

Claims

1. An antibody that binds B cell maturation antigen (BCMA), wherein the antibody comprises a light chain variable region (VL) comprising light chain complementarity determining region (LCDR) 1, 2, and 3 and comprises a heavy chain variable region (VH) comprising heavy chain complementarity determining region (HCDR) 1, 2, and 3; wherein the antibody is selected from the group consisting of:

(a) an antibody comprising HCDR1 as shown in SEQ ID NO: 1, HCDR2 as shown in SEQ ID NO: 2, HCDR3 as shown in SEQ ID NO: 3, LCDR1 as shown in SEQ ID NO: 6, LCDR2 as shown in SEQ ID NO: 7, and LCDR3 as shown in SEQ ID NO: 8;

(b) an antibody comprising HCDR1 as shown in SEQ ID NO: 1, HCDR2 as shown in SEQ ID NO: 2, HCDR3 as shown in SEQ ID NO: 4, LCDR1 as shown in SEQ ID NO: 6, LCDR2 as shown in SEQ ID NO: 7, and LCDR3 as shown in SEQ ID NO: 9;

(c) an antibody comprising HCDR1 as shown in SEQ ID NO: 1, HCDR2 as shown in SEQ ID NO: 2, HCDR3 as shown in SEQ ID NO: 5, LCDR1 as shown in SEQ ID NO: 6, LCDR2 as shown in SEQ ID NO: 7, and LCDR3 as shown in SEQ ID NO: 10;

(d) an antibody comprising HCDR1 as shown in SEQ ID NO: 60, HCDR2 as shown in SEQ ID NO: 61, HCDR3 as shown in SEQ ID NO: 5, LCDR1 as shown in SEQ ID NO: 6, LCDR2 as shown in SEQ ID NO: 7, and LCDR3 as shown in SEQ ID NO: 10; and

(e) an antibody comprising HCDR1 as shown in SEQ ID NO: 62, HCDR2 as shown in SEQ ID NO: 63, HCDR3 as shown in SEQ ID NO: 5, LCDR1 as shown in SEQ ID NO: 6, LCDR2 as shown in SEQ ID NO: 7, and LCDR3 as shown in SEQ ID NO: 10.

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

(a) an antibody comprising a heavy chain variable region that has the amino acid sequence shown in SEQ ID NO: 13 and a light chain variable region that has the amino acid sequence shown in SEQ ID NO: 11;

(b) an antibody comprising a heavy chain variable region that has the amino acid sequence shown in SEQ ID NO: 17 and a light chain variable region that has the amino acid sequence shown in SEQ ID NO: 15;

(c) an antibody comprising a heavy chain variable region that has the amino acid sequence shown in SEQ ID NO: 21 and a light chain variable region that has the amino acid sequence shown in SEQ ID NO: 19;

(d) an antibody comprising a heavy chain variable region that has the amino acid sequence shown in SEQ ID NO: 56 and a light chain variable region that has the amino acid sequence shown in SEQ ID NO: 19; and

(e) an antibody comprising a heavy chain variable region that has the amino acid sequence shown in SEQ ID NO: 58 and a light chain variable region that has the amino acid sequence shown in SEQ ID NO: 19.

3. A pharmaceutical composition comprising an antibody of claim **1** and a pharmaceutically acceptable carrier.

4. A nucleic acid encoding the antibody of claim **1**.

5. An expression vector comprising the nucleic acid of claim **4**.

6. A host cell comprising the expression vector of claim **5**.

7. A multifunctional immunoconjugate, comprising an antibody of claim **1** and a functional molecule linked thereto, wherein the functional molecule is selected from the group consisting of a molecule that targets a tumor surface marker, a molecule that inhibits tumors, a molecule that targets a surface marker of an immune cell, and a detectable label; wherein the multifunctional immunoconjugate optionally includes a linker peptide between the antibody and functional molecule.

8. The multifunctional immunoconjugate of claim **7**, wherein the molecule that inhibits tumors is an antitumor cytokine or an antitumor toxin.

9. The multifunctional immunoconjugate of claim **7**, wherein the molecule that targets a surface marker of an immune cell is an antibody that binds to a surface marker of an immune cell.

10. A pharmaceutical composition comprising a multifunctional immunoconjugate of claim **7** and a pharmaceutically acceptable carrier.

11. A B cell maturation antigen (BCMA)-targeting chimeric antigen receptor (CAR) that comprises an extracellular domain, a hinge domain, transmembrane domain and an intracellular signal domain sequentially linked, wherein the extracellular domain comprises a BCMA-binding antibody of claim **1**.

12. The BCMA-targeting chimeric antigen receptor of claim **11**, wherein the intracellular signal domain further comprises one or more co-stimulatory signal domains.

13. The BCMA-targeting chimeric antigen receptor of claim **12**, wherein the transmembrane domain is selected from the group consisting of alpha, beta, zeta chain of TCR, or the transmembrane domain is a transmembrane region selected from the group consisting of CD3 ϵ , CD3 ζ , CD4, CD5, CD8 α , CD9, CD16, CD22, CD27, CD28, CD33, CD37, CD45, CD64, CD80, CD86, CD134, CD137, CD152, CD154 and PD1; and/or

the co-stimulatory signal domain is selected from the group consisting of an intracellular signal region of CARD11, CD2, CD7, CD27, CD28, CD30, CD40, CD54, CD83, OX40, CD137, CD134, CD150, CD152, CD223, CD270, PD-L2, PD-L1, CD278, DAP10, LAT, NKD2C, SLP76, TRIM, FcεRIγ, MyD88 and 41BBL.

