

Claims

1. An antibody targeting CLL1 having:

HCDR1 shown in SYX₁MX₂, HCDR2 shown in X₃X₄X₅X₆SGGSTX₇YAX₈X₉X₁₀X₁₁G, HCDR3 shown in SEQ ID NO: 40 or 41, and LCDR1 shown in RASQSISSX₁₂LX₁₃, LCDR2 shown in X₁₄ASX₁₅LX₁₆S, LCDR3 shown in QQX₁₇YSX₁₈PX₁₉X₂₀T,

Wherein, X₁ is selected from A or Y, X₂ is selected from S or H, X₃ is A or I, X₄ is selected from I or F, X₅ is selected from S or N, X₆ is selected from G or P, X₇ is selected from Y or S, X₈ is selected from D or Q, X₉ is selected from S or K, X₁₀ is selected from V or F, X₁₁ is selected from K or Q, X₁₂ is selected from W or Y, X₁₃ is selected from A or N, X₁₄ is selected from D or V, X₁₅ is selected from N or S, X₁₆ is selected from E or Q, X₁₇ is selected from Y or S, X₁₈ is selected from Y or T, X₁₉ is selected from M or L, and X₂₀ is I or absent.

2. The antibody of claim 1, wherein the antibody is selected from the following group:

(1) an antibody, the heavy chain variable region of which comprises HCDR1 shown in SEQ ID NO: 35 or 36, and/or comprises HCDR2 shown in SEQ ID NO: 37, 38 or 39, and/or comprises HCDR3 shown in SEQ ID NO: 40 or 41;

(2) an antibody, the light chain variable region of which comprises LCDR1 shown in SEQ ID NO: 42, 43 or 44, and/or comprises LCDR2 shown in SEQ ID NO: 45, 46, 47 or 48, and/or comprises LCDR3 shown in SEQ ID NO: 49 or 50;

(3) an antibody, comprising the heavy chain variable region described in (1) and the light chain variable region described in (2);

(4) a variant of the antibody described in any one of (1) to (3), which has the same or similar activities as the antibody described in any one of (1) to (3).

3. The antibody of claim 1, wherein the LCDR1 of the antibody is mutated from RASQSISSX₁₂LX₁₃ to RASQWIARX₁₂LX₁₃;

preferably, the sequence of the mutated LCDR1 is shown in SEQ ID NO: 44.

4. The antibody of claim 1, wherein the X₃X₄X₅X₆ of the HCDR2 of the antibody is AISG or IFNP.

5. The antibody of claim 1 or 4, wherein the HCDR2 of the antibody is mutated from X₃X₄X₅X₆SGGSTX₇YAX₈X₉X₁₀X₁₁G to X₃X₄X₅X₆GGGSTX₇YAX₈X₉X₁₀X₁₁G;

preferably, the sequence of the mutated HCDR2 is shown in SEQ ID NO: 39.

6. The antibody of claim 2, wherein the antibody is selected from any one of the following groups:

(1) An antibody comprising HCDR1 shown in SEQ ID NO: 35, HCDR2 shown in SEQ ID NO: 37, HCDR3 shown in SEQ ID NO: 40, and LCDR1 shown in SEQ ID NO: 42 : LCDR2 shown in SEQ ID NO: 45 and LCDR3 shown in SEQ ID NO: 49;

(2) An antibody comprising the HCDR1 shown in SEQ ID NO: 36, HCDR2 shown in SEQ ID NO: 38, HCDR3 shown in SEQ ID NO: 41, and LCDR1 shown in SEQ ID NO: 43 : LCDR2 shown in SEQ ID NO: 46, LCDR3 shown in SEQ ID NO: 50;

(3) An antibody comprising HCDR1 shown in SEQ ID NO: 35, HCDR2 shown in SEQ ID NO: 37, HCDR3 shown in SEQ ID NO: 40, and LCDR1 shown in SEQ ID NO: 44, LCDR2 shown in SEQ ID NO: 47, LCDR3 shown in SEQ ID NO: 49;

(4) An antibody comprising the HCDR1 shown in SEQ ID NO: 36, HCDR2 shown in SEQ ID NO: 38, HCDR3 shown in SEQ ID NO: 41, and LCDR1 shown in SEQ ID NO: 43 : LCDR2 shown in SEQ ID NO: 48, LCDR3 shown in SEQ ID NO: 50;

(5) An antibody comprising the HCDR1 shown in SEQ ID NO: 36, HCDR2 shown in SEQ ID NO: 39, HCDR3 shown in SEQ ID NO: 41, and LCDR1 shown in SEQ ID NO: 43, LCDR2 shown in SEQ ID NO: 48, LCDR3 shown in SEQ ID NO: 50;

(6) An antibody, which is a variant of the antibody described in any one of (1) to (5), and has the same or similar activity as the antibody described in any one of (1) to (5).

7. The antibody of claim 2, wherein the antibody is selected from any one of the following groups:

(1) An antibody, wherein the heavy chain variable region of the antibody has the amino acid sequence shown in SEQ ID NO: 1, the amino acid sequence shown in SEQ ID NO: 5, the amino acid sequence shown in SEQ ID NO: 13, the amino acid sequence shown in SEQ ID NO: 67, the amino acid sequence shown in SEQ ID NO: 68, or the amino acid sequence shown in SEQ ID NO: 69;

(2) An antibody, wherein the light chain variable region of the antibody has the amino acid sequence shown in SEQ ID NO: 3, the amino acid sequence shown in SEQ ID NO: 7, the amino acid sequence shown in SEQ ID NO: 11, or the amino acid sequence shown in SEQ ID NO: 15;

(3) An antibody, comprising the heavy chain variable region of the antibody described in (1) and the light chain variable region of the antibody described in (2);

(4) A variant of the antibody described in any one of (1) to (3), which has the same or similar activity as the antibody described in any one of (1) to (3).

