C10orf54 have also been shown to prevent acute graft-versus-host disease in mice (Flies et al., *J. Immunology* 187(4):1537-1541 (2011)).

Citation or discussion of a reference herein shall not be construed as an admission that such is prior art to the present invention.

SUMMARY

In one aspect, the present disclosure refers to an isolated antibody that binds to C10orf54, said antibody being selected from:

a. an antibody comprising:
   i. a heavy chain variable (VH) region comprising three CDRs having the amino acid sequences SEQ ID NO. 36, SEQ ID NO. 37, and SEQ ID NO. 38, and
   ii. a light chain variable (VL) region comprising three CDRs having the amino acid sequences SEQ ID NO. 45, SEQ ID NO. 46, and SEQ ID NO. 47;

b. an antibody comprising:
   i. a heavy chain variable (VH) region comprising three CDRs having the amino acid sequences SEQ ID NO. 30, SEQ ID NO. 31, and SEQ ID NO. 32, and
   ii. a light chain variable (VL) region comprising three CDRs having the amino acid sequences SEQ ID NO. 45, SEQ ID NO. 40, and SEQ ID NO. 41; and

c. an antibody comprising:
   i. a heavy chain variable (VH) region comprising three CDRs having the amino acid sequences SEQ ID NO. 33, SEQ ID NO. 34, and SEQ ID NO. 35, and
   ii. a light chain variable (VL) region comprising three CDRs having the amino acid sequences SEQ ID NO. 42, SEQ ID NO. 43, and SEQ ID NO. 44.

In another aspect, the present disclosure refers to an isolated nucleic acid molecule encoding an antibody as disclosed herein, said nucleic acid molecule comprising or consisting of a nucleic acid sequence that encodes the V_H region and/or V_L region of said antibody. In yet another aspect, the present disclosure refers to a vector comprising the nucleic acid molecule as disclosed herein. In another aspect, the present disclosure refers to a host cell comprising the vector as disclosed herein. In

yet a further aspect, the present disclosure refers to a method of producing an antibody comprising culturing the host cell as disclosed herein under conditions that promotes the production of the antibody. In a further aspect, disclosed herein is a pharmaceutical composition comprising the antibody as disclosed herein and a pharmaceutically-acceptable excipient. In still another aspect, the present disclosure refers to the antibody or the composition as disclosed herein for use as a medicament. In another aspect, the present disclosure refers to the use of the antibody as disclosed herein or the composition as disclosed herein in the manufacture of a medicament for treating, preventing or alleviating one or more symptoms of a disease, wherein the disease is a cancer or graft-versus-host disease. In a further aspect, the present disclosure refers to the antibody or the composition as disclosed herein for use in modulating an immune response in a subject. In another aspect, the present disclosure refers to the use of the anti-C10orf54 antibody as disclosed herein or an antibody-drug conjugate as disclosed herein, in the manufacture of a medicament for treating cancer. In another aspect, the present disclosure refers to the use of the anti-C10orf54 antibody as disclosed herein or an antibody-drug conjugate as disclosed herein, in the manufacture of a medicament for killing a tumor cell.

In a first example, provided herein are antibodies that bind to C10orf54, including a C10orf54 polypeptide, a C10orf54 polypeptide fragment or a C10orf54 epitope, collectively referred to herein as anti-C10orf54 antibodies. Also provided herein are anti-C10orf54 antibodies that are conjugated to drugs as antibody-drug conjugates (ADCs), including ADCs of the formula A-L-CTX, wherein A is an antibody, L is a linker, and CTX is cytotoxin. In some examples the anti-C10orf54 antibodies are humanized antibodies that bind to a C10orf54 polypeptide, a C10orf54 polypeptide fragment or a C10orf54 epitope. In certain examples, the anti-C10orf54 antibody comprises a VH domain, VL domain, VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and/or VL CDR3 of monoclonal antibody 175A, 76E1 or 141A described herein, or a humanized variant thereof. In certain examples, the anti-C10orf54 antibody can further comprise a VH FR1, VH FR2, VH FR3, VH FR4, VL FR1, VL FR2, VL FR3, and/or VL FR4 of a human germline immunoglobulin amino acid sequence or a variant thereof.

