-290 of human PD-L1 polypeptide (SEQ ID NO: 1).
2. The antibody of claim 1, wherein the antibody comprises the following hypervariable regions (HVRs):
 - (a) an HVR-H1 comprising the amino acid sequence of SNGLT (SEQ ID NO: 2);
 - (b) an HVR-H2 comprising the amino acid sequence of TINKDASAYYASWAKG (SEQ ID NO: 3); and
 - (c) an HVR-H3 comprising the amino acid sequence of IAFKTGTSI (SEQ ID NO: 4).
3. The antibody of claim 2, further comprising the following heavy chain variable domain framework regions (FRs):
 - (a) FR-H1 comprising the amino acid sequence of QSLEESGGRLVKPDETLTITCTVSGIDLS (SEQ ID NO: 5);
 - (b) FR-H2 comprising the amino acid sequence of WVRQAPGEGLEWIG (SEQ ID NO: 6);
 - (c) FR-H3 comprising the amino acid sequence of RLISKPSSTKVDLKITSPTTEDTATYFCGR (SEQ ID NO: 7); and
 - (d) FR-H4 comprising the amino acid sequence of WPGGTLVTVSS (SEQ ID NO: 8).
4. The antibody of claim 2 or 3, further comprising the following HVRs:
 - (a) an HVR-L1 comprising the amino acid sequence of QASESVYSNNYLS (SEQ ID NO: 9);
 - (b) an HVR-L2 comprising the amino acid sequence of LASTLAS (SEQ ID NO: 10); and
 - (c) an HVR-L3 comprising the amino acid sequence of IGGKSSTDGNA (SEQ ID NO: 11).
5. The antibody of claim 4, further comprising the following light chain variable domain FRs:
 - (a) FR-L1 comprising the amino acid sequence of AIVMTQTPSPVSAVGGTVTINC (SEQ ID NO: 12);
 - (b) FR-L2 comprising the amino acid sequence of WFQQKPGQPPKLLIY (SEQ ID NO: 13);
 - (c) FR-L3 comprising the amino acid sequence of GVPSRFKGSQSGTQFTLTISGVQCDDAATYYC (SEQ ID NO: 14); and
 - (d) FR-L4 comprising the amino acid sequence of FGGGTEVVVR (SEQ ID NO: 15).
6. The antibody of claim 1, wherein the antibody comprises the following HVRs:
 - (a) an HVR-L1 comprising the amino acid sequence of QASESVYSNNYLS (SEQ ID NO: 9);
 - (b) an HVR-L2 comprising the amino acid sequence of LASTLAS (SEQ ID NO: 10); and
 - (c) an HVR-L3 comprising the amino acid sequence of IGGKSSTDGNA (SEQ ID NO: 11).

7 The antibody of claim 6, further comprising the following light chain variable domain FRs:

- (a) FR-L1 comprising the amino acid sequence of AIVMTQTPSPVSAAVGGTVTINC (SEQ ID NO: 12);
- (b) FR-L2 comprising the amino acid sequence of WFQQKPGQPPKLLIY (SEQ ID NO: 13);
- (c) FR-L3 comprising the amino acid sequence of GVPSRFKGS GSGTQFTLTISGVQCDDAATYYC (SEQ ID NO: 14); and
- (d) FR-L4 comprising the amino acid sequence of FGGGTEVVVR (SEQ ID NO: 15).

8. The antibody of claim 1, comprising (a) a VH sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 16; (b) a VL sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 17; or (c) a VH sequence as in (a) and a VL sequence as in (b).

9. The antibody of claim 8, comprising a VH sequence of SEQ ID NO: 16.

10. The antibody of claim 8, comprising a VL sequence of SEQ ID NO: 17.

11. An isolated antibody that specifically binds PD-L1, wherein the antibody comprises the following HVRs:

- (a) an HVR-H1 comprising the amino acid sequence of SNGLT (SEQ ID NO: 2);
- (b) an HVR-H2 comprising the amino acid sequence of TINKDASYYASWAKG (SEQ ID NO: 3);
- (c) an HVR-H3 comprising the amino acid sequence of IAFKTGTSTI (SEQ ID NO: 4);
- (d) an HVR-L1 comprising the amino acid sequence of QASESVYSNNYLS (SEQ ID NO: 9);
- (e) an HVR-L2 comprising the amino acid sequence of LASTLAS (SEQ ID NO: 10); and
- (f) an HVR-L3 comprising the amino acid sequence of IGGKSSSTDGNA (SEQ ID NO: 11).

