

CLAIMS

1. An isolated anti-OX40 antibody, comprising

(1) heavy chain complementarity determining regions (HCDRs), HCDR1, HCDR2 and HCDR3, wherein the HCDR1 comprises the amino acid sequence as set forth in SEQ ID NO: 11, the HCDR2 comprises the amino acid sequence as set forth in SEQ ID NO: 12, and the HCDR3 comprises the amino acid sequence as set forth in SEQ ID NO: 13;

(2) light chain complementarity determining regions (LCDRs), LCDR1, LCDR2 and LCDR3, wherein the LCDR1 comprises the amino acid sequence as set forth in SEQ ID NO: 14, the LCDR2 comprises the amino acid sequence as set forth in SEQ ID NO: 15, and the LCDR3 comprises the amino acid sequence as set forth in SEQ ID NO: 16; and

(3) Fc region variant, which is human IgG1 N297A, wherein the amino acid residues in the Fc region are numbered in accordance with the EU numbering system.

2. The antibody of claim 1, comprising a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH comprises the amino acid sequence as set forth in SEQ ID NO: 2, and wherein the VL comprises the amino acid sequence as set forth in SEQ ID NO: 7.

3. The antibody of any one of claims 1-2, which comprises the human IgG1 constant region sequence as set forth in SEQ ID NO: 21 with mutation N297A.

4. The antibody of any one of claims 1-3, which is a full-length antibody.

5. The antibody of any one of claims 1-4, which has a binding affinity (K_D) to human OX40 of less than 10 nM.

6. The antibody of any one of claims 1-5, which is an OX40 antagonist antibody and has an activity for blocking OX40-mediated signal transduction.

7. The antibody of claim 6, wherein the binding of the Fc region variant to Fc γ R is reduced or eliminated compared to a native Fc region.

8. The antibody of claim 1, which comprises:

- the heavy chain variable region (VH) having the amino acid sequence as set forth in SEQ ID NO: 2;
- the light chain variable region (VL) having the amino acid sequence as set forth in SEQ ID NO: 7; and
- the heavy chain constant region of human IgG1 as set forth in SEQ ID NO: 21 with mutation N297A.

9. An isolated nucleic acid encoding the antibody of any one of claims 1-8.

10. A recombinant vector or an expression vector, comprising one or more nucleic acids of claim 9, wherein the vector is suitable for recombinant production of the antibody of any one of claims 1-8.

11. A host cell, comprising one or more recombinant vectors or expression vectors of claim 10.
12. An immunoconjugate or immune fusion, comprising the antibody of any one of claims 1-8.
13. A pharmaceutical composition, comprising the antibody of any one of claims 1-8, the nucleic acid of claim 9, the vector of claim 10, or the immunoconjugate or immune fusion of claim 12, and optionally comprising at least one pharmaceutically acceptable excipient.
14. Use of the antibody of any one of claims 1-8, the nucleic acid of claim 9, the vector of claim 10, or the immunoconjugate or immune fusion of claim 12 in the manufacture of a medicament for treating an OX40-related disease or condition, wherein the OX40-related disease or condition is inflammation and/or autoimmune disease.
15. The use of claim 14, wherein the OX40-related disease or condition is selected from atopic dermatitis, rheumatoid arthritis, asthma (e.g., allergic asthma), COPD, autoimmune uveitis, multiple sclerosis, lupus (such as systemic lupus erythematosus), ulcerative colitis, scleroderma, and graft-versus-host disease (GVHD).
16. The use of claim 15, wherein the OX40-related disease or condition is graft-versus-host disease.
17. The use of claim 15, wherein the OX40-related disease or condition is atopic dermatitis.
18. A method for detecting OX40 in a sample, comprising:
 - (a) contacting the sample with the antibody of any one of claims 1-8 or the immunoconjugate or immune fusion of claim 12; and
 - (b) detecting the formation of the complex of the antibody or the immunoconjugate or the immune fusion with the OX40 protein.