CLAIMS:

1. A method for screening for a molecule capable of binding to CD4 comprising:

(a) providing one or more candidate molecules;

(b) determining whether the one or more candidate molecules is capable of binding to one or more of the following regions of human CD4: amino acids 148 to 154, amino acids 164 to 168 and amino acids 185 to 192; and

(c) selecting a molecule determined in step (b) to be capable of binding to CD4.

2. A method according to claim 1 wherein the one or more candidate molecules is an antibody, an antibody derived molecule, a humanized antibody, a camelid antibody, a peptide, an oligonucleotide, a siRNA, a mimotope, a peptidomimetic, a foldamer, a small molecule, a recognition protein based on a natural or an engineered lipocalin, a DARPin, a fibronectin, an affibody, a Kunitz-type inhibitor, a peptidic aptamer, a ribozyme, or a toxin.

3. A method according to claim 1 or claim 2 wherein the one or more candidate molecules are antibodies or antibody fragments comprising CDR1 and CDR2 of BT061 light chain and CDR1 and CDR3 of BT061 heavy chain.

4. A method according to claim 3, wherein the CDR1 of BT061 light chain, the CDR2 of BT061 light chain, the CDR1 of BT061 heavy chain, and/or CDR3 of BT061 heavy chain sequences comprise amino acid substitutions provided that:

(i) the light chain CDR1 comprises: Ser32; Gly33; and Tyr 34;

(ii) the light chain CDR2 comprises: Leu54; and Ile57;

(iii) the heavy chain CDR1 comprises: Asp31, Glu31, Thr31, Cys31, Pro31, Met31 or Tyr31; and/or

(iv) the heavy chain CDR3 comprises: Tyr103, Phe103 or His103; Arg104; Tyr105; Asp106; and Trp110, Phe110, His 110 or Tyr110.

5. A method according to claim 3 or claim 4 wherein the antibody or antibody fragment further comprises the CDR3 of BT061 light chain and the CDR2 of BT061 heavy chain, and wherein the sequences of at least one of the CDR1 of BT061 light chain, the CDR2 of BT061 light chain, the CDR3 of BT061 light chain, the CDR1 of BT061 heavy chain, the CDR2 of BT061 heavy chain and/or the CDR3 of BT061 heavy chain comprise amino acid substitutions selected from those set out in Table 4 and Table 5.

6. A method according to any one of claims 3 to 5 wherein the antibody or antibody fragment comprises: (i) a light chain comprising Tyr53 or Phe53; (ii) a light chain comprising Asp64; (iii) a heavy chain comprising Ser28; or (iv) a heavy chain comprising Glu56.

7. A method according to any one of claims 1 to 6 wherein steps (a) to (c) are conducted on a computer system.

8. A method according to any one of claims 1 to 7 further comprising a step (d) of producing the molecule selected in step (c).

9. A method according to claim 8 further comprising a step (e) of contacting in vitro the molecule produced in step (d) with a CD4+ cell or with a peptide or polypeptide comprising one or more of the following regions of human CD4: amino acids 148 to 154, amino acids 164 to 168 and amino acids 185 to 192.

10. A method according to claim 9 wherein step (e) comprises determining whether the molecule produced in step (d):

(i) binds to a peptide comprising one or more of the following regions of human CD4: amino acids 148 to 154, amino acids 164 to 168, and amino acids 185 to 192;

(ii) activates CD4+CD25+ regulatory T cells; and/or

(iii) reduces CD4 receptor expression on a CD4-expressing cell.

11. A method according to any one of claims 1 to 6 wherein steps (a) to (c) are conducted *in vitro* and step (b) comprises contacting the one or more candidate molecules with a peptide or polypeptide comprising one or more of the following regions of human CD4: amino acids 148 to 154, amino acids 164 to 168 and amino acids 185 to 192.

12. A method according to claim 11 further comprising a step (d) of screening a molecule selected in step (c) for its ability to activate CD4+CD25+ regulatory T cells, and/or a step (e) of screening a molecule selected in step (c) for its ability to reduce CD4 receptor expression on a CD4-expressing cell.