In certain examples, the antibody comprises less than six CDRs. In some examples, the antibody comprises or consists of one, two, three, four, or five CDRs selected from the group consisting of VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and/or VL CDR3. In specific examples, the antibody comprises or consists of one, two, three, four, or five CDRs selected from the group consisting of VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and/or VL CDR3 of the monoclonal antibody 175A, 76E1 or 141A described herein, or a humanized variant thereof. In specific examples, the antibody further comprises a VH FR1, VH FR2, VH FR3, VH FR4, VL FR1, VL FR2, VL FR3, and/or VL FR4 of a human germline immunoglobulin amino acid sequence or a variant thereof.

In specific examples, the antibody is a humanized antibody, a monoclonal antibody, a recombinant antibody, an antigen binding fragment or any combination thereof. In particular examples, the antibody is a humanized monoclonal antibody, or antigen binding fragment thereof, that binds to a C10orf54 polypeptide (*e.g.,* a cell surface-expressed or soluble C10orf54), a C10orf54 fragment, or a C10orf54 epitope.

In a second example, provided herein are antibodies, including humanized antibodies, (i) that competitively block (*e.g.,* in a dose-dependent manner) an anti-C10orf54 antibody provided herein from binding to a C10orf54 polypeptide (*e.g.,* a cell surface-expressed or soluble C10orf54), a C10orf54 fragment, or a C10orf54 epitope and/or (ii) that bind to a C10orf54 epitope that is bound by an anti-C10orf54 antibody (*e.g.*, humanized anti-C10orf54 antibodies) provided herein. In other examples, the antibody competitively blocks (*e.g.,* in a dose-dependent manner) monoclonal antibody 175A, 76E1 or 141A described herein or a humanized variant thereof from binding to a C10orf54 polypeptide (*e.g.,* a cell surface-expressed or soluble C10orf54), a C10orf54 fragment, or a C10orf54 epitope. In other examples, the antibody binds to a C10orf54 epitope that is bound (*e.g.,* recognized) by monoclonal antibody 175A, 76E1, or 141A described herein or a humanized variant thereof (e.g. humanized anti-C10orf54 antibodies).

In certain examples, the anti-C10orf54 antibodies (*e.g.*, humanized anti-C10orf54 antibodies) provided herein are conjugated or recombinantly fused to a diagnostic agent, detectable agent or therapeutic agent. In some examples, the therapeutic agent is a chemotherapeutic agent (*e.g.,* a cystotoxic agent such as cytotoxin). In

some examples, the detectable agent is a radioisotope, an enzyme, a fluorescent compound, a bioluminescent compound or a chemiluminescent compound. In certain examples, the anti-C10orf54 antibodies provided herein are conjugated to drugs as antibody-drug conjugates (ADCs). In some examples, the antibody-drug conjugate (ADC) is of the formula A-L-CTX, wherein A is an antibody, L is a linker, and CTX is a cytotoxin.

In certain examples, provided are compositions comprising an anti-C10orf54 antibody (*e.g.*, humanized anti-C10orf54 antibodies) described herein. In some examples, the compositions comprise an antibody-drug conjugate wherein the antibody is an anti-C10orf54 antibody. Also provided herein are pharmaceutical compositions comprising an anti-C10orf54 antibody, including a humanized anti-C10orf54 antibody, provided herein.

In a third example, provided are isolated nucleic acid molecules encoding a VH chain, VL chain, VH domain, VL domain, VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and/or VL CDR3 of anti-C10orf54 antibodies, including humanized anti-C10orf54 antibodies, that bind to a C10orf54 polypeptide, a C10orf54 polypeptide fragment, or a C10orf54 epitope. In certain examples, the nucleic acid molecule encodes a VH domain, VL domain, VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and/or VL CDR3 of monoclonal antibody 175A, 76E1 or 141A described herein, or a humanized variant thereof. In certain examples, the nucleic acid molecule further encodes a VH FR1, VH FR2, VH FR3, VH FR4, VL FR1, VL FR2, VL FR3, and/or VL FR4 of a human germline immunoglobulin amino acid sequence or a variant thereof. Also provided herein are vectors and host cells comprising the nucleic acid molecules encoding an anti-C10orf54 antibody (*e.g.*, humanized anti-C10orf54 antibodies), as well as methods of producing an anti-C10orf54 antibody by culturing the host cells provided herein under conditions that promote the production of the anti-C10orf54 antibody.

