

Claims

1. A bispecific antibody comprising anti-CLDN18.2 binding domain and anti-CD3 binding domain, the first binding domain being capable of binding to a CLDN18.2 protein, the second binding domain being capable of binding to CD3.
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2. The bispecific antibody according to claim 1, wherein the anti-CLDN18.2 binding domain comprises: a heavy chain variable region in which the sequences of three CDRs, i.e., HCDR1, HCDR2, and HCDR3, are as set forth in SEQ ID NO: 11, 12, and 13, respectively; and a light chain variable region in
10 which sequences of three CDRs, i.e., LCDR1, LCDR2, and LCDR3, are as set forth in SEQ ID NO: 14, 15, and 16, respectively.
3. The bispecific antibody according to claim 1, wherein the anti-CD3 binding domain comprises: a heavy chain variable region in which the sequences of three CDRs, i.e., HCDR1, HCDR2, and HCDR3, are as set forth in SEQ ID NO:
15 17, 18, and 19, respectively; and a light chain variable region in which sequences of three CDRs, i.e., LCDR1, LCDR2, and LCDR3, are as set forth in SEQ ID NO: 20, 21, and 22, respectively.
4. The bispecific antibody according to any one of claims 1-3, wherein the anti-
20 CLDN18.2 binding domain comprises a heavy chain variable

region and a light chain variable region, the heavy chain variable region has at least 80% to 100% sequence identity to SEQ ID NO: 23; and the light chain variable region has at least 80% to 100% sequence identity to SEQ ID NO: 24.

5 5. The bispecific antibody according to any one of claims 1-4, wherein the anti-CD3 binding domain comprises a heavy chain variable region and a light chain variable region, the heavy chain variable region has at least 80% to 100% sequence identity to SEQ ID NO: 6; and the light chain variable region has at least 80% to 100% sequence identity to SEQ ID NO: 7.

10 6. The bispecific antibody according to any one of claims 1-5, wherein the binding domain comprises a Fab, Fv, scFv, F(ab')₂, a linear antibody, a single domain antibody, or a full-length antibody.

7. The bispecific antibody according to any one of claims 1-6, further comprising a heavy chain constant region and/or a light chain constant region, preferably the heavy chain constant region comprising a native Fc or a variant Fc.

8. The bispecific antibody according to any one of claims 1-7, wherein the anti-CLDN18.2 binding domain is a full-length antibody and the anti-CD3 binding domain is scFv;

preferably, the anti-CLDN18.2 binding domain is a full-length antibody, the

full-length antibody has a heavy chain sequence as set forth in SEQ ID NO: 1, a light chain sequence as set forth in SEQ ID NO: 5; the anti-CD3 binding domain is scFv, the scFv has a sequence as set forth in SEQ ID NO: 8.

9. The bispecific antibody according to any one of claims 1-8, having a structure
5 of linking anti-CD3 scFv at the C-terminus of the heavy or light chain of the full-length anti-CLDN18.2 antibody.

10. The bispecific antibody according to any one of claims 1-9, having a structure of fusing the anti-CD3 scFv to the C-terminus of the two light chains of the full-length anti-CLDN18.2 antibody to form two homologous light chains
10 and two homologous heavy chains, wherein the fused light chain has a sequence as set forth in in SEQ ID NO: 2, the heavy chain has a sequence as set forth in SEQ ID NO: 1.

11. The bispecific antibody according to any one of claims 1-9, having a structure of fusing the anti-CD3 scFv to the C-terminus of one heavy chain of
15 the full-length anti-CLDN18.2 antibody to form two homologous light chains and two heterologous heavy chains, wherein the heavy chain containing the scFv has a sequence as set forth in SEQ ID NO: 3, the heavy chain without the scFv has a sequence as set forth in SEQ ID NO: 4, the light chain has a sequence as set forth in SEQ ID NO: 5.

20 12. A nucleic acid encoding a bispecific antibody according to any one of claims 1-11.

13. A recombinant vector comprising the nucleic acid according to claim 12.

14. A host cell comprising the recombinant vector according to claim 13 or

comprising the nucleic acid according to claim 12.

preferably the host cell is a prokaryotic cell, such as *E. coli*; or a eukaryotic cell, such as yeast or mammalian cells, such as CHO cells, HEK293 cells, HEK293E cells, or Expi293 cells.

5 15. A method of preparing a bispecific antibody, comprising culturing the host cell according to claim 14 under suitable conditions and purifying the expression product from the cell.

16. Use of the bispecific antibody according to any one of claims 1-11 for the preparation of a drug specifically targeting CLDN18.2-expressing tumor cells;
10 the CLDN18.2-expressing tumor comprises: gastric cancer, pancreatic cancer, esophageal cancer, lung cancer, ovarian cancer, colon cancer, rectal cancer, liver cancer, head and neck cancer, and gallbladder cancer and metastases thereof, the gastric cancer metastasis being such as Kuckenberg tumor.

17. A pharmaceutical composition comprising an effective amount of the
15 bispecific antibody according to any one of claims 1-11, or comprising an effective amount of the nucleic acid according to claim 12, or comprising an

effective amount of the recombinant vector according to claim 14, or comprising an effective amount of the host cell according to claim 14;

preferably, the pharmaceutical composition further comprising a pharmaceutically acceptable carrier;

- 5 preferably, the pharmaceutical composition further comprising one or more additional other therapeutic agents; the additional therapeutic agents comprise: cytotoxic agents, cytostatic agents, anti-angiogenic agents, anti-neoplastic agents, chemotherapeutic agents, radio therapeutic agents, targeted anti-cancer agents, biological response modifiers, cancer vaccines, cytokines, hormones,
10 anti-metastatic agents, and immunotherapeutic agents.

18. A drug box or kit comprising a container, and the pharmaceutical composition according to claim 17 in the container.

19. Use of the pharmaceutical composition according to claim 17 characterized by being in the manufacture of a medicament for inducing cell death in
15 CLDN18.2-expressing cells, comprising contacting the cells with the pharmaceutical composition according to claim 17.

- preferably, the cells are cancer cells, preferably solid tumor cells; more preferably, the cells are selected from the group consisting of: gastric cancer cells, esophageal cancer cells, intestinal cancer cells, pancreatic cancer cells,
20 nephroblastoma cells, lung cancer cells, ovarian cancer cells, colon cancer cells, rectal cancer cells, liver cancer cells,

head and neck cancer cells, chronic myelogenous leukemia cells, and gallbladder cancer cells.

20. Use of the pharmaceutical composition according to claim 17 characterized by being in the manufacture of a medicament for treating a disease associated
5 with expression of CLDN18.2 in a subject, comprising administering to a subject in need thereof the pharmaceutical composition according to claim 17; preferably, the disease is a tumor; preferably gastric cancer, esophageal cancer, intestinal cancer, pancreatic cancer, nephroblastoma, lung cancer, ovarian cancer, colon cancer, rectal cancer, liver cancer, head and neck cancer, chronic
10 myelogenous leukemia, or gallbladder cancer.

preferably, the method further comprising administering to the subject one or more additional therapeutic agents;

preferably, the one or more additional therapeutic agents comprising: chemotherapeutic agents, cytotoxic agents, radio therapeutic agents, cancer
15 vaccines, anti-neoplastic agents, targeted anti-cancer agents, anti-angiogenic agents, biological response modifiers, cytokines, hormones, anti-metastatic agents, and immunotherapeutic agents.