

CLAIMS

1. An isolated antibody or the antigen binding portion thereof, wherein the isolated antibody or the antigen binding portion thereof comprises:—

A) one or more heavy chain CDRs (CDRHs) selected from at least one of the group consisting of:

- (i) a CDRH1 with at least 90% sequence identity to a CDRH1 as set forth in one of the sequences selected from the group consisting of SEQ ID NOs: 1, 7, 13, 15, 21 and 27;—
- (ii) a CDRH2 with at least 90% sequence identity to a CDRH2 as set forth in one of the sequences selected from the group consisting of SEQ ID NOs: 3, 9, 17, 23 and 29; and
- (iii) a CDRH3 with at least 90% sequence identity to a CDRH3 as set forth in one of the sequences selected from the group consisting of SEQ ID NOs: 5, 11, 19, 25 and 31;—

B) one or more light chain CDRs (CDRLs) selected from at least one of the group consisting of:—

- (i) a CDRL1 with at least 90% sequence identity to a CDRL1 as set forth in one of the sequences selected from the group consisting of SEQ ID NOs: 2, 8, 14, 16, 22 and 28;—
- (ii) a CDRL2 with at least 90% sequence identity to a CDRL2 as set forth in one of the sequences selected from the group consisting of SEQ ID NOs: 4, 10, 18, 24 and 30; and—
- (iii) a CDRL3 with at least 90% sequence identity to a CDRL3 as set forth in one of the sequences selected from the group consisting of SEQ ID NOs: 6, 12, 20, 26 and 32; or—

C) one or more CDRHs of A) and one or more CDRLs of B).

2. The isolated antibody or the antigen binding portion thereof of claim 1, wherein the isolated antibody or the antigen binding portion thereof comprises:—

A) one or more heavy chain CDRs (CDRHs) selected from at least one of the group consisting of:

- (i) a CDRH1 selected from the group consisting of SEQ ID NOs: 1, 7, 13, 15, 21 and 27, or a CDRH1 that differs in amino acid sequence from the CDRH1 by an amino acid addition, deletion or substitution of not more than 2 amino acids;—
- (ii) a CDRH2 selected from the group consisting of SEQ ID NOs: 3, 9, 17, 23 and 29, or a CDRH2 that differs in amino acid sequence from the CDRH2 by an amino acid addition, deletion or substitution of not more than 2 amino acids; and
- (iii) a CDRH3 selected from the group consisting of SEQ ID NOs: 5, 11, 19, 25 and 31, or a CDRH3 that differs in amino acid sequence from the CDRH3 by an amino acid addition, deletion or substitution of not more than 2 amino acids;—

B) one or more light chain CDRs (CDRLs) selected from at least one of the group consisting of:—

- (i) a CDRL1 selected from the group consisting of SEQ ID NOs: 2, 8, 14, 16, 22 and 28, or a CDRL1 that differs in amino acid sequence from the CDRL1 by an amino acid addition, deletion or substitution of not more than 2 amino acids;—

(ii) a CDRL2 selected from the group consisting of SEQ ID NOs: 4, 10, 18, 24 and 30, or a CDRL2 that differs in amino acid sequence from the CDRL2 by an amino acid addition, deletion or substitution of not more than 2 amino acids; and

(iii) a CDRL3 selected from the group consisting of SEQ ID NOs: 6, 12, 20, 26 and 32, or a CDRL3 that differs in amino acid sequence from the CDRL3 by an amino acid addition, deletion or substitution of not more than 2 amino acids; or

C) one or more CDRHs of A) and one or more CDRLs of B).

31. The An isolated antibody that binds to OX40 or the an antigen-binding portion thereof of claim 1, wherein the isolated antibody or the antigen-binding portion thereof comprises:

- (a) a CDRH1 comprising or consisting of SEQ ID NO: 1;
- (b) a CDRH2 comprising or consisting of SEQ ID NO: 3;
- (c) a CDRH3 comprising or consisting of SEQ ID NO: 5;
- (d) a CDRL1 comprising or consisting of SEQ ID NO: 2;
- (e) a CDRL2 comprising or consisting of SEQ ID NO: 4; and
- (f) a CDRL3 comprising or consisting of SEQ ID NO: 6.

