CLAIMS

1. An immuno-responsive T-cell or Natural Killer (NK)-cell expressing

(i) a second generation chimeric antigen receptor (CAR) comprising:

(a) a signalling region;

(b) a co-stimulatory signalling region;

(c) a transmembrane domain; and

(d) a binding element that specifically interacts with a first epitope on a target antigen; and

(ii) a chimeric costimulatory receptor (CCR) comprising:

(e) a co-stimulatory signalling region which is different to that of (b);

(f) a transmembrane domain; and

(g) a binding element that specifically interacts with a second epitope on a target antigen.

2. The immuno-responsive cell according to claim 1 which is a T-cell.

3. The immuno-responsive cell according to claim 1 or claim 2 wherein co-stimulatory signalling regions for (b) and (e) are selected from CD28, CD27, ICOS, 4-1BB, OX40, CD30, GITR, HVEM, DR3 or CD40.

4. The immuno-responsive cell according to claim 3, wherein one of (b) or (e) is CD28 and the other is 4-1BB or OX40.

5. The immuno-responsive cell according to claim 3 wherein (b) is CD28 and (e) is 4-1BB or CD27.

6. The immuno-responsive cell according to any one of the preceding claims wherein the transmembrane domains of (c) and (f) are selected from CD8α and CD28 transmembrane domains.

7. The immuno-responsive cell according to any one of the preceding claims wherein the first and second epitopes are associated with the same receptor or antigen.

8. The immuno-responsive cell according to any one of the preceding claims which co-expresses a chimeric cytokine receptor, such as 4αβ.

9. The immuno-responsive cell according to any one of the preceding claims wherein at least one of binding element (d) or binding element (g) is a ligand for an ErbB dimer, a receptor for colony stimulating factor-1 (CSF-1R) or an $\alpha_v\beta_6$ integrin-specific binding agent.

10. The immuno-responsive cell according to any one of the preceding claims wherein binding element (d) comprises CSF-1 and binding element (g) comprises IL-34; or wherein binding element (d) is an $\alpha_v\beta_6$ integrin-specific binding agent which is a peptide comprising the sequence motif
RGDLX^{5}X^{6}L (SEQ ID NO 7) or
RGDLX^{5}X^{6}I (SEQ ID NO 8),
wherein LX^{5}X^{6}L or LX^{5}X^{6}I is contained within an alpha helical structure, wherein X^5 and X^6 are helix promoting residues; and binding element (g) is a T1E peptide, wherein said T1E peptide is a chimeric fusion protein composed of the entire mature human EGF protein, but wherein the five most N-terminal amino acids of said EGF protein are replaced by the seven most N-terminal amino acids of the mature human TGF-α isoform 1 protein.

11. The immuno-responsive cell according to any one of the preceding claims wherein binding affinity of binding element (d) is lower than that of binding element (g).

12. A method for preparing the immuno-responsive cell according to any one of the preceding claims, said method comprising transducing a cell with a first nucleic acid encoding the CAR of structure (i) as defined in claim 1; and also a second nucleic acid encoding the CCR of structure (ii) as defined in claim 1.

13. The method according to claim 12 wherein the immuno-responsive cell comprises a chimeric cytokine receptor, and wherein an expansion step is carried out in the presence of said cytokine.

14. A combination of a first nucleic acid encoding the CAR of (i) as defined in claim 1 and a second nucleic acid encoding the CCR of (ii) as defined in claim 1.

15. A vector or combination of vectors comprising the combination according to claim 14.

16. A kit comprising the combination according to claim 14 or claim 15.