

European Union to treat diseases such as unresectable or metastatic melanoma and metastatic non-small cell lung cancer. Treatment of patients with these agents has resulted in anti-tumor responses as measured by improvement in either progression free survival and/or overall survival.

[0008] The recent failure of OPDIVO® to slow progression of advanced lung cancer in a treatment-naïve patient population in a clinical trial comparing OPDIVO® with conventional chemotherapy highlights the need for alternative approaches and additional cancer treatments to complement existing therapeutic standards of care.

5. SUMMARY

[0009] The present disclosure provides anti-OX40 antibodies that specifically bind to and activate OX40. The amino acid sequences of exemplary complementarity determining regions (CDRs), the heavy chain variable domain (V_H) and light chain variable domain (V_L) regions (*i.e.*, the V_H and V_L chains, respectively), and the heavy and light chains of exemplary anti-OX40 antibodies are provided in the Detailed Description below. Anti-OX40 antibodies provided herein result in activation of the adaptive immune response.

[0009a] In one aspect, there is provided an anti-OX40 antibody which comprises (i) a V_H chain comprising three CDRs; and a V_L chain comprising three CDRs wherein

VH CDR#1 has an amino acid sequence of: GFTFSRYGMS (SEQ ID NO:101);

VH CDR#2 has an amino acid sequence of: TINSNGGRTYYPD SVKG
(SEQ ID NO:102);

VH CDR#3 has an amino acid sequence of: EGITTAYAMDY (SEQ ID NO:103);

VL CDR#1 has an amino acid sequence of: KASQSVDYDGDSYMH (SEQ ID NO:104);

VL CDR#2 has an amino acid sequence of: AASILES (SEQ ID NO:105); and

VL CDR#3 has an amino acid sequence of: QQSNE DPRT (SEQ ID NO:106).

[0009b] In one aspect, there is provided an anti-human OX40 antibody which is an IgG antibody consisting of heavy chains each consisting of the amino acid sequence of SEQ ID NO:41 and light chains each consisting of the amino acid sequence of SEQ ID NO:51.

[0009c] In one aspect, there is provided an anti-human OX40 antibody which is an IgG antibody consisting of heavy chains each consisting of the amino acid sequence of SEQ ID NO:42 and light chains each consisting of the amino acid sequence of SEQ ID NO:51.

[0010] The anti-OX40 antibodies may include modifications and/or mutations that alter the properties of the antibodies, such as increase half-life, increase or decrease antigen-dependent cellular cytotoxicity (ADCC), as is known in the art.

[0010a] In another aspect, there is provided one or more nucleic acids comprising nucleotide sequences encoding the anti-OX40 antibody disclosed herein.

[0010b] In another aspect, there is provided one or more vectors comprising the one or more nucleic acids disclosed herein.

[0010c] In another aspect, there is provided a eukaryotic host cell transformed with the one or more vectors disclosed herein.

[0010d] In another aspect, there is provided a eukaryotic host cell engineered to express the one or more nucleic acids disclosed herein.

[0010e] In another aspect, there is provided a method of producing an anti-OX40 antibody, comprising: (a) culturing the host cell disclosed herein and (b) recovering the anti-OX40 antibody.

[0011] Nucleic acids comprising nucleotide sequences encoding the anti-OX40 antibodies of the disclosure are provided herein, as are vectors comprising nucleic acids. Additionally, prokaryotic and eukaryotic host cells transformed with a vector comprising a nucleotide sequence encoding a disclosed anti-OX40 antibody are provided herein, as well as eukaryotic (such as mammalian) host cells engineered to express the nucleotide sequences. Methods of producing antibodies, by culturing host cells and recovering the antibodies are also provided, and discussed further in the Detailed Description below.

[0011a] In another aspect, there is provided a pharmaceutical composition comprising the anti-OX40 antibody disclosed herein, and a pharmaceutically acceptable carrier.

[0012] In another example, the present disclosure provides compositions including the anti-OX40 antibodies described herein. The compositions generally comprise one or more anti-OX40 antibodies as described herein, and one or more excipients, carriers or diluents.

[0012a] In another aspect, there is provided use of the anti-OX40 antibody disclosed herein, or the pharmaceutical composition disclosed herein in the manufacture of a medicament for activating the immune system in a patient in need thereof. In another aspect, there is provided use of the anti-OX40 antibody disclosed herein, or the pharmaceutical composition disclosed herein in the manufacture of a medicament for treating cancer in a patient in need thereof.

[0013] The present disclosure provides methods of treating subjects, such as human subjects, diagnosed with a solid tumor with an anti-OX40 antibody. The method generally involves administering to the subject an amount of an anti-OX40 antibody described herein effective to

WHAT IS CLAIMED IS:

1. An anti-OX40 antibody which comprises (i) a V_H chain comprising three CDRs; and a V_L chain comprising three CDRs wherein
VH CDR#1 has an amino acid sequence of: GFTFSRYGMS (SEQ ID NO:101);
VH CDR#2 has an amino acid sequence of: TINSNGGRITYYPDSVKG
(SEQ ID NO:102);
VH CDR#3 has an amino acid sequence of: EGITTAYAMDY (SEQ ID NO:103);
VL CDR#1 has an amino acid sequence of: KASQSVDYDGDSYMH (SEQ ID NO:104);
VL CDR#2 has an amino acid sequence of: AASILES (SEQ ID NO:105); and
VL CDR#3 has an amino acid sequence of: QQSNEPRT (SEQ ID NO:106).
2. The anti-OX40 antibody of claim 1, which is monoclonal.
3. The anti-OX40 antibody of claim 1, which is humanized.
4. The anti-OX40 antibody of any one of claims 1-3, which comprises a V_H chain having an amino acid sequence according to SEQ ID NO:22; and a V_L chain having an amino acid sequence according to SEQ ID NO:32.
5. The anti-OX40 antibody of any one of claims 1-4, which is an IgG.
6. The anti-OX40 antibody of claim 5, which is an IgG₁.
7. The anti-OX40 antibody of claim 4, which comprises a heavy chain having an amino acid sequence according to SEQ ID NOS:41 or 42; and a light chain having an amino acid sequence according to SEQ ID NO:51.
8. An anti-human OX40 antibody which is an IgG antibody consisting of heavy chains each consisting of the amino acid sequence of SEQ ID NO:41 and light chains each consisting of the amino acid sequence of SEQ ID NO:51.
9. An anti-human OX40 antibody which is an IgG antibody consisting of heavy chains each consisting of the amino acid sequence of SEQ ID NO:42 and light chains each consisting of the amino acid sequence of SEQ ID NO:51.

10. One or more nucleic acids comprising nucleotide sequences encoding the anti-OX40 antibody of any one of claims 1-9.
11. One or more vectors comprising the one or more nucleic acids of claim 10.
12. A eukaryotic host cell transformed with the one or more vectors of claim 11.
13. A eukaryotic host cell engineered to express the one or more nucleic acids of claim 12.
14. The eukaryotic host cell of claim 12 or 13, which is a mammalian host cell.
15. A method of producing an anti-OX40 antibody, comprising: (a) culturing the host cell of any one of claims 12-14 and (b) recovering the anti-OX40 antibody.