Claims

1. An antibody specifically recognizing EGFRvIII expressed or EGFR overexpressed by tumor cells, wherein the antibody comprises a light chain variable region and a heavy chain variable region, and

CDR1 of the light chain variable region has an amino acid sequence selected from a group consisting of SEQ ID NO: 41, SEQ ID NO: 47, SEQ ID NO: 55;

CDR2 of the light chain variable region has an amino acid sequence selected from a group consisting of SEQ ID NO: 42, SEQ ID NO: 53;

CDR3 of the light chain variable region has an amino acid sequence selected from a group consisting of SEQ ID NO: 43, SEQ ID NO: 48, SEQ ID NO: 54, SEQ ID NO: 56, SEQ ID NO: 57;

CDR1 of the heavy chain variable region has the amino acid sequence of SEQ ID NO: 44;

CDR2 of the heavy chain variable region has an amino acid sequence selected from a group consisting of SEQ ID NO: 45, SEQ ID NO: 49, SEQ ID NO: 51, SEQ ID NO: 52;

CDR3 of the heavy chain variable region has an amino acid sequence selected from a group consisting of SEQ ID NO: 46, SEQ ID NO: 50;

preferably, the antibody includes:

antibody (a), wherein the light chain variable region thereof has CDR1 of SEQ ID NO: 41, CDR2 of SEQ ID NO: 42, CDR3 of SEQ ID NO: 43, and the heavy chain variable region thereof has CDR1 of SEQ ID NO: 44, CDR2 of SEQ ID NO: 45, CDR3 of SEQ ID NO: 46,

antibody (b), wherein the light chain variable region thereof has CDR1 of SEQ ID NO: 47, CDR2 of SEQ ID NO: 42, CDR3 of SEQ ID NO: 48, and the heavy chain variable region thereof has CDR1 of SEQ ID NO: 44, CDR2 of SEQ ID NO: 49, CDR3 of SEQ ID NO: 50,

antibody (c), wherein the light chain variable region thereof has CDR1 of SEQ ID NO: 41, CDR2 of SEQ ID NO: 42, CDR3 of SEQ ID NO: 48, and the heavy chain variable region thereof has CDR1 of SEQ ID NO: 44, CDR2 of SEQ ID NO: 51, CDR3 of SEQ ID NO: 50,

antibody (d), wherein the light chain variable region thereof has CDR1 of SEQ ID NO: 41, CDR2 of SEQ ID NO: 42, CDR3 of SEQ ID NO: 43, and the heavy chain variable region thereof has CDR1 of SEQ ID NO: 44, CDR2 of SEQ ID NO: 52, CDR3 of SEQ ID NO: 50,

antibody (e), wherein the light chain variable region thereof has CDR1 of SEQ ID NO: 41, CDR2 of SEQ ID NO: 42, CDR3 of SEQ ID NO: 43, and the heavy chain variable region thereof has CDR1 of SEQ ID NO: 44, CDR2 of SEQ ID NO: 45, CDR3 of SEQ ID NO: 50,

antibody (f), wherein light chain variable region thereof has CDR1 of SEQ ID NO: 41, CDR2 of SEQ ID NO: 53, CDR3 of SEQ ID NO: 54, and the heavy chain variable region thereof has CDR1 of SEQ ID NO: 44, CDR2 of SEQ ID NO: 51, CDR3 of SEQ ID NO: 50,

antibody (g), wherein the light chain variable region has CDR1 of SEQ ID NO: 41, CDR2 of

SEQ ID NO: 42, CDR3 of SEQ ID NO: 54, and the heavy chain variable region thereof has CDR1 of SEQ ID NO: 44, CDR2 of SEQ ID NO: 51, CDR3 of SEQ ID NO: 50,

antibody (h), wherein the light chain variable region thereof has CDR1 of SEQ ID NO: 55, CDR2 of SEQ ID NO: 42, CDR3 of SEQ ID NO: 56, and the heavy chain variable region thereof has CDR1 of SEQ ID NO: 44, CDR2 of SEQ ID NO: 45, CDR3 of SEQ ID NO: 50,

antibody (i), wherein the light chain variable region thereof has CDR1 of SEQ ID NO: 41, CDR2 of SEQ ID NO: 53, CDR3 of SEQ ID NO: 56, and the heavy chain variable region thereof has CDR1 of SEQ ID NO: 44, CDR2 of SEQ ID NO: 52, CDR3 of SEQ ID NO: 50,

antibody (j), wherein the light chain variable region thereof has CDR1 of SEQ ID NO: 41, CDR2 of SEQ ID NO: 42, CDR3 of SEQ ID NO: 56, and the heavy chain variable region thereof has CDR1 of SEQ ID NO: 44, CDR2 of SEQ ID NO: 52, CDR3 of SEQ ID NO: 50, or

antibody (k), wherein the light chain variable region thereof has CDR1 of SEQ ID NO: 41, CDR2 of SEQ ID NO: 42, CDR3 of SEQ ID NO: 57, and the heavy chain variable region thereof has CDR1 of SEQ ID NO: 44, CDR2 of SEQ ID NO: 52, CDR3 of SEQ ID NO: 50.

