

CLAIMS

~~What is claimed is:~~

1. A chimeric antigen receptor (CAR) comprising:
 - (a) an extracellular domain that specifically binds to the human Kallikrein-2 (hK2) antigen,
 - (b) a transmembrane domain, and
 - (c) an intracellular signaling domain optionally comprising at least one co-stimulatory domain.
2. The CAR of claim 1, further comprising
 - (d) a CD8a-hinge region,wherein the transmembrane domain comprises a CD8a transmembrane region (CD8a-TM) polypeptide; and
wherein the intracellular signaling domain comprises a co-stimulatory domain comprising a TNF receptor superfamily member 9 (CD137) component and a primary signaling domain comprising a T-cell surface glycoprotein CD3 zeta chain (CD3z) component.
3. The CAR of claim 2, wherein
 - the CD8a-hinge region comprises an amino acid sequence that is at least 90% identical to SEQ ID NO: 25, 269, 270, 271, or 272;
 - the transmembrane domain comprises an amino acid sequence that is at least 90% identical to SEQ ID NO: 26; and/or
 - the intracellular signaling domain comprises a co-stimulatory domain having an amino acid sequence that is at least 90% identical to SEQ ID NO: 27, and a primary signaling domain having an amino acid sequence that is at least 90% identical to SEQ ID NO: 28.

4. A chimeric antigen receptor (CAR), comprising an extracellular antigen-binding domain, a transmembrane domain and an intracellular signaling domain, wherein the extracellular antigen-binding domain comprises:

a heavy chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 63, a heavy chain CDR2 having the amino acid sequence of SEQ ID NO: 64, and a heavy chain CDR3 having the amino acid sequence of SEQ ID NO: 66; a heavy chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 314, a heavy chain CDR2 having the amino acid sequence of SEQ ID NO: 315, and a heavy chain CDR3 having the amino acid sequence of SEQ ID NO: 311;

a heavy chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 309, a heavy chain CDR2 having the amino acid sequence of SEQ ID NO: 310, and a heavy chain CDR3 having the amino acid sequence of SEQ ID NO: 311;

a heavy chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 63, a heavy chain CDR2 having the amino acid sequence of SEQ ID NO: 65, and a heavy chain CDR3 having the amino acid sequence of SEQ ID NO: 66;

a heavy chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 72, a heavy chain CDR2 having the amino acid sequence of SEQ ID NO: 73, and a heavy chain CDR3 having the amino acid sequence of SEQ ID NO: 66;

a heavy chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 86, a heavy chain CDR2 having the amino acid sequence of SEQ ID NO: 87, and a heavy chain CDR3 having the amino acid sequence of SEQ ID NO: 88;

a heavy chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 92, a heavy chain CDR2 having the amino acid sequence of SEQ ID NO: 93, and a heavy chain CDR3 having the amino acid sequence of SEQ ID NO: 94;

a heavy chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 102, a heavy chain CDR2 having the amino acid sequence of SEQ ID NO: 103, and a heavy chain CDR3 having the amino acid sequence of SEQ ID NO: 104;

a heavy chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 105, a heavy chain CDR2 having the amino acid sequence of SEQ ID NO: 106, and a heavy chain CDR3 having the amino acid sequence of SEQ ID NO: 104;

a heavy chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 107, a heavy chain CDR2 having the amino acid sequence of SEQ ID NO: 108, and a heavy chain CDR3 having the amino acid sequence of SEQ ID NO: 109;

a heavy chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 110, a heavy chain CDR2 having the amino acid sequence of SEQ ID NO: 111, and a heavy chain CDR3 having the amino acid sequence of SEQ ID NO: 109;

a heavy chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 102, a heavy chain CDR2 having the amino acid sequence of SEQ ID NO: 112, and a heavy chain CDR3 having the amino acid sequence of SEQ ID NO: 113;

a heavy chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 105, a heavy chain CDR2 having the amino acid sequence of SEQ ID NO: 114, and a heavy chain CDR3 having the amino acid sequence of SEQ ID NO: 113;

a heavy chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 115, a heavy chain CDR2 having the amino acid sequence of SEQ ID NO: 116, and a heavy chain CDR3 having the amino acid sequence of SEQ ID NO: 117;

a heavy chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 118, a heavy chain CDR2 having the amino acid

sequence of SEQ ID NO: 119, and a heavy chain CDR3 having the amino acid sequence of SEQ ID NO: 117;

a heavy chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 120, a heavy chain CDR2 having the amino acid sequence of SEQ ID NO: 121, and a heavy chain CDR3 having the amino acid sequence of SEQ ID NO: 122; or

a heavy chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 123, a heavy chain CDR2 having the amino acid sequence of SEQ ID NO: 124, and a heavy chain CDR3 having the amino acid sequence of SEQ ID NO: 122,

wherein the extracellular antigen-binding domain binds the hK2 antigen.

