

CLAIMS

1. A chimeric antigen receptor (CAR) comprising a polypeptide comprising:
 - (a) an extracellular antigen binding domain comprising a first single-domain antibody (sdAb) specifically binding to a first antigen and a second single-domain antibody (sdAb) specifically binding to a second antigen, wherein the first sdAb is an anti-BCMA sdAb;
 - (b) a transmembrane domain; and
 - (c) an intracellular signaling domain.
2. The CAR of claim 1, wherein the first antigen is different from the second antigen or wherein the first antigen is the same as the second antigen.
3. The CAR of claim 1 or claim 2, wherein the first sdAb is located at the N-terminus of the second sdAb or the C-terminus of the second sdAb.
4. The CAR of claim 1, wherein the second antigen are selected from the group consisting of CD19, CD20, CD22, CD33, CD38, BCMA, CSI, ROR1, GPC3, CD123, IL-13R, CD138, c-Met, EGFRvIII, GD-2, NY-ESO-1, MAGE A3, and glycolipid F77.
5. The CAR of claim 4, wherein the first sdAb is an anti-BCMA sdAb, and the second sdAb is an anti-CD38 sdAb or an anti-CD19 sdAb.
6. The CAR of claim 5, wherein the first sdAb and the second sdAb specifically bind to the same epitope or to different epitopes.
7. The CAR of any one of claims 1-6, wherein the first sdAb and/or the second sdAb are camelid, chimeric, human, or humanized.
8. The CAR of any one of claims 1-7, wherein the first sdAb and the second sdAb are directly fused to each other via a peptide bond or via a peptide linker of no more than about 50 amino acids in length.
9. An anti-BCMA single-domain antibody (sdAb) comprising any one of the following:
 - (1) a CDR1 comprising the amino acid sequence of SEQ ID NO:7; a CDR2 comprising the amino acid sequence of SEQ ID NO:18; and a CDR3 comprising the amino acid sequence of SEQ ID NO:29;
 - (2) a CDR1 comprising the amino acid sequence of SEQ ID NO:8; a CDR2 comprising the amino acid sequence of SEQ ID NO:19; and a CDR3 comprising the amino acid sequence of SEQ ID NO:30;

- (3) a CDR1 comprising the amino acid sequence of SEQ ID NO:9; a CDR2 comprising the amino acid sequence of SEQ ID NO:20; and a CDR3 comprising the amino acid sequence of SEQ ID NO:31;
- (4) a CDR1 comprising the amino acid sequence of SEQ ID NO:10; a CDR2 comprising the amino acid sequence of SEQ ID NO:21; and a CDR3 comprising the amino acid sequence of SEQ ID NO:32;
- (5) a CDR1 comprising the amino acid sequence of SEQ ID NO:11; a CDR2 comprising the amino acid sequence of SEQ ID NO:22; and a CDR3 comprising the amino acid sequence of SEQ ID NO:33;
- (6) a CDR1 comprising the amino acid sequence of SEQ ID NO:12; a CDR2 comprising the amino acid sequence of SEQ ID NO:23; and a CDR3 comprising the amino acid sequence of SEQ ID NO:34;
- (7) a CDR1 comprising the amino acid sequence of SEQ ID NO:13; a CDR2 comprising the amino acid sequence of SEQ ID NO:24; and a CDR3 comprising the amino acid sequence of SEQ ID NO:35;
- (8) a CDR1 comprising the amino acid sequence of SEQ ID NO:14; a CDR2 comprising the amino acid sequence of SEQ ID NO:25; and a CDR3 comprising the amino acid sequence of SEQ ID NO:36;
- (9) a CDR1 comprising the amino acid sequence of SEQ ID NO:15; a CDR2 comprising the amino acid sequence of SEQ ID NO:26; and a CDR3 comprising the amino acid sequence of SEQ ID NO:37;
- (10) a CDR1 comprising the amino acid sequence of SEQ ID NO:16; a CDR2 comprising the amino acid sequence of SEQ ID NO:27; and a CDR3 comprising the amino acid sequence of SEQ ID NO:38; or
- (11) a CDR1 comprising the amino acid sequence of SEQ ID NO:17; a CDR2 comprising the amino acid sequence of SEQ ID NO:28; and a CDR3 comprising the amino acid sequence of SEQ ID NO:39.

10. A chimeric antigen receptor comprising:

- (a) an extracellular antigen binding domain comprising the anti-BCMA sdAb of claim 9;
- (b) a transmembrane domain; and
- (c) an intracellular signaling domain.

11. The CAR of any one of claims 1-8 and 10, wherein the intracellular signaling domain comprises a primary intracellular signaling domain of an immune effector cell and is derived from CD3 ζ .
12. The CAR of any one of claims 1-8 and 10-11, wherein the intracellular signaling domain comprises a co-stimulatory signaling domain derived from a co-stimulatory molecule selected from the group consisting of CD27, CD28, CD137, OX40, CD30, CD40, CD3, LFA-1, CD2, CD7, LIGHT, NKG2C, B7-H3, Ligands of CD83 and combinations thereof.
13. The CAR of any one of claims 1-8 and 10-12, further comprising a hinge domain located between the C-terminus of the extracellular antigen binding domain and the N-terminus of the transmembrane domain and a signal peptide located at the N-terminus of the polypeptide.
14. A chimeric antigen receptor, comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: SEQ ID NO: 207-216.
15. An isolated nucleic acid comprising a nucleic acid sequence encoding the CAR of any one of claims 1-8 and 10-14.
16. A vector comprising the isolated nucleic acid of claim 15.
17. An engineered immune effector cell, comprising the CAR of any one of claims 1-14, the isolated nucleic acid of claim 15, or the vector of claim 16 and wherein the immune effector cell is a T cell.
18. A pharmaceutical composition, comprising the anti-BCMA sdAb of claim 9, and a pharmaceutically acceptable carrier.
19. Use of the anti-BCMA sdAb of claim 9 in the manufacture of a pharmaceutical composition for treating cancer in an individual.