42. The An isolated antibody that binds to OX40 or an the antigen-binding portion thereof of claim 1, wherein the isolated antibody or the antigen-binding portion thereof comprises:

- (a) a CDRH1 comprising or consisting of SEQ ID NO: 7;
- (b) a CDRH2 comprising or consisting of SEQ ID NO: 9;
- (c) a CDRH3 comprising or consisting of SEQ ID NO: 11;
- (d) a CDRL1 comprising or consisting of SEQ ID NO: 8;
- (e) a CDRL2 comprising or consisting of SEQ ID NO: 10; and
- (f) a CDRL3 comprising or consisting of SEQ ID NO: 12.

53. The An isolated antibody that binds to OX40 or an the antigen-binding portion thereof of claim 1, wherein the isolated antibody or the antigen-binding portion thereof comprises:

- (a) a CDRH1 comprising or consisting of SEQ ID NO: 13;
- (b) a CDRH2 comprising or consisting of SEQ ID NO: 9;
- (c) a CDRH3 comprising or consisting of SEQ ID NO: 11;
- (d) a CDRL1 comprising or consisting of SEQ ID NO: 14;
- (e) a CDRL2 comprising or consisting of SEQ ID NO: 10; and
- (f) a CDRL3 comprising or consisting of SEQ ID NO: 12.

~~64. The~~ An isolated antibody that binds to OX40 or an ~~the~~ antigen-binding portion thereof of claim 1, wherein the isolated antibody or the antigen-binding portion thereof comprises:

- (a) a CDRH1 comprising or consisting of SEQ ID NO: 15;
- (b) a CDRH2 comprising or consisting of SEQ ID NO: 17;
- (c) a CDRH3 comprising or consisting of SEQ ID NO: 19;
- (d) a CDRL1 comprising or consisting of SEQ ID NO: 16;
- (e) a CDRL2 comprising or consisting of SEQ ID NO: 18; and
- (f) a CDRL3 comprising or consisting of SEQ ID NO: 20.

~~75. The~~ An isolated antibody that binds to OX40 or an ~~the~~ antigen-binding portion thereof of claim 1, wherein the isolated antibody or the antigen-binding portion thereof comprises:

- (a) a CDRH1 comprising or consisting of SEQ ID NO: 21;
- (b) a CDRH2 comprising or consisting of SEQ ID NO: 23;
- (c) a CDRH3 comprising or consisting of SEQ ID NO: 25;
- (d) a CDRL1 comprising or consisting of SEQ ID NO: 22;
- (e) a CDRL2 comprising or consisting of SEQ ID NO: 24; and
- (f) a CDRL3 comprising or consisting of SEQ ID NO: 26.

~~86. The~~ An isolated antibody that binds to OX40 or an ~~the~~ antigen-binding portion thereof of claim 1, wherein the isolated antibody or the antigen-binding portion thereof comprises:

- (a) a CDRH1 comprising or consisting of SEQ ID NO: 27;
- (b) a CDRH2 comprising or consisting of SEQ ID NO: 29;
- (c) a CDRH3 comprising or consisting of SEQ ID NO: 31;
- (d) a CDRL1 comprising or consisting of SEQ ID NO: 28;
- (e) a CDRL2 comprising or consisting of SEQ ID NO: 30; and
- (f) a CDRL3 comprising or consisting of SEQ ID NO: 32.

~~9. The isolated antibody or the antigen-binding portion thereof of claim 1, wherein the isolated antibody or the antigen-binding portion thereof comprises:—~~

~~(A) a heavy chain variable region:—~~

- ~~(i) comprising the amino acid sequence selected from the group consisting of SEQ ID NO: 33, 35, 37, 39, 41 and 43;~~
- ~~(ii) comprising an amino acid sequence at least 85%, at least 90%, or at least 95% identical to the amino acid sequence selected from the group consisting of SEQ ID NO: 33, 35, 37, 39, 41 and 43; or~~

