CLAIMS

1. An antibody which binds to human CC chemokine receptor 4 (CCR4) and which is capable of inhibiting the binding of macrophage-derived chemokine (MDC) and/or thymus and activation regulated chemokine (TARC) to CCR4, and which comprises at least one heavy chain variable region that comprises three CDRs and at least one light chain variable region that comprises three CDRs,
wherein said heavy chain variable region comprises
(i) a variable heavy (VH) CDR1 that has the amino acid sequence of SEQ ID NO: 1,
(ii) a variable heavy (VH) CDR2 that has the amino acid sequence of SEQ ID NO: 2, and
(iii) a variable heavy (VH) CDR3 that has the amino acid sequence of SEQ ID NO: 20 or 3.

2. An antibody according to claim 1, wherein said light chain variable region of said antibody comprises:
(iv) a variable light (VL) CDR1 that has the amino acid sequence of SEQ ID NO: 22, 17 or 4;
(v) a VL CDR2 that has the amino acid sequence of SEQ ID NO: 5; and
(vi) a VL CDR3 that has the amino acid sequence of SEQ ID NO: 24 or 6.

3. An antibody according to any one of claims 1 to 2, wherein said antibody has a VH domain having the sequence of SEQ ID NO: 39 or a sequence having at least 70% identity thereto and/or a VL domain having the sequence of SEQ ID NO: 40 or a sequence having at least 70% identity thereto.

4. An antibody according to any one of claims 1-3, wherein said antibody is a fully human antibody.

5. The antibody of any one of claims 1-4, wherein said antibody is an IgG antibody, preferably IgG_1.

6. The antibody of any one of claims 1-5, wherein said antibody has an altered glycosylation pattern, preferably wherein at least 10, 20, 30, 40 50, 60, 75, 80, 85, 90, 91, 92, 93, 94, 95, 96, 97, 98 or at least 99% of the total complex N-glycoside-linked sugar chains bound to the Fc region of said antibody are sugar chains in which fucose is not bound to N- acetylglucosamine in the reducing end in the sugar chain.

7. The antibody of any one of claims 1-6, wherein said antibody is an antigen binding fragment of an antibody, preferably a Fab', Fab, $F(ab')_2$, single domain antibody, TandAbs dimer, Fv, scFv, dsFv, ds-scFv, Fd, linear antibody, minibody, diabody, bispecific antibody fragment, bibody, tribody, sc-diabody, kappa(lamda) body, BiTE, DVD-Ig, SIP, SMIP, DART or a small antibody mimetic comprising one or more CDRs.

8. The antibody of any one of claims 1-7, wherein said antibody is attached to at least a therapeutic or diagnostic agent, preferably at least a radiotherapeutic agent, chemotherapeutic agent, anti-angiogenic agent, apoptosis-inducing agent, anti-tubulin drug, anti-cellular or cytotoxic agent, steroid, cytokine antagonist, cytokine expression inhibitor, chemokine antagonist, chemokine expression inhibitor, anti-inflammatory corticosteroid or NSAIDs, coagulant or anti-viral agent, wherein said anti-viral agent is preferably selected from the group consisting of a nucleoside, a nucleoside reverse transcriptase inhibitor, a non-nucleoside reverse transcriptase inhibitor and a protease inhibitor.

9. A composition comprising at least an antibody according to any one of claims 1-8, wherein said composition is preferably a pharmaceutically acceptable composition such as a liposome or nanoparticle composition and optionally further comprises at least a second therapeutic agent.

10 A nucleic acid molecule comprising a nucleotide sequence region encoding the antibody of any one of claims 1-8.

11. The nucleic acid molecule of claim 10, wherein said nucleotide sequence region has the nucleotide sequence of SEQ ID NO: 111 and/or 112, or a sequence having at least 70% identify to any of said sequences.

12. An expression vector comprising the nucleic acid molecule of claim 10 or 11.

13. A host cell or virus comprising the nucleic acid molecule of claim 10 or 11 or the expression vector of claim 12.

14. A kit comprising, in at least a first container:

(a) the antibody of any one of claims 1-8;

(b) the composition of claim 9;

(c) the nucleic acid molecule of claim 10 or 11;

(d) the expression vector of claim 12; and/or

(e) the host cell or virus of claim 13.

