

CLAIMS:

1. An antibody or a fragment thereof, that specifically binds to hOX40L,

wherein the antibody or fragment

(i) comprises a VH domain which comprises a HCDR3 comprising the motif VRGXYYY,
5 wherein X is any amino acid and

(ii) comprises six CDRs corresponding to HCDR1, HCDR2, HCDR3, LCDR1, LCDR2 and LCDR3.
2. The antibody or fragment according to claim 1 wherein said antibody or fragment competes
for binding to said hOX40L with the antibody 02D10, wherein the antibody 02D10
10 comprises the heavy chain variable region of SEQ ID NO:34 and the light chain variable
region of SEQ ID NO:48.
3. The antibody or fragment according to claim 1 or 2, where X is a neutral amino acid,
optionally P or G.
4. An antibody or a fragment thereof, optionally according to any one of claims 1 to 3, that
15 specifically binds to hOX40L and competes for binding to said hOX40L with the antibody
02D10, wherein the antibody or fragment comprises a VH domain which comprises the
HCDR3 sequence of SEQ ID NO:40 or 46 or the HCDR3 sequence of SEQ ID NO:40 or 46
comprising less than 5 amino acid substitutions.
5. An antibody or fragment according to any one of claims 1 to 4, the VH domain comprising a
20 HCDR3 of from 16 to 27 amino acids and which is derived from the recombination of a
human VH gene segment, a human D gene segment and a human JH gene segment,
wherein the human JH gene segment is IGHJ6 (e.g. IGHJ6*02).
6. The antibody or fragment according to any one of claims 1 to 5, the VH domain comprising
the HCDR1 sequence of SEQ ID NO:36 or 42 or the HCDR1 sequence of SEQ ID NO:36 or
25 42 comprising less than 4 amino acid substitutions.
7. The antibody or fragment according to any preceding claim, the VH domain comprising the
HCDR2 sequence of SEQ ID NO:38 or 44, or the HCDR2 sequence of SEQ ID NO:38 or 44
comprising less than 5 amino acid substitutions.
8. The antibody or fragment according to any preceding claim, the VH domain comprising an
30 amino acid sequence of SEQ ID NO: 34, or a heavy chain variable domain amino acid
sequence that is at least 90% identical to SEQ ID NO:34.

9. The antibody or fragment according to any preceding claim comprising a first and a second copy of said VH domain.
10. The antibody or fragment according to any preceding claim, comprising a VL domain which comprises the LCDR1 sequence of SEQ ID NO:54 or 60, or the LCDR3 sequence of SEQ ID NO:54 or 60 comprising less than 5 amino acid substitutions.
11. The antibody or fragment according to any preceding claim, comprising a or said VL domain, which VL domain comprises the LCDR2 sequence of SEQ ID NO:52 or 58, or the LCDR2 sequence of SEQ ID NO:52 or 58 comprising less than 2 amino acid substitutions.
12. The antibody or fragment according to any preceding claim, comprising a or said VL domain, which VL domain comprises the LCDR1 sequence of SEQ ID NO:54 or 60, or the LCDR1 sequence of SEQ ID NO:54 or 60 comprising less than 4 amino acid substitutions.
13. The antibody or fragment according to any preceding claim, comprising a or said VL domain, which VL domain comprises an amino acid sequence of SEQ ID NOs: 48, or a light chain variable domain amino acid sequence that is at least 90% identical to SEQ ID NO:48.
14. The antibody or fragment according to any one of claims 10 to 13, comprising a first and a second copy of said VL domain.
15. The antibody or fragment according to any one of claims 10 to 14, wherein the antibody or fragment comprises a kappa light chain.
16. The antibody or fragment according to any one of claims 4 to 15, wherein the amino acid substitutions are conservative amino acid substitutions, optionally wherein the conservative substitutions are from one of six groups (each group containing amino acids that are conservative substitutions for one another) selected from:
- 1) Alanine (A), Serine (S), Threonine (T);
 - 2) Aspartic acid (D), Glutamic acid (E);
 - 3) Asparagine (N), Glutamine (Q);
 - 4) Arginine (R), Lysine (K);
 - 5) Isoleucine (I), Leucine (L), Methionine (M), Valine (V); and
 - 6) Phenylalanine (F), Tyrosine (Y), Tryptophan (W).
17. The antibody or fragment according to claim 1, wherein the antibody is 02D10 which comprises the heavy chain variable region of SEQ ID NO: 34 and the light chain variable region of SEQ ID NO: 48.

