

CLAIMS

1. A T cell or NK cell which co-expresses a first chimeric antigen receptor (CAR) and second CAR as separate molecules 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 T cell or NK 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 T cell or NK 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 encoding both the first and second chimeric antigen receptors (CARs) as defined in any of Claims 1, 2 or 3.
5. A nucleic acid according to Claim 4, which has the following structure:

AgB1-spacer1-TM1-coexpr-AgB2-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 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 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 a cleavage site such that the first and second CARs are co-expressed at the T cell surface.

6. A nucleic acid according to Claim 5, in which coexpr encodes a sequence comprising a self-cleaving peptide.
7. A nucleic acid 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 vector comprising a nucleic acid according to any of Claims 4 to 7.
9. A retroviral vector or a lentiviral vector or a transposon according to Claim 8.
10. A method for making a cell according to any of Claims 1 to 3, which comprises the step of introducing: a nucleic acid according to any of Claims 4 to 7; or a vector according to Claim 8 or 9, into a cell.
11. A method according to Claim 10, in which the cell is from a sample isolated from a subject.
12. A pharmaceutical composition comprising a plurality of cells according to any of Claims 1 to 3.
13. A pharmaceutical composition according to Claim 12 for use in treating a disease.
14. A pharmaceutical composition for use according to Claim 13, in which the plurality of cells is prepared by:
 - (i) isolating a cell-containing sample from a subject; and
 - (ii) transducing or transfecting the cells with: a nucleic acid sequence according to any of Claims 4 to 7; or a vector according to Claim 8 or 9.
15. A pharmaceutical composition for use according to Claim 13 or 14, in which the disease is a cancer.
16. A pharmaceutical composition for use according to Claim 15, in which the cancer is a B cell malignancy.

17. Use of a cell according to any of Claims 1 to 3 in the manufacture of a medicament for treating a B-cell malignancy.