12. The antibody of claim 11, wherein the antibody further comprises the following heavy chain variable domain and light chain variable domain FRs:

- (a) FR-H1 comprising the amino acid sequence of QSLEESGGRLVKPDETLTITCTVSGIDLS (SEQ ID NO: 5);
- (b) FR-H2 comprising the amino acid sequence of WVRQAPGEGLEWIG (SEQ ID NO: 6);
- (c) FR-H3 comprising the amino acid sequence of RLTISKPSSTKVDLKITSPTTEDTATYFCGR (SEQ ID NO: 7);
- (d) FR-H4 comprising the amino acid sequence of WPGGTLVTVSS (SEQ ID NO: 8);
- (e) FR-L1 comprising the amino acid sequence of AIVMTQTPSPVSAAVGGTVTINC (SEQ ID NO: 12);
- (f) FR-L2 comprising the amino acid sequence of WFQQKPGQPPKLLIY (SEQ ID NO: 13);
- (g) FR-L3 comprising the amino acid sequence of GVPSRFKGS GSGTQFTLTISGVQCDDAATYYC (SEQ ID NO: 14); and
- (h) FR-L4 comprising the amino acid sequence of FGGGTEVVVR (SEQ ID NO: 15).

13. The antibody of claim 11 or 12, wherein the antibody comprises a VH sequence of SEQ ID NO: 16 and a VL sequence of SEQ ID NO: 17.
14. An isolated antibody that competes for binding to PD-L1 with the antibody of any one of claims 1-13.
15. An isolated antibody that binds to the same epitope as the antibody of any one of claims 1-13.
16. The antibody of any one of claims 1-15, wherein the antibody is a monoclonal antibody.
17. The antibody of claim 16, wherein the monoclonal antibody is a rabbit monoclonal antibody.
18. The antibody of any one of claims 1-15, wherein the antibody is an IgG antibody.
19. The antibody of any one of claims 1-15, wherein the antibody is an antibody fragment that specifically binds PD-L1.
20. The antibody of claim 19, wherein the antibody fragment is selected from the group consisting of Fab, single chain variable fragment (scFv), Fv, Fab', Fab'-SH, F(ab')₂, and diabody.
21. An isolated nucleic acid encoding an isolated antibody of any one of claims 1-20.
22. A vector comprising the nucleic acid of claim 21.
23. A host cell comprising the vector of claim 22.
24. An immunoconjugate comprising the antibody of any one of claims 1-20.
25. The antibody of any one of claims 1-20 for use in detecting the presence or expression level of PD-L1 in a biological sample.
26. The antibody of claim 25, wherein the detecting is by immunohistochemistry (IHC), immunofluorescence (IF), flow cytometry, Enzyme-Linked Immunosorbant Assay (ELISA), or immunoblotting.
27. The antibody of claim 26, wherein the detecting is by IHC.
28. The antibody of any one of claims 25-27, wherein the sample comprises a fixed tissue.

29. The antibody of claim 28, wherein the fixed tissue is a formalin-fixed paraffin-embedded (FFPE) tissue.

30. The antibody of any one of claims 25-29, wherein the sample is from a subject having, or at risk of, a cancer or an immune dysfunction.

31. The antibody of claim 30, wherein the immune dysfunction is a T-cell dysfunctional disorder.

32. The antibody of claim 31, wherein the T-cell dysfunctional disorder is an unresolved acute infection, chronic infection, or tumor immunity.

33. A method of detecting the presence or expression level of PD-L1 in a biological sample comprising contacting the biological sample with the antibody of any one of claims 1-20 and detecting the presence of the bound antibody.

34. The method of claim 33, wherein the detecting is by IHC, IF, flow cytometry, ELISA, or immunoblotting.

35. The method of claim 34, wherein the detecting is by IHC.

36. The method of any one of claims 33-35, wherein the sample comprises a fixed tissue.

37. The method of claim 36, wherein the fixed tissue is a FFPE tissue.

38. The method of any one of claims 33-37, wherein the sample is from a subject having, or at risk of, a cancer or an immune dysfunction.

39. The method of claim 38, wherein the immune dysfunction is a T-cell dysfunctional disorder.

40. The method of claim 39, wherein the T-cell dysfunctional disorder is an unresolved acute infection, chronic infection, or tumor immunity.

41. The method of claim 38, wherein the sample is from a subject having a cancer.

42. The method of any one of claims 33-41, wherein the presence or expression level of PD-L1 in the sample indicates that the subject is likely to respond to treatment with an anti-cancer therapy.

43. The method of any one of claims 33-41, wherein the presence or expression level of PD-L1 in the sample indicates that the subject is more likely to respond to treatment with an anti-cancer therapy.

44. The method of any one of claims 33-41, wherein the presence or expression level of PD-L1 in the sample indicates the likelihood that the subject will exhibit benefit from treatment with an anti-cancer therapy.

45. The method of any one of claims 41-44, wherein the method further comprises selecting an anti-cancer therapy for the subject based on the presence or expression level of PD-L1 in the sample.

46. The method of any one of claims 41-45, wherein the method further comprises administering a therapeutically effective amount of an anti-cancer therapy to the subject.