15. A method of producing an antibody, comprising:

(a) culturing the host cell of claim 13 under conditions effective to express the encoded antibody; and

(b) obtaining the expressed antibody from said host cell.

16. An *in vitro* method of detecting or measuring CCR4, comprising contacting a sample known to contain CCR4 or suspected of containing CCR4 with the antibody of any one of claims 1-8 under conditions effective to allow the formation of complexes between said CCR4 and said antibody and detecting or measuring said complexes so formed.

17. The antibody of any one of claims 1-8 for use in therapy, imaging or diagnosis.

18. The antibody of claim 17 for use in therapy, imaging or diagnosis, of a condition associated with CCR4 expression or activity, or for use in reducing immunosuppression associated with CCR4 expression in an animal.

19. The antibody of claim 18 for use according to claim 18 wherein said condition is a disease mediated by CCR4 or characterised by aberrant proliferation of CCR4+ cells, preferably cancer, an inflammatory disease, an immune disease or an infection, wherein said condition is preferably selected from (a) allergic diseases such as systemic anaphylaxis or hypersensitivity responses, drug allergies, allergic bronchopulmonary aspergillosis (ABPA), insect sting allergies and food allergies, (b) inflammatory bowel diseases, such as Crohn's disease, ulcerative colitis, ileitis and enteritis, (c) vaginitis, (d) psoriasis and inflammatory dermatoses such as dermatitis, eczema, atopic dermatitis, allergic contact dermatitis, urticaria and pruritus, (e) vasculitis, (f) spondyloarthropathies, (g) scleroderma, (h) asthma and respiratory allergic diseases such as allergic asthma, allergic rhinitis, chronic obstructive pulmonary disease and hypersensitivity lung diseases, (i) autoimmune diseases, such as arthritis (including rheumatoid and psoriatic), multiple sclerosis, systemic lupus erythematosus, type I diabetes, glomerulonephritis, (j) graft rejection (including

allograft rejection and graft-v-host disease), (k) other diseases in which undesired inflammatory responses are to be inhibited, such as atherosclerosis, myositis, T-cell mediated neurodegenerative diseases, multiple sclerosis, encephalitis, meningitis, hepatitis, nephritis, sepsis, sarcoidosis, allergic conjunctivitis, otitis, Castleman's disease, sinusitis, LPS-induced endotoxic shock, Behcet's syndrome and gout, (l) cancers, preferably breast cancer, colorectal cancer, esophageal cancer, gastric cancer, hepatocellular carcinoma, lung cancer, melanoma, ovarian cancer, renal cancer, pancreatic cancer, cervical cancer, brain cancer, prostate cancer, stomach cancer, Adult T-cell leukemia/lymphoma (ATL), Peripheral T-cell lymphoma, unspecified Diffuse large B-cell lymphoma, Hodgkin's lymphoma, B-cell chronic lymphocytic leukemia, Mycosis fungoides, Sézary syndrome (m) infections such as Epstein-Barr virus (EBV) infection, HIV infection and other viral infections.

20. The antibody of claim 17 for use according to claim 17, wherein said use is diagnosing a disease associated with CCR4 expression in an animal, and comprises the step of:

(a) contacting an animal with said antibody; and, optionally

(b) measuring or detecting the presence and/or amount and/or location of antibody-antigen complex in the animal; and, optionally

(c) comparing the presence and/or amount of antibody-antigen complex in the animal to a control.

21. An *in vitro* method of diagnosing a condition associated with CCR4 expression or activity, comprising detecting or measuring CCR4 according to claim 16 and using this information to diagnose a condition associated with CCR4 expression or activity.

22. The antibody of claim 20 for use in diagnosis according to claim 20, or the method of claim 21, wherein an increased amount of CCR4 in said animal or sample is diagnostic for tumour cells or for virally infected cells, preferably wherein said virally infected cells are infected with a virus selected from Epstein-Barr and HIV.

