CLAIMS

1. A humanized anti-human CD154 antibody that comprises

(i) a variable heavy chain polypeptide comprising ~~or consisting of~~ a polypeptide having a sequence selected from SEQ ID NO: 1 or 17~~15, 17 and 18 shown in **Figures 2A-2C**~~, and (ii) ~~and~~ a variable light chain polypeptide comprising ~~or consisting of~~ a polypeptide having a sequence selected from SEQ ID NO: ~~20,~~ 2 or 21, 22, 23, 24, 25, 26, 27, 28, 29, 30 and 31.~~shown in in **Figures 2A-2C,** with the proviso that the humanized anti-human CD154 antibody does not comprise the variable heavy polypeptide of SEQ ID NO:15 and the variable light polypeptide of SEQ ID NO:20.~~

2. A humanized anti-human CD154 antibody according to claim 1, that comprises

(i) a variable heavy chain polypeptide comprising ~~or consisting of~~ a polypeptide having the sequence of SEQ ID NO:1~~ as shown in **Figures 1A-C**~~, and

(ii)~~ and~~ a variable light chain polypeptide comprising~~ or consisting of~~ a polypeptide having the sequence of SEQ ID NO:2~~ shown in **Figures 1A-C**~~.

3. The anti-human CD154 antibody ~~-~~of claim 1 or 2, which comprises IgG1, IgG2, IgG3 or IgG4 constant regions lacking the ability to bind C1Q and/or to bind to FcγR2 and/or FcγR3.

4. The anti-human CD154 antibody ~~-~~of claim 1 or 2, which comprises human IgG1 constant regions lacking the ability to bind C1Q and to bind to Fcγ~~γ~~2 and/or Fcγ~~γ~~3.

5. The humanized anti-human CD154 antibody of claim 4 wherein said human IgG1 constant regions comprise E269R and K322A mutations (numbering according to Kabat).

6. The humanized anti-human CD154 antibody of any one of claims 1-5, that comprises the IgG1 ~~light and heavy~~heavy and light constant regions of SEQ ID NO:3 and SEQ ID NO:24~~ shown in **Figures 1A-C**~~.

7. The humanized anti-human CD154 antibody of any one of Claims 1-6, wherein the antibody is of the IgG1 isotype and the Fc region of the antibody is further mutated to introduce at least one other mutation that affects effector function such as a mutation which impairs FcRn binding, one which impairs or eliminates glycosylation or another mutation which impairs the ability of the antibody to bind to an FcR such as FcγR2 or FcγR3 or another FcR or a mutation which impairs binding to complement.

8. The humanized anti-human CD154 antibody of any one of Claims 1-7, wherein the antibody is of the IgG1 isotype and the Fc region of the antibody is mutated to ~~further~~ introduce a E233P and/or a D265A mutation or any of the Fc mutations ~~identified in **Table 1, 2 or 3**~~selected from the following: E269R, E233P, D265A, D265N, D270N, N297A, S298N, P329A, D270A, K326V, V369R, F405K, L410P, V427R, L234N, G237M, S239F, V262E, V264F, V266T, S267N, N268E, N297R, T299A, R301D, N325L, N325E and L328R (wherein numbering is according to Kabat).

9. The humanized anti-human CD154 antibody of any one of Claims 1-8, wherein the antibody is of the IgG1 isotype and the Fc region of the antibody is mutated to introduce a E233P mutation.

10. The humanized anti-human CD154 antibody of any one of Claims 1-9, wherein the Fc region of the antibody is further mutated to introduce one or more other mutations that improve *in vivo* half-life.

11. A pharmaceutical composition comprising a therapeutically or prophylactically effective amount of at least one humanized anti-human CD154 antibody according to any one of Claims 1-10 and a pharmaceutically acceptable carrier.

12. The pharmaceutical composition of claim 11, which further comprises an antigen, cell, tissue, or organ.

13. The pharmaceutical composition of claim 12 wherein the antigen is an autoantigen, allergen, inflammatory agent, drug, or a non-HLA matched (allo) or xeno (non-human) donor cell.