13. A method according to any one of claims 9 to 12 wherein the contacting step comprises contacting the peptide and the molecule with a competitor antibody or antibody fragment having

the heavy and light chain variable domains of BT061 to determine if the candidate or selected molecule is able to block binding of the competitor antibody or antibody fragment to the regions of the peptide or polypeptide.

14. A method for screening for an antibody or antibody fragment capable of binding CD4 comprising:

(a) providing an antibody or antibody fragment comprising CDR1, CDR2 and CDR3 of BT061 light chain and CDR1, CDR2 and CDR3 of BT061 heavy chain wherein at least one of said CDRs comprises one or more amino acid substitutions provided that:

(i) the light chain CDR1 comprises: Ser32; Gly33; and Tyr34;

(ii) the light chain CDR2 comprises: Leu54; and Ile57;

(iii) the heavy chain CDR1 comprises Asp31, Glu31, Thr31, Cys31, Pro31, Met31 or Tyr31; and/or

(iv) the heavy chain CDR3 comprises Tyr103, Phe103 or His103; Arg104; Tyr105; Asp106; and Trp110, Phe110, His 110 or Tyr110,

(b) determining whether the antibody or antibody fragment is capable of binding to CD4, and

(c) selecting the antibody or antibody fragment determined in step (b) to be capable of binding to CD4.

15. A method according to claim 14 wherein the amino acid substitutions in the sequences of at least one of the CDR1 of BT061 light chain, the CDR2 of BT061 light chain, the CDR3 of BT061 light chain, the CDR1 of BT061 heavy chain, the CDR2 of BT061 heavy chain and/or the CDR3 of BT061 heavy chain comprise one or more amino acid substitutions selected from those set out in Table 4 and Table 5.

16. A method according to claim 14 or claim 15 wherein the antibody or antibody fragment comprises: (i) a light chain comprising Tyr53 or Phe53; (ii) a light chain comprising Asp64; (iii) a heavy chain comprising Ser28; or (iv) a heavy chain comprising Glu56.

17. A method according to any one of claims 14 to 16 wherein steps (a) to (c) are conducted on a computer system.

18. A method according to any one of claims 14 to 17 further comprising a step (d) of producing the antibody or antibody fragment selected in step (c).

19. A method according to claim 18 further comprising determining whether the antibody or antibody fragment produced in step (d):

(i) activates CD4+CD25+ regulatory T cells;

(ii) binds to one or more of the following regions of CD4: amino acids 148 to 154; amino acids 164 to 168 and amino acids 185 to 192; and/or

(iii) down-regulates expression of CD4 on a CD4-expressing cell.

20. A method according to any one of claims 14 to 16 wherein steps (a) to (c) are conducted *in vitro*.

21. A method according to claim 20 wherein step (b) comprises determining whether the antibody or antibody fragment:

(i) activates CD4+CD25+ regulatory T cells;

(ii) binds to one or more of the following regions of CD4: amino acids 148 to 154; amino acids 164 to 168 and amino acids 185 to 192; and/or

(iii) down-regulates expression of CD4 on a CD4-expressing cell.

22. A method for producing a therapeutic composition comprising:

(a) selecting: (i) a molecule determined as being capable of activating CD4+CD25+ regulatory T cells using the method of claim 10 or claim 12; or (ii) the antibody or antibody fragment determined according to claim 19 or 21 as being capable of activating CD4+CD25+ regulatory T cells; and

(b) producing a therapeutic composition comprising the selected molecule.

23. An antibody or antibody fragment capable of activating CD4+CD25+ regulatory T cells comprising CDR1, CDR2 and CDR3 of BT061 light chain and CDR1, CDR2 and CDR3 of BT061 heavy chain, wherein at least one of said CDRs comprises one or more amino acid substitutions provided that:

(i) the light chain CDR1 comprises: Ser32; Gly33; and Tyr34;

(ii) the light chain CDR2 comprises: Leu54; and Ile57;

(iii) the heavy chain CDR1 comprises: Asp31, Glu31, Thr31, Cys31, Pro31, Met31 or Tyr31; and/or

(iv) the heavy chain CDR3 comprises: Tyr103, Phe103 or His103; Arg104; Tyr105; Asp106; and Trp110, Phe110, His 110 or Tyr110.