23. Use of an antibody according to any one of claims 1-8 for detecting the presence or measuring the amount of CCR4 expressed by a cell, target site, tissue or organ of a subject suffering from a CCR4-related disorder, wherein an increased presence or amount of CCR4 detected or measured compared to a healthy control indicates that said subject may benefit from anti-CCR4 therapy.

CLAIMS

1. An antibody which binds to human CC chemokine receptor 4 (CCR4) and which is capable of inhibiting the binding of macrophage-derived chemokine (MDC) and/or thymus and activation regulated chemokine (TARC) to CCR4, and which comprises at least one heavy chain variable region that comprises three CDRs and at least one light chain variable region that comprises three CDRs, in which the heavy chain variable region comprises:

(i) a variable heavy (VH) CDR1 that has the amino acid sequence of SEQ ID NO: 1,

(ii) a variable heavy (VH) CDR2 that has the amino acid sequence of SEQ ID NO: 2, and

(iii) a variable heavy (VH) CDR3 that has the amino acid sequence of SEQ ID NO: 20 or 3.

2. An antibody according to Claim 1, in which the light chain variable region of the antibody comprises:

(iv) a variable light (VL) CDR1 that has the amino acid sequence of SEQ ID NO: 22, 17 or 4;

(v) a VL CDR2 that has the amino acid sequence of SEQ ID NO: 5; and

(vi) a VL CDR3 that has the amino acid sequence of SEQ ID NO: 24 or 6.

3. An antibody according to Claim 1 or 2, in which the antibody has a VH domain having the sequence of SEQ ID NO: 39 or a sequence having at least 70% identity thereto and/or a VL domain having the sequence of SEQ ID NO: 40 or a sequence having at least 70% identity thereto.

4. An antibody according to Claim 1, 2 or 3, in which the antibody is a fully human antibody.

5. An antibody according to any preceding claim, in which the antibody is an IgG antibody, preferably IgG_1.

6. An antibody according to any preceding claim, in which the antibody has an altered glycosylation pattern, preferably in which at least 10, 20, 30, 40 50, 60, 75, 80, 85, 90, 91, 92, 93, 94, 95, 96, 97, 98 or at least 99% of the total complex N-glycoside-linked sugar chains

bound to the Fc region of the antibody are sugar chains in which fucose is not bound to N-acetylglucosamine in the reducing end in the sugar chain.

7. An antibody according to Claim 1, in which the antibody is an antigen binding fragment of an antibody, preferably a Fab', Fab, $F(ab')_2$, single domain antibody, TandAbs dimer, Fv, scFv, dsFv, ds-scFv, Fd, linear antibody, minibody, diabody, bispecific antibody fragment, bibody, tribody, sc-diabody, kappa(lamda) body, BiTE, DVD-Ig, SIP, SMIP, DART.

8. An antibody according to any preceding claim, in which the antibody is attached to at least a therapeutic or diagnostic agentselected froma radiotherapeutic agent, chemotherapeutic agent, anti-angiogenic agent, apoptosis-inducing agent, anti-tubulin drug, anti-cellular or cytotoxic agent, steroid, cytokine antagonist, cytokine expression inhibitor, chemokine antagonist, chemokine expression inhibitor, anti-inflammatory corticosteroid or NSAIDs, coagulant or anti-viral agent, in which the anti-viral agent is preferably selected from the group consisting of a nucleoside, a nucleoside reverse transcriptase inhibitor, a non-nucleoside reverse transcriptase inhibitor and a protease inhibitor.

9. A pharmaceutically acceptable composition comprising at least an antibody according to any preceding claim, in which the composition optionally further comprises at least a second therapeutic agent selected from a radiotherapeutic agent, chemotherapeutic agent, anti-angiogenic agent, apoptosis-inducing agent, anti-tubulin drug, anti-cellular or cytotoxic agent, steroid, cytokine antagonist, cytokine expression inhibitor, chemokine antagonist, chemokine expression inhibitor, anti-inflammatory corticosteroid or NSAIDs, coagulant or anti-viral agent, in which the anti-viral agent is preferably selected from the group consisting of a nucleoside, a nucleoside reverse transcriptase inhibitor, a non-nucleoside reverse transcriptase inhibitor and a protease inhibitor.

