

Claims

1. An antibody or antigen binding unit thereof that specifically binds to claudin 18A2, wherein,

(a) HCDR1 is SEQ ID NO:31, HCDR2 is SEQ ID NO:32, HCDR3 is SEQ ID NO:33, LCDR1 is SEQ ID NO:34, LCDR2 is SEQ ID NO:35, and LCDR3 is SEQ ID NO:36;

(b) HCDR1 is SEQ ID NO:37, HCDR2 is SEQ ID NO:38, HCDR3 is SEQ ID NO:39, LCDR1 is SEQ ID NO:40, LCDR2 is SEQ ID NO:41, and LCDR3 is SEQ ID NO:42;

(c) HCDR1 is SEQ ID NO:43, HCDR2 is SEQ ID NO:44, HCDR3 is SEQ ID NO:45, LCDR1 is SEQ ID NO:46, LCDR2 is SEQ ID NO:47, and LCDR3 is SEQ ID NO:48;

(d) HCDR1 is SEQ ID NO:49, HCDR2 is SEQ ID NO:50, HCDR3 is SEQ ID NO:51, LCDR1 is SEQ ID NO:52, LCDR2 is SEQ ID NO:53, and LCDR3 is SEQ ID NO:54;

(e) HCDR1 is SEQ ID NO:31, HCDR2 is SEQ ID NO:83, HCDR3 is SEQ ID NO:33, LCDR1 is SEQ ID NO:34, LCDR2 is SEQ ID NO:35, and LCDR3 is SEQ ID NO:36;

(f) HCDR1 is SEQ ID NO:31, HCDR2 is SEQ ID NO:84, HCDR3 is SEQ ID NO:33, LCDR1 is SEQ ID NO:34, LCDR2 is SEQ ID NO:35, and LCDR3 is SEQ ID NO: 36; or

(g) HCDR1 is SEQ ID NO:49, HCDR2 is SEQ ID NO:85, HCDR3 is SEQ ID NO:51, LCDR1 is SEQ ID NO:52, LCDR2 is SEQ ID NO:53, and LCDR3 is SEQ ID NO: 54.

2. The antibody or antigen binding unit of claim 1, comprising a heavy chain variable region (VH) and a light chain variable region (VL), wherein

VH comprises an amino acid sequence of SEQ ID NO:3, SEQ ID NO:7, SEQ ID NO:11, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:23, SEQ ID NO:27 or SEQ ID NO:29; and

VL comprises an amino acid sequence of SEQ ID NO:1, SEQ ID NO:5, SEQ ID NO:9, SEQ ID NO:13, SEQ ID NO:21 or SEQ ID NO:25.

3. The antibody or antigen binding unit of claim 2, wherein:

(a) VH comprises an amino acid sequence of SEQ ID NO:3 and VL comprises an amino acid sequence of SEQ ID NO:1;

(b) VH comprises an amino acid sequence of SEQ ID NO:7 and VL comprises an amino acid sequence of SEQ ID NO:5;

(c) VH comprises an amino acid sequence of SEQ ID NO:11 and VL comprises an amino acid sequence of SEQ ID NO:9;

(d) VH comprises an amino acid sequence of SEQ ID NO:15 and VL comprises an amino acid sequence of SEQ ID NO:13;

(e) VH comprises an amino acid sequence of SEQ ID NO:17 and VL comprises an amino acid sequence of SEQ ID NO:1;

(f) VH comprises an amino acid sequence of SEQ ID NO:19 and VL comprises an amino acid sequence of SEQ ID NO:1;

(g) VH comprises an amino acid sequence of SEQ ID NO:23 and VL comprises an amino acid sequence of SEQ ID NO:21;

(h) VH comprises an amino acid sequence of SEQ ID NO:27 and VL comprises an amino acid sequence of SEQ ID NO:25; or

(i) VH comprises an amino acid sequence of SEQ ID NO:29 and VL comprises an amino acid sequence of SEQ ID NO:25.

4. The antibody or antigen binding unit of any one of claims 1-3, which is a humanized antibody, a chimeric antibody, a fully humanized antibody, a monoclonal antibody, a single chain antibody, a multivalent antibody, a chimeric antigen receptor, an scFv, an Fv, a Fab, or a F(ab')₂.