5. A chimeric antigen receptor (CAR), comprising an extracellular antigen-binding domain, a transmembrane domain and an intracellular signaling domain, wherein the extracellular antigen-binding domain comprises:

a light chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 67, a light chain CDR2 having the amino acid sequence of SEQ ID NO: 69, and a light chain CDR3 having the amino acid sequence of SEQ ID NO: 71;

a light chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 68, a light chain CDR2 having the amino acid sequence of SEQ ID NO: 70, and a light chain CDR3 having the amino acid sequence of SEQ ID NO: 71;

a light chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 89, a light chain CDR2 having the amino acid sequence of SEQ ID NO: 90, and a light chain CDR3 having the amino acid sequence of SEQ ID NO: 91;

a light chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 95, a light chain CDR2 having the amino acid sequence of SEQ ID NO: 96, and a light chain CDR3 having the amino acid sequence of SEQ ID NO: 71;

a light chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 312, a light chain CDR2 having the amino acid sequence of SEQ ID NO: 313, and a light chain CDR3 having the amino acid sequence of SEQ ID NO: 91;

a light chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 89, a light chain CDR2 having the amino acid sequence of SEQ ID NO: 90, and a light chain CDR3 having the amino acid sequence of SEQ ID NO: 91;

a light chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 67, a light chain CDR2 having the amino acid sequence of SEQ ID NO: 126, and a light chain CDR3 having the amino acid sequence of SEQ ID NO: 71;

a light chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 128, a light chain CDR2 having the amino acid sequence of SEQ ID NO: 129, and a light chain CDR3 having the amino acid sequence of SEQ ID NO: 130;

a light chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 125, a light chain CDR2 having the amino acid sequence of SEQ ID NO: 131, and a light chain CDR3 having the amino acid sequence of SEQ ID NO: 132;

a light chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 133, a light chain CDR2 having the amino acid sequence of SEQ ID NO: 134, and a light chain CDR3 having the amino acid sequence of SEQ ID NO: 135;

a light chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 136, a light chain CDR2 having the amino acid sequence of SEQ ID NO: 137, and a light chain CDR3 having the amino acid sequence of SEQ ID NO: 138; or

a light chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 97, a light chain CDR2 having the amino acid sequence

of SEQ ID NO: 127, and a light chain CDR3 having the amino acid sequence of SEQ ID NO: 139,

wherein the extracellular antigen-binding domain binds the hK2 antigen.

6. The CAR according to claim 4, wherein the extracellular antigen-binding domain further comprises:

a light chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 67, a light chain CDR2 having the amino acid sequence of SEQ ID NO: 69, and a light chain CDR3 having the amino acid sequence of SEQ ID NO: 71;

a light chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 68, a light chain CDR2 having the amino acid sequence of SEQ ID NO: 70, and a light chain CDR3 having the amino acid sequence of SEQ ID NO: 71;

a light chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 89, a light chain CDR2 having the amino acid sequence of SEQ ID NO: 90, and a light chain CDR3 having the amino acid sequence of SEQ ID NO: 91;

a light chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 95, a light chain CDR2 having the amino acid sequence of SEQ ID NO: 96, and a light chain CDR3 having the amino acid sequence of SEQ ID NO: 71;

a light chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 89, a light chain CDR2 having the amino acid sequence of SEQ ID NO: 90, and a light chain CDR3 having the amino acid sequence of SEQ ID NO: 91;

a light chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 67, a light chain CDR2 having the amino acid sequence of SEQ ID NO: 126, and a light chain CDR3 having the amino acid sequence of SEQ ID NO: 71;

a light chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 128, a light chain CDR2 having the amino acid sequence of SEQ ID NO: 129, and a light chain CDR3 having the amino acid sequence of SEQ ID NO: 130;

a light chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 125, a light chain CDR2 having the amino acid sequence of SEQ ID NO: 131, and a light chain CDR3 having the amino acid sequence of SEQ ID NO: 132;

a light chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 133, a light chain CDR2 having the amino acid sequence of SEQ ID NO: 134, and a light chain CDR3 having the amino acid sequence of SEQ ID NO: 135;

a light chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 136, a light chain CDR2 having the amino acid sequence of SEQ ID NO: 137, and a light chain CDR3 having the amino acid sequence of SEQ ID NO: 138; or

a light chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 97, a light chain CDR2 having the amino acid sequence of SEQ ID NO: 127, and a light chain CDR3 having the amino acid sequence of SEQ ID NO: 139.