In a fourth example, provided herein are methods of treating, preventing or alleviating a disease, disorder or condition, including one or more symptoms of a disease, disorder or condition, comprising administering a therapeutically effective amount of an anti-C10orf54 antibody, including an antibody-drug conjugate (ADC) comprising an anti-C10orf54 antibody, provided herein to a subject, thereby treating, preventing or

alleviating the disease, disorder or condition, including one or more symptoms of the disease, disorder or condition. In some examples the anti-C10orf54 antibodies are humanized antibodies that bind to a C10orf54 polypeptide, a C10orf54 polypeptide fragment or a C10orf54 epitope. In one example, the disease, disorder or condition is caused by or otherwise associated with C10orf54, including by or associated with C10orf54-expressing cells (*e.g.*, tumor cells, myeloid-derived suppressor cells (MDSC), suppressive dendritic cells (suppressive DC), and /or regulatory T cells (T regs)). In certain examples, the disease is a cancer, such as a leukemia, a bladder cancer or a fibrosarcoma. In one example, the leukemia is an acute myeloid leukemia (AML). In other examples, the disease is graft-versus-host disease (GVHD). Additional methods provided include using an anti-C10orf54 antibody with C10orf54 binding activity for C10orf54-expressing cells, provided herein, for example, as an unconjugated antibody or conjugated antibody (ADC), including to inhibit and/or kill the C10orf54-expressing cells (*e.g.*, with anti-tumor activity to mediate an anti-tumor effect). In certain examples, the anti-C10orf54 antibodies, including ADCs comprising the anti-C10orf54 antibodies, provided herein inhibit C10orf54-mediated suppressor activity on T cells (*e.g.*, to allow an effective anti-tumor immune response). In certain examples, the anti-C10orf54 antibodies provided herein directly kill C10orf54-expressing cells (*e.g.*, C10orf54-bearing tumor cells, myeloid-derived suppressor cells (MDSC), suppressive dendritic cells (suppressive DC), and /or regulatory T cells (T regs)), for example, via antibody-dependent cellular cytotoxicity (ADCC) and/or complement-dependent cytotoxicity (CDC) In certain examples, antibody drug conjugates (ADCs) comprising anti-C10orf54 antibodies provided herein directly kill C10orf54-expressing cells including by binding to cells expressing C10orf54 (*e.g.*, tumor cells, myeloid-derived suppressor cells (MDSC), suppressive dendritic cells (suppressive DC), and/or regulatory T cells (T regs)), for example, by allowing internalization of the cytotoxic drug. In any of the above examples, the anti-C10orf54 antibody can be a humanized anti-C10orf54 antibody provided herein that binds to a C10orf54 polypeptide, a C10orf54 polypeptide fragment or a C10orf54 epitope.

In a fifth example, provided herein are methods of inhibiting the growth of cells and/or killing cells having cell surface expression of C10orf54 comprising contacting the cells with an effective amount of an anti-C10orf54 antibody or antibody-drug conjugates

provided herein. In one example, the cell is a regulatory T cell (*e.g.*, a $CD4^+$ $Foxp3^+$ regulatory T cell). In other examples, the cell is a myeloid-derived suppressor cell (*e.g.*,a $CD11b^+$ or $CD11b^{high}$ myeloid-derived suppressor cell) or a suppressive dendritic cell (e.g., a $CD11b^+$ or $CD11b^{high}$ dendritic cell).. In other examples, the cell is a cancerous or pre-cancerous cell. Additional methods provided include using an anti-C10orf54 antibody with C10orf54 binding activity for C10orf54-expressing cells provided herein, for example, as an unconjugated antibody or conjugated antibody (ADC) including to inhibit and/or kill C10orf54-expressing cells (*e.g.*, with anti-tumor activity to mediate an anti-tumor effect). In certain examples, the anti-C10orf54 antibodies, including ADCs comprising the anti-C10orf54 antibodies, provided herein inhibit C10orf54-mediated suppressor activity on T cells (*e.g.*, to allow an effective anti-tumor immune response). In certain examples, the anti-C10orf54 antibodies provided herein directly kill C10orf54-expressing cells (*e.g.*, C10orf54-bearing tumor cells, myeloid-derived suppressor cells (MDSC), suppressive dendritic cells (suppressive DC), and /or regulatory T cells (T regs)), for example, via antibody-dependent cellular cytotoxicity (ADCC) and/or complement-dependent cytotoxicity (CDC) In certain examples, antibody drug conjugates (ADCs) comprising anti-C10orf54 antibodies provided herein directly kill C10orf54-expressing cells including by binding to cells expressing C10orf54 (*e.g.*, tumor cells, myeloid-derived suppressor cells (MDSC), suppressive dendritic cells (suppressive DC), and/or regulatory T cells (T regs)), for example, by allowing internalization of the cytotoxic drug. In any of the above examples, the anti-C10orf54 antibody can be a humanized anti-C10orf54 antibody provided herein that binds to a C10orf54 polypeptide, a C10orf54 polypeptide fragment or a C10orf54 epitope.

