

Claims

1. An isolated antibody which binds to human OX40, comprising heavy chain CDR1 (SEQ ID NO: 87), CDR2 (SEQ ID NO: 317), and CDR3 (SEQ ID NO: 89) sequences, and light chain CDR1 (SEQ ID NO: 90), CDR2 (SEQ ID NO: 91), and CDR3 (SEQ ID NO: 92) sequences.
2. An isolated antibody which binds to human OX40, comprising a heavy chain variable region sequence (SEQ ID NO: 318) and a light chain variable region sequence (SEQ ID NO: 94).
3. An isolated antibody which binds to human OX40, comprising a heavy chain sequence (SEQ ID NO: 124) and a light chain sequence (SEQ ID NO: 116).
4. The antibody of claim 1 or 2, wherein the antibody comprises heavy and light chain constant regions.
5. The antibody of any one of claims 1-4, wherein the heavy chain constant region either lacks a C-terminal lysine or comprises an amino acid other than lysine at the C-terminus.
6. The antibody of any one of claims 1-5, wherein the antibody stimulates an antigen-specific T cell response.
7. The antibody of any one of claims 1-6, wherein the antibody binds to soluble human OX40 with a KD of 1 nM or less, as measured by Biacore.
8. The antibody of any one of claims 1-7, wherein the antibody binds to all or a portion of the sequence DVVSSKPCKPCTWCNLR (SEQ ID NO: 178) of human OX40 (SEQ ID NO: 2).
9. The antibody of any one of claims 1-8, which is an IgG1 isotype.
10. The antibody of any one of claims 1-9, which is a human antibody.
11. A nucleic acid encoding the heavy and/or light chain variable region of the antibody of any one of claims 1-10.
12. An expression vector comprising the nucleic acid of claim 11.
13. A cell transformed with the expression vector of claim 12.
14. A composition comprising the antibody of any one of claims 1-10 and a carrier.
15. The composition of claim 14, further comprising one or more additional therapeutics.
16. The composition of claim 15, wherein the one or more additional therapeutics are selected from the group consisting of: an anti-PD1 antibody and a CTLA-4 antibody.

17. Use of an antibody of any one of claims 1-10 in the manufacture of a medicament for treating a cancer.

18. Use of a composition of any one of claims 14-16 in the manufacture of a medicament for treating a cancer.

19. The use of claim 17 or 18, wherein the cancer is selected from the group consisting of: cervical cancer, colorectal cancer, bladder cancer, and ovarian cancer.

20. An isolated monoclonal antibody which binds to OX40, comprising:

(a) heavy chain CDR1, CDR2, and CDR3 sequences comprising SEQ ID NOs: 11-13, respectively, and light chain CDR1, CDR2, and CDR3 sequences comprising SEQ ID NOs: 14-16, respectively;

(b) heavy chain CDR1, CDR2, and CDR3 sequences comprising SEQ ID NOs: 19-21, respectively, and light chain CDR1, CDR2, and CDR3 sequences comprising SEQ ID NOs: 22-24, respectively;

(c) heavy chain CDR1, CDR2, and CDR3 sequences comprising SEQ ID NOs: 19-21, respectively, and light chain CDR1, CDR2, and CDR3 sequences comprising SEQ ID NOs: 25-27, respectively;

(d) heavy chain CDR1, CDR2, and CDR3 sequences comprising SEQ ID NOs: 31-33, respectively, and light chain CDR1, CDR2, and CDR3 sequences comprising SEQ ID NOs: 34-36, respectively;

(e) heavy chain CDR1, CDR2, and CDR3 sequences comprising SEQ ID NOs: 39-41, respectively, and light chain CDR1, CDR2, and CDR3 sequences comprising SEQ ID NOs: 42-44, respectively;

(f) heavy chain CDR1, CDR2, and CDR3 sequences comprising SEQ ID NOs: 39-41, respectively, and light chain CDR1, CDR2, and CDR3 sequences comprising SEQ ID NOs: 45-47, respectively;

(g) heavy chain CDR1, CDR2, and CDR3 sequences comprising SEQ ID NOs: 51-53, respectively, and light chain CDR1, CDR2, and CDR3 sequences comprising SEQ ID NOs: 54-56, respectively;

(h) heavy chain CDR1, CDR2, and CDR3 sequences comprising SEQ ID NOs: 59-61, respectively, and light chain CDR1, CDR2, and CDR3 sequences comprising SEQ ID NOs: 62-64, respectively;

(i) heavy chain CDR1, CDR2, and CDR3 sequences comprising SEQ ID NOs: 67-69, respectively, and light chain CDR1, CDR2, and CDR3 sequences comprising SEQ ID NOs: 70-72, respectively;

(j) heavy chain CDR1, CDR2, and CDR3 sequences comprising SEQ ID NOs: 75-77, respectively, and light chain CDR1, CDR2, and CDR3 sequences comprising SEQ ID NOs: 78-80, respectively, wherein, optionally, the Asp-Gly sequence in SEQ ID NO: 76 is replaced with an amino acid sequence that does not undergo isomerization;

(k) heavy chain CDR1, CDR2, and CDR3 sequences comprising SEQ ID NOs: 75-77, respectively, and light chain CDR1, CDR2, and CDR3 sequences comprising SEQ ID NOs: 81-83, respectively; or

(l) heavy chain CDR1, CDR2, and CDR3 sequences comprising SEQ ID NOs: 87-89, respectively, and light chain CDR1, CDR2, and CDR3 sequences comprising SEQ ID NOs: 90-92, respectively.