

CLAIMS

1. A kit comprising (1) an anti-CD73 antibody or an antigen-binding fragment thereof, a conjugate comprising the anti-CD73 antibody or an antigen-binding fragment thereof, a fusion protein comprising the anti-CD73 antibody or an antigen-binding fragment thereof or a multispecific antibody comprising the anti-CD73 antibody or an antigen-binding fragment thereof, and

(2) anti-PD-1/CTLA-4 bispecific antibody, wherein the anti-PD-1/CTLA-4 bispecific antibody comprises the following CDRs:

HCDR1 consisting of the sequence represented by SEQ ID NO: 23,

HCDR2 consisting of the sequence represented by SEQ ID NO:24,

HCDR3 consisting of the sequence represented by SEQ ID NO: 25,

HCDR4 consisting of the sequence represented by SEQ ID NO: 26,

HCDR5 consisting of the sequence represented by SEQ ID NO: 27,

HCDR6 consisting of the sequence represented by SEQ ID NO: 28,

HCDR7 consisting of the sequence represented by SEQ ID NO: 29,

HCDR8 consisting of the sequence represented by SEQ ID NO: 30,

HCDR9 consisting of the sequence represented by SEQ ID NO:31,

LCDR1 consisting of the sequence represented by SEQ ID NO: 32,

LCDR2 consisting of the sequence represented by SEQ ID NO: 33,

LCDR3 consisting of the sequence represented by SEQ ID NO: 34,

wherein according to an IMGT numbering system, the anti-CD73 antibody comprises:

HCDR1, HCDR2 and HCDR3 of a heavy chain variable region set forth in SEQ ID NO: 2; and LCDR1, LCDR2 and LCDR3 of a light chain variable region set forth in SEQ ID NO: 4;

wherein the antigen-binding fragment is selected from Fab, Fab', F(ab')₂, Fv, Fab/c, single chain antibody, humanized antibody, chimeric antibody or bispecific antibody.

2. The kit according to claim 1, wherein CD73 is human CD73.

3. The kit according to claim 1, wherein according to the IMGT numbering system, the anti-CD73 antibody comprises:

HCDR1 consisting of an amino acid sequence set forth in SEQ ID NO: 15,

HCDR2 consisting of an amino acid sequence set forth in SEQ ID NO: 16,

HCDR3 consisting of an amino acid sequence set forth in SEQ ID NO: 17,

LCDR1 consisting of an amino acid sequence set forth in SEQ ID NO: 18,

LCDR2 consisting of an amino acid sequence set forth in SEQ ID NO: 19,

and

LCDR3 consisting of an amino acid sequence set forth in SEQ ID NO: 20.

4. The kit according to claim 1, wherein a heavy chain variable region of the anti-CD73 antibody consists of SEQ ID NO: 2, or a sequence having at least 85% sequence identity to SEQ ID NO: 2, and a light chain variable region of the anti-CD73 antibody consists of SEQ ID NO: 4 or a sequence having at least 90% sequence identity to SEQ ID NO: 4, or

a heavy chain variable region of the anti-CD73 antibody consists of SEQ ID NO: 6 or a sequence having at least 90% sequence identity to SEQ ID NO: 6, and a light chain variable region of the antibody consists of SEQ ID NO: 8, or a sequence having at least 93% sequence identity to SEQ ID NO: 8, or

a heavy chain variable region of the anti-CD73 antibody consists of SEQ ID NO: 10, or a sequence having at least 85% sequence identity to SEQ ID NO: 10, and a light chain variable region of the anti-CD73 antibody consists of SEQ ID NO: 12 or a sequence having at least 92% sequence identity to SEQ ID NO: 12, or

a heavy chain variable region of the anti-CD73 antibody consists of SEQ ID NO: 10, or a sequence having at least 85% sequence identity to SEQ ID NO: 10, and a light chain variable region of the anti-CD73 antibody consists of SEQ ID NO: 14 or a sequence having at least 90% sequence identity to SEQ ID NO: 14.