7. The CAR according to claim 6, wherein the extracellular antigen-binding domain comprises:

a heavy chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 63, a heavy chain CDR2 having the amino acid sequence of SEQ ID NO: 64, a heavy chain CDR3 having the amino acid sequence of SEQ ID NO: 66, and a light chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 67, a light chain CDR2 having the amino acid sequence of SEQ ID NO: 69, a light chain CDR3 having the amino acid sequence of SEQ ID NO: 71;

a heavy chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 63, a heavy chain CDR2 having the amino acid sequence of SEQ ID NO: 65, a heavy chain CDR3 having the amino acid sequence of SEQ ID NO: 66, and a light chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 68, a light chain CDR2 having the amino acid sequence of SEQ ID NO: 70, a light chain CDR3 having the amino acid sequence of SEQ ID NO: 71;

a heavy chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 63, a heavy chain CDR2 having the amino acid sequence of SEQ ID NO: 65, a heavy chain CDR3 having the amino acid sequence of SEQ ID NO: 66, and a light chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 67, a light chain CDR2 having the amino acid sequence of SEQ ID NO: 126, a light chain CDR3 having the amino acid sequence of SEQ ID NO: 71;

a heavy chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 63, a heavy chain CDR2 having the amino acid sequence of SEQ ID NO: 65, a heavy chain CDR3 having the amino acid sequence of SEQ ID NO: 66, and a light chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 67, a light chain CDR2 having the amino acid sequence of SEQ ID NO: 69, a light chain CDR3 having the amino acid sequence of SEQ ID NO: 71;

a heavy chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 63, a heavy chain CDR2 having the amino acid sequence of SEQ ID NO: 65, a heavy chain CDR3 having the amino acid sequence of SEQ ID NO: 66, and a light chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 67, a light chain CDR2 having the amino acid sequence of SEQ ID NO: 126, a light chain CDR3 having the amino acid sequence of SEQ ID NO: 71;

a heavy chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 314, a heavy chain CDR2 having the amino acid sequence of SEQ ID NO: 315, a heavy chain CDR3 having the amino acid sequence of SEQ ID NO:

311, and a light chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 312, a light chain CDR2 having the amino acid sequence of SEQ ID NO: 313, a light chain CDR3 having the amino acid sequence of SEQ ID NO: 91;

a heavy chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 102, a heavy chain CDR2 having the amino acid sequence of SEQ ID NO: 103, a heavy chain CDR3 having the amino acid sequence of SEQ ID NO: 104, and a light chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 128, a light chain CDR2 having the amino acid sequence of SEQ ID NO: 129, a light chain CDR3 having the amino acid sequence of SEQ ID NO: 130;

a heavy chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 107, a heavy chain CDR2 having the amino acid sequence of SEQ ID NO: 108, a heavy chain CDR3 having the amino acid sequence of SEQ ID NO: 109, and a light chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 125, a light chain CDR2 having the amino acid sequence of SEQ ID NO: 131, a light chain CDR3 having the amino acid sequence of SEQ ID NO: 132;

a heavy chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 102, a heavy chain CDR2 having the amino acid sequence of SEQ ID NO: 112, a heavy chain CDR3 having the amino acid sequence of SEQ ID NO: 113, and a light chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 133, a light chain CDR2 having the amino acid sequence of SEQ ID NO: 134, a light chain CDR3 having the amino acid sequence of SEQ ID NO: 135;

a heavy chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 115, a heavy chain CDR2 having the amino acid sequence of SEQ ID NO: 116, a heavy chain CDR3 having the amino acid sequence of SEQ ID NO: 117, and a light chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 136, a light chain CDR2 having the amino acid sequence

of SEQ ID NO: 137, a light chain CDR3 having the amino acid sequence of SEQ ID NO: 138; or

a heavy chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 120, a heavy chain CDR2 having the amino acid sequence of SEQ ID NO: 121, a heavy chain CDR3 having the amino acid sequence of SEQ ID NO: 122, and a light chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 97, a light chain CDR2 having the amino acid sequence of SEQ ID NO: 127, a light chain CDR3 having the amino acid sequence of SEQ ID NO: 138.