18. The antibody or fragment according to any preceding claim, wherein the antibody or fragment comprises a constant region, e.g. an IgG4 constant region, optionally wherein the constant region is IgG4-PE (Seq ID No:128).
19. The antibody according to any preceding claim wherein the antibody comprises a heavy chain and a light chain, the heavy chain amino acid sequence consisting of the sequence of SEQ ID No:62 and the light chain amino acid sequence consisting of the sequence of SEQ ID No:64.
20. An antibody or fragment according to any preceding claim, wherein the antibody or fragment maintains a naïve population of CD4⁺ T cells of >20% of total CD4⁺ T cell population at day 12 in a *Rhesus macaque* model of haploidentical hematopoietic stem cell transplantation.
21. An antibody or fragment as defined in any one of claims 1 to 20 for use in treating or preventing a hOX40L-mediated disease or condition, wherein said hOX40L-mediated disease or condition is selected from an autoimmune disease or condition, a systemic inflammatory disease or condition, or transplant rejection; for example inflammatory bowel disease (IBD), Crohn's disease, rheumatoid arthritis, transplant rejection, allogenic transplant rejection, graft-versus-host disease (GvHD), ulcerative colitis, systemic lupus erythematosus (SLE), diabetes, uveitis, ankylosing spondylitis, contact hypersensitivity, multiple sclerosis or atherosclerosis, in particular GvHD.
22. Use of an antibody or fragment as defined in any one of claims 1 to 20 in the manufacture of a medicament for administration to a human for treating or preventing a hOX40L mediated disease or condition in the human, wherein said hOX40L mediated disease or condition is selected from an autoimmune disease or condition, a systemic inflammatory disease or condition, or transplant/host rejection; for example inflammatory bowel disease (IBD), Crohn's disease, rheumatoid arthritis, transplant rejection, allogenic transplant rejection, graft-versus-host disease (GvHD), ulcerative colitis, systemic lupus erythematosus (SLE), diabetes, uveitis, ankylosing spondylitis, contact hypersensitivity, multiple sclerosis or atherosclerosis, in particular GvHD.
23. The antibody or fragment according to claim 21, the use according to claim 22, wherein the hOX40L-mediated disease or condition is GvHD.
24. The antibody or fragment or the use according to any one of claims 21 to 23, wherein the antibody is to be administered prophylactically.
25. The antibody or fragment, or use according to any one of claims 21 to 24, further comprising a further therapeutic agent to be administered to the human optionally, wherein

the further therapeutic agent is independently selected from the group consisting of rapamycin (sirolimus), racrolimus, ciclosporin, corticosteroids (e.g. methylprednisolone), methotrexate, mycophenolate mofetil, anti-CD28 antibodies, anti-IL12/IL-23 antibodies (e.g. ustekinumab), anti-CD20 antibodies (e.g. rituximab), anti-CD30 antibodies (e.g. brentuximab), CTLA4-Fc molecules (e.g. abatacept), CCR5 receptor antagonists (e.g. maraviroc), anti-CD40L antibodies, anti-VLA4 antibodies (e.g. natalizumab), anti-LFA1 antibodies, fludarabine, anti-CD52 antibodies (e.g. alemtuzumab), anti-CD45 antibodies, cyclophosphamide, anti-thymocyte globulins, anti-complement C5 antibodies (e.g. eculizumab), anti- α 4 β 7 integrin antibodies (e.g. vedolizumab), anti-IL6 antibodies (e.g. tocilizumab), anti-IL2R antibodies (e.g. basilixumab), anti-CD25 antibodies (e.g. daclizumab), anti-TNF α / TNF α -Fc molecules (e.g. etanercept, adalimumab, infliximab, golimumab or certolizumab pegol) and Vorinostat, in particular rapamycin (sirolimus), racrolimus, ciclosporin, corticosteroids (e.g. methylprednisolone), methotrexate, mycophenolate mofetil, anti-CD28 antibodies, CTLA4-Fc molecules (e.g. abatacept), anti-CD40L antibodies, anti-LFA1 antibodies, anti-CD52 antibodies (e.g. alemtuzumab), cyclophosphamide and anti-thymocyte globulins.

