CLAIMS

1. A cell which co-expresses a first chimeric antigen receptor (CAR) and second CAR at the cell surface, each CAR comprising an antigen-binding domain, wherein the antigen-binding domain of the first CAR binds to CD19 and the antigen-binding domain of the second CAR binds to CD22.

2. A cell according to Claim 1, in which each CAR comprises:

(i) an antigen-binding domain;

(ii) a spacer; and

(iii) a trans-membrane domain;

in which the spacer of the first CAR is different to the spacer of the second CAR.

3. A cell according to Claim 2, in which the antigen-binding domain of the second CAR binds to an epitope on Ig domain 1, 2, 3 or 4 of CD22.

4. A nucleic acid sequence encoding both the first and second chimeric antigen receptors (CARs) as defined in any of Claims 1, 2 or 3.

5. A nucleic acid sequence according to Claim 4, which has the following structure:

AgB1-spacer1-TM1 -coexpr-AbB2-spacer2-TM2

in which

AgB1 is a nucleic acid sequence encoding the antigen-binding domain of the first CAR;

spacer 1 is a nucleic acid sequence encoding the spacer of the first CAR;

TM1 is a a nucleic acid sequence encoding the transmembrane domain of the first CAR;

coexpr is a nucleic acid sequence enabling co-expression of both CARs

AgB2 is a nucleic acid sequence encoding the antigen-binding domain of the second CAR;

spacer 2 is a nucleic acid sequence encoding the spacer of the second CAR;

TM2 is a a nucleic acid sequence encoding the transmembrane domain of the second CAR;

which nucleic acid sequence, when expressed in a T cell, encodes a polypeptide which is cleaved at the cleavage site such that the first and second CARs are co-expressed at the T cell surface.

6. A nucleic acid sequence according to Claim 5, in which coexpr encodes a sequence comprising a self-cleaving peptide.

7. A nucleic acid sequence according to Claim 5 or 6, in which alternative codons are used in regions of sequence encoding the same or similar amino acid sequences, in order to avoid homologous recombination.

8. A kit which comprises

(i) a first nucleic acid sequence encoding the first chimeric antigen receptor (CAR) as defined in any of Claims 1 to 3, which nucleic acid sequence has the following structure:

AgB1-spacer1-TM1

in which

AgB1 is a nucleic acid sequence encoding the antigen-binding domain of the first CAR;

spacer 1 is a nucleic acid sequence encoding the spacer of the first CAR;

TM1 is a nucleic acid sequence encoding the transmembrane domain of the first CAR;

and

(ii) a second nucleic acid sequence encoding the second chimeric antigen receptor (CAR) as defined in any of Claims 1 to 3, which nucleic acid sequence has the following structure:

AgB2-spacer2-TM2

AgB2 is a nucleic acid sequence encoding the antigen-binding domain of the second CAR;

spacer 2 is a nucleic acid sequence encoding the spacer of the second CAR; and

TM2 is a nucleic acid sequence encoding the transmembrane domain of the second CAR.

9. A kit comprising: a first vector which comprises the first nucleic acid sequence as defined in Claim 8; and a second vector which comprises the second nucleic acid sequence as defined in Claim 8.

10. A kit according to Claim 9, in which the vectors are integrating viral vectors or transposons.

11. A vector comprising a nucleic acid sequence according to any of Claims 4 to 7.

12. A retroviral vector or a lentiviral vector or a transposon according to Claim 11.

13. A method for making a cell according to any of Claims 1 to 3, which comprises the step of introducing: a nucleic acid sequence according to any of Claims 4 to 7; a first nucleic acid sequence and a second nucleic acid sequence as defined in Claim 8; and/or a first vector and a second vector as defined in Claim 9 or a vector according to Claim 11 or 12, into a cell.

14. A method according to Claim 13, in which the cell is from a sample isolated from a subject.

15. A pharmaceutical composition comprising a plurality of cells according to any of Claims 1 to 3.

16. A pharmaceutical composition according to Claim 15 for use in treating a disease.

17. A pharmaceutical composition for use according to Claim 16, which comprises the following steps:

(i) isolation of a cell-containing sample from a subject;

(ii) transduction or transfection of the cells with: a nucleic acid sequence according to any of Claims 4 to 7; a first nucleic acid sequence and a second nucleic acid sequence as defined in Claim 8; a first vector and a second vector as defined in Claim 9 or 10 or a vector according to Claim 11 or 12; and

(iii) administering the cells from (ii) to a the subject.

18. A pharmaceutical composition for use according to Claim 16 or 17, in which the disease is a cancer.

19. A pharmaceutical composition for use according to Claim 18, in which the cancer is a B cell malignancy.

20. Use of a cell according to any of Claims 1 to 3 in the manufacture of a medicament for treating and/or preventing a disease.

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