Claims

1. A modified T cell adapted to over-express SLC1A5, an isoform of SLC1A5 or a tryptophan or glutamine transporter.

2. The modified T cell of claim 1 wherein the T cell is adapted to express SLC1A5, an isoform of SLC1A5 or a tryptophan or glutamine transporter at a level at least twice the expression level observed in an unmodified T cell.

3. The modified T cell of claim 1 wherein the T cell is adapted to express SLC1A5, an isoform of SLC1A5 or a tryptophan or glutamine transporter at a level at least twice the expression level observed in an unmodified activated T cell.

4. The modified T cell of any of any one of claims 1 to 3 wherein the T cell expresses at least one of
   (i) a gamma delta T cell receptor,
   (ii) an alpha beta T cell receptor,
   (iii) a T cell receptor and at least one chimeric antigen receptor (CAR).

5. The modified T cell of claim 4 wherein the T cell expresses a gamma delta T cell receptor and a co-stimulatory chimeric antigen receptor (CAR) wherein the costimulatory CAR comprises, an antigen binding domain, a transmembrane domain and an intracellular signalling domain wherein the intracellular signalling domain provides a co-stimulatory signal (signal 2 only) to the T cell following binding of antigen to the extracellular antigen binding domain.

6. The modified T cell of claim 4 wherein the T cell expresses a T cell receptor and a chimeric antigen receptor (CAR) wherein the CAR comprises, an antigen binding domain, a transmembrane domain and an intracellular signalling domain wherein the intracellular signalling domain

provides a signal 1 response only to the T cell following binding of antigen to the antigen binding domain.

7. The modified T cell of claim 4 wherein the T cell expresses a T cell receptor and a chimeric antigen receptor (CAR) wherein the CAR comprises, an antigen binding domain, a transmembrane domain and an intracellular signalling domain wherein the intracellular signalling domain provides a signal 1 response and a signal 2 response (from a co-stimulatory domain) to the T cell following binding of antigen to the antigen binding domain.

8. The modified T cell of claim 5 wherein the T cell expresses a gamma delta T cell receptor and a chimeric antigen receptor (CAR) wherein, in use, signal 1 is provided by a first binding event of the TCR on the gamma delta T cell to the cell binding target recognised by the TCR and signal 2 is provided by a second binding event of antigen to the antigen binding domain of the co-stimulatory CAR and in combination signal 1 and signal 2 from both first and second binding events respectively activate the T cell.

9. The modified T cell of any one of claims 1 to 8 wherein the T cell expresses a gamma delta T cell receptor wherein the gamma delta (γδ) T cell is of the Vγ9Vδ2 subtype.

10. The modified T cell of any preceding claim wherein SLC1A5 is overexpressed in conjunction with SLC7A5 and SLC3A2 to form a LAT1 transporter.

11. A method of treating a cancer, the method comprising administration of an effective amount of a modified T cell of any one of claims 1 to 10 to a subject in need thereof.

12. A modified T cell of any one of claims 1 to 10 for use in medicine.

13. A modified T cell of any one of claims 1 to 10 for use in the treatment of cancer or a virus.

14. An isolated nucleic acid encoding SLC1A5, an isoform of SLC1A5 or a tryptophan or glutamine transporter operably linked to control sequences adapted to allow a T cell transformed by the nucleic acid to express the encoded SLC1A5, an isoform of SLC1A5, or tryptophan or glutamine transporter, optionally wherein the tryptophan or glutamine transporter is selected from a high-affinity glutamate and neutral amino acid transporter family (SLC1A1, SLC1A2, SLC1A3, SLC1A4, SLC1A5, SLC1A6, SLC1A7); heavy subunits of heterodimeric amino acid transporters (SLC3A1, SLC3A2); a member of the sodium- and chloride-dependent sodium:neurotransmitter symporter family (SLC6A1, SLC6A2, SLC6A3, SLC6A4, SLC6A5, SLC6A6, SLC6A7, SLC6A8, SLC6A9, SLC6A10, SLC6A11, SLC6A12, SLC6A13, SLC6A14, SLC6A15, SLC6A16, SLC6A17, SLC6A18, SLC6A19, SLC6A20) or a member of a cationic amino acid transporter/glycoprotein-associated family (SLC7A1, SLC7A2, SLC7A3, SLC7A4, SLC7A5, SLC7A6, SLC7A7, SLC7A8, SLC7A9, SLC7A10, SLC7A11, SLC7A13, SLC7A14).

15. A vector comprising a nucleic acid of claim 14.

16. A host T cell transfected or transduced with the nucleic acid of claim 14 or vector of claim 15.

17. A method of culturing a T cell to express the transporter encoded by the nucleic acid of claim 14 or the vector of claim 15 wherein the method comprises the step of introducing a nucleic acid according to claim 14 or a vector according to claim 15 into a T cell.

18. The method of claim 17 wherein the T cell is a T cell isolated from a subject with a disease to be treated.

19. A pharmaceutical composition comprising a T cell of any one of claims 1 to 10 and a therapeutic agent.

20. Use of a modified T cell according to any one of claims 1 to 10 in the manufacture of a medicament for treating or preventing disease.

21. Use of a modified T cell in the manufacture of a medicament according to claim 20 wherein the disease is cancer.

22. A method to provide a modified T cell to a subject comprising the steps

a. providing a T cell containing sample which has been isolated from a subject
b. transducting or transfecting a T cell of the T cell containing sample with a nucleic acid of claim 14 or a vector of claim 15, and
c. administering the cells from (b) to the subject.

23. A method of selecting a modified T cell adapted to overexpress SLC1A5, an isoform of SLC1A5 or a tryptophan or glutamine transporter, as claimed in any one of claims 1 to 10, wherein the method comprises the steps:

a. culturing a population of T cells comprising modified T cells adapted to overexpress SLC1A5, an isoform of SLC1A5 or an alternative tryptophan or glutamine transporter in a media with at least one of L-tryptophan at a concentration of less than 5μM and L-glutamine at a concentration of less than 3μM, or in the presence of an inhibitor of SLC1A5, optionally wherein said inhibitor is O-Benzyl-L-Serine;

b. selecting those modified T cells which proliferate when cultured according to step a.

24. A method of selecting a modified T cell adapted to overexpress SLC1A5, an isoform of SLC1A5 or a tryptophan or glutamine transporter, as claimed in any one of claims 1 to 10, wherein the method comprises
    a. providing a binding member with binding specificity to at least one of SLC1A5, an isoform of SLC1A5 or an alternative tryptophan or glutamine transporter, to a T cell expressing at least one of SLC1A5, an isoform of SLC1A5 or an alternative tryptophan or glutamine transporter,
    b. optionally, detecting the binding of the binding member to the T cell in step a, and
    c. selecting the T cell to which the binding member is bound.

25. A method of isolating a modified T cell adapted to overexpress SLC1A5, an isoform of SLC1A5 or an alternative tryptophan or glutamine transporter, the method comprising the steps:
    a. providing a binding member with binding specificity to SLC1A5, an isoform of SLC1A5 or an alternative tryptophan or glutamine transporter to a culture comprising T cells,
    b. isolating a T cell to which the binding member is bound form the culture.

26. A method of treating a cancer as claimed in claim 11 wherein the, the method comprises administering at a first time point an effective amount of a modified T cell of any one of claims 1 to 10 to a subject in need thereof, wherein the method further comprises a step of administering to the subject at a second later time point a binding member with binding specificity to SLC1A5, an isoform of SLC1A5 or a tryptophan or glutamine transporter capable of binding to the modified T cell to selectively bind to and reduce the modified T cells present in the subject.