

CLAIMS

1. An antibody or antigen-binding fragment thereof that specifically binds to the human PD-L1 protein, wherein the antibody comprises heavy chain CDR sequences of SEQ ID NOs: 13-15 and light chain CDR sequences of SEQ ID NOs: 16-18.
2. The antibody of claim 1, wherein the antibody exhibits a binding affinity to the human PD-L1 protein that is between 3 and 300 nM.
3. The antibody of claim 1 or 2, wherein the antibody exhibits a binding affinity to the human PD-L1 protein that is between 3 and 15 nM.
4. The antibody of any of claims 1-3, wherein the antibody further exhibits a total internalization that is higher than the total internalization of an antibody comprising the heavy chain variable region sequence of SEQ ID NO: 1 and the light chain variable region sequence of SEQ ID NO: 2.
5. The antibody of claim 4, wherein the total internalization is between a 9% and 155% increase of AUC over the AUC of an antibody comprising the heavy chain variable region sequence of SEQ ID NO: 1 and the light chain variable region sequence of SEQ ID NO: 2.
6. The antibody of claim 5, wherein the total internalization is determined by a FabFluor internalization assay.
7. The antibody of any of claims 1-6, wherein the antibody further exhibits an x50 that is higher than the IC₅₀ of an antibody comprising the heavy chain variable region sequence of SEQ ID NO: 1 and the light chain variable region sequence of SEQ ID NO: 2.
8. The antibody of any of claims 1-7, wherein the antibody comprises a heavy chain variable region sequence having at least 80% sequence identity to SEQ ID NO: 11 and a light chain variable region sequence having at least 80% sequence identity to SEQ ID NO: 12.
9. The antibody of any of claims 1-8, wherein the antibody comprises a heavy chain variable region sequence having at least 90% sequence identity to SEQ ID NO: 11 and a light chain variable region sequence having at least 90% sequence identity to SEQ ID NO: 12.

10. The antibody of any of claims 1-9, wherein the antibody comprises a heavy chain variable region sequence having at least 95% sequence identity to SEQ ID NO: 11 and a light chain variable region sequence having at least 95% sequence identity to SEQ ID NO: 12.

11. The antibody of any of claims 1-10, wherein the antibody comprises a heavy chain variable region sequence of SEQ ID NO: 11 and a light chain variable region sequence of SEQ ID NO: 12.

12. The antibody of any of claims 1-11, wherein the antibody comprises a heavy chain of SEQ ID NO: 9 and a light chain of SEQ ID NO: 10.

13. The antibody of any of claims 1-12, wherein the fragment is a Fab, Fab', F(ab')₂, Fab'-SH, Fv, diabody, linear antibody, or single-chain antibody fragment.

14. The antibody of any of claims 1-13, wherein the antibody contains L234A and L235A mutations in the heavy chain of the antibody, wherein the residues are numbered according to EU numbering.

15. The antibody of any of claims 1-14, wherein the heavy chain constant region is of the IgG1 isotype.

16. The antibody of any of claims 1-15, wherein the antibody is a humanized or chimeric antibody.

17. The antibody of any of claims 1-16, wherein the antibody is conjugated to a MMAE or camptothecin via a linker.

18. The antibody of claim 17, wherein the antibody is conjugated to monomethyl auristatin E (MMAE).

19. The antibody of claim 18, wherein the antibody is conjugated to MMAE via an enzyme-cleavable linker unit.

20. The antibody of claim 19, wherein the enzyme-cleavable linker unit comprises a Val-Cit linker.

21. The antibody of any one of claims 18-20, wherein the antibody is conjugated to MMAE via a linker forming an antibody-drug conjugate having the structure:



22. The antibody of claim 21, wherein p is 4.
23. The antibody of claim 21, wherein p is 8.
24. The antibody of claim 17, wherein the antibody is conjugated to camptothecin.
25. The antibody of claim 24, wherein the antibody is conjugated to camptothecin via an enzyme-cleavable linker unit.
26. The antibody of claim 25, wherein the enzyme-cleavable linker unit comprises a Val-Lys-Gly linker.
27. The antibody of any one of claims 24-26, wherein the antibody is conjugated to camptothecin via a linker forming an antibody-drug conjugate having the structure:



28. The antibody of claim 27, wherein p is 4.
29. The antibody of claim 27, wherein p is 8.

30. A pharmaceutical composition that comprises a therapeutically effective amount of the antibody of any of claims 1-29 and a pharmaceutically acceptable excipient.
31. The antibody of any of claims 1-29 for use in therapy.
32. Use of the antibody of any of claims 1-29 in the manufacture of a medicament for treating cancer in a subject.
33. The use of claim 32, wherein the subject is a human subject.
34. The use of claim 32 or 33, wherein the cancer is melanoma, non-small cell lung cancer (NSCLC), small cell lung cancer (SCLC), head and neck cancer, triple negative breast cancer (TNBC), ovarian cancer, urothelial cancer, hepatocellular carcinoma (HCC), gastric cancer, or cervical cancer.
35. A nucleic acid encoding the antibody as defined by any one of claims 1-29.
36. A vector comprising the nucleic acid of claim 35.
37. A host cell comprising the nucleic acid of claim 36.
38. The host cell of claim 37, wherein the host cell is a Chinese hamster ovary (CHO) cell.
39. A method of producing an antibody or antigen-binding fragment thereof that specifically binds to the human PD-L1 protein, comprising culturing the host cell of claim 37 or 38 under a condition suitable for production of the antibody.
40. A method of producing an antibody drug-conjugate that specifically binds to the human PD-L1 protein, comprising culturing the host cell of claim 37 or 38 under a condition suitable for production of the antibody; and conjugating the antibody to a cytotoxic agent.
41. The method of claim 40, wherein the cytotoxic agent is MMAE or camptothecin.