

Claims

1. A chimeric antigen receptor (CAR) comprising an extracellular spacer which comprises at least part of the extracellular domain of human low affinity nerve growth factor (LNGFR), wherein at least part of the LNGFR is suitable for facilitating immunoselection and identification of cells transduced with said CAR.
2. A CAR according to claim 1 wherein the spacer lacks the intracellular domain of LNGFR.
3. A CAR according to any preceding claim wherein the extracellular spacer comprises the first three TNFR-Cys domains of LNGFR.
4. A CAR according to claim 3 wherein spacer comprises all four TNFR-Cys domains of LNGFR.
5. A CAR according to any preceding claim wherein the spacer comprises the fourth TNFR-Cys domain (TNFR-Cys 4) but wherein the following amino acid sequence is removed from said domain: NHVDPCLPCTVCEdTERQLRECTRW and replaced with the following amino acid sequence: ARA.
6. A CAR according to any preceding claim wherein the spacer comprises the serine /threonine-rich stalk of LNGFR.
7. A CAR according to claims 1 to 5 wherein the spacer lacks the serine /threonine-rich stalk of LNGFR.
8. A CAR according to claim 1 or 2 wherein said spacer comprises the entire extracellular domain of LNGFR.
9. A CAR according to claim 1 or 2 wherein the spacer comprises the extracellular domain of LNGFR with the exception of the serine /threonine-rich stalk of said domain.
10. A chimeric antigen receptor (CAR) comprising an extracellular spacer wherein the spacer comprises the sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5 or SEQ ID NO:7 or a sequence at least 90% identical thereto.
11. A CAR according to claim 10 wherein the spacer consists of a sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5 or SEQ ID NO:7 or a sequence at least 90% identical thereto.
12. A chimeric antigen receptor (CAR) comprising
 - (i) an antigen-specific targeting domain;
 - (ii) an extracellular spacer domain as defined in any one of claims 1 to 11;
 - (iii) a transmembrane domain;
 - (iv) optionally at least one costimulatory domain; and
 - (v) an intracellular signaling domain.

13. A CAR according to claim 12 wherein the antigen-specific targeting domain comprises an antibody or fragment there.
14. A CAR according to claim 13 wherein the antigen-specific targeting domain is a single chain variable fragment.
15. A CAR according to any one of claims 12 to 14 wherein the antigen-specific targeting domain targets a tumour antigen.
16. A CAR according to claim 15 wherein the tumour antigen is selected from the group consisting of CD44, CD19, CD20, CD22, CD23, CD123, CS-1, ROR1, mesothelin, c-Met, PSMA, Her2, GD-2, CEA, MAGE A3 TCR and combinations thereof.
17. A CAR according to claim 15 wherein the tumour antigen is isoform 6 of CD44 (CD44v6).
18. A CAR according to any one of claims 12 to 17 wherein the transmembrane domain comprises any one or more of a transmembrane domain of a zeta chain of a T cell receptor complex, CD28, CD8a, and combinations thereof.
19. A CAR according to claim any one of claims 12 to 18 wherein the costimulatory domain comprises a costimulating domain from any one or more of CD28, CD137 (4-1BB), CD134 (OX40), Dap10, CD27, CD2, CD5, ICAM-1, LFA-1, Lck, TNFR-I, TNFR-II, Fas, CD30, CD40 and combinations thereof.
20. A CAR according to any one of claims 12 to 19 wherein the intracellular signaling domain comprises an intracellular signaling domain of one or more of a human CD3 zeta chain, FcγRIII, FcεRI, a cytoplasmic tail of a Fc receptor, an immunoreceptor tyrosine-based activation motif (ITAM) bearing cytoplasmic receptors, and combinations thereof.
21. A CAR according to any one of claims 12 to 20 wherein the antigen-specific targeting domain targets CD44v6, the transmembrane domain comprises a transmembrane domain of CD28, the intracellular signaling domain comprises an intracellular signaling domain of human CD3 zeta chain and the costimulatory domain comprises a CD28 endo-costimulating domain.
22. A polynucleotide encoding a CAR of any one of claims 1 to 21.
23. A vector comprising the polynucleotide of claim 22.
24. A vector according to claim 23 wherein the vector is a viral vector.
25. A cell comprising a CAR according to any one of claims 1 to 21, a polynucleotide according to claim 22 or a vector according to claim 23 or 24.
26. A cell according to claim 25 wherein the cell is a T-cell.
27. A pharmaceutical composition comprising the cell of claim 25 or 26.
28. A CAR according to any one of claims 12 to 21, or a polynucleotide according to claim 22, a vector according to claim 23 or 24 or a cell according to claim 25 or 26, for use in treating cancer.

29. A CAR according to claim 21, a polynucleotide encoding said CAR, a vector comprising said polynucleotide or a host cell comprising said CAR, polynucleotide or vector, for use in treating tumours that express CD44.