

Claims

1. A chimeric antigen receptor (CAR), comprising: an anti-BCMA antigen-binding region which comprises a light chain variable region (V_L) and a heavy chain variable region (V_H), V_L comprising
5 three complementarity determining regions (CDRs), LCDR1, LCDR2 and LCDR3, V_H comprising three CDRs, HCDR1, HCDR2 and HCDR3,

(a) wherein LCDR1, LCDR2 and LCDR3 have amino acid sequences about 80% to about 100% identical to the amino acid sequences set forth in SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 21, respectively, wherein HCDR1, HCDR2 and HCDR3 have amino acid sequences about
10 80% to about 100% identical to the amino acid sequences set forth in SEQ ID NO: 24, SEQ ID NO: 26, SEQ ID NO: 28, respectively;

(b) wherein LCDR1, LCDR2 and LCDR3 have amino acid sequences about 80% to about 100% identical to the amino acid sequences set forth in SEQ ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 35, respectively, wherein HCDR1, HCDR2 and HCDR3 have amino acid sequences about
15 80% to about 100% identical to the amino acid sequences set forth in SEQ ID NO: 38, SEQ ID NO: 40, SEQ ID NO: 42, respectively; or

(c) wherein LCDR1, LCDR2 and LCDR3 have amino acid sequences about 80% to about 100% identical to the amino acid sequences set forth in SEQ ID NO: 45, SEQ ID NO: 47, SEQ ID NO: 49, respectively, wherein HCDR1, HCDR2 and HCDR3 have amino acid sequences about
20 80% to about 100% identical to the amino acid sequences set forth in SEQ ID NO: 52, SEQ ID NO: 54, SEQ ID NO: 56, respectively.

2. The CAR of claim 1, wherein V_L is located at the N-terminus of V_H .

3. The CAR of claim 1, wherein V_L and V_H have amino acid sequences about 80% to about 100% identical to amino acid sequences set forth in (a) SEQ ID NO: 1 and SEQ ID NO: 2, respectively; (a) SEQ ID NO: 3 and SEQ ID NO: 4, respectively; or (a) SEQ ID NO: 5 and SEQ ID NO: 6, respectively.

4. The CAR of claim 1, wherein the anti-BCMA antigen-binding region is a single-chain variable fragment (scFv) that specifically binds BCMA.

5. The CAR of claim 1, wherein the CAR further comprises one or more of the following:

- (a) a signal peptide,
- (b) a hinge region,
- (c) a transmembrane domain,
- (d) a co-stimulatory region, and
- (e) a cytoplasmic signaling domain.

6. The CAR of claim 5, wherein the co-stimulatory region comprises a co-stimulatory region of 4-1BB (CD137), CD28, OX40, CD2, CD7, CD27, CD30, CD40, CD70, CD134, PD1, Dap10, CDS, ICAM-1, LFA-1 (CD11a/CD18), ICOS (CD278), NKG2D, GITR, TLR2, or combinations thereof.

7. The CAR of claim 5, wherein the cytoplasmic signaling domain comprises a cytoplasmic signaling domain of CD3 ζ .

8. The CAR of claim 5, wherein the hinge region comprises a hinge region of CD8, CD28, CD137, Ig4, or combinations thereof.

9. The CAR of claim 5, wherein the transmembrane domain comprises a transmembrane domain of CD8, CD28, CD3 ϵ , CD45, CD4, CD5, CD9, CD16, CD22, CD33, CD37, CD64, CD80, CD86, CD134, CD137, CD154, or combinations thereof.

10. An immune cell expressing the CAR of claim 1.

11. The immune cell of claim 10, wherein the immune cell is a T cell or a natural killer (NK) cell.

12. A nucleic acid encoding the CAR of claim 1.

13. A vector comprising the nucleic acid of claim 12.

14. ~~A method of treating cancer, the method comprising administering~~ Use of the immune cell of claim 10 in the manufacture of a medicament for the treatment of cancer, wherein the medicament is to be administered to a subject in need thereof.