24. An antibody or antibody fragment according to claim 23 comprising the sequence SGYSY from CDR1 of BT061 light chain and/or the sequence LASILE from CDR2 of BT061 light chain and/or the sequence YYRYD from CDR3 of BT061 heavy chain.

25. An antibody or antibody fragment according to claim 23 or claim 24 wherein the amino acids substitutions in the sequences of the CDRs are isosteric variations.

26. An antibody or antibody fragment capable of activating CD4+CD25+ regulatory T cells comprising V domains that are at least 80% identical to the V domains of the antibody BT061, the V domains comprising:

(i) the sequence motif SGYSY in CDR1 of the light chain V domain;

(ii) the sequence motif LASILE in CDR2 of the light chain V domain; and

(iii) the sequence motif SYXRYD in CDR3 of the heavy chain V domain where X is Y, F or H,

and wherein the antibody or antibody fragment does not comprise CDR1, CDR2 and CDR3 of BT061 heavy chain and CDR1, CDR2 and CDR3 of BT061 light chain.

27. An antibody or antibody fragment according to any one of claims 23 to 26 wherein the amino acid substitutions in the sequences of CDR1 of BT061 light chain, CDR2 of BT061 light chain, CDR3 of BT061 light chain, CDR1 of BT061 heavy chain, CDR2 of BT061 heavy chain and/or CDR3 of BT061 heavy chain are selected from those set out in Table 4 and Table 5.

28. An antibody or antibody fragment according to claim 23 or claim 27 wherein the antibody or antibody fragment comprises: (i) a light chain comprising Tyr53 or Phe53; (ii) a light chain comprising Asp64; (iii) a heavy chain comprising Ser28; or (iv) a heavy chain comprising Glu56.

29. An antibody or antibody fragment according to any one of claims 23, 27 or 28, comprising the CDR sequences of BT061 light chain and the CDR sequences of BT061 heavy chain with a single amino acid substitution wherein the substitution is:

(i) A63G in the heavy chain;

(ii) R33K in the heavy chain; or

(iii) L98I in the light chain.

30. An antibody or antibody fragment according to any one of claims 23, 27 or 28, comprising the CDR sequences of BT061 light chain and the CDR sequences of BT061 heavy chain with a double amino acid substitution wherein the substitutions are:

(i) R33K and A63G in the heavy chain; or

(ii) L98I in the light chain and R33K in the heavy chain.

31. An antibody or antibody fragment according to claim 29 or claim 30 further comprising the remaining variable domain sequences of BT061.

32. An antibody or antibody fragment according to any one of claims 23 to 31, wherein the antibody of antibody fragment further comprising an Fc receptor capable of binding to CD64, or wherein the antibody is an IgG antibody.

33. An isolated peptide comprising less than 50 amino acids of human CD4 protein and including the following regions of human CD4: amino acids 148 to 154, amino acids 164 to 168, and amino acids 185 to 192.

34. A nucleic acid encoding the antibody or antibody fragment according to any one of claims 23 to 32.

35. A vector comprising the nucleic acid of claim 34.

36. A host cell or hybridoma comprising the nucleic acid of claim 34 or the vector of claim 35.

37. A method for the production of an antibody or antibody fragment according to any one of claims 23 to 32 comprising a step of culturing the host cell according to claim 36 in a culture medium under conditions allowing the expression of the antibody or antibody fragment and separating the antibody or fragment from the culture medium.

38. A pharmaceutical composition comprising the antibody or antibody fragment according to any one of claims 23 to 32 and further comprising a pharmaceutically acceptable carrier.

39. A method for the activation of CD4+CD25+ regulatory T cells comprising contacting the cells with the antibody or antibody fragment according to any one of claims 23 to 32.

40. Use of an antibody or antibody fragment according to any one of claims 23 to 32 for the manufacture of a medicament for treating or preventing an autoimmune disease or transplant rejection.

41. Use of an antibody or antibody fragment according to any one of claims 23 to 32 for identifying or for activating CD4+CD25+ regulatory T cells *in vitro*.

42. Use of the isolated peptide of claim 33 for screening for molecules capable of binding to CD4 and/or activating CD4+CD25+ regulatory T cells.