

CLAIMS

1. A chimeric transmembrane protein which comprises two polypeptides:
 - (i) a first polypeptide which comprises:
 - (a) a heavy chain constant domain (CH)
 - 5 (b) a first chain of the cytokine receptor endodomain; and
 - (ii) a second polypeptide which comprises:
 - (a) a light chain constant domain (CL)
 - (b) a second chain of the cytokine-receptor endodomain, in which the cytokine receptor endodomain comprises:
 - 10 (i) IL-2 receptor β -chain endodomain
 - (ii) IL-7 receptor α -chain endodomain; or
 - (iii) IL-15 receptor α -chain endodomain; and
 - (iv) common γ -chain receptor endodomain.
2. A cell which comprises a chimeric transmembrane protein according to Claim 1.
- 15 3. A cell which comprises a chimeric antigen receptor (CAR) and a chimeric transmembrane protein which comprises two polypeptides:
 - (i) a first polypeptide which comprises:
 - (a) a heavy chain constant domain (CH)
 - (b) a first chain of a type I cytokine receptor endodomain; and
 - 20 (ii) a second polypeptide which comprises:
 - (a) a light chain constant domain (CL)
 - (b) a second chain of a type I cytokine-receptor endodomain.
4. A cell according to Claim 3, in which the cytokine receptor endodomain of the chimeric transmembrane protein comprises:
 - 25 (i) IL-2 receptor β -chain endodomain

- (ii) IL-7 receptor α -chain endodomain; or
- (iii) IL-15 receptor α -chain endodomain; and
- (iv) common γ -chain receptor endodomain.

5. A cell according to Claim 3 or 4, in which the chimeric antigen receptor binds a tumour-associated cell surface antigen.
6. A nucleic acid sequence encoding a chimeric transmembrane protein according to Claim 1.
7. A nucleic acid construct encoding a chimeric transmembrane protein according to Claim 1, which comprises a first nucleic acid sequence encoding the first polypeptide and a second nucleic acid sequence encoding the second polypeptide, the nucleic acid construct having the structure:

CH -TM1-endo1-coexpr-CL -TM2-endo2

in which

CH is a nucleic acid sequence encoding the heavy chain constant domain of the first polypeptide;

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

endo 1 is a nucleic acid sequence encoding the endodomain of the first polypeptide;

coexpr is a nucleic acid sequence enabling co-expression of both the first and second polypeptide;

CL is a nucleic acid sequence encoding the light chain constant domain of the second polypeptide;

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

endo 2 is a nucleic acid sequence encoding the endodomain of the second polypeptide.

8. A nucleic acid construct encoding a chimeric transmembrane protein as defined in Claim 3, which comprises a first nucleic acid sequence encoding the first polypeptide and a

second nucleic acid sequence encoding the second polypeptide, the nucleic acid construct having the structure:

CH -TM1-endo1-coexpr-CL -TM2-endo2

in which

5 CH is a nucleic acid sequence encoding the heavy chain constant domain of the first polypeptide;

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

endo 1 is a nucleic acid sequence encoding the endodomain of the first polypeptide;

10 coexpr is a nucleic acid sequence enabling co-expression of the first and second polypeptides

CL is a nucleic acid sequence encoding the light chain constant domain of the second polypeptide;

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

endo 2 is a nucleic acid sequence encoding the endodomain of the second polypeptide,

in which the nucleic acid construct also comprises a nucleic acid sequence which encodes a chimeric antigen receptor (CAR).

20 9. A nucleic acid construct according to Claim 7 or 8, in which coexpr encodes a sequence comprising a self-cleaving peptide.

10. A nucleic acid construct according to Claim 7, 8 or 9, in which alternative codons are used in regions of sequence encoding the same or similar amino acid sequences, in order to avoid homologous recombination.

25 11. A vector comprising a nucleic acid sequence according to Claim 6 or a nucleic acid construct according to any of Claims 7 to 10.

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

13. A kit which comprises:
 - (i) a vector comprising a nucleic acid sequence encoding a first polypeptide as defined in Claim 1; and
 - (ii) a vector comprising a nucleic acid sequence encoding a second polypeptide as defined in Claim 1.
14. A kit which comprises:
 - (i) a vector comprising a nucleic acid sequence encoding a first polypeptide as defined in Claim 3; and
 - (ii) a vector comprising a nucleic acid sequence encoding a second polypeptide as defined in Claim 3; and
 - (iii) a vector comprising a nucleic acid sequence encoding a chimeric antigen receptor.
15. A kit which comprises:
 - (i) a vector comprising a nucleic acid sequence encoding a chimeric transmembrane protein as defined in Claim 3; and
 - (ii) a vector comprising a nucleic acid sequence encoding a chimeric antigen receptor.
16. A method for making a cell according to any of Claims 2 to 5, which comprises the step of introducing: a nucleic acid sequence according to Claim 6; a nucleic acid construct according to any of Claims 7 to 10; a vector according to Claim 11 or 12; or a kit of vectors according to any Claims 13 to 15, into a cell.
17. A method according to Claim 16, in which the cell is from a sample isolated from a subject.
18. A pharmaceutical composition comprising a plurality of cells according to any of Claims 2 to 5.
19. A pharmaceutical composition according to Claim 18 for use in treating a disease.
20. A pharmaceutical composition for use according to Claim 19, in which the disease is cancer.

21. Use of a cell according to any of Claims 2 to 5 in the manufacture of a medicament for treating a disease.