5

15. The ~~method-use~~ of claim 14, wherein the cancer is a hematologic cancer.

16. The ~~method-use~~ of claim 14, wherein the cancer is a plasma-cell malignancy.

10

17. The ~~method-use~~ of claim 14, wherein the cancer is a BCMA-positive malignancy.

18. The ~~method-use~~ of claim 14, wherein the cancer is multiple myeloma (MM), or plasma cell leukemia.

15

19. The ~~method-use~~ of claim 14, wherein the ~~immune cell~~ medicament is to be administered by infusion, injection, transfusion, implantation, and/or transplantation.

20

20. The ~~method-use~~ of claim 14, wherein the ~~immune cell~~ medicament is to be administered intravenously, subcutaneously, intradermally, intranodally, intratumorally, intramedullary, intramuscularly, or intraperitoneally.

21. The ~~method-use~~ of claim 14, wherein the ~~immune cell~~ medicament is to be administered via intravenous infusion.

25

22. The ~~method-use~~ of claim 14, wherein the immune cell is allogeneic or autologous.

23. The ~~method-use~~ of claim 14, wherein the subject is a human.

30

24. ~~A method for treating cancer, the method comprising administering the~~ Use of the immune cell of claim 10 in the manufacture of a medicament for the treatment of cancer, wherein the medicament is to be administered to a subject in need thereof, wherein the chimeric antigen

receptor (CAR) generates an area under the curve (AUC) ranging from about $5.0\text{e}+05$ copies/ μg genomic DNA (copies/gDNA) to about $1.3\text{e}+07$ copies/gDNA in the blood of the subject in about 28 days after the medicament is to be administered~~administration~~.

5 25. The ~~method~~use of claim 24, wherein the AUC ranges from about $5.0\text{e}+06$ copies/ μg genomic DNA (copies/gDNA) to about $1.0\text{e}+07$ copies/gDNA in the blood of the subject in about 28 days after the medicament is to be administered~~administration~~.

10 26. The ~~method~~use of claim 24, wherein the AUC ranges from about $5.0\text{e}+06$ copies/ μg genomic DNA (copies/gDNA) to about $1.3\text{e}+07$ copies/gDNA in the blood of the subject in about 28 days after the medicament is to be administered~~administration~~.

15 27. The ~~method~~use of claim 24, wherein the AUC ranges from about $7.0\text{e}+06$ copies/ μg genomic DNA (copies/gDNA) to about $1.0\text{e}+07$ copies/gDNA in the blood of the subject in about 28 days after the medicament is to be administered~~administration~~.

20 28. ~~A method for treating cancer, the method comprising administering~~Use of the immune cell of claim 10 in the manufacture of a medicament for the treatment of cancer, wherein the medicament is to be administered to a subject in need thereof, wherein the chimeric antigen receptor (CAR) generates a maximum plasma concentration (C_{max}) ranging from about $5\text{x}10^4$ copies/ μg genomic DNA (copies/gDNA) to about $1.3\text{x}10^6$ copies/gDNA in the blood of the subject.

25 29. The ~~method~~use of claim 28, wherein the C_{max} ranges from about $5\text{x}10^5$ copies/ μg genomic DNA (copies/gDNA) to about $1.3\text{x}10^6$ copies/gDNA in the blood of the subject in about 28 days after the medicament is to be administered~~administration~~.

30 30. The ~~method~~use of claim 28, wherein the C_{max} ranges from about $7.5\text{x}10^5$ copies/ μg genomic DNA (copies/gDNA) to about $1\text{x}10^6$ copies/gDNA in the blood of the subject in about 28 days after the medicament is to be administered~~administration~~.

31. The ~~method~~use of claim 28, wherein the CAR has a $T_{\max}$ ranging from about 12 days to about 25 days.

32. The ~~method~~use of claim 28, wherein the CAR has a $T_{\max}$ ranging from about 14 days to about 20 days.

33. The ~~method~~use of claim 28, wherein the CAR has a $T_{\max}$ ranging from about 6 days to about 22 days.

34. The CAR of claim 1, comprising an amino acid sequence about 80% to about 100% identical to the amino acid sequence set forth in SEQ ID NO: 59, SEQ ID NO: 61, or SEQ ID NO: 63.