

CLAIMS

1. An anti-human CD154 antibody that comprises
 - (i) a variable heavy chain polypeptide comprising a polypeptide having SEQ ID NO: 17, and
 - (ii) a variable light chain polypeptide comprising a polypeptide having a sequence selected from SEQ ID NO: 21, 22, 23, 24, 25, 26, 27, 28, 29, 30 and 31.
2. An anti-human CD154 antibody according to claim 1, that comprises
 - (i) a variable heavy chain polypeptide comprising a polypeptide having the sequence of SEQ ID NO:17, and
 - (ii) a variable light chain polypeptide comprising a polypeptide having the sequence of SEQ ID NO:21.
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 FcγR2 and/or FcγR3.
5. The anti-human CD154 antibody of claim 4, wherein said human IgG1 constant regions comprise E269R and K322A mutations (numbering according to Kabat).
6. The anti-human CD154 antibody of any one of claims 1-5, that comprises the IgG1 heavy and light constant regions of SEQ ID NO:3 and SEQ ID NO:4.
7. The anti-human CD154 antibody of any one of Claims 1-5, wherein the antibody is of the IgG1 isotype and the Fc region of the antibody is mutated to introduce at least one other mutation that affects effector function.
8. The anti-human CD154 antibody of any one of Claims 1-3, wherein the antibody is of the IgG1 isotype and the Fc region of the antibody is mutated to introduce a E233P and/or a D265A mutation or any of the Fc mutations selected from the following: E269R, K322A, 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 anti-human CD154 antibody of Claim 8, wherein the Fc region of the antibody comprises a E233P mutation.

10. The anti-human CD154 antibody of any one of Claims 1-5, 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 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 immunosuppression of a T or B cell mediated immune response associated with a pathologic condition in a subject in need thereof.

15. An antibody or composition according to any one of claims 1- 13, for use in the treatment of a subject with an allergic, inflammatory, or autoimmune disorder or for treatment of a subject comprising a transplanted tissue or organ.

16. An antibody or composition according to any one of claims 1- 13, for use in the treatment or prevention of graft versus host disease (GVHD) in a subject before, concurrent or after transplant of donor tissue, organ, or cells, which optionally may be genetically engineered.

17. The 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 eliciting prolonged immunosuppression against an antigen associated with a disease condition in a subject in need thereof.
19. The antibody or composition for use according to claim 18, wherein said use further includes the use of a cell, antigen, tissue, or organ which comprises an antigen against which the anti-human CD154 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 gene, cell, tissue or organ therapy.
21. The antibody or composition for use according to claim 15, wherein the disorder is selected from psoriasis, rheumatoid arthritis, psoriatic arthritis, oophoritis, lupus or systemic lupus erythematosus (SLE), diabetes, Crohn's disease, thyroiditis, rheumatoid arthritis, Myasthenia gravis, Graves' disease, idiopathic thrombocytopenia purpura, hemolytic anemia, diabetes mellitus, inflammatory bowel disease, multiple sclerosis, drug-induced autoimmune diseases, and drug-induced lupus.
22. A method for suppressing an immune response against bone marrow, an organ or immune cells which are for use in cell therapy or for use in organ or bone marrow transplant, which method comprises incubating said bone marrow, organ, tissue or immune cells *in vitro* with an anti-human CD154 antibody or composition containing according to any one of claims 1- 13.
23. The method of claim 22, wherein the treated bone marrow, tissue, organ or immune cells comprise donor and/or recipient T cells.
24. An antibody according to claim 4 or 5, for use in suppressing a B or T cell mediated immune response associated with a pathologic condition in a subject in need thereof without eliciting thrombotic events.
25. The antibody for use according to claim 24, which further includes the use of an antigen.
26. The antibody 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 antibody for use according to any one of claims 24-26, wherein the subject is to receive or has received transplanted cells, organ or tissue.
28. The antibody for use according to claim 26, wherein the drug is a therapeutic antibody, receptor, fusion protein, hormone, growth factor or cytokine.
29. An antibody or composition according to any one of claims 1-11, for use in the treatment of a T cell mediated autoimmune disorder in a subject in need thereof.
30. An antibody or composition according to any one of claims 1-11, for use in the treatment of a B cell mediated autoimmune disorder in a subject in need thereof.
31. The antibody or composition for use according to claim 29 or 30, wherein the 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 including drug-induced lupus.
32. The antibody or composition for use according to any one of claims 29-31, which further includes the use of an antigen.
33. An antibody or composition according to any one of claims 1-11, for use in the treatment or prevention of graft versus host disease (GVHD), for use in eliciting immunosuppression against a bone marrow transplant (BMT), or for use in the treatment or prevention of multiple sclerosis, lupus, immune thrombocytopenic purpura (ITP), rheumatoid arthritis, asthma, inflammatory bowel disease (IBD) or another inflammatory bowel disorder in a subject in need thereof.
34. An antibody or composition according to any one of claims 1-13, for use in the treatment of a human disorder or disease mediated in whole or in part by CD40 signaling.
35. The antibody or composition for use according to claim 34, wherein the human disorder or disease is associated with inflammation, allergy, an autoimmune response or fibrosis.

36. The antibody or composition for use according to claim 34 or 35, wherein the human 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 antibody or composition for use according to claim 34, wherein the human 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 dermatomyositis, and vitiligo.

38. The antibody or composition for use according to claim 34, wherein the human 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 syndrome; juvenile
 dermatomyositis; juvenile rheumatoid arthritis (juvenile chronic arthritis); Kawasaki's
 disease; keratitis; keratoconjunctivitis sicca; Guillain-Barre 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.