8. The CAR according to claim 6, wherein the extracellular antigen-binding domain comprises: a heavy chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 86, a heavy chain CDR2 having the amino acid sequence of SEQ ID NO: 87, a heavy chain CDR3 having the amino acid sequence of SEQ ID NO: 88, and a light chain complementarity determining region 1 (CDR1) having the amino acid sequence of SEQ ID NO: 89, a light chain CDR2 having the amino acid sequence of SEQ ID NO: 90, a light chain CDR3 having the amino acid sequence of SEQ ID NO: 91.

9. A chimeric antigen receptor (CAR), comprising an extracellular antigen-binding domain, a transmembrane domain and an intracellular signaling domain, wherein the extracellular antigen-binding domain comprises:

a light chain variable domain (VL) comprising an amino acid sequence selected from SEQ ID NOS: 1, 2, 3, 74, 75, 147, 148, 149, 150, 151, 152 and 318; and/or

a heavy chain variable domain (VH) comprising an amino acid sequence selected from SEQ ID NOS: 4, 5, 6, 76, 77, 140, 141, 142, 143, 144, 145, 146 and 317;

wherein the extracellular antigen-binding domain binds the human Kallikrein-2 (hK2) antigen.

10. The CAR of claim 9, wherein the extracellular antigen-binding domain comprises:
- a light chain variable region comprising an amino acid sequence of SEQ ID NO: 1 and a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 4;
 - a light chain variable region comprising an amino acid sequence of SEQ ID NO: 2 and a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 4;
 - a light chain variable region comprising an amino acid sequence of SEQ ID NO: 3 and a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 6;
 - a light chain variable region comprising an amino acid sequence of SEQ ID NO: 3 and a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 4;
 - a light chain variable region comprising an amino acid sequence of SEQ ID NO: 2 and a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 6;
 - a light chain variable region comprising an amino acid sequence of SEQ ID NO: 3 and a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 4;
 - a light chain variable region comprising an amino acid sequence of SEQ ID NO: 1 and a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 6;
 - a light chain variable region comprising an amino acid sequence of SEQ ID NO: 3 and a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 5;
 - a light chain variable region comprising an amino acid sequence of SEQ ID NO: 1 and a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 5;
 - a light chain variable region comprising an amino acid sequence of SEQ ID NO: 2 and a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 5;

a light chain variable region comprising an amino acid sequence of SEQ ID NO: 3 and a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 5;

a light chain variable region comprising an amino acid sequence of SEQ ID NO: 74 and a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 76;

a light chain variable region comprising an amino acid sequence of SEQ ID NO: 75 and a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 77;

a light chain variable region comprising an amino acid sequence of SEQ ID NO: 147 and a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 140;

a light chain variable region comprising an amino acid sequence of SEQ ID NO: 75 and a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 141;

a light chain variable region comprising an amino acid sequence of SEQ ID NO: 75 and a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 140;

a light chain variable region comprising an amino acid sequence of SEQ ID NO: 148 and a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 142;

a light chain variable region comprising an amino acid sequence of SEQ ID NO: 149 and a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 143;

a light chain variable region comprising an amino acid sequence of SEQ ID NO: 150 and a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 144;

a light chain variable region comprising an amino acid sequence of SEQ ID NO: 151 and a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 145;

a light chain variable region comprising an amino acid sequence of SEQ ID NO: 152 and a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 146;

a light chain variable region comprising an amino acid sequence of SEQ ID NO: 318 and a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 317.

11. The CAR of any of claims 1-10, wherein the extracellular antigen-binding domain comprises a single-chain variable fragment (scFv), the scFv comprising a light chain variable region (VL) and a heavy chain variable region (VH).
12. The CAR of claim 11, wherein the scFv comprises a linker polypeptide between the light chain variable region (VL) and the heavy chain variable region (VH).
13. The CAR of claim 12, wherein the linker polypeptide comprises an amino acid sequence of SEQ ID NO: 7.
14. The CAR of any of claims 11-13, wherein the scFv comprises an amino acid sequence selected from the group consisting of SEQ ID NOS: 8-23, 169-184 and 340-343.
15. The CAR of any of claims 1-14, wherein the extracellular antigen-binding domain comprises a signal polypeptide.
16. The CAR of claim 15, wherein the signal polypeptide comprises an amino acid sequence of SEQ ID NO: 24.
17. The CAR of any of claims 4-16, wherein the intracellular signaling domain comprises a polypeptide component selected from the group consisting of a TNF receptor superfamily member 9 (CD137) component, a T-cell surface glycoprotein CD3 zeta chain

(CD3z) component, a cluster of differentiation (CD27) component, a cluster of differentiation superfamily member component, and a combination thereof.