8. The antibody of claim 7, wherein the antibody is selected from:

(1) An antibody, wherein the heavy chain variable region of the antibody has the amino

acid sequence shown in SEQ ID NO: 1 and the light chain variable region of the antibody has the amino acid sequence shown in SEQ ID NO: 3;

(2) An antibody, wherein the heavy chain variable region of the antibody has the amino acid sequence shown in SEQ ID NO: 5 and the light chain variable region of the antibody has the amino acid sequence shown in SEQ ID NO: 7;

(3) An antibody, wherein the heavy chain variable region of the antibody has the amino acid sequence shown in SEQ ID NO: 1 and the light chain variable region of the antibody has the amino acid sequence shown in SEQ ID NO: 11;

(4) An antibody, wherein the heavy chain variable region of the antibody has the amino acid sequence shown in SEQ ID NO: 13 and the light chain variable region of the antibody has the amino acid sequence shown in SEQ ID NO: 15;

(5) An antibody, wherein the heavy chain variable region of the antibody has the amino acid sequence shown in SEQ ID NO: 5 and the light chain variable region of the antibody has the amino acid sequence shown in SEQ ID NO: 15;

(6) A variant of the antibody described in any one of (1) to (5), which has the same or similar activity as the antibody described in any one of (1) to (5).

9. The antibody of claim 2, wherein the light chain variable region of the antibody has LCDR1 shown in SEQ ID NO: 43, LCDR2 shown in SEQ ID NO: 48, and LCDR3 shown in SEQ ID NO: 50;

Preferably, the light chain variable region has the amino acid sequence shown in SEQ ID NO: 15;

More preferably, the light chain variable region of the antibody has the amino acid sequence shown in SEQ ID NO: 15, and the heavy chain variable region of the antibody has the amino acid sequence shown in SEQ ID NO: 5, 13, 67, 68 or 69.

~~10. An antibody that recognizes the same epitope as the antibody of any one of claims 1-9.~~

~~11~~10. The antibody of any one of claims 1-~~10~~9, wherein the antibody is a fully human antibody.

~~12~~11. The antibody of any one of claims 1-~~11~~10, wherein the antibody is a full antibody, scFv, single domain antibody, Fab fragment, Fv fragment, and F(ab')₂ fragment.

~~13~~12. A nucleic acid encoding the antibody of any one of claims 1-~~12~~11.

~~14~~13. An expression vector comprising the nucleic acid of claim ~~13~~12.

~~15~~14. A host cell comprising the expression vector of claim ~~14~~13 or having the nucleic acid of claim ~~13~~12 integrated into the genome.

~~46~~15. Use of the antibody of any one of claims ~~1-42-11~~ for preparing a medicament for treating tumors or preparing a reagent for diagnosing tumors.

~~47~~16. An immunoconjugate, comprising:

The antibody of any one of claims ~~1-42-11~~, and a functional molecule connected thereto; and the functional molecule is selected from: a molecule targeting tumor surface markers, a tumor-inhibiting molecule, a molecule targeting immune cell surface markers, and a detectable marker.

~~48~~17. The immunoconjugate of claim ~~47~~16, wherein the tumor-inhibiting molecule is an anti-tumor cytokine or an anti-tumor toxin.

~~49~~18. The immunoconjugate of claim ~~47~~16, wherein the molecule targeting the immune cell surface markers is an antibody or ligand binding to the immune cell surface markers.

~~20~~19. The immunoconjugate of claim ~~49~~18, wherein the molecule targeting the immune cell surface markers is an antibody binding to the surface marker of T cells, NK cells or NKT cells.

~~24~~20. A nucleic acid encoding the multifunctional immunoconjugate of any one of claims ~~47~~16-~~20~~19.

~~22~~21. A chimeric antigen receptor, wherein the chimeric antigen receptor comprises the antibody of any one of claims ~~1-42-11~~.

~~23~~22. The chimeric antigen receptor of claim ~~22~~21, wherein the antibody is a single-chain antibody or a single-domain antibody.

~~24~~23. A nucleic acid encoding the chimeric antigen receptor of claim ~~22~~21.

~~25~~24. An expression vector comprising the nucleic acid of claim ~~24~~23.

~~26~~25. A virus comprising the vector of claim ~~25~~24.

~~27~~26. A genetically modified immune cell transduced with the nucleic acid of claim ~~24~~23, or expressing the chimeric antigen receptor of claim ~~22~~21.

~~28~~27. The genetically modified immune cell of claim ~~27~~26, wherein the immune cell also expresses a second sequence other than the chimeric antigen receptor.

~~29~~28. The immune cell of claim ~~28~~27, wherein the second sequence includes a cytokine, or another chimeric antigen receptor, or chemokine receptor, or siRNA that reduces PD-1 expression, or protein that blocks PD-L1, or TCR, or safety switch.

~~30~~29. Use of the genetically modified immune cell of claim ~~28-27~~ in the preparation of a medicament for treating tumors.

~~34~~30. A pharmaceutical composition comprising:

The antibody of any one of claims ~~1-42-11~~ or the nucleic acid encoding the antibody; or

The immunoconjugate of any one of claims ~~17~~16-20~~19~~ or the nucleic acid encoding the conjugate; or

The genetically modified immune cell of any one of claims ~~27~~26-29~~28~~.