14. An antibody or composition according to any one of claims 1- 13, for use in eliciting ~~method of~~ immunosuppression of a T or B cell mediated immune response associated with a pathologic condition in a subject in need thereof~~or immunotherapy using an antibody or composition according to any of claims 1- 13~~.

15. An antibody or composition according to any one of claims 1- 13, for use ~~method of~~ in the treatment~~ing~~ of a subject with an allergic, inflammatory, or autoimmune disorder or for inhibiting an immune response against a transplanted tissue or organ in a transplant recipient ~~by administering an antibody or composition according to any of claims 1- 13~~.

16. An antibody or composition according to any one of claims 1- 13, for use in the ~~method of~~ treatment~~ing~~ or prevention~~ing~~ of GVHD in a subject ~~by administering an antibody or composition according to any of claims 1- 13~~ before, concurrent or after transplant of donor tissue, organ, or cells which optionally may be genetically engineered.

17. The ~~method of~~antibody or composition for use according to claim 16, wherein the cells are CAR-T or NK cells.

18. An antibody or composition according to any one of claims 1- 13, for use in ~~method of~~ eliciting ~~tolerance or~~ prolonged ~~antigen specific~~ immunosuppression ~~by administering an antibody or composition according to any of claims 1- 13~~ against an antigen associated with a disease condition in a subject in need thereof.

19. The ~~method of~~antibody or composition for use according to claim 18, ~~wherein the method~~said use further includes the ~~administration~~use of a cell, antigen, tissue, or organ which comprises an antigen against which ~~tolerance or prolonged immunosuppression is to be elicited~~the antibody or composition containing suppresses a T or B cell mediated immune response.

20. An antibody or composition according to any one of claims 1- 13, for use in ~~method of~~ gene, cell, tissue or organ therapy ~~which includes administering an antibody or composition according to any of claims 1- 13~~.

21. The ~~method of~~antibody or composition for use according to claim 15, wherein the ~~condition treated~~disorder is selected from psoriasis, rheumatoid arthritis, psoriatic arthritis, oophoritis, lupus or SLE, diabetes, IBD, Crohn's disease, ITP, thyroiditis, rheumatoid arthritis, Myasthenia gravis, systemic lupus erythematosus, Graves' disease, idiopathic thrombocytopenia purpura, hemolytic anemia, diabetes mellitus, inflammatory bowel disease, ~~Crohn's disease,~~ multiple sclerosis, ~~psoriasis,~~ drug-induced autoimmune diseases, ~~or~~and drug-induced lupus.

22. An antibody or composition according to any one of claims 1- 13, for use in suppressing an immune response against ~~method of treating~~ bone marrow, an organ or immune cells which are for use in cell therapy or an organ or bone marrow transplant, wherein said use comprises~~comprising~~ incubating said bone marrow, organ, tissue or immune cells *in vitro* with an antibody or composition according to any one of claims 1-13 prior to said use.

23. The ~~method of~~antibody or composition for use according to claim 22, wherein the treated bone marrow, tissue, ~~an~~ organ or immune cells comprise donor and/or recipient T cells.

24. An antibody or composition according to any one of claims 1- 13, for use in suppressing a B or T cell mediated immune response in a subject in need thereof ~~method of inducing tolerance~~ without eliciting thrombotic events ~~in a patient in need thereof comprising administering to a patient an effective amount of an antibody or composition according to any one of claims 1-13~~.

25. The ~~method of~~antibody or composition for use according to claim 24 which further includes ~~administration~~the use of an antigen.

26. The ~~method of~~antibody or composition for use according to claim 25, wherein the antigen is an autoantigen, allergen, inflammatory agent, drug, or a non-HLA matched (allo) donor cell.

27. The ~~method of~~antibody or composition for use according to claims 24-26, wherein the ~~patient~~subject is to receive or has received transplanted cells, organ or tissue.