5. The kit according to claim 4, wherein
the heavy chain variable region of the anti-CD73 antibody is represented
by a sequence having at least 86% sequence identity to SEQ ID NO:2, or
the light chain variable region of the anti-CD73 antibody is represented by
a sequence having at least 91% sequence identity to SEQ ID NO:4, or
the heavy chain variable region of the anti-CD73 antibody is represented
by a sequence having at least 91% sequence identity to SEQ ID NO:6, or
the light chain variable region of the anti-CD73 antibody is represented by
a sequence having at least 94% sequence identity to SEQ ID NO:8, or
the heavy chain variable region of the anti-CD73 antibody is represented
by a sequence having at least 86% sequence identity to SEQ ID NO:10, or
the light chain variable region of the anti-CD73 antibody is represented by
a sequence having at least 93% sequence identity to SEQ ID NO:12, or
the light chain variable region of the anti-CD73 antibody is represented by
a sequence having at least 91% sequence identity to SEQ ID NO:14.

6. The kit according to claim 4, wherein
the heavy chain variable region of the anti-CD73 antibody is represented
by a sequence having at least 87% sequence identity to SEQ ID NO:2, or
the light chain variable region of the anti-CD73 antibody is represented by
a sequence having at least 92% sequence identity to SEQ ID NO:4, or
the heavy chain variable region of the anti-CD73 antibody is represented
by a sequence having at least 92% sequence identity to SEQ ID NO:6, or
the light chain variable region of the anti-CD73 antibody is represented by
a sequence having at least 95% sequence identity to SEQ ID NO:8, or
the heavy chain variable region of the anti-CD73 antibody is represented
by a sequence having at least 87% sequence identity to SEQ ID NO:10, or
the light chain variable region of the anti-CD73 antibody is represented by
a sequence having at least 94% sequence identity to SEQ ID NO:12, or
the light chain variable region of the anti-CD73 antibody is represented by

a sequence having at least 92% sequence identity to SEQ ID NO:14.

7. The kit according to claim 4, wherein

the heavy chain variable region of the anti-CD73 antibody is represented by a sequence having at least 88% sequence identity to SEQ ID NO:2, or

the light chain variable region of the anti-CD73 antibody is represented by a sequence having at least 93% sequence identity to SEQ ID NO:4, or

the heavy chain variable region of the anti-CD73 antibody is represented by a sequence having at least 93% sequence identity to SEQ ID NO:6, or

the light chain variable region of the anti-CD73 antibody is represented by a sequence having at least 96% sequence identity to SEQ ID NO:8, or

the heavy chain variable region of the anti-CD73 antibody is represented by a sequence having at least 88% sequence identity to SEQ ID NO:10, or

the light chain variable region of the anti-CD73 antibody is represented by a sequence having at least 95% sequence identity to SEQ ID NO:12, or

the light chain variable region of the anti-CD73 antibody is represented by a sequence having at least 93% sequence identity to SEQ ID NO:14.

8. The kit according to claim 4, wherein

the heavy chain variable region of the anti-CD73 antibody is represented by a sequence having at least 89% sequence identity to SEQ ID NO:2, or

the light chain variable region of the anti-CD73 antibody is represented by a sequence having at least 94% sequence identity to SEQ ID NO:4, or

the heavy chain variable region of the anti-CD73 antibody is represented by a sequence having at least 94% sequence identity to SEQ ID NO:6, or

the light chain variable region of the anti-CD73 antibody is represented by a sequence having at least 97% sequence identity to SEQ ID NO:8, or

the heavy chain variable region of the anti-CD73 antibody is represented by a sequence having at least 89% sequence identity to SEQ ID NO:10, or

the light chain variable region of the anti-CD73 antibody is represented by a sequence having at least 96% sequence identity to SEQ ID NO:12, or

the light chain variable region of the anti-CD73 antibody is represented by a sequence having at least 94% sequence identity to SEQ ID NO:14.

9. The kit according to claim 4, wherein

the heavy chain variable region of the anti-CD73 antibody is represented by a sequence having at least 90% sequence identity to SEQ ID NO:2, or

the light chain variable region of the anti-CD73 antibody is represented by a sequence having at least 95% sequence identity to SEQ ID NO:4, or

the heavy chain variable region of the anti-CD73 antibody is represented by a sequence having at least 95% sequence identity to SEQ ID NO:6, or

the light chain variable region of the anti-CD73 antibody is represented by a sequence having at least 98% sequence identity to SEQ ID NO:8, or

the heavy chain variable region of the anti-CD73 antibody is represented by a sequence having at least 90% sequence identity to SEQ ID NO:10, or

the light chain variable region of the anti-CD73 antibody is represented by a sequence having at least 97% sequence identity to SEQ ID NO:12, or

the light chain variable region of the anti-CD73 antibody is represented by a sequence having at least 95% sequence identity to SEQ ID NO:14.