5. The antibody of any one of claims 1-4, having

(a) a heavy chain comprising an amino acid sequence of SEQ ID NO:63 and a light chain comprising an amino acid sequence of SEQ ID NO:65;

(b) a heavy chain comprising an amino acid sequence of SEQ ID NO:59 and a light chain comprising an amino acid sequence of SEQ ID NO:61; or

(c) a heavy chain comprising an amino acid sequence of SEQ ID NO:67 and a light chain comprising an amino acid sequence of SEQ ID NO:65.

6. A pharmaceutical composition comprising the antibody or antigen binding unit of any one of claims 1-5, and a pharmaceutically acceptable carrier.

7. A nucleic acid encoding the antibody or antigen binding unit of any one of claims 1-5.

8. An expression vector comprising the nucleic acid of claim 7.

9. A host cell comprising the expression vector of claim 8.

10. A method for producing an antibody or antigen binding unit that specifically binds to claudin 18A2, comprising culturing the host cell of claim 9 under suitable conditions, and obtaining the product expressed by the host cell.

11. A method for preparing an anti-claudin 18A2 targeting drug, an anti-claudin 18A2 antibody-drug conjugate, a multifunctional anti-claudin 18A2 antibody, a reagent for diagnosing a tumor expressing claudin 18A2, or an anti claudin 18A2 chimeric antigen receptor modified immune cell, wherein the method comprises providing the antibody or antigen binding unit of claim 1 and incorporating said antibody or antigen binding unit into the claudin 18A2 targeting drug, the anti-claudin 18A2 antibody-drug conjugate, the multifunctional anti-claudin 18A2 antibody, the reagent for diagnosing a tumor expressing claudin 18A2, or the anti claudin 18A2 chimeric antigen receptor modified immune cell.

12. A chimeric antigen receptor comprising the following sequentially linked components: the antibody or antigen binding unit of any one of claims 1-5, a transmembrane region, and an intracellular signal region.

13. The chimeric antigen receptor of claim 12, wherein the intracellular signal region is selected from: an intracellular signal region sequence of CD3 ζ , Fc ϵ RI γ , CD27, CD28, CD137, CD134, MyD88, CD40, and combinations thereof; and/or the transmembrane region comprises a transmembrane region of CD8 or CD28.

14. A nucleic acid encoding the chimeric antigen receptor of any one of claims 12-13.

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

16. A virus comprising the vector of claim 15.
17. A chimeric antigen receptor-modified immune cell having the chimeric antigen receptor of any one of claims 12-13 expressed on the surface.
18. The chimeric antigen receptor-modified immune cell of claim 17, wherein the immune cell is selected from a T lymphocyte, a NK cell, and a NKT lymphocyte.
19. The chimeric antigen receptor-modified immune cell of claim 18, further comprising:
- (a) an encoding sequence for an exogenous cytokine;
 - (b) another expressed chimeric antigen receptor which does not contain CD3 ζ but contains an intracellular signal domain of CD28, an intracellular signal domain of CD137, or a combination of the both;
 - (c) an expressed chemokine receptor;
 - (d) an expressed siRNA which can reduce expression of PD-1;
 - (e) an expressed protein which can block PD-L1;
 - (f) a knock-out of endogenous PD-1 in the immune cell by gene editing techniques;
 - (g) an expressed safety switch; or
 - (h) an expressed Type I interferon.
20. A multifunctional immunoconjugate comprising:
- an antibody or antigen binding unit of any one of claims 1-5; and
 - a functional molecule linked thereto, wherein the functional molecule is selected from a molecule targeting a surface marker on a tumor, a tumor-inhibiting molecule, a molecule targeting a surface marker of an immune cell, and a detectable label.
21. The multifunctional immunoconjugate of claim 20, which is bifunctional and wherein the function molecule is a molecule targeting a surface marker of an immune cell that is a T cell.
22. A nucleic acid encoding the multifunctional immunoconjugate of claim 20 or claim 21.
23. A kit comprising:
- a container, and

the antibody or antigen binding unit of any one of claims 1-5.

24. The composition of claim 6, further comprising a Type I interferon.

25. The antibody or antigen binding unit of any one of claims 1-5 for use as a medicament.

26. Use of the antibody or antigen binding unit of any one of claims 1-5 for the preparation of a medicament for treating a tumor, wherein the tumor is associated with gastric cancer, esophageal cancer, intestinal cancer, pancreatic cancer, neuroblastoma, lung cancer, ovarian cancer, colon cancer, rectal cancer, liver cancer, head and neck cancer, chronic myelogenous leukemia, or gallbladder cancer.