10. A nucleic acid molecule comprising a nucleotide sequence region encoding an antibody according to any of Claims 1 to 8.

11. A nucleic acid molecule according to Claim 10, in which the nucleotide sequence region has the nucleotide sequence of SEQ ID NO: 111 and/or 112, or a sequence having at least 70% identify to any of the sequences.

12. An expression vector comprising a nucleic acid molecule according to Claim 10 or 11.

13. A host cell or virus comprising a nucleic acid molecule according to Claim 10 or 11 or an expression vector according to Claim 12.

14. A kit comprising, in at least a first container: (a) the antibody according to any of Claims 1 to 8; (b) a composition according to Claim 9; (c) a nucleic acid molecule according to Claim 10 or 11; (d) a expression vector according to Claim 12; and/or (e) a host cell or virus according to Claim 13.

15. A method of producing an antibody, comprising: (a) culturing a host cell according to Claim 13 under conditions effective to express the encoded antibody; and (b) obtaining the expressed antibody from the host cell.

16. An *in vitro* method of detecting or measuring CCR4, comprising contacting a sample known to contain CCR4 or suspected of containing CCR4 with the antibody according to any of Claims 1 to 8 under conditions effective to allow the formation of complexes between the CCR4 and the antibody and detecting or measuring the complexes so formed.

17. An antibody according to any of Claims 1 to 8 for use in therapy, imaging or diagnosis.

18. An antibody according to Claim 17 for use in therapy, imaging or diagnosis of a condition associated with CCR4 expression or activity, or for use in reducing immunosuppression associated with CCR4 expression in an animal.

19. An antibody according to Claim 18 for a use as specified therein in which the condition is a disease mediated by CCR4 or characterised by aberrant proliferation of CCR4+ cells, preferably cancer, an inflammatory disease, an immune disease or an infection, in which the condition is preferably selected from (a) allergic diseases such as systemic anaphylaxis or hypersensitivity responses, drug allergies, allergic bronchopulmonary aspergillosis (ABPA), insect sting allergies and food allergies, (b) inflammatory bowel diseases, such as Crohn's disease, ulcerative colitis, ileitis and enteritis, (c) vaginitis, (d) psoriasis and inflammatory dermatoses such as dermatitis, eczema, atopic dermatitis, allergic contact dermatitis, urticaria and pruritus, (e) vasculitis, (f) spondyloarthropathies, (g) scleroderma, (h) asthma and respiratory allergic diseases such as allergic asthma, allergic rhinitis, chronic obstructive pulmonary disease and hypersensitivity lung diseases, (i) autoimmune diseases, such as arthritis (including rheumatoid and psoriatic), multiple sclerosis, systemic lupus erythematosus, type I diabetes, glomerulonephritis, (j) graft rejection (including allograft

rejection and graft-v-host disease), (k) other diseases in which undesired inflammatory responses are to be inhibited, such as atherosclerosis, myositis, T-cell mediated neurodegenerative diseases, multiple sclerosis, encephalitis, meningitis, hepatitis, nephritis, sepsis, sarcoidosis, allergic conjunctivitis, otitis, Castleman's disease, sinusitis, LPS-induced endotoxic shock, Behcet's syndrome and gout, (l) cancers, preferably breast cancer, colorectal cancer, esophageal cancer, gastric cancer, hepatocellular carcinoma, lung cancer, melanoma, ovarian cancer, renal cancer, pancreatic cancer, cervical cancer, brain cancer, prostate cancer, stomach cancer, Adult T-cell leukemia/lymphoma (ATL), Peripheral T-cell lymphoma, unspecified Diffuse large B-cell lymphoma, Hodgkin’s lymphoma, B-cell chronic lymphocytic leukemia, Mycosis fungoides, Sézary syndrome (m) infections such as Epstein-Barr virus (EBV) infection, HIV infection and other viral infections.