~~(iii) comprising an amino acid sequence with addition, deletion and/or substitution of one or more amino acids compared with the amino acid sequence selected from the group consisting of SEQ ID NO: 33, 35, 37, 39, 41 and 43; and/or~~

~~(B) a light chain variable region:~~

~~(i) comprising the amino acid sequence selected from the group consisting of SEQ ID NO: 34, 36, 38, 40, 42 and 44;~~

~~(ii) comprising an amino acid sequence at least 85%, at least 90%, or at least 95% identical to the amino acid sequence selected from the group consisting of SEQ ID NO: 34, 36, 38, 40, 42 and 44; or~~

~~(iii) comprising an amino acid sequence with addition, deletion and/or substitution of one or more amino acids compared with the amino acid sequence selected from the group consisting of SEQ ID NO: 34, 36, 38, 40, 42 and 44.~~

~~107.~~ The isolated antibody or the antigen-binding portion thereof of any one of claims 91 to 6, wherein the isolated antibody or the antigen-binding portion thereof comprises:

(a) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 33 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 34; or

(b) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 35 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 36; or

(c) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 37 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 38; or

(d) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 39 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 40; or

(e) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 41 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 42; or

(f) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 43 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 44.

~~118.~~ The isolated antibody or the antigen-binding portion thereof of any one of claims 1 to 6, wherein the antibody is a monoclonal antibody, ~~a chimeric antibody, a humanized antibody, or a fully human monoclonal antibody.~~

~~129.~~ The isolated antibody or the antigen-binding portion thereof of any one of claims 1 to 6, wherein the antibody is fused to a constant region of an IgG.

~~13~~10. An isolated nucleic acid molecule, comprising a nucleic acid sequence encoding the heavy chain variable region and/or the light chain variable region of the isolated antibody ~~as defined of any one of~~ claims 1 to 6.

~~14~~11. A vector comprising the nucleic acid molecule of claim ~~13~~10.

~~15~~12. A host cell comprising the vector of claim ~~14~~11.

~~16~~13. A pharmaceutical composition comprising at least one antibody or antigen-binding portion thereof ~~as defined in of any one of~~ claims 1 to 6 and a pharmaceutically acceptable carrier.

~~17~~14. A method for preparing antibody or antigen-binding portion thereof ~~as defined in of any one of~~ claims 1 to 6, comprising the steps of:

- expressing the antibody or antigen-binding portion thereof in ~~a the~~ the host cell of claim 12 ~~which comprises a vector comprising a nucleic acid molecule, wherein the nucleic acid molecule comprises a nucleic acid sequence encoding the heavy chain variable region and/or the light chain variable region of the antibody or antigen-binding portion thereof; and~~

- isolating the antibody or antigen-binding portion thereof from the host cell.

~~18~~15. Use of the antibody or antigen-binding portion thereof ~~as defined in of any one of~~ claims 1 to 6 in the manufacture of a medicament for reducing tumor cell metastasis in a subject.

~~19~~16. Use of the antibody or antigen-binding portion thereof of any one of ~~as defined in~~ claims 1 to 6 in the manufacture of a medicament for treating ~~or preventing~~ proliferative disorders (such as cancers), in which OX40 is implicated, ~~autoimmune diseases, inflammatory disease or infectious diseases~~ in a subject.

~~20~~17. A kit for treating or diagnosing ~~proliferative disorders (such as cancers) in which OX40 is implicated,~~ autoimmune diseases, inflammatory disease or infectious diseases, comprising a container comprising at least one antibody or antigen-binding portion thereof ~~as defined in of any one of~~ claims 1 to 6.

~~21~~18. The antibody or antigen-binding portion thereof of any one of ~~as defined in~~ claims 1 to 6 for use as a medicament.

2219. The antibody or antigen-binding portion thereof of any one of as defined in claims 1 to 6 for use in reducing tumor cell metastasis in a subject.

2320. The antibody or antigen-binding portion thereof of any one of as defined in claims 1 to 6 for use in treating ~~or preventing~~ diseases comprising ~~proliferative disorders (such as cancers)~~ in which OX40 is implicated, ~~autoimmune diseases, inflammatory disease or infectious diseases~~ in a subject.