Claims

1. A monoclonal antibody, or an antigen-binding portion thereof, which cross-competes for binding to human Programmed Death Ligand 1 (PD-L1) with a reference antibody or reference antigen-binding portion thereof comprising:

(a) a heavy chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:1 and a light chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:11;

(b) a heavy chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:2 and a light chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:12;

(c) a heavy chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:6 and a light chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:16;

(d) a heavy chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:7 and a light chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:17;

(e) a heavy chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:8 and a light chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:18;

(f) a heavy chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:9 and a light chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:19; or

(g) a heavy chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:10 and a light chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:20.

2. The monoclonal antibody or antigen-binding portion thereof of claim 1, wherein the reference antibody or reference antigen-binding portion thereof comprises a heavy chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:2 and a light chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:12.

3. The monoclonal antibody or an antigen-binding portion thereof of claim 1, comprising:
(a) a heavy chain variable region derived from a human VH 1-18 gene; and
(b) a light chain variable region derived from a human Vk L6 gene;
wherein the antibody specifically binds to PD-Ll.

4. The monoclonal antibody or an antigen-binding portion thereof of claim 1, comprising:
(a) a heavy chain variable region derived from a human VH 1-69 gene; and
(b) a light chain variable region derived from a human Vk L6 gene;
wherein the antibody specifically binds to PD-Ll.

5. The monoclonal antibody or an antigen-binding portion thereof of claim 1, comprising:
(a) a heavy chain variable region derived from a human VH 1-3 gene; and
(b) a light chain variable region derived from a human Vk L15 gene;
wherein the antibody specifically binds to PD-Ll.

6. The monoclonal antibody, or an antigen-binding portion thereof of claim 1, comprising:
(a) a heavy chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:27; (b) a heavy chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:37; (c) a heavy chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:47; (d) a light chain variable region CDR1 comprising amino acids having the sequence set forth in SEQ ID NO:57; (e) a light chain variable region CDR2 comprising amino acids having the sequence set forth in SEQ ID NO:67; and (f) a light chain variable region CDR3 comprising amino acids having the sequence set forth in SEQ ID NO:77;
wherein the antibody, or antigen-binding portion thereof, specifically binds to Programmed Death Ligand 1 (PD-L1).

7. The monoclonal antibody, or an antigen binding portion thereof of claim 1 comprising:
(a) a heavy chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:7, and (b) a light chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:17;
wherein the antibody or antigen-binding portion thereof specifically binds to Programmed Death Ligand 1 (PD-L1).

8. The antibody or antigen-binding portion thereof of any one of claims 1-7, which exhibits one or more properties selected from:
(a) increases T-cell proliferation in a mixed lymphocyte reaction (MLR) assay;
(b) increases interferon-γ production in an MLR assay; and
(c) increases IL-2 secretion in an MLR assay.

9. An immunoconjugate comprising the antibody, or antigen-binding portion thereof, of any one of claims 1-8, linked to a therapeutic agent.

10. The immunoconjugate of claim 9, wherein the therapeutic agent is a cytotoxin or a radioactive isotope.

11. A bispecific molecule comprising the antibody, or antigen-binding portion thereof, of any one of claims 1-8, linked to a second functional moiety having a different binding specificity than said antibody, or antigen-binding portion thereof.

12. A composition comprising (a) the monoclonal antibody, or antigen-binding portion thereof, of any one of claims 1-8; (b) the immunoconjugate of claim 9 or 10; or (c) the bispecific molecule of claim 11, and a pharmaceutically acceptable carrier.

13. An isolated nucleic acid encoding the antibody, or antigen-binding portion thereof, of any one of claims 1-8.

14. An expression vector comprising the nucleic acid of claim 13.

15. A host cell comprising the expression vector of claim 14.

16. A transgenic mouse comprising human immunoglobulin heavy and light chain transgenes, wherein the mouse expresses the antibody of any one of claims 1-8.

17. A hybridoma prepared from the mouse of claim 16, wherein the hybridoma produces said antibody, or antigen-binding portion thereof.

18. Use of the monoclonal antibody, or antigen-binding portion thereof, of any one of claims 1-8 for the preparation of a medicament for modulating an immune response in a subject.

19. Use of the monoclonal antibody, or antigen-binding portion thereof, of any one of claims 1-8 for the preparation of a medicament for inhibiting growth of tumor cells in a subject.

20. The use of claim 19, wherein the tumor cells are of a cancer selected from melanoma, renal cancer, prostate cancer, breast cancer, colon cancer and lung cancer.