10. The kit according to claim 4, wherein

the heavy chain variable region of the anti-CD73 antibody is represented by a sequence having at least 91% sequence identity to SEQ ID NO:2, or

the light chain variable region of the anti-CD73 antibody is represented by a sequence having at least 96% sequence identity to SEQ ID NO:4, or

the heavy chain variable region of the anti-CD73 antibody is represented by a sequence having at least 96% sequence identity to SEQ ID NO:6, or

the light chain variable region of the anti-CD73 antibody is represented by a sequence having at least 99% sequence identity to SEQ ID NO:8, or

the heavy chain variable region of the anti-CD73 antibody is represented by a sequence having at least 91% sequence identity to SEQ ID NO:10, or

the light chain variable region of the anti-CD73 antibody is represented by

a sequence having at least 98% sequence identity to SEQ ID NO:12, or
the light chain variable region of the anti-CD73 antibody is represented by
a sequence having at least 96% sequence identity to SEQ ID NO:14.

11. The kit according to claim 4, wherein
the heavy chain variable region of the anti-CD73 antibody is represented
by a sequence having at least 92% sequence identity to SEQ ID NO:2, or
the light chain variable region of the anti-CD73 antibody is represented by
a sequence having at least 97% sequence identity to SEQ ID NO:4, or
the heavy chain variable region of the anti-CD73 antibody is represented
by a sequence having at least 97% sequence identity to SEQ ID NO:6, or
the heavy chain variable region of the anti-CD73 antibody is represented
by a sequence having at least 92% sequence identity to SEQ ID NO:10, or
the light chain variable region of the anti-CD73 antibody is represented by
a sequence having at least 99% sequence identity to SEQ ID NO:12, or
the light chain variable region of the anti-CD73 antibody is represented by
a sequence having at least 97% sequence identity to SEQ ID NO:14.

12. The kit according to claim 4, wherein
the heavy chain variable region of the anti-CD73 antibody is represented
by a sequence having at least 93% sequence identity to SEQ ID NO:2, or
the light chain variable region of the anti-CD73 antibody is represented by
a sequence having at least 98% sequence identity to SEQ ID NO:4, or
the heavy chain variable region of the anti-CD73 antibody is represented
by a sequence having at least 98% sequence identity to SEQ ID NO:6, or
the heavy chain variable region of the anti-CD73 antibody is represented
by a sequence having at least 93% sequence identity to SEQ ID NO:10, or
the light chain variable region of the anti-CD73 antibody is represented by
a sequence having at least 98% sequence identity to SEQ ID NO:14.

13. The kit according to claim 4, wherein
the heavy chain variable region of the anti-CD73 antibody is represented

by a sequence having at least 94% sequence identity to SEQ ID NO:2, or
the light chain variable region of the anti-CD73 antibody is represented by
a sequence having at least 99% sequence identity to SEQ ID NO:4, or
the heavy chain variable region of the anti-CD73 antibody is represented
by a sequence having at least 99% sequence identity to SEQ ID NO:6, or
the heavy chain variable region of the anti-CD73 antibody is represented
by a sequence having at least 94% sequence identity to SEQ ID NO:10, or
the light chain variable region of the anti-CD73 antibody is represented by
a sequence having at least 99% sequence identity to SEQ ID NO:14.

14. The kit according to claim 4, wherein
the heavy chain variable region of the anti-CD73 antibody is represented
by a sequence having at least 95% sequence identity to SEQ ID NO:2, or
the heavy chain variable region of the anti-CD73 antibody is represented
by a sequence having at least 95% sequence identity to SEQ ID NO:10.

15. The kit according to claim 4, wherein
the heavy chain variable region of the anti-CD73 antibody is represented
by a sequence having at least 96% sequence identity to SEQ ID NO:2, or
the heavy chain variable region of the anti-CD73 antibody is represented
by a sequence having at least 96% sequence identity to SEQ ID NO:10.

16. The kit according to claim 4, wherein
the heavy chain variable region of the anti-CD73 antibody is represented
by a sequence having at least 97% sequence identity to SEQ ID NO:2, or
the heavy chain variable region of the anti-CD73 antibody is represented
by a sequence having at least 97% sequence identity to SEQ ID NO:10.

17. The kit according to claim 4, wherein
the heavy chain variable region of the anti-CD73 antibody is represented
by a sequence having at least 98% sequence identity to SEQ ID NO:2, or
the heavy chain variable region of the anti-CD73 antibody is represented
by a sequence having at least 98% sequence identity to SEQ ID NO:10.