47. The method of any one of claims 38 and 41-46, wherein the cancer is selected from the group consisting of non-small cell lung cancer, squamous cell cancer, small-cell lung cancer, cancer of the peritoneum, hepatocellular cancer, gastrointestinal cancer, pancreatic cancer, glioma, cervical cancer, ovarian cancer, liver cancer, bladder cancer, hepatoma, breast cancer, colon cancer, colorectal cancer, endometrial or uterine carcinoma, salivary gland carcinoma, kidney cancer, liver cancer, prostate cancer, vulval cancer, thyroid cancer, hepatic carcinoma, leukemia, and head and neck cancer.

48. The method of claim 47, wherein the cancer is non-small cell lung cancer (NSCLC).

49. The method of claim 48, wherein the NSCLC is adenocarcinoma of the lung or squamous carcinoma of the lung.

50. The method of any one of claims 38 and 41-49, wherein the sample is a tumor sample.

51. The method of claim 50, wherein the tumor sample comprises tumor-infiltrating immune cells, tumor cells, stromal cells, or any combination thereof.

52. The method of claim 51, wherein the tumor sample has a detectable expression level of PD-L1 in tumor-infiltrating immune cells that comprise about 1% or more of the tumor sample by area.

53. The method of claim 52, wherein the tumor sample has a detectable expression level of PD-L1 in tumor-infiltrating immune cells that comprise about 5% or more of the tumor sample by area.

54. The method of claim 53, wherein the tumor sample has a detectable expression level of PD-L1 in tumor-infiltrating immune cells that comprise about 10% or more of the tumor sample by area.

55. The method of any one of claims 50-54, wherein the tumor sample has a detectable expression level of PD-L1 in about 1% or more of the tumor cells in the tumor sample.

56. The method of claim 55, wherein the tumor sample has a detectable expression level of PD-L1 in about 5% or more of the tumor cells in the tumor sample.

57. The method of claim 56, wherein the tumor sample has a detectable expression level of PD-L1 in about 10% or more of the tumor cells in the tumor sample.

58. The method of any one of claims 46-57, wherein the anti-cancer therapy comprises a PD-1 axis binding antagonist.

59. The method of claim 58, wherein the PD-1 axis binding antagonist is selected from the group consisting of a PD-L1 binding antagonist, a PD-1 binding antagonist, and a PD-L2 binding antagonist.

60. The method of claim 59, wherein the PD-1 axis binding antagonist is a PD-L1 binding antagonist.

61. The method of claim 60, wherein the PD-L1 binding antagonist inhibits the binding of PD-L1 to one or more of its ligand binding partners.

62. The method of claim 61, wherein the PD-L1 binding antagonist inhibits the binding of PD-L1 to PD-1.

63. The method of claim 61, wherein the PD-L1 binding antagonist inhibits the binding of PD-L1 to B7-1.

64. The method of any one of claims 61-63, wherein the PD-L1 binding antagonist inhibits the binding of PD-L1 to both PD-1 and B7-1.

65. The method of any one of claims 60-64, wherein the PD-L1 binding antagonist is an antibody.

66. The method of claim 65, wherein the antibody is selected from the group consisting of: YW243.55.S70, MPDL3280A (atezolizumab), MDX-1105, and MEDI4736 (durvalumab), and MSB0010718C (avelumab).

67. The method of claim 59, wherein the PD-1 axis binding antagonist is a PD-1 binding antagonist.

68. The method of claim 67, wherein the PD-1 binding antagonist inhibits the binding of PD-1 to one or more of its ligand binding partners.

69. The method of claim 68, wherein the PD-1 binding antagonist inhibits the binding of PD-1 to PD-L1.

70. The method of claim 68, wherein the PD-1 binding antagonist inhibits the binding of PD-1 to PD-L2.

71. The method of any one of claims 68-70, wherein the PD-1 binding antagonist inhibits the binding of PD-1 to both PD-L1 and PD-L2.

72. The method of any one of claims 67-71, wherein the PD-1 binding antagonist is an antibody.

73. The method of claim 72, wherein the antibody is selected from the group consisting of: MDX 1106 (nivolumab), MK-3475 (pembrolizumab), CT-011 (pidilizumab), MEDI-0680 (AMP-514), PDR001, REGN2810, and BGB-108.

74. The method of any one of claims 67-71, wherein the PD-1 binding antagonist is an Fc-fusion protein.

75. The method of claim 74, wherein the Fc-fusion protein is AMP-224.

76. The method of any one of claims 46-75, further comprising administering to the patient an effective amount of a second therapeutic agent.

77. The method of claim 76, wherein the second therapeutic agent is selected from the group consisting of a cytotoxic agent, a growth-inhibitory agent, a radiation therapy agent, an anti-angiogenic agent, and combinations thereof.

78. The method of any one of claims 33-77, wherein the subject is a human.