

CLAIMS

1. An isolated anti-OX40 antibody or antigen-binding fragment thereof, comprising HCDR1, HCDR2 and HCDR3 of the VH and LCDR1, LCDR2 and LCDR3 of the VL, wherein the VH and VL are selected from

(1) a VH comprising the amino acid sequence as set forth in SEQ ID NO: 1, and a VL comprising the amino acid sequence as set forth in SEQ ID NO: 6;

(2) a VH comprising the amino acid sequence as set forth in SEQ ID NO: 2, and a VL comprising the amino acid sequence as set forth in SEQ ID NO: 7 or 9;

(3) a VH comprising the amino acid sequence as set forth in SEQ ID NO: 3, and a VL comprising the amino acid sequence as set forth in SEQ ID NO: 9; or

(4) a VH comprising the amino acid sequence as set forth in SEQ ID NO: 4 and a VL comprising the amino acid sequence as set forth in SEQ ID NO: 7 or 8,

wherein, the antibody or antigen-binding fragment thereof does not comprise an Fc region variant which is human IgG1 N297A, and wherein the amino acid residues in the Fc region are numbered in accordance with the EU numbering system.

2. The antibody or antigen-binding fragment thereof of claim 1, 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; and

(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.

3. The antibody or antigen-binding fragment thereof of any one of claims 1-2, comprising

(1) a heavy chain variable region (VH) comprising an amino acid sequence identical to or having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to the amino acid sequence as set forth in SEQ ID NO: 1, 2, 3, 4 or 5; and/or

(2) a light chain variable region (VL) comprising an amino acid sequence identical to or having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to the amino acid sequence as set forth in SEQ ID NO: 6, 7, 8, 9 or 10.

4. The antibody or antigen-binding fragment thereof of any one of claims 1-2, comprising a heavy chain variable region (VH) and/or a light chain variable region (VL), wherein the VH comprises the amino acid sequence as set forth in any one of SEQ ID NO: 2, 3, 4 or 5, and the VL comprises the amino acid sequence as set forth in any one of SEQ ID NO: 7, 8, 9 or 10.

5. The antibody or antigen-binding fragment thereof of claim 1 or 2, comprising a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH and VL are selected from

(1) a VH comprising the amino acid sequence as set forth in SEQ ID NO: 1, and a VL comprising the amino acid sequence as set forth in SEQ ID NO: 6;

(2) a VH comprising the amino acid sequence as set forth in SEQ ID NO: 2, and a VL comprising the amino acid sequence as set forth in SEQ ID NO: 7 or 9;

(3) a VH comprising the amino acid sequence as set forth in SEQ ID NO: 3, and a VL comprising the amino acid sequence as set forth in SEQ ID NO: 9; or

(4) a VH comprising the amino acid sequence as set forth in SEQ ID NO: 4 and a VL comprising the amino acid sequence as set forth in SEQ ID NO: 7 or 8.

6. The antibody or antigen-binding fragment thereof of claim 5, 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.

7. The antibody or antigen-binding fragment thereof of any of claims 1-6, which is a murine antibody, a chimeric antibody or a humanized antibody.

8. The antibody or antigen-binding fragment thereof of any of claims 1-7, which is a full-length antibody, a Fab, a Fab' antibody, a Fab'-SH, a (Fab')₂ antibody, a single-chain antibody (such as a scFv), a Fv, or a bis(multi)-specific antibody.

9. The antibody or antigen-binding fragment thereof of any of claims 1-7, wherein said antibody comprises an Fc region, wherein the amino acid sequence of the Fc region is identical to the sequence of the Fc region of human IgG1, IgG2 or IgG4, or is a variant of the Fc region of human IgG1, IgG2 or IgG4.

10. The antibody or antigen-binding fragment thereof of any one of claims 1-7, which has a binding affinity (K_D) for human OX40 of less than 10 nM.

11. The antibody or antigen-binding fragment thereof of any one of claims 1-7, which blocks the binding of OX40 to its ligand OX40L.

12. The antibody or antigen-binding fragment thereof of any one of claims 1-7, wherein said antibody comprises an Fc region that binds to Fc γ R, and is an OX40 agonist antibody and has an activity of activating OX40-mediated signal transduction.

13. The antibody or antigen-binding fragment thereof of claim 12, wherein said antibody comprises an Fc region, wherein the amino acid sequence of the Fc region is identical to the sequence of the Fc region of human IgG1, IgG2 or IgG4.

14. The antibody or antigen-binding fragment thereof of any one of claims 1-7, wherein said antibody substantially does not bind to Fc γ R, and is an OX40 antagonist antibody and has an activity of blocking OX40-mediated signal transduction.

15. The antibody or antigen-binding fragment thereof of claim 14, wherein said antibody comprises a variant of a native Fc region, wherein the binding of the Fc region variant to Fc γ R is reduced or eliminated compared to the native Fc region.

16. An isolated nucleic acid, encoding the antibody or antigen-binding fragment thereof of any one of claims 1-15.

17. A recombinant vector or an expression vector, comprising one or more nucleic acids of claim 16, wherein the vector is suitable for recombinant production of the antibody or antigen-binding fragment thereof of any one of claims 1-15.

18. A host cell, comprising one or more recombinant vectors or expression vectors of claim 17.

19. An immunoconjugate or immune fusion, comprising the antibody or antigen-binding fragment thereof of any one of claims 1-15.

20. A pharmaceutical composition, comprising the antibody or antigen-binding fragment thereof of any one of claims 1-15, the nucleic acid of claim 16, the vector of claim 17, or the immunoconjugate or immune fusion of claim 19, and optionally comprising at least one pharmaceutically acceptable excipient.

21. Use of the antibody or antigen-binding fragment thereof of any one of claims 12-13 in the manufacture of a medicament for treating a cancer, wherein the cancer is selected from breast cancer, urothelial cancer, melanoma, kidney cancer, ovarian cancer, head and neck cancer, stomach cancer, liver cancer, small-cell lung cancer, non-small cell lung cancer, skin cancer, mesothelioma, lymphoma, leukemia, myeloma, prostate cancer, lymphatic leukemia and sarcoma.

22. The use of claim 21, wherein the cancer is melanoma, preferably metastatic melanoma.

23. Use of the antibody or antigen-binding fragment thereof of any one of claims 14-15 in the manufacture of a medicament for treating inflammation and/or autoimmune disease, wherein the disease is selected from atopic dermatitis, rheumatoid arthritis, asthma, allergic asthma, COPD, autoimmune uveitis, multiple sclerosis, lupus, systemic lupus erythematosus, ulcerative colitis, scleroderma, and graft-versus-host disease.

24. The use of claim 23, wherein the disease is graft-versus-host disease.

25. A method for detecting OX40 in a sample, comprising:

(a) contacting the sample with the antibody or antigen-binding fragment thereof of any one of claims 1-15 or the immunoconjugate or immune fusion of claim 19; and

(b) detecting the formation of the complex of the antibody or antigen-binding fragment thereof or the immunoconjugate or the immune fusion with the OX40 protein.