28. The ~~method of~~antibody or composition for use according to claim 26 wherein the drug is a biologic such as a therapeutic antibody, receptor, fusion protein, hormone, growth factor or cytokine.

29. An antibody or composition according to any one of claims 1- 13, for use in ~~method of~~the treatment~~ing~~ of a T cell mediated autoimmune disorder in a subject in need thereof~~by administering an effective amount of an antibody or composition according to any of claims 1- 13~~.

30. An antibody or composition according to any one of claims 1- 13, for use in ~~method of~~the treatment~~ing~~ of a B cell mediated autoimmune disorder in a subject in need thereof~~by administering an effective amount of an antibody or composition according to any of claims 1- 13~~.

31. The ~~method of~~antibody or composition according to claim 29 or 30, wherein the ~~disease~~T or B cell mediated autoimmune disorder is an autoimmune disease selected from rheumatoid arthritis, Myasthenia gravis, systemic lupus erythematosus, Graves' disease, Huntington's disease, idiopathic thrombocytopenia purpura, hemolytic anemia, diabetes mellitus, Parkinson's disease, psoriasis, Addison's disease, multiple sclerosis, lupus, and drug-induced autoimmune diseases~~, e.g.,~~including drug-induced lupus.

32. The ~~method of~~antibody or composition according to one of claims 29-31 which includes ~~administration~~the use of an antigen.

33. An antibody or composition according to any one of claims 1- 13, for use in ~~method of~~the treatment~~ing~~ or prevention~~ing~~ of GVHD, eliciting immunosuppression against a bone marrow transplant (BMT), or for the treatment or prevention of multiple sclerosis, lupus, ITP, rheumatoid arthritis, asthma, IBD or another inflammatory bowel disorder ~~by administering an effective amount of an antibody or composition according to any of claims 1- 13~~in a subject in need thereof.

34. An antibody or composition according to any one of claims 1- 13, for use in the ~~method for~~ treatment of~~ing~~ a human condition, disorder or disease mediated in whole or in part by CD40 signaling, or a symptom of any of the foregoing~~, the method comprising~~

~~administering an effective amount of an antibody or composition according to any of claims 1- 13~~.

35. The ~~method of~~antibody or composition for use according to claim 34, wherein the human condition, disorder or disease ~~is an~~is associated with inflammation~~ory~~ or, allergic, or autoimmune response or fibrosis.

36. The ~~method of~~antibody or composition for use according to claim 34 or 35, wherein the human condition, disorder or disease is selected from lupus nephritis, rheumatoid arthritis, systemic lupus erythematosus, spondyloarthritis, drug-induced lupus erythematosus , inflammatory bowel disease, Crohn's disease, psoriasis and multiple sclerosis.

37. The ~~method of~~antibody or composition for use according to claim 34 wherein the human condition, disorder or disease is selected from allergic contact dermatitis, alopecia universalis, anaphylactoid purpura asthma, severe asthma, metabolic asthma, allergic asthma, atopic dermatitis, dermatitis herpetiformis, erythema elevatum diutinum, erythema marginatum, erythema multiforme; erythema nodosum, allergic granulomatosis, granuloma annulare, granulocytopenia, hypersensitivity pneumonitis, keratitis, nephrotic syndrome, overlap syndrome, pigeon breeder's disease, idiopathic polyneuritis, urticaria, uveitis, juvenile dermatomyosistitis, and vitiligo.