20. An antibody according to Claim 17 for use in diagnosing a disease associated with CCR4 expression in an animal, comprising the steps of: (a) contacting an animal with the antibody; and, optionally (b) measuring or detecting the presence and/or amount and/or location of antibody-antigen complex in the animal; and, optionally (c) comparing the presence and/or amount of antibody-antigen complex in the animal to a control.

21. An *in vitro* method of diagnosing a condition associated with CCR4 expression or activity, comprising detecting or measuring CCR4 according to Claim 16 and using this information to diagnose a condition associated with CCR4 expression or activity.

22. An antibody according to Claim 20 for use in diagnosis according to Claim 20, or in a method according to Claim 21, in which an increased amount of CCR4 in the animal or sample is diagnostic for tumour cells or for virally infected cells, preferably in which the virally infected cells are infected with a virus selected from Epstein-Barr and HIV.

23. Use of an antibody according to any of Claims 1 to 8 in the manufacture of a diagnostic agent for detecting the presence or measuring the amount of CCR4 expressed by a cell, target site, tissue or organ of a subject suffering from a CCR4-related disorder, in which an increased presence or amount of CCR4 detected or measured compared to a healthy control indicates that the subject may benefit from anti-CCR4 therapy.

24. Use of antibody according to any of Claims 1 to 8 in the manufacture of a preparation for therapy, imaging or diagnosis.

25. Use of an antibody according to Claim 24 in the manufacture of a preparation for therapy, imaging or diagnosis of a condition associated with CCR4 expression or activity, or for use in reducing immunosuppression associated with CCR4 expression in an animal.

26. Use of an antibody according to Claim 25 in which the condition is a disease mediated by CCR4 or characterised by aberrant proliferation of CCR4+ cells, preferably cancer, an inflammatory disease, an immune disease or an infection, in which the condition is preferably selected from (a) allergic diseases such as systemic anaphylaxis or hypersensitivity responses, drug allergies, allergic bronchopulmonary aspergillosis (ABPA), insect sting allergies and food allergies, (b) inflammatory bowel diseases, such as Crohn's disease, ulcerative colitis, ileitis and enteritis, (c) vaginitis, (d) psoriasis and inflammatory dermatoses such as dermatitis, eczema, atopic dermatitis, allergic contact dermatitis, urticaria and pruritus, (e) vasculitis, (f) spondyloarthropathies, (g) scleroderma, (h) asthma and respiratory allergic diseases such as allergic asthma, allergic rhinitis, chronic obstructive pulmonary disease and hypersensitivity lung diseases, (i) autoimmune diseases, such as arthritis (including rheumatoid and psoriatic), multiple sclerosis, systemic lupus erythematosus, type I diabetes, glomerulonephritis, (j) graft rejection (including allograft rejection and graft-v-host disease), (k) other diseases in which undesired inflammatory responses are to be inhibited, such as atherosclerosis, myositis, T-cell mediated neurodegenerative diseases, multiple sclerosis, encephalitis, meningitis, hepatitis, nephritis, sepsis, sarcoidosis, allergic conjunctivitis, otitis, Castleman's disease, sinusitis, LPS-induced endotoxic shock, Behcet's syndrome and gout, (l) cancers, preferably breast cancer, colorectal cancer, esophageal cancer, gastric cancer, hepatocellular carcinoma, lung cancer, melanoma, ovarian cancer, renal cancer, pancreatic cancer, cervical cancer, brain cancer, prostate cancer, stomach cancer, Adult T-cell leukemia/lymphoma (ATL), Peripheral T-cell lymphoma, unspecified Diffuse large B-cell lymphoma, Hodgkin’s lymphoma, B-cell chronic lymphocytic leukemia, Mycosis fungoides, Sézary syndrome (m) infections such as Epstein-Barr virus (EBV) infection, HIV infection and other viral infections.

27. Use of an antibody according to Claim 24 in the manufacture of a preparation for diagnosing a disease associated with CCR4 expression in an animal, comprising the steps of: (a) contacting an animal with the antibody; and, optionally (b) measuring or detecting the presence and/or amount and/or location of antibody-antigen complex in the animal; and, optionally (c) comparing the presence and/or amount of antibody-antigen complex in the animal to a control.