

CLAIMS

1. An isolated antibody or antigen-binding fragment thereof which specifically binds to CD73 comprising an antibody V_L and an antibody V_H, wherein the V_L comprises the amino acid sequence comprising SEQ ID NO: 68; and wherein the V_H comprises the amino acid sequence comprising SEQ ID NO: 82.
2. An isolated antibody or antigen-binding fragment thereof which specifically binds to CD73 comprising a V_L and a V_H comprising VL-CDR1, VL-CDR2, VL-CDR3, VH-CDR1, VH-CDR2, and VH-CDR3, wherein VL-CDR1 comprises SEQ ID NO: 46, VL-CDR2 comprises SEQ ID NO: 51, VL-CDR3 comprises SEQ ID NO: 56, VH-CDR1 comprises SEQ ID NO: 36, VH-CDR2 comprises SEQ ID NO: 39, and VH-CDR3 comprises SEQ ID NO: 45.
3. The isolated antibody or antigen-binding fragment thereof according to either one of claims 1 or 2, which comprises a heavy chain constant region or fragment thereof.
4. A nucleic acid comprising a sequence encoding the isolated antibody or antigen-binding fragment thereof according to either one of claims 1 or 2.
5. A host cell comprising a nucleic acid sequence according to claim 4.
6. A method of making the isolated antibody or antigen-binding fragment thereof according to either one of claims 1 or 2, comprising (a) culturing the host cell of claim 4; and (b) isolating the antibody or antigen-binding fragment thereof.
7. The isolated antibody or antigen-binding fragment thereof according to either one of claims 1 or 2, which is an antagonist of CD73.
8. The isolated antibody or antigen-binding fragment thereof according to claim 7, wherein the CD73 is human CD73.
9. The isolated antibody or antigen-binding fragment thereof of claims 1 or 2 for use in treating a CD73-associated cancer.
10. The isolated antibody or antigen-binding fragment thereof for use according to claim 9, wherein the CD73-associated cancer is selected from the group consisting of colorectal cancer, pancreatic cancer, bladder cancer, leukemia, lymphoma, glioma, glioblastoma,

melanoma, ovarian cancer, thyroid cancer, esophageal cancer, prostate cancer, and breast cancer.

11. The isolated antibody or antigen-binding fragment thereof for use according to claim 9 additionally comprising the use in combination of a therapeutically effective amount of a second agent, which is an anti-cancer agent other than antibody recited in claim 9.

12. The isolated antibody or antigen-binding fragment thereof for use according to claim 11, wherein the combination is additively or synergistically effective.

13. The isolated antibody or antigen-binding fragment thereof for use according to claim 11, wherein the second agent specifically binds to PD-1 (programmed death 1 protein), PD-L1 (programmed death 1 protein ligand 1), PD-L2 (programmed death 1 protein ligand 2), or CTLA-4 (cytotoxic T lymphocyte antigen 4 protein).

14. The isolated antibody or antigen-binding fragment thereof for use according to claim 9, wherein the subject being treated for the CD73-associated cancer is identified as having a tumor that has increased expression of CD73 relative to a reference.

15. The isolated antibody or antigen-binding fragment thereof for use according to claim 14, wherein the subject is undergoing, has undergone, or will undergo an anti-PD-1, anti-PD-L1, or anti-CTLA4 therapy.

16. The use of the isolated antibody or antigen-binding fragment thereof of claims 1 or 2 in the manufacture of a medicament for treating a CD73-associated cancer.

17. The use according to claim 16, wherein the CD73-associated cancer is selected from the group consisting of colorectal cancer, pancreatic cancer, bladder cancer, leukemia, lymphoma, glioma, glioblastoma, melanoma, ovarian cancer, thyroid cancer, esophageal cancer, prostate cancer, and breast cancer.

18. The use according to claim 16 additionally comprising the use in combination of a therapeutically effective amount of a second agent, which is an anti-cancer agent other than antibody recited in claim 16.

19. The use according to claim 18, wherein the combination is additively or synergistically effective.

20. The use according to claim 18, wherein the second agent specifically binds to PD-1 (programmed death 1 protein), PD-L1 (programmed death 1 protein ligand 1), PD-L2 (programmed death 1 protein ligand 2), or CTLA-4 (cytotoxic T lymphocyte antigen 4 protein).
21. The use according to claim 16, wherein the subject being treated for the CD73-associated cancer is identified as having a tumor that has increased expression of CD73 relative to a reference.
22. The use according to claim 21, wherein the subject is undergoing, has undergone, or will undergo an anti-PD-1, anti-PD-L1, or anti-CTLA4 therapy.
23. A pharmaceutical formulation comprising an effective amount of an anti-CD73 antibody, or antigen binding fragment thereof and an anti-PD-L1 antibody, or an antigen binding fragment thereof, wherein the anti-CD73 antibody is MEDI9447, Phen0203 hIgG1, or an antigen binding fragment thereof.
24. The pharmaceutical formulation of claim 23, wherein the anti-PD-L1 is MEDI4736, BMS-936559, or MPDL3280A, or an antigen binding fragment thereof.
25. A pharmaceutical formulation comprising an effective amount of an anti-CD73 antibody, or an antigen binding fragment thereof and anti-CTLA4 antibody, or an antigen binding fragment thereof, wherein the anti-CD73 antibody is MEDI9447, Phen0203 hIgG1, or an antigen binding fragment thereof.
26. The pharmaceutical formulation of claim 25, wherein the anti-CTLA4 antibody is ipilimumab or tremelimumab (ticilimumab, CP-675,206) or an antigen binding fragment thereof.