CLAIMS

1. A method for enhancing the ability of a regulatory T cell (Treg) to suppress immune responses comprising introducing a polynucleotide encoding a FOXP3 polypeptide into the Treg.

2. A method according to claim 1 wherein:

(i) the FOXP3 polypeptide comprises an amino acid sequence which is at least 80 % identical to SEQ ID NO: 3 or 4 or a functional fragment thereof; or

(ii) the polynucleotide encoding the FOXP3 polypeptide comprises a polynucleotide sequence which is at least 80 % identical to SEQ ID NO: 1 or 2 or a functional fragment thereof.

3. A method according to claim 1 or 2 wherein the polynucleotide encoding FOXP3 is a contiguous portion of an expression vector.

4. A method according to any preceding claim which further comprises introducing a polynucleotide encoding an exogenous T cell receptor (TCR) or a polynucleotide encoding a chimeric antigen receptor (CAR) into the Treg.

5. A method according to claim 4 wherein the polynucleotide encoding a FOXP3 polypeptide and the polynucleotide encoding the exogenous TCR or the CAR are provided by a single expression vector.

6. A method according to claim 5 wherein the vector comprises a nucleic acid with the orientation: 5' FOXP3 – X – TCR/CAR; wherein X is an internal self-cleaving sequence.

7. A method according to any preceding claim wherein the polynucleotide encoding FOXP3 is introduced into the isolated Treg by viral transduction; optionally wherein the polynucleotide encoding FOXP3 is introduced into the isolated Treg by retroviral transduction.

8. A method according to any preceding claim comprising:

(a) isolating a Treg from a cell population; and

(b) increasing FOXP3 expression in the Treg.

9. A method according to claim 8 wherein the cell population comprises or consists of peripheral blood mononuclear cells (PBMCs).

10. A method according to claim 8 or 9 wherein isolating the Treg comprises

isolating $CD4^+$ T cells; and

isolating the Treg from the $CD4^+$ T cells.

11. A method according to any of claims 8-10 wherein the isolation of the Treg comprises selection using immuno-magnetic beads or fluorescence-activated cell sorting (FACS).

12. A method according to any of claims 8-11 wherein the Treg is isolated by selecting for (i) $CD4^+CD25^+CD127^-$ and/or $CD4^+CD25^+CD127^{low}$ cells; (ii) $CD4^+CD25^{hi}CD127^-$ and/or $CD4^+CD25^+CD127^{low}$ cells.

13. A method according to any of claims 8-12 wherein the Treg is isolated by selecting for $FOXP3^+$ cells; preferable wherein the Treg is isolated by selecting for $CD4^+CD25^+FOXP3^+Helios^+Neuropilin1^+$ cells.

14. An engineered Treg obtainable or obtained by the method of any of claims 1-13.

15. An engineered Treg comprising an exogenous polynucleotide encoding a FOXP3 polypeptide and having higher FOXP3 expression than a corresponding non-engineered Treg.

16. An engineered Treg according to claim 15 wherein the FOXP3 polypeptide (i) comprises an amino acid sequence which is at least 80 % identical to SEQ ID NO: 3 or 4 or a functional fragment thereof or (ii) is encoded by a polynucleotide sequence which is at least 80 % identical to SEQ ID NO: 1 or 2 or a functional fragment thereof.

17. An engineered Treg according to claim 16 wherein the exogenous polynucleotide encoding FOXP3 is a contiguous portion of an expression vector.

18. An engineered Treg according to any of claims 14 to 17 further comprising a polynucleotide encoding an exogenous T cell receptor (TCR) or a polynucleotide encoding a chimeric antigen receptor (CAR).

19. An engineered Treg according to claim 18 wherein the polynucleotide encoding a FOXP3 polypeptide and the polynucleotide encoding the exogenous TCR or the CAR are provided by a single expression.

20. An engineered Treg according to claim 19 wherein the vector comprises a nucleic acid with the orientation: 5' FOXP3 – X – TCR/CAR; wherein X is an internal self-cleaving sequence

21. A pharmaceutical composition comprising an engineered Treg according to any of claims 14-20.

22. An engineered Treg according to any of claims 14-20, or a pharmaceutical composition according to claim 21, for use in prevention and/or treatment of a disease.

23. Use of an engineered Treg according to any of claims 14-20 in the manufacture of a medicament for prevention and/or treatment of a disease.

24. A method of prevention and/or treatment of a disease comprising administering to a subject an engineered Treg or a pharmaceutical composition according to any of claims 14-21.

25. An engineered Treg for use, or a pharmaceutical composition for use, according to claim 22, use of an engineered Treg according to claim 23, or a method according to claim 24, wherein the disease is an autoimmune disease; preferably wherein the disease is multiple sclerosis.

26. An engineered Treg according to any of claims 13 to 17 for use in prevention and/or treatment of a disease wherein the disease is transplant rejection or graft-vs-host disease.

27. Use of a polynucleotide encoding a FOXP3 polypeptide to enhance the ability of a regulatory T cell (Treg) to suppress immune responses.