

CLAIMS

1. A cell which comprises a chimeric antigen receptor (CAR) and a signal transduction modifying protein, selected from one of the following:
 - (i) a truncated protein which comprises an SH2 domain from a protein which binds a phosphorylated immunoreceptor tyrosine-based activation motif (ITAM), but lacks a kinase domain;
 - (ii) a truncated protein which comprises an SH2 domain from a protein which binds a phosphorylated immunoreceptor tyrosine-based inhibition motif (ITIM) but lacks a phosphatase domain;
 - (iii) a fusion protein which comprises (a) an SH2 domain from a protein which binds a phosphorylated immunoreceptor tyrosine-based activation motif (ITAM) or from a protein which binds a phosphorylated immunoreceptor tyrosine-based inhibition motif (ITIM); and (ii) a heterologous domain.
2. A cell according to Claim 1, in which the signal transduction modifying protein is a truncated protein which comprises an PTPN6 SH2 but lacks a PTPN6 phosphatase domain.
3. A cell according to Claim 1, in which the signal transduction modifying protein is a truncated protein which comprises a SHP-2 SH2 domain but lacks a SHP-2 phosphatase domain.
4. A nucleic acid construct, which comprises:
 - a first nucleic acid sequence encoding a chimeric antigen receptor; and
 - a second nucleic acid sequence encoding a truncated protein or a fusion protein as defined in any preceding claim.
5. A vector which comprises a nucleic acid construct according to Claim 4.
6. A vector according to Claim 5, which is a retroviral or lentiviral vector.
7. A pharmaceutical composition comprising a plurality of cells according Claim 1, 2 or 3.
8. A pharmaceutical composition according to Claim 7 for use in treating and/or preventing a disease.

9. A method for treating and/or preventing a disease, which comprises the step of administering a pharmaceutical composition according to Claim 8 to a subject.
10. A method according to Claim 9, which comprises the following steps:
 - (i) isolation of a cell containing sample from a subject;
 - 5 (ii) transduction or transfection of the cells with a nucleic acid construct according to Claim 4 or a vector according to Claim 5 or 6; and
 - (iii) administering the cells from (ii) to the subject.
11. Use of a pharmaceutical composition according to Claim 8 in the manufacture of a medicament for the treatment and/or prevention of a disease.
- 10 12. A pharmaceutical composition for use according to Claim 8 or a method according to Claim 9 or 10 or a use according to Claim 11, in which the disease is cancer.
13. A method for making a cell according to Claim 1, 2 or 3, which comprises the step of introducing: a nucleic acid construct according to Claim 4 or a vector according to Claim 5 or 6, into the cell.
- 15 14. A method according to Claim 13, in which the cell is from a sample isolated from a subject.