

Claims

1. An isolated antibody which binds to human OX40, wherein the antibody comprises a heavy chain variable region CDR1 comprising the sequence of SEQ ID NO: 87, a heavy chain variable region CDR2 comprising the sequence of SEQ ID NO: 317, and a heavy chain variable region CDR3 comprising the sequence of SEQ ID NO: 89, and a light chain variable region CDR1 comprising the sequence of SEQ ID NO: 90, a light chain variable region CDR2 comprising the sequence of SEQ ID NO: 91, and a light chain variable region CDR3 comprising the sequence of SEQ ID NO: 92.
2. An isolated antibody which binds to human OX40, wherein the antibody comprises a heavy chain variable region comprising the sequence of SEQ ID NO: 318 and a light chain variable region comprising the sequence of SEQ ID NO: 94.
3. An isolated antibody which binds to human OX40, wherein the antibody comprises a heavy chain comprising the sequence of SEQ ID NO: 124 and a light chain comprising the sequence of 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, an anti-PD-L1 antibody, an anti-CTLA-4 antibody, and combination thereof.

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. Use of an antibody of any one of claims 1-10 in combination with the anti-PD-1 antibody nivolumab in the manufacture of a medicament for treating a cancer.

21. Use of an antibody of any one of claims 1-10 in combination with the anti-CTLA-4 antibody ipilimumab in the manufacture of a medicament for treating a cancer.

22. Use of an antibody of any one of claims 1-10 in combination with the anti-PD-1 antibody nivolumab and the anti-CTLA-4 antibody ipilimumab in the manufacture of a medicament for treating cancer.

23. A method of making an antibody which binds to human OX40, comprising culturing the cell of claim 13 under suitable conditions and isolating the antibody.