18. The CAR of claim 17, wherein the CD137 component comprises an amino acid sequence of SEQ ID NO: 27.

19. The CAR of claim 17 or claim 18, wherein the CD3z component comprises an amino acid sequence of SEQ ID NO: 28.

20. The CAR of any one of claims 17-19, wherein the intracellular signaling domain comprises an amino acid sequence of SEQ ID NO: 45, or, optionally, the intracellular signaling domain comprises a co-stimulatory domain comprising an amino acid sequence of SEQ ID NO: 27, and a primary signaling domain comprising an amino acid sequence of SEQ ID NO: 28.

21. The CAR of any of claims 4-20, wherein the transmembrane domain comprises a CD8a transmembrane region (CD8a-TM) polypeptide.

22. The CAR of claim 21, wherein the CD8a-TM polypeptide comprises an amino acid sequence of SEQ ID NO: 26.

23. The CAR of any of claims 4-22, further comprising a hinge region linking the transmembrane domain to the extracellular antigen-binding domain.

24. The CAR of claim 23, wherein the hinge region is a CD8a-hinge region.

25. The CAR of claim 24, wherein the CD8a-hinge region comprises an amino acid sequence of SEQ ID NO: 25, 269, 270, 271, or 272.

26. The CAR of any of claims 1-25, wherein the extracellular antigen-binding domain comprises an amino acid sequence selected from the group consisting of SEQ ID NOS: 29-44, 78-81, 221-236, and 273-308.
27. The CAR of any of claims 1-26, wherein the CAR comprises an amino acid sequence selected from the group consisting of SEQ ID NOS: 46-61, 82-85 and 205-220.
28. An isolated lymphocyte expressing the CAR of any of claims 1-27.
29. The isolated lymphocyte of claim 28, wherein the lymphocyte is a T lymphocyte.
30. The isolated lymphocyte of claim 28, wherein the lymphocyte is a natural killer (NK) cell.
31. An isolated nucleic acid molecule encoding the CAR of any of claims 1-27.
32. A vector comprising the nucleic acid molecule of claim 31.
33. A cell expressing the nucleic acid molecule of claim 31.
34. A pharmaceutical composition, comprising an effective amount of the lymphocyte of any of claims 28-30.
35. A pharmaceutical composition, comprising an effective amount of the lymphocyte of any of claims 28-30 and a pharmaceutically acceptable excipient.
36. The CAR of any of claims 1-27 or the pharmaceutical composition of claims 34 or 35 for use in therapy.

37. The CAR of any of claims 1-27 or the pharmaceutical composition of claims 34 or 35 for use in a method of treating a subject having cancer.

38. ~~A method of treating a subject having cancer, the method comprising:~~
~~administering a therapeutically effective amount~~ Use of the lymphocyte of any of
claims 28-30 ~~in the manufacture of a medicament for treating cancer, to a subject in~~
~~need thereof, wherein a therapeutically effective amount of the lymphocyte is to be~~
~~administered to the subject in need thereof, and~~ whereby the lymphocyte induces killing
of cancer cells in the subject.

39. The ~~method-use~~ of claim 38, or the CAR or the pharmaceutical composition for
use in a method of claim 37, wherein the cancer is prostate cancer or androgen receptor-
expressing breast cancer.

40. ~~A method of targeted killing of a cancer cell, the method comprising:~~
~~contacting the cancer cell with~~ Use of the lymphocyte of any of claims 28-30 in the
manufacture of a medicament for treating cancer, whereby the lymphocyte is to be
contacted with the cancer cell and, whereby
the lymphocyte induces killing of the cancer cell.

41. The ~~method-use~~ of claim 40, wherein the cancer cell is a prostate cancer cell or
androgen receptor-expressing breast cancer cell.

42. A method of detecting the presence of cancer in a subject, comprising:
contacting a cell sample obtained from the subject with the CAR of any one
of claims 1-27, thereby forming a CAR-cell complex, and
detecting the complex, wherein detection of the complex is indicative of the
presence of cancer in the subject.

43. The lymphocyte of any of claims 28-30 for use in therapy.