21. The use of claim 19, wherein the tumor cells are of a cancer of the bladder.

22. The use of claim 19 wherein the tumor cells are of a cancer selected from the list consisting of bone cancer, pancreatic cancer, skin cancer, cancer of the head or neck, cutaneous or intraocular malignant melanoma, uterine cancer, ovarian cancer, rectal cancer, cancer of the anal region, stomach cancer, testicular cancer, uterine cancer, carcinoma of the fallopian tubes, carcinoma of the endometrium, carcinoma of the cervix, carcinoma of the vagina, carcinoma of the vulva, Hodgkin's Disease, non-Hodgkin's lymphoma, cancer of the esophagus, cancer of the small intestine, cancer of the endocrine system, cancer of the thyroid gland, cancer of the parathyroid gland, cancer of the adrenal gland, sarcoma of soft tissue, cancer of the urethra, cancer of the penis, chronic or acute leukemias including acute myeloid leukemia, chronic myeloid leukemia, acute lymphoblastic leukemia, chronic lymphocytic leukemia, solid tumors of childhood, lymphocytic lymphoma, cancer of the kidney or ureter, carcinoma of the renal pelvis, neoplasm of the central nervous system (CNS), primary CNS lymphoma, tumor angiogenesis, spinal axis tumor, brain stem glioma, pituitary adenoma, Kaposi's sarcoma, epidermoid cancer,

squamous cell cancer, T-cell lymphoma, environmentally induced cancers including those induced by asbestos, and combinations of said cancers.

23. Use of the monoclonal antibody, or antigen-binding portion thereof, of any one of claims 1-8 for the preparation of a medicament for treating an infectious disease in a subject.

24. The use of claim 23, wherein the infectious disease is

(a) a disease selected from the group consisting of Influenza, Herpes, Giardia, Malaria, and Leishmania;

(b) a pathogenic infection by a virus selected from the group consisting of human immunodeficiency virus (HIV), Hepatitis virus, herpes virus, adenovirus, influenza virus, flaviviruses, echovirus, rhinovirus, coxsackie virus, cornovirus, respiratory syncytial virus, mumps virus, rotavirus, measles virus, rubella virus, parvovirus, vaccinia virus, HTLV virus, dengue virus, papillomavirus, molluscum virus, poliovirus, rabies virus, JC virus and arboviral encephalitis virus;

(c) a pathogenic infection by a bacterium selected from the group consisting of chlamydia, rickettsial bacteria, mycobacteria, staphylococci, streptococci, pneumonococci, meningococci and conococci, klebsiella, proteus, serratia, pseudomonas, legionella, diphtheria, salmonella, bacilli, cholera, tetanus, botulism, anthrax, plague, leptospirosis, and Lyme's disease bacteria;

(d) a pathogenic infection by a fungus selected from the group consisting of Candida, Cryptococcus neoformans, Aspergillus, Mucorales, Sporothrix schenkii, Blastomyces dermatitidis, Paracoccidioides brasiliensis, Coccidioides immitis and Histoplasma capsulatum; and

(e) a pathogenic infection by a parasite selected from the group consisting of Entamoeba histolytica, Balantidium coli, Naegleriafowleri, Acanthamoeba sp., Giardia lambia, Cryptosporidium sp., Pneumocystis carinii, Plasmodium vivax, Babesia microti, Trypanosoma brucei, Trypanosoma cruzi, Leishmania donovani, Toxoplasma gondi, Nippostrongylus brasiliensis.

25. The use of claim 24, wherein:

(a) the Hepatitis virus is selected from Hepatitis A, Hepatitis B, Hepatitis C, and any combination thereof,

(b) the herpes virus is selected from VZV, HSV-1, HAV-6, HSV-II, CMV, Epstein Barr virus, and any combination thereof,

(c) the Candida fungus is selected from Candida albicans, Candida krusei, Candida glabrata, Candida tropicalis, and any combination thereof,

(d) the Aspergillus fungus is selected from the group consisting of Aspergillus fumigatus, Aspergillus niger, and any combination thereof, and/or

(e) the Mucorales fungus is selected from Mucor, Absidia, Rhizophus, and any combination thereof.

26. Use of the antibody, or antigen-binding portion thereof, of any one of claims 1-8 for the preparation of a medicament for enhancing an immune response to the antigen in a subject.

27. The use of claim 26, wherein the antigen is a tumor antigen, a viral antigen, a bacterial antigen or an antigen from a pathogen.

28. Use of the monoclonal antibody, or antigen-binding portion thereof, of any one of claims 1-8 for the preparation of a medicament for treating or preventing an inflammatory disease in a subject.

29. The use of claim 28, wherein the inflammatory disease is lichen planus (LP).