CLAIMS

1. A method of selecting a modified T cell adapted to overexpress SLC1A5, an isoform of SLC1A5 or an alternative tryptophan or glutamine transporter, in which 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 the presence of an inhibitor of SLC1A5; and

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

2. A method of selecting a modified T cell adapted to overexpress SLC1A5, an isoform of SLC1A5 or an alternative tryptophan or glutamine transporter, according to Claim 1, in which the method further comprises the steps:

(c) providing an antibody with binding specificity to at least one of SLC1A5, an isoform of SLC1A5 or an alternative tryptophan or glutamine transporter, to a cell expressing at least one of SLC1A5, an isoform of SLC1A5 or an alternative tryptophan or glutamine transporter,

(d) optionally, detecting the binding of the antibody to the cell in step (a), and

(e) selecting the cell to which the antibody is bound.

3. A method of selecting a modified T cell adapted to overexpress SLC1A5, an isoform of SLC1A5 or an alternative tryptophan or glutamine transporter according to Claim 2, in which the method further comprises the step:

(f) isolating a cell to which the antibody is bound.

4. A method of selecting a modified T cell according to Claim 1, in which the inhibitor of SLC1A5 is O-Benzyl-L-Serine.

5. A method according to any preceding claim, in which the modified T cell co-expresses a chimeric antigen receptor and a glutamine and/or tryptophan transporter provided by the same construct.

6. A modified T cell provided by a method according to Claim 5.

7. A modified T cell according to Claim 6, in which 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.

8. A modified T cell according to Claim 6 or 7, in which the T cell expresses a gamma delta T cell receptor and a co-stimulatory chimeric antigen receptor (CAR) in which the costimulatory CAR comprises, an antigen binding domain, a transmembrane domain and an intracellular signalling domain in which 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.

9. A modified T cell according to Claim 6 or 7, in which the T cell expresses a T cell receptor and a chimeric antigen receptor (CAR) in which the CAR comprises, an antigen binding domain, a transmembrane domain and an intracellular signalling domain in which the intracellular signalling domain provides a signal 1 response only, for example from a CD3zeta domain, to the T cell following binding of antigen to the antigen binding domain.

10. A modified T cell according to Claim 6 or 7, in which the T cell expresses a T cell receptor and a chimeric antigen receptor (CAR) in which the CAR comprises, an antigen binding domain, a transmembrane domain and an intracellular signalling domain in which the intracellular signalling domain provides a signal 1 response, for example from a CD3zeta domain, and a signal 2 response from a co-stimulatory domain to the T cell following binding of antigen to the antigen binding domain.

11. A modified T cell according to Claim 10, in which the T cell expresses a gamma delta T cell receptor and a chimeric antigen receptor (CAR) in which, 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.

12. A modified T cell according to any of Claims 6 to 11, in which the T cell expresses a gamma delta T cell receptor in which the gamma delta (γδ) T cell is of the Vγ9Vδ2 subtype.

13. A modified T cell according to any of Claims 6 to 12, in which SLC1A5 is overexpressed in conjunction with SLC7A5 and SLC3A2 to form a LAT1 transporter.

14. A method according to any of Claims 1 to 5 or a modified T cell according to any of Claims 6 to 13, in which the transporter is encoded by an isolated nucleic acid, in which the isolated nucleic acid 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 modified T cell according to any of Claims 6 to 14, for use in a method of treating a cancer, in which an effective amount of the modified T cell is to be administered to a subject in need thereof.

16. A modified T cell according to any of Claims 6 to 14 for use in medicine.

17. A modified T cell according to any of Claims 6 to 14 for use in the treatment of cancer or a viral infection.

18. A modified T cell for use according to Claim 15, in which the modified T cell is isolated from a subject with a disease to be treated.

19. A pharmaceutical composition comprising a modified T cell according to any of Claims 6 to 14 and a therapeutic agent.

20. A modified T cell for use according to Claim 15, in which an effective amount of a modified T cell according to any of Claims 6 to 14 is to be administered at a first time point to a subject in need thereof, in which an antibody with binding specificity to SLC1A5, an isoform of SLC1A5 or an alternative tryptophan or glutamine transporter capable of binding to the modified T cell is to be administered to the subject at a second later time point to selectively bind to and reduce the modified T cells present in the subject.