

WHAT IS CLAIMED IS:

1. A method of generating a population of genetically modified veto cells, the method comprising:
 - (a) providing a population of cells comprising T cells, said T cells comprising at least 40 % memory CD8⁺ T cells;
 - (b) culturing said population of cells comprising T cells with an antigen or antigens under conditions which allow enrichment of tolerance-inducing antigen-specific cells having a central memory T-lymphocyte (Tcm) phenotype, the cells being depleted of graft versus host (GVH) reactivity; and
 - (c) transducing said cells with a polynucleotide encoding a heterologous cell surface receptor comprising a T cell receptor signaling module, thereby generating the population of genetically modified veto cells.
2. The method of claim 1, wherein said step (b) is affected concomitantly with step (c).
3. The method of any one of claims 1-2, wherein step (a) is affected by treating peripheral blood mononuclear cells (PBMCs),
 - (i) with an agent capable of depleting CD4⁺, CD56⁺ and CD45RA⁺ cells; or
 - (ii) with an agent capable of selecting CD45RO⁺, CD8⁺ cells,
 so as to obtain a population of cells comprising T cells enriched of memory CD8⁺ T cells comprising a CD45RO⁺CD45RA⁻CD8⁺ phenotype.
4. The method of any one of claims 1-3, wherein said heterologous cell surface receptor comprises a chimeric antigen receptor (CAR) or a transgenic T cell receptor (tg-TCR).
5. The method of claim 4, wherein said CAR comprises at least one co-stimulatory domain and/or at least one signaling domain.
6. The method of any one of claims 4-5, wherein said CAR or said tg-TCR binds an antigen selected from the group consisting of a tumor antigen, a viral antigen, a bacterial antigen, a fungal antigen, a protozoa antigen, and a parasite antigen.

7. The method of any one of claims 1-6, wherein said culturing said population of cells comprising T cells with an antigen or antigens under conditions which allow enrichment of tolerance-inducing antigen-specific cells having a Tcm phenotype, is affected by a method comprising:

- (a) contacting said population of cells comprising T cells with said antigen or antigens in the presence of IL-21 so as to allow enrichment of antigen reactive cells; and
- (b) culturing said cells resulting from step (a) in the presence of IL-21, IL-15 and/or IL-7 so as to allow proliferation of cells comprising said Tcm phenotype.

8. The method of any one of claims 1-7, wherein said antigen or antigens comprise third-party antigen or antigens.

9. The method of any one of claims 7-8, wherein said Tcm phenotype comprises a CD3⁺, CD8⁺, CD62L⁺, CD45RA⁻, CD45RO⁺ signature.

10. An isolated population of genetically modified veto cells obtainable according to the method of any one of claims 1-9.

11. A therapeutically effective amount of the isolated population of genetically modified veto cells of claim 10 for use in the treatment of a disease in a subject in need thereof.

12. The therapeutically effective amount of the isolated population of genetically modified veto cells for use of claim 11, further comprises a cell or tissue transplant.

13. A therapeutically effective amount of the isolated population of genetically modified veto cells of claim 10 for use as an adjuvant treatment for a cell or tissue transplant into a subject, wherein said subject is in need of a cell or tissue transplantation.

14. The therapeutically effective amount for use according to any one of claims 11-13, wherein the disease is selected from the group consisting of a malignant disease, a viral disease, a bacterial disease, a fungal disease, a protozoa disease, and a parasite disease.

15. The therapeutically effective amount for use according to any one of claims 11-14, wherein said genetically modified veto cells are non-syngeneic with the subject.