26. The antibody or fragment, or use according to claim 25, wherein the further therapeutic agent is to be administered sequentially or simultaneously with the anti-hOX40L antibody or fragment.

27. A pharmaceutical composition comprising an antibody or fragment as defined in any one of claims 1 to 20 and a pharmaceutically acceptable excipient, diluent or carrier and optionally further comprising a further therapeutic agent independently selected from the group consisting of rapamycin (sirolimus), racrolimus, ciclosporin, corticosteroids (e.g. methylprednisolone), methotrexate, mycophenolate mofetil, anti-CD28 antibodies, anti-IL12/IL-23 antibodies (e.g. ustekinumab), anti-CD20 antibodies (e.g. rituximab), anti-CD30 antibodies (e.g. brentuximab), CTLA4-Fc molecules (e.g. abatacept), CCR5 receptor antagonists (e.g. maraviroc), anti-CD40L antibodies, anti-VLA4 antibodies (e.g. natalizumab), anti-LFA1 antibodies, fludarabine, anti-CD52 antibodies (e.g. alemtuzumab), anti-CD45 antibodies, cyclophosphamide, anti-thymocyte globulins, anti-complement C5 antibodies (e.g. eculizumab), anti- α 4 β 7 integrin antibodies (e.g. vedolizumab), anti-IL6 antibodies (e.g. tocilizumab), anti-IL2R antibodies (e.g. basilixumab), anti-CD25 antibodies (e.g. daclizumab), anti-TNF α / TNF α -Fc molecules (e.g. etanercept, adalimumab, infliximab, golimumab or certolizumab pegol) and Vorinostat, in particular rapamycin (sirolimus), racrolimus, ciclosporin, corticosteroids (e.g. methylprednisolone), methotrexate, mycophenolate mofetil, anti-CD28 antibodies, CTLA4-Fc molecules (e.g. abatacept), anti-CD40L antibodies, anti-LFA1 antibodies, anti-CD52 antibodies (e.g. alemtuzumab), cyclophosphamide and anti-thymocyte globulins.

28. A pharmaceutical composition according to claim 27, or a kit comprising a pharmaceutical composition as defined in claim 27, wherein the composition is for treating and/or preventing a hOX40L-mediated condition or disease selected from an autoimmune disease or condition, a systemic inflammatory disease or condition, or transplant rejection; for example inflammatory bowel disease (IBD), Crohn's disease, rheumatoid arthritis, transplant rejection, allogenic transplant rejection, graft-versus-host disease (GvHD), ulcerative colitis, systemic lupus erythematosus (SLE), diabetes, uveitis, ankylosing spondylitis, contact hypersensitivity, multiple sclerosis and atherosclerosis, in particular GvHD.
29. A pharmaceutical composition according to claim 27 or claim 28 in combination with, or kit according to claim 28 comprising a label or instructions for use to treat and/or prevent said disease or condition in a human; optionally wherein the label or instructions comprise a marketing authorisation number (e.g., an FDA or EMA authorisation number); optionally wherein the kit comprises an IV or injection device that comprises the antibody or fragment.
30. A nucleic acid that encodes the HCDR3 of an antibody or fragment as defined in any one of claims 1 to 20.
31. A nucleic acid that encodes a VH domain and/or a VL domain of an antibody or fragment as defined in any one of claims 1 to 20.
32. A nucleic acid according to claim 31 comprising a nucleotide sequence that is at least 90% identical to the sequence of SEQ ID NO: 33 and/or SEQ ID NO: 47.
33. A nucleic acid that encodes a heavy chain or a light chain of an antibody recited in any one of claims 1 to 20.
34. A vector comprising the nucleic acid of any one of claims 30 to 33; optionally wherein the vector is a CHO or HEK293 vector.
35. A host comprising the nucleic acid of any one of claims 30 to 33 or the vector of claim 34.