18. The kit according to claim 4, wherein
the heavy chain variable region of the anti-CD73 antibody is represented by a sequence having at least 99% sequence identity to SEQ ID NO:2, or
the heavy chain variable region of the anti-CD73 antibody is represented by a sequence having at least 99% sequence identity to SEQ ID NO:10.

19. The kit according to claim 1 or 2, wherein
the heavy chain variable region of the anti-CD73 antibody is set forth in SEQ ID NO: 2, and the light chain variable region of the anti-CD73 antibody is set forth in SEQ ID NO: 4;

the heavy chain variable region of the anti-CD73 antibody is set forth in SEQ ID NO: 6, and the light chain variable region of the anti-CD73 antibody is set forth in SEQ ID NO: 8;

the heavy chain variable region of the anti-CD73 antibody is set forth in SEQ ID NO: 10, and the light chain variable region of the anti-CD73 antibody is set forth in SEQ ID NO: 12; or

the heavy chain variable region of the anti-CD73 antibody is set forth in SEQ ID NO: 10, and the light chain variable region of the anti-CD73 antibody is set forth in SEQ ID NO: 14.

20. The kit according to claim 1 or 2, wherein a heavy chain constant region of the anti-CD73 antibody is an Ig gamma-1 chain C region, ACCESSION: P01857; a light chain constant region is an Ig kappa chain C region, ACCESSION: P01834.

21. The kit according to claim 1 or 2, wherein a heavy chain constant region of the anti-CD73 antibody is represented by a sequence as set forth in SEQ ID NO:21, a light chain constant region of the anti-CD73 antibody is represented by a sequence as set forth in SEQ ID NO:22.

22. The kit according to claim 1 or 2, wherein the anti-CD73 antibody is a monoclonal antibody, a humanized antibody, a chimeric antibody or a bispecific antibody.

23. The kit according to claim 1 or 2, wherein the antigen-binding fragment is scFv.

24. The kit according to claim 1, wherein the conjugate comprises a conjugated moiety, wherein the conjugated moiety is a purification tag or a detectable label.

25. The kit according to claim 24, wherein the conjugate moiety is a His tag, a radioisotope, a fluorescent substance, a chemiluminescent substance, a colored substance, polyethylene glycol or an enzyme.

26. The kit according to claim 1 or 2, wherein the anti-PD-1/CTLA-4 bispecific antibody comprises a heavy chain amino acid sequence set forth in SEQ ID NO: 35 and a light chain amino acid sequence set forth in SEQ ID NO: 36.

27. A pharmaceutical composition, comprising (1) the anti-CD73 antibody or the antigen-binding fragment thereof as defined in any one of claims 1 to 23, the conjugate as defined in any one of claims 1, 24 and 25, or the fusion protein or the multispecific antibody as defined in claim 1, and (2) an anti-PD-1/CTLA-4 bispecific antibody as defined in claim 1 or 26.

28. The pharmaceutical composition according to claim 27, wherein the pharmaceutical composition further comprises a pharmaceutically acceptable carrier and/or excipient.

29. The pharmaceutical composition according to claim 27 or 28, wherein the pharmaceutical composition is in a form suitable for administration by subcutaneous injection, intradermal injection, intravenous injection, intramuscular injection or intralesional injection.

30. Use of the antibody or the antigen-binding fragment thereof as defined in any one of claims 1 to 23, the conjugate as defined in any one of claim 1, 24 and 25, or the fusion protein or the multispecific antibody as defined in claim 1 in the manufacture of a medicament for treating a tumor or in the manufacture of a medicament for diagnosing a tumor.

31. Use according to claim 30, wherein the tumor is a solid tumor.

32. Use according to claim 30, wherein the tumor is non-small cell lung cancer, prostate cancer, triple-negative breast cancer, ovarian cancer, colorectal cancer, gastric cancer, melanoma, head and neck cancer, renal cell carcinoma or pancreatic ductal adenocarcinoma.

33. Use according to claim 32, wherein the prostate is metastatic castration-resistant prostate cancer (mCRPC),

colorectal cancer is microsatellite stability (MSS) or mismatch repair dysfunction/microsatellite high instability (dMMR/MSI-high) type,

gastric cancer is microsatellite stability (MSS) or mismatch repair dysfunction/microsatellite high instability (dMMR/MSI-high) type.