38. The ~~method of~~antibody or composition for use according to claim 34 wherein the human condition, disorder or disease is selected from allergic bronchopulmonary aspergillosis; autoimmune hemolytic anemia; acanthosis nigricans; allergic contact dermatitis; Addison’s disease; atopic dermatitis; alopecia areata; alopecia universalis; amyloidosis; anaphylactoid purpura; anaphylactoid reaction; aplastic anemia; angioedema, hereditary; angioedema, idiopathic; ankylosing spondylitis; arteritis, cranial; arteritis, giant cell; arteritis, Takayasu’s; arteritis, temporal; asthma; ataxia-telangiectasia; autoimmune oophoritis; autoimmune orchitis; autoimmune polyendocrine failure; Behçet’s disease; Berger’s disease; Buerger’s disease; bullous pemphigus; candidiasis, chronic mucocutaneous; Caplan’s syndrome; post-myocardial infarction syndrome; post-pericardiotomy syndrome; carditis; celiac sprue; Chagas’s disease; Chédiak-Higashi

syndrome; Churg-Strauss disease; Cogan’s syndrome; cold agglutinin disease; crest syndrome; Crohn’s disease; cryoglobulinemia; cryptogenic fibrosing alveolitis; dermatitis herpetiformis; dermatomyositis; diabetes mellitus; Diamond-Blackfan syndrome; DiGeorge syndrome; discoid lupus erythematosus; eosinophilic fasciitis; episcleritis; erythema elevatum diutinum; erythema marginatum; erythema multiforme; erythema nodosum; familial Mediterranean fever; Felty’s syndrome; fibrosis pulmonary; glomerulonephritis, anaphylactoid; glomerulonephritis, autoimmune; glomerulonephritis, post-streptococcal; glomerulonephritis, post-transplantation; glomerulopathy, membranous; Goodpasture’s syndrome; graft-vs.-host disease; granulocytopenia, immune-mediated; granuloma annulare; granulomatosis, allergic; granulomatous myositis; grave's disease; Hashimoto’s thyroiditis; hemolytic disease of the newborn; hemochromatosis, idiopathic; Henoch-Schönlein purpura; hepatitis, chronic active and chronic progressive; histiocytosis x; hypereosinophilic syndrome; idiopathic thrombocytopenic purpura; job's syndrome; juvenile dermatomyositis; juvenile rheumatoid arthritis (juvenile chronic arthritis); Kawasaki’s disease; keratitis; keratoconjunctivitis sicca; landry-guillain-barre-strohl syndrome; leprosy, lepromatous; Loeffler’s syndrome; Lyell's syndrome; lyme disease; lymphomatoid granulomatosis; mastocytosis, systemic; mixed connective tissue disease; mononeuritis multiplex; Muckle-Wells syndrome; mucocutaneous lymph node syndrome; mucocutaneous lymph node syndrome; multicentric reticulohistiocytosis; multiple sclerosis; myasthenia gravis; mycosis fungoides; necrotizing vasculitis, systemic; nephrotic syndrome; overlap syndrome; panniculitis; paroxysmal cold hemoglobinuria; paroxysmal nocturnal hemoglobinuria; pemphigoid; pemphigus; pemphigus erythematosus; pemphigus foliaceus; pemphigus vulgaris; pigeon breeder's disease; pneumonitis, hypersensitivity; polyarteritis nodosa; polymyalgia rheumatica; polymyositis; polyneuritis, idiopathic; Portuguese familial polyneuropathics; pre-eclampsia/eclampsia; primary biliary cirrhosis; progressive systemic sclerosis (scleroderma); psoriasis; psoriatic arthritis; pulmonary alveolar proteinosis; pulmonary fibrosis, Raynaud’s phenomenon/syndrome; Reidel’s thyroiditis; Reiter’s syndrome, relapsing polychondritis; rheumatic fever; rheumatoid arthritis; sarcoidosis; scleritis; sclerosing cholangitis; serum sickness; Sézary syndrome; Sjögren’s syndrome; Stevens-Johnson syndrome; Still's disease; subacute sclerosing

panencephalitis; sympathetic ophthalmia; systemic lupus erythematosus; transplant rejection; ulcerative colitis; undifferentiated connective tissue disease; urticaria, chronic; urticaria, cold; uveitis; vitiligo; Weber-Christian disease; Wegener's granulomatosis; and Wiskott-Aldrich syndrome.