

CLAIMS

1. A population of CD4⁺ T cells that have been genetically modified to comprise an exogenous polynucleotide encoding IL-10, wherein:
 - (a) the CD4⁺ T cells were obtained from at least three different T cell donors (poly-donor CD4^{IL-10} cells); and
 - (b) the exogenous polynucleotide is integrated into the T cell nuclear genome.
2. The population of CD4⁺ T cells of claim 1, wherein the CD4⁺ T cells in the population collectively have six, seven, eight, nine, ten, eleven, twelve, or more different HLA haplotypes.
3. The population of CD4⁺ T cells of claim 1, wherein:
 - (a) all the CD4⁺ T cells in the population have:
 - (i) at least 5/10, 6/10, 7/10, 8/10, or 9/10 match at the HLA-A, HLA-B, HLA-C, HLA-DRB1, and HLA-DQB1 loci to each other;
 - (ii) at least 4/8, 5/8, 6/8, 7/8, or 8/8 match at the HLA-A, HLA-B, HLA-C, and HLA-DRB1 loci to each other;
 - (iii) 2/2 match at the HLA-A locus to each other;
 - (iv) 2/2 match at the HLA-B locus to each other;
 - (v) 2/2 match at the HLA-C locus to each other; and/or
 - (vi) all the CD4⁺ T cells in the population have at least 3/4 or 4/4 match at the HLA-DRB1 and HLA-DQB1 loci with each other; and/or
 - (b) all the CD4⁺ T cells in the population have an A*02 allele.

4. The population of CD4⁺ T cells of claim 1 or claim 2, wherein the exogenous polynucleotide further comprises:
 - (a) a sequence encoding a selection marker, optionally wherein the selection marker is Δ NGFR; and/or
 - (b) lentiviral vector sequences.
5. The population of CD4⁺ T cells of any one of the above claims, wherein:
 - (a) at least 90% of the CD4⁺ T cells within the population express IL-10;
 - (b) the genetically modified CD4⁺ T cells constitutively express at least 100pg, 200pg, 500pg, 1ng, 5ng, 10ng, or 50ng IL-10 per 10⁶ of the CD4⁺ T cells/ml of culture medium; and/or
 - (c) the genetically modified CD4⁺ T cells express at least 1ng, 2ng, 5ng, 10ng, 100ng, 200ng, or 500ng IL-10 per 10⁶ of the CD4⁺ T cells/ml after activation with anti-CD3 and anti-CD28 antibodies.
6. The population of CD4⁺ T cells of claim 4(a), wherein at least 90%, at least 95%, or at least 98% of the CD4⁺ T cells within the population express the selection marker from the exogenous polynucleotide.
7. The population of CD4⁺ T cells of any one of the above claims, wherein the genetically modified CD4⁺ T cells express CD49b, LAG-3, TGF- β , IFN γ , GzB, perforin, CD18, CD2, CD226, and/or IL-22.
8. The population of CD4⁺ T cells of any one of the above claims, wherein the CD4⁺ T cells are in:
 - (a) a frozen suspension; or
 - (b) a liquid suspension, optionally wherein the liquid suspension has previously been frozen.

9. A method of making poly-donor CD4^{IL-10} cells, comprising the steps of:
- (i) modifying primary CD4⁺ T cells which have been obtained from at least three different T cell donors, wherein each donor's CD4⁺ T cells are separately modified by introducing an exogenous polynucleotide encoding IL-10, and
 - (ii) pooling the genetically modified CD4⁺ T cells,
- thereby obtaining the poly-donor CD4^{IL-10} cells.
10. The method of claim 9, further comprising the step, before step (i), after step (i), after step (i) and before step (ii), or after step (ii), of:
- incubating the primary CD4⁺ T cells in the presence of:
- (a) an anti-CD3 antibody, and anti-CD28 antibody; or
 - (b) anti-CD3 antibody and anti-CD28 antibody coated beads,
- optionally wherein the method further comprises incubating the primary CD4⁺ T cells in the presence of IL-2.
11. The method of claim 9 or claim 10, wherein the exogenous polynucleotide further comprises a segment encoding a selection marker, optionally wherein the encoded selection marker is ΔNGFR;
- optionally wherein the method further comprises the step, after step (i), of:
- isolating the genetically-modified CD4⁺ T cells expressing the selection marker, thereby generating an enriched population of genetically-modified CD4⁺ T cells.
12. The method of any one of claims 9-11, wherein in step (i), the primary CD4⁺ T cells are obtained from one or more frozen stocks.
13. Use of the population of CD4⁺ cells according to any one of claims 1-8 in the manufacture of a medicament for treating a patient in need of immune tolerization, wherein the poly-donor CD4^{IL-10} cells are to be administered to the patient.

14. The use of the population of CD4⁺ cells according to claim 13, further comprising hematopoietic stem cells (HSC) of an HSC donor to be administered to the patient either prior to or subsequent to the pooled donor CD4^{IL-10} cells to be administered.
15. The use of the population of CD4⁺ cells according to claim 13, wherein the patient has:
- (a) an inflammatory or autoimmune disease, optionally wherein the inflammatory or autoimmune disease is selected from the group consisting of type-1 diabetes, Crohn's disease, autoimmune uveitis, rheumatoid arthritis, psoriasis, psoriatic arthritis, multiple sclerosis, systemic lupus, inflammatory bowel disease, Addison's disease, Graves' disease, Sjögren's syndrome, Hashimoto's thyroiditis, myasthenia gravis, autoimmune vasculitis, pernicious anemia, ulcerative colitis, bullous diseases, scleroderma, and celiac disease;
 - (b) a disease or disorder involving hyperactivity of NLPR3 inflammasome;
 - (c) type 2 diabetes, a neurodegenerative disease, a cardiovascular disease or inflammatory bowel disease; and/or
 - (d) an allergic or atopic disease, optionally wherein the allergic or atopic disease is selected from the group consisting of: asthma, atopic dermatitis, and rhinitis.
16. The use of the population of CD4⁺ cells according to claim 13, further comprising an organ to be transplanted to the patient, either prior to or subsequent to the population of CD4⁺ T cells to be administered.
17. Use of the population of CD4⁺ cells according to any one of claims 1-8 in the manufacture of a medicament for treating a hematological cancer, wherein an amount of poly-donor CD4^{IL-10} cells sufficient to induce anti-cancer effect are to be administered to a hematological cancer patient, and wherein the poly-donor CD4^{IL-10} cells are genetically modified by vector-mediated gene transfer of the coding sequence of human IL-10 under control of a constitutive promoter.
18. The use of the population of CD4⁺ cells according to claim 17, wherein:
- (a) the poly-donor CD4^{IL-10} cells are to be administered to the patient prior to or subsequent to an allogenic hematopoietic stem cell transplant (allo HSCT) to be

administered, and the amount of poly-donor CD4^{IL-10} cells to be administered to the patient is sufficient to suppress GvHD without suppressing graft versus leukemia (GvL) or graft versus tumor (GvT) efficacy of the allo HSCT; and/or

(b) the hematological cancer is a myeloid leukemia.

19. The use of the population of CD4⁺ cells according to claim 13, wherein the patient has Crohn's disease.
20. The population of CD4⁺ cells according to claim 1 for use as a medicament.