

CLAIMS

1. A multimeric chimeric antigen receptor (CAR) which comprises at least three CAR-forming polypeptides, each CAR-forming polypeptide comprising:

- (i) an antigen-binding domain;
- (ii) a coiled-coil spacer domain;
- (iii) a transmembrane domain; and
- (iv) an endodomain.

2. A multimeric chimeric antigen receptor (CAR) comprising one or more CAR-forming polypeptide(s) as defined in Claim 1, together with one or more accessory polypeptide(s), the or each accessory polypeptide comprising:

- (i) a coiled-coil spacer domain;
- (ii) a transmembrane domain; and
- (iii) an endodomain;

in which the total number of CAR-forming polypeptides and accessory polypeptides in the multimeric CAR is at least three.

3. A multimeric CAR according to Claim 1 or 2, in which the coiled-coil spacer domain is selected from: cartilage-oligomeric matrix protein (COMP), mannose-binding protein A, coiled-coil serine-rich protein 1, polypeptide release factor 2, SNAP-25, SNARE, Lac repressor or apolipoprotein E.

4. An engaged complex which comprises first and second multimeric CARs according to any preceding claim, in which the first multimeric CAR forms a bridge with the second multimeric CAR, such that the first and second multimeric CARs engage to form a complex.

5. A chimeric antigen receptor (CAR) signalling system, which comprises:

- (i) a multimeric CAR according to Claim 1, 2 or 3, in which the endodomain comprises a first heterodimerization domain; and
- (ii) an intracellular signalling component comprising a signalling domain and a second heterodimerization domain;

in which heterodimerization between the first and second heterodimerization domains causes the multimeric CAR and signalling component to form a functional CAR complex.

6. A nucleic acid sequence which encodes a CAR-forming polypeptide or accessory polypeptide as defined in Claim 1, 2 or 3.
7. A nucleic acid construct which encodes two or more CAR forming polypeptides as defined in Claim 1.
8. A nucleic acid construct which encodes at least one CAR-forming polypeptide as defined in Claim 1 and at least one accessory polypeptide as defined in Claim 2.
9. A nucleic acid construct which encodes:
 - (i) at least one CAR-forming polypeptide or accessory polypeptide which forms a CAR signalling system according to Claim 5; and
 - (ii) an intracellular signalling component.
10. A vector which comprises a nucleic acid sequence according to Claim 6 or a nucleic acid construct according to Claim 7, 8 or 9.
11. A cell which expresses a multimeric CAR according to Claim 1, 2 or 3; an engaged complex according to Claim 4; or a CAR signalling system according to Claim 5.
12. A pharmaceutical composition which comprises a cell according to Claim 11.
13. A cell according to Claim 11 for use in treating a disease.
14. Use of a cell according to Claim 11 in the manufacture of a medicament for treating a disease.
15. A cell for use according to Claim 13 or use according to Claim 14, in which the disease is cancer.
16. A cell or use according to Claim 15, in which the cancer is Chronic lymphocytic leukaemia (CLL), melanoma or myeloma.

17. A method for making a cell according to Claim 11, which comprises the step of introducing a nucleic acid sequence according to Claim 6, a nucleic acid construct according to Claim 7, 8 or 9 or a vector according to Claim 10 into the cell.