more preferably, the amino acid sequence of the heavy chain variable region of the antibody is shown in positions 124 to 239 of SEQ ID NO: 13; and the amino acid sequence of the light chain variable region of the antibody is shown in positions 1-108 of SEQ ID NO: 13;

The amino acid sequence of the heavy chain variable region of the antibody is shown in positions 124 to 239 of SEQ ID NO: 59; and the amino acid sequence of the light chain variable region of the antibody is shown in positions 1-108 of SEQ ID NO: 59;

The amino acid sequence of the heavy chain variable region of the antibody is shown in positions 124 to 239 of SEQ ID NO: 61; and the amino acid sequence of the light chain variable region of the antibody is shown in positions 1-108 of SEQ ID NO: 61;

The amino acid sequence of the heavy chain variable region of the antibody is shown in positions 124 to 239 of SEQ ID NO: 63; and the amino acid sequence of the light chain variable region of the antibody is shown in positions 1-108 of SEQ ID NO: 63;

The amino acid sequence of the heavy chain variable region of the antibody is shown in positions 124 to 239 of SEQ ID NO: 65; and the amino acid sequence of the light chain variable region of the antibody is shown in positions 1-108 of SEQ ID NO: 65;

The amino acid sequence of the heavy chain variable region of the antibody is shown in positions 124 to 239 of SEQ ID NO: 67; and the amino acid sequence of the light chain variable region of the antibody is shown in positions 1-108 of SEQ ID NO: 67;

The amino acid sequence of the heavy chain variable region of the antibody is shown in positions 124 to 239 of SEQ ID NO: 69; and the amino acid sequence of the light chain variable region of the antibody is shown in positions 1-108 of SEQ ID NO: 69;

The amino acid sequence of the heavy chain variable region of the antibody is shown in

positions 124 to 239 of SEQ ID NO: 71; and the amino acid sequence of the light chain variable region of the antibody is shown in positions 1-108 of SEQ ID NO: 71;

The amino acid sequence of the heavy chain variable region of the antibody is shown in positions 124 to 239 of SEQ ID NO: 73; and the amino acid sequence of the light chain variable region of the antibody is shown in positions 1-108 of SEQ ID NO: 73;

The amino acid sequence of the heavy chain variable region of the antibody is shown in positions 124 to 239 of SEQ ID NO: 75; and the amino acid sequence of the light chain variable region of the antibody is shown in positions 1-108 of SEQ ID NO: 75; or

The amino acid sequence of the heavy chain variable region of the antibody is shown in positions 124 to 239 of SEQ ID NO: 77; and the amino acid sequence of the light chain variable region of the antibody is shown in positions 1-108 of SEQ ID NO: 77.

2. The antibody of claim 1, wherein the antibody is antibody (a); more preferably, the amino acid sequence of the heavy chain variable region of the antibody is shown in positions 124 to 239 of SEQ ID NO: 13; and the amino acid sequence of the light chain variable region of the antibody is shown in positions 1-108 of SEQ ID NO: 13.

3. A nucleic acid encoding the antibody of claim 1 or 2.

4. An expression vector comprising the nucleic acid of claim 3.

5. A host cell, comprising the expression vector of claim 4 or having the nucleic acid of claim 3 integrated into its genome.

6. Use of the antibody of claim 1 or 2 for the manufacture of a targeting drug, antibody drug conjugate, or multi-functional antibody specifically targeting tumor cells expressing EGFRvIII or over-expressing EGFR; or

for the manufacture of an agent for diagnosis of tumors that expresse EGFRvIII or overexpress EGFR; or

for the manufacture of a chimeric antigen receptor modified immune cell; preferably, the immune cell includes: T lymphocyte, NK cell or NKT lymphocyte.