In a sixth example, provided herein are methods of modulating an immune response in a subject comprising administering an effective amount of an anti-C10orf54 antibody (e.g., a humanized anti-C10orf54 antibody) provided herein to a subject. In one example, the modulating comprises increasing T cell activation. In other example, the modulating comprises increasing T cell

proliferation. In another example, the modulating comprises increasing cytokine production.

In a seventh example, provided herein are methods for detecting C10orf54 in a sample comprising contacting the sample with an anti-C10orf54 antibody (e.g., a humanized anti-C10orf54 antibody) provided herein, such as an antibody that comprises a detectible agent. In certain examples, the sample comprises a cell expressing C10orf54 on its surface.

In an eighth example, provided herein are methods of treating cancers comprising administering to a subject an anti-C10orf54 antibody or an antibody-drug conjugate (ADC) comprising an anti-C10orf54 (*e.g.,* an ADC of the formula A-L-CTX, wherein A is the antibody, L is a linker, and CTX is a cytotoxic agent) in a therapeutically effective amount, including in an amount effective to kill a C10orf54-expressing cell (*e.g.*, tumor cell, myeloid-derived suppressor cell (MDSC), suppressive dendritic cell (suppressive DC), and /or regulatory T cell (T reg)). In some examples the cancer is acute myeloid leukemia (AML). In any of the above examples, the anti-C10orf54 antibody can be a humanized anti-C10orf54 antibody provided herein that binds to a C10orf54 polypeptide, a C10orf54 polypeptide fragment or a C10orf54 epitope.

In a ninth example, provided herein are methods of killing C10orf54-expressing cells (*e.g.*, tumor cells, myeloid-derived suppressor cells (MDSC), suppressive dendritic cells (suppressive DC), and /or regulatory T cells (T reg)) comprising contacting a C10orf54-expressing cell (*e.g.*, tumor cell, myeloid-derived suppressor cell (MDSC), suppressive dendritic cell (suppressive DC), and /or regulatory T cell (T regs)) with an amount of an anti-C10orf54 antibody or an antibody-drug conjugate (ADC) comprising an anti-C10orf54 antibody (*e.g.,* an ADC of the formula A-L-CTX, wherein A is the antibody, L is a linker, and CTX is a cytotoxic agent) effective to kill the cell (*e.g.*, tumor cell, myeloid-derived suppressor cell (MDSC), suppressive dendritic cell (suppressive DC), and /or regulatory T cell (T reg)). In some examples, the tumor cell is an AML cell. In any of the above examples, the anti-C10orf54 antibody can be a humanized anti-C10orf54

antibody provided herein that binds to a C10orf54 polypeptide, a C10orf54 polypeptide fragment or a C10orf54 epitope.

In a tenth example, provided herein is a kit comprising an anti-C10orf54 antibody (e.g., a humanized anti-C10orf54 antibody) that binds to a C10orf54 polypeptide, a C10orf54 polypeptide fragment, or a C10orf54 epitope provided herein. In some examples, the kits comprise an antibody-drug conjugate (ADC) wherein the antibody is an anti-C10orf54 antibody (e.g., a humanized anti-C10orf54 antibody).

TERMINOLOGY

Unless defined otherwise, all technical and scientific terms used herein have the same meaning as is commonly understood by one of ordinary skill in the art. All patents, applications, published applications and other publications are incorporated by reference in their entirety. In the event that there are a plurality of definitions for a term herein, those in this section prevail unless stated otherwise.

The term “about” or “approximately” means within 20%, such as within 10%, or within 5% (or 1% or less) of a given value or range.