5 **14.** The BCMA-targeting chimeric antigen receptor of claim **13**, wherein the transmembrane domain is the transmembrane region of CD8 or CD28, and/or the co-stimulatory signal domain is the intracellular signal domain of CD137 or CD28.

10 **15.** The BCMA-targeting chimeric antigen receptor of claim **11**, wherein the extracellular domain is a scFv antibody comprising a heavy chain variable region that has HCDR1 as shown in SEQ ID NO: 60, HCDR2 as shown in SEQ ID NO: 61 and HCDR3 as shown in SEQ ID NO: 5 and a light chain variable region that has LCDR1 as shown in SEQ ID NO: 6, LCDR2 as shown in SEQ ID NO: 7 and LCDR3 as shown in SEQ ID NO: 10.

15 **16.** A genetically modified immune cell which expresses the BCMA-targeting chimeric antigen receptor of claim **11**.

20 **17.** The genetically modified immune cell of claim **16**, wherein the genetically modified immune cell further expresses a sequence that encodes a cytokine selected from IL-12, IL-15, IL-21, and type I interferon; another chimeric antigen receptor; a chemokine receptor; an siRNA that reduces PD-1 expression; a protein that blocks PD-L1; a TCR; or a sequence that is a safety switch.

18. A genetically modified T cell which expresses the BCMA-targeting chimeric antigen receptor of claim **11**.

19. A pharmaceutical composition comprising genetically modified immune cells of claim **16**.

25 **20.** A B cell maturation antigen (BCMA)-targeting chimeric antigen receptor (CAR), wherein the chimeric antigen receptor is selected from the group consisting of:

30 (a) a chimeric antigen receptor that has an extracellular domain as shown in SEQ ID NO: 64, a CD8 hinge domain as shown in SEQ ID NO: 25, a transmembrane region as shown in SEQ ID NO: 33, a CD137 intracellular signaling domain as shown in SEQ ID NO: 35, and a CD3ξ primary signal domain as shown in SEQ ID NO: 31;

 (b) a chimeric antigen receptor that has an extracellular domain as shown in SEQ ID NO: 66, a CD8 hinge domain as shown in SEQ ID NO: 25, a transmembrane region as shown in SEQ ID NO: 33, a CD137 intracellular signaling domain as shown in SEQ ID NO: 35, and a CD3ξ primary signal domain as shown in SEQ ID NO: 31;

(c) a chimeric antigen receptor that has an extracellular domain as shown in SEQ ID NO: 47, a CD8 hinge domain as shown in SEQ ID NO: 25, a transmembrane region as shown in SEQ ID NO: 33, a CD137 intracellular signaling domain as shown in SEQ ID NO: 35, and a CD3 ξ primary signal domain as shown in SEQ ID NO: 31;

5 (d) a chimeric antigen receptor that has a CD8 α signal peptide as shown in SEQ ID NO: 23, a 7A12 scFv as shown in SEQ ID NO: 47, a CD8 hinge as shown in SEQ ID NO: 25, a CD28 transmembrane region as shown in SEQ ID NO: 27, an intracellular signaling domain as shown in SEQ ID NO: 29 and an intracellular segment CD3 ξ of CD3 as shown in SEQ ID NO: 31;

10 (e) a chimeric antigen receptor that has a CD8 α signal peptide as shown in SEQ ID NO: 23, a 7A12 scFv as shown in SEQ ID NO: 47, a CD8 hinge as shown in SEQ ID NO: 25, a transmembrane region as shown in SEQ ID NO: 33, a CD137 intracellular signaling domain as shown in SEQ ID NO: 35 and a CD3 ξ as shown in SEQ ID NO: 31;

(f) a chimeric antigen receptor that has a CD8 α signal peptide as shown in SEQ ID
15 NO: 23, a 7A12-scFv as shown in SEQ ID NO: 47, CD8 hinge as shown in SEQ ID NO: 25, a CD28 transmembrane region as shown in SEQ ID NO: 27, an intracellular segment as shown in SEQ ID NO: 29, a CD137 intracellular signaling domain as shown in SEQ ID NO: 35 and a CD3 ξ as shown in SEQ ID NO: 31;

(g) a chimeric antigen receptor that has a CD8 α signal peptide as shown in SEQ ID
20 NO: 23, a 7G2 scFv as shown in SEQ ID NO: 48, a CD8 hinge as shown in SEQ ID NO: 25, a CD28 transmembrane region as shown in SEQ ID NO: 27, an intracellular signaling domain as shown in SEQ ID NO: 29 and an intracellular segment CD3 ξ of CD3 as shown in SEQ ID NO: 31;

(h) a chimeric antigen receptor that has a CD8 α signal peptide as shown in SEQ
25 ID NO: 23, a 7G2 scFV as shown in SEQ ID NO: 48, a CD8 hinge as shown in SEQ ID NO: 25, a transmembrane region as shown in SEQ ID NO: 33, a CD137 intracellular signaling domain as shown in SEQ ID NO: 35 and a CD3 ξ as shown in SEQ ID NO: 31;
and

(i) a chimeric antigen receptor that has a CD8 α signal peptide as shown in SEQ ID
30 NO: 23, a 7G2-scFv as shown in SEQ ID NO: 48, a CD8 hinge as shown in SEQ ID NO: 25, a CD28 transmembrane region as shown in SEQ ID NO: 27, an intracellular segment as shown in SEQ ID NO: 29, a CD137 intracellular signaling domain as shown in SEQ ID NO: 35 and a CD3 ξ as shown in SEQ ID NO: 31.

21. A genetically modified T cell which expresses a BCMA-targeting chimeric antigen receptor of claim **20**.

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22. A pharmaceutical composition comprising genetically modified T cells of claim **21**.