7. A multi-functional immunoconjugate, comprising:

The antibody of claim 1 or 2; and

a functional molecule linked thereto; and the functional molecule is selected from a group consisting of a molecule that targets a tumor surface marker, a tumor-suppressing molecule, a molecule that targets a surface marker of an immune cell, a detectable label;

preferably, the molecule that targets the tumor surface marker is an antibody or ligand that binds to a tumor surface marker; or

the tumor-suppressing molecule is an anti-tumor cytokine or an anti-tumor toxin; preferably, the cytokines include but are not limited to: IL-12, IL-15, IFN-beta, TNF-alpha; or

the detectable label includes a fluorescent label and a chromogenic label; or

the molecule targeting the surface marker of the immune cell is an antibody or ligand that binds to an immune cell surface marker; preferably, the immune cell surface markers include: CD3, CD16, CD28;or

the multi-functional immunoconjugate is a fusion polypeptide, and further comprises a linker peptide between the antibody of claim 1 or 2 and the functional molecule linked thereto;

more preferably, wherein the molecule that targets the surface marker of the immune cell is an antibody that binds to a T cell surface marker, which forms a T-cell-engaging bifunctional antibody with the antibody of claim 1 or 2;

more preferably, the antibody that binds to the immune cell surface marker is an anti-CD3 antibody.

8. A nucleic acid encoding the multi-functional immunoconjugate of claim 7.

9. Use of the multi-functional immunoconjugate of claim 7 for the preparation of an antineoplastic agent, or

for the preparation of an agent for diagnosis of tumors that express EGFRvIII or overexpress EGFR; or

for the preparation of chimeric antigen receptor modified immune cells; preferably, the immune cells include T lymphocyte, NK cell or NKT lymphocyte.

10. A chimeric antigen receptor expressed on the surface of an immune cell comprising the antibody of claim 1 or 2, wherein the chimeric antigen receptor comprises: the antibody of claim 1 or 2, a transmembrane region and an intracellular signal region, which are sequentially linked;

preferably, the intracellular signal region is selected from a group consisting of intracellular signal region sequences of CD3ζ, FcεRIγ, CD27, CD28, CD137 and CD134, or a combination thereof;

more preferably, the transmembrane region comprises a transmembrane region of CD8 or CD28; or

the immune cells include T lymphocyte, NK cell or NKT cell; or

the chimeric antigen receptor comprises the following sequentially linked antibody, transmembrane region and intracellular signal region:

Antibody of any one of claims 1-4, CD8 and CD3ζ;

Antibody of any one of claims 1-4, CD8, CD137 and CD3ζ;

Antibody of any one of claims 1-4, a transmembrane region of a CD28 molecule, an intracellular signal region of a CD28 molecule, and CD3ζ; or

Antibody of any one of claims 1-4, a transmembrane region of a CD28 molecule, an intracellular signal region of a CD28 molecule, CD137 and CD3ζ; or

the antibody is a single chain antibody or a domain antibody; or

the chimeric antigen receptor comprises:

SEQ ID NO: 36 or the amino acid sequence shown in positions 285-601; or

SEQ ID NO: 37 or the amino acid sequence shown in positions 285-702; or

SEQ ID NO: 38 or the amino acid sequence shown in positions 285-744; or

SEQ ID NO: 39 or the amino acid sequence shown in positions 285-749; or

SEQ ID NO: 40 or the amino acid sequence shown in positions 285-791.

11. A nucleic acid encoding the chimeric antigen receptor of claim 10.

12. An expression vector comprising the nucleic acid of claim 11.

13. A virus comprising the vector of claim 12.

14. Use of the chimeric antigen receptor of claim 10 or the nucleic acid of claim 11, or the expression vector of claim 12, or the virus of claim 13, for the preparation of genetically modified immune cells that target tumor cells that express EGFRvIII or overexpress EGFR.

15. A genetically modified immune cell, wherein it is transduced with the nucleic acid of claim 11, or the expression vector of claim 12 or the virus of claim 13; or

it expresses the chimeric antigen receptor of claim 10 at its surface;

preferably, the immune cell further carries an exogenous encoding sequence for cytokine; preferably, the cytokine includes: IL-12, IL-15 or IL-21; or

the immune cell further expresses another chimeric antigen receptor that does not contain CD3ζ, but contains the intracellular signaling domain of CD28, the intracellular signaling domain of CD137, or a combination of both; or

the immune cell further expresses a chemokine receptor; preferably, the chemokine receptor includes CCR2; or

the immune cell further expresses siRNA that can reduce PD-1 expression or a protein that can block PD-L1; or

the immune cell further expresses a safety switch; preferably, the safety switch includes iCaspase-9, Truncated EGFR or RQR8.

16. Use of the genetically modified immune cells of claim 15 for the preparation of a tumor-inhibiting drug, and said tumor is the tumor that expresses EGFRvIII or overexpresses EGFR.

17. A pharmaceutical composition, comprising:

The antibody of claim 1 or 2 or a nucleic acid encoding the antibody; or

The immunoconjugate of claim 7 or a nucleic acid encoding the conjugate; or

The chimeric antigen receptor of claim 10 or a nucleic acid encoding the chimeric antigen receptor; or

The genetically modified immune cell of claim 15.