WHAT IS CLAIMED:

1 An isolated antibody that binds to C10orf54, said antibody being selected from:

a. an antibody comprising:

i. a heavy chain variable (VH) region comprising three CDRs having the amino acid sequences SEQ ID NO. 36, SEQ ID NO. 37, and SEQ ID NO. 38, and

ii. a light chain variable (VL) region comprising three CDRs having the amino acid sequences SEQ ID NO. 45, SEQ ID NO. 46, and SEQ ID NO. 47;

b. an antibody comprising:

i. a heavy chain variable (VH) region comprising three CDRs having the amino acid sequences SEQ ID NO. 30, SEQ ID NO. 31, and SEQ ID NO. 32, and

ii. a light chain variable (VL) region comprising three CDRs having the amino acid sequences SEQ ID NO. 45, SEQ ID NO. 40, and SEQ ID NO. 41; and

c. an antibody comprising:

i. a heavy chain variable (VH) region comprising three CDRs having the amino acid sequences SEQ ID NO. 33, SEQ ID NO. 34, and SEQ ID NO. 35, and

ii. a light chain variable (VL) region comprising three CDRs having the amino acid sequences SEQ ID NO. 42, SEQ ID NO. 43, and SEQ ID NO. 44.

2 The antibody of claim 1 which is a monoclonal antibody.

3 The antibody of any one of claims 1 or 2, wherein the antibody is selected from:

a. an antibody comprising:

i. a VH region having the amino acid sequence SEQ ID NO. 3, and

ii. a VL region having the amino acid sequence SEQ ID NO. 6;

b. an antibody comprising:

i. a VH region having the amino acid sequence SEQ ID NO. 1, and

ii. a VL region having the amino acid sequence SEQ ID NO. 4; and

c. an antibody comprising:

i. a VH region having the amino acid sequence SEQ ID NO. 2, and

ii. a VL region having the amino acid sequence SEQ ID NO. 5.

4 The antibody of any one of claims 1 or 2, wherein the antibody is humanised.

5 The antibody of claim 3, wherein the antibody is selected from:

a. an antibody comprising:

i. a VH region having an amino acid sequence selected from the group consisting of SEQ ID NOs. 20, 21, 22, and 23, and

ii. a VL region having an amino acid sequence selected from the group consisting of SEQ ID NOs. 28 and 29;

b. an antibody comprising:

i. a VH region having an amino acid sequence selected from the group consisting of SEQ ID NOs. NO. 12, 13, 14, 15, and

ii. a VL region having an amino acid sequence selected from the group consisting of SEQ ID NOs. 24 and 25; and

c. an antibody comprising:

i. a VH region having an amino acid sequence selected from the group consisting of SEQ ID NOs. 16, 17, 18, 19, and

ii. a VL region having an amino acid sequence selected from the group consisting of SEQ ID NOs.26 and 27.

6. The antibody of any one of claims 1 to 4, wherein the antibody is a humanised antibody, a monoclonal antibody, a recombinant antibody, a fusion protein, an antigen binding fragment, a Fab Fragment, F(ab')2 fragment, single chain Fv (sFv), diabody, triabody, or minibody.

7. An antibody of any one of claims 1 to 6, wherein the antibody is conjugated or recombinantly fused to a diagnostic agent, detectable agent or therapeutic agent.

8. An isolated nucleic acid molecule encoding an antibody according to claims 1 to 6, said nucleic acid molecule comprising or consisting of a nucleic acid sequence that encodes the V_H region and/or V_L region of said antibody.

9. A vector comprising the nucleic acid molecule of claim 8.

10. A host cell comprising the vector of claim 9.

11. A method of producing an antibody comprising culturing the host cell of claim 10 under conditions that promotes the production of the antibody.

12. A pharmaceutical composition comprising the antibody of any one claims 1 to 6 and a pharmaceutically-acceptable excipient.

13 The antibody of any one of claims 1 to 6 or the composition of claim 12 for use as a medicament.

14. Use of the antibody of any one of claims 1 to 6 or the composition of claim 12 in the manufacture of a medicament for treating, preventing or alleviating one or more symptoms of a disease, wherein the disease is a cancer or graft-versus-host disease.

15. The use of claim 14, wherein the cancer is a leukemia, a bladder cancer or a fibrosarcoma.

16. The antibody of any one of claims 1 to 6 or the composition of claim 12 for use in modulating an immune response in a subject.

17. Use of the anti-C10orf54 antibody of any one of claims 1 to 6 or an antibody-drug conjugate of claim 7, in the manufacture of a medicament for treating cancer.

18. Use of the anti-C10orf54 antibody of any one of claims 1 to 6 or antibody-drug conjugate of claim 7, in the manufacture of a medicament for killing a tumor cell.