ANTI-SIGLEC-7 ANTIBODIES FOR THE TREATMENT OF CANCER

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claim priority benefit of U. S. provisional application no. 62/371,680, filed August 5, 2016, which is herein incorporated by reference.

BACKGROUND OF THE INVENTION

[0002] Siglec-7, also known as p75 or AIRM, is a member of the sialic acid-binding lectins (Siglec) of the immunoglobulin (Ig) superfamily. Siglec receptors bind glycans containing sialic acid, but differ in their recognition of the linkage regiochemistry and spatial distribution of sialic residues. The members of the family also have distinct expression patterns. High level expression of Siglec-7 has been observed on Natural Killer (NK) cells. Expression has also been observed on a subset CD8+ T cells. Siglec-7 has also been observed to have an inhibitory role on NK cell-mediated tumor clearance (Jandus, *et al., J. Clin. Invest*. 124: 1810-20, 2014); Hudak *et al., Nat. Chem. Biol.* 10:69-77, 2014).

[0003] A broad range of human malignancies overexpress Siglec-7 ligands sialoglycans, including sialocglycans that are the ligands for Siglec-7. Siglec-7 has also been observed to have an inhibitory role on NK cell-mediated tumor clearance (Jandus, *et al., J. Clin. Invest*. 124: 1810-20, 2014).

~~BRIEF~~ SUMMARY ~~OF ASPECTS OF THE DISCLOSURE~~

[0004] The disclosure is based, in part, on the discovery that an elevated level of tumor-infiltrating CD8+ T cells express Siglec-7; and further, that an antibody that blocks Siglec-7-ligand binding interactions and/or decreases the level of Siglec-7 that is expressed on CD8+ cells increases killing of tumor cells. Accordingly, the disclosure provides antibodies and uses of such antibodies for inhibiting tumor growth.

[0004a] In one aspect, the present disclosure refers to an anti-Siglec-7 antibody that binds to Siglec-7 and comprises: a heavy chain variable region comprising: an HCDR1 sequence GYDFSNF (SEQ ID NO:79) or a variant HCDR1 sequence GYDFSNY (SEQ ID NO:89); an HCDR2 sequence YPGDGE (SEQ ID NO:80); and an HCDR3 sequence DDYLRAMDY (SEQ ID NO:81), or a variant HCDR3 sequence DDYLRAMDV (SEQ ID NO:91) or DDYLRAMDI (SEQ ID NO:92); and a light chain variable region comprising: an LCDR1 sequence RASGNIHNYLA (SEQ ID NO:93) or a variant LCDR1 sequence RASQNIHNYLA

(SEQ ID NO:100); an LCDR2 sequence SAKALAD or a variant LCDR2 sequence SAKRLES (SEQ ID NO:94), or SAKRLED (SEQ ID NO:103); and an LCDR3 sequence QHFWSSPYT (SEQ ID NO:95).

[0004b] In another aspect, the present disclosure refers to an anti-Siglec-7 antibody that binds Siglec-7, wherein the antibody comprises: a heavy chain variable region comprising 100 % identity in CDRs, and at least 90 % identity in the remaining regions to the amino acid sequence of any one of SEQ ID NOS:41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 57, 58, or 59; and a light chain variable region comprising 100 % identity in CDRs, and at least 90 % identity in the remaining regions to the amino acid sequence of any one of SEQ ID NOS:69, 70, 71, 76, 77, or 78.

[0004c] In another aspect, the present disclosure refers to an anti-Siglec-7 antibody of claim 8, wherein the antibody comprises: a heavy chain variable region comprising the amino acid sequence of any one of SEQ ID NOS:51, 52, 54, 55, 57, 58, or 59; and a light chain variable region comprising the amino acid sequence of SEQ ID NO:78.

[0004d] In another aspect, the present disclosure refers to a bispecific or multi-specific antibody that comprises an antibody as disclosed herein.

[0004e] In another aspect, the present disclosure refers to a pharmaceutical composition comprising an antibody as disclosed herein or a bispecific or multi-specific antibody as disclosed herein for the treatment of a tumor that expresses sialylated Siglec-7 ligands.

[0004f] In another aspect, the present disclosure refers to the antibody as disclosed herein, the bispecific or multi-specific antibody as disclosed herein, or the pharmaceutical composition as disclosed herein for use in therapy

[0004g] In another aspect, the present disclosure refers to use of the antibody as disclosed herein, the bispecific or multi-specific antibody as disclosed herein, or the pharmaceutical composition as disclosed herein in the manufacture of a medicament for the treatment of a tumor that expresses sialylated Siglec-7 ligands

[0005] In one ~~aspect~~example, the disclosure provides a method of inhibiting proliferation of tumor cells, the method comprising administering a therapeutically effective amount of an anti-Siglec-7 antibody to a patient that has cancer, wherein the patient has a primary tumor or metastatic lesion that comprises an elevated level of CD8+ infiltrating-T cells that express Siglec-7, and further, wherein the tumor or metastatic lesion comprises cancer cells that express sialylated Siglec-7 ligands. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has a K_D

of 50 pM or less. In some ~~embodiment~~examples, the anti-Siglec-7 antibody blocks ligand binding at an IC_{50} of less than about 4000 pM, or blocks ligand binding at an IC_{50} of less than about 3500 pM, and optionally may have a K_D of 50 pM or less. In some ~~embodiment~~examples, which may be combined with the foregoing ~~embodiment~~examples, the anti-Siglec-7 antibody has an internalization activity of less than about 70 pM or than about 25 pM. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has an internalization activity of less than about 70 pM or than about 25 pM; and does not block ligand binding.

[0006] In some ~~embodiment~~examples, the anti-Siglec-7 antibody for use in the method blocks binding of ligand to Siglec-7 and competes with an antibody QA79 produced from the hybridoma deposited under accession number ICLC PD99003 for binding to Siglec-7, but does not compete with antibody Z176 or antibody S7.7 for binding to Siglec-7. In some ~~embodiment~~examples, the antibody competes with an antibody comprising the V_H and V_L of 2G12 as designated in Figures 1 and 2 for binding to Siglec-7. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has a V_H region that comprises at least one CDR, or at least two CDRs, of a heavy chain variable region sequence of SEQ ID NO:2. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has a V_H region that comprises a CDR3 of a heavy chain variable region sequence of SEQ ID NO:2. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has a V_H region that comprises a CDR1, CDR2, and CDR3 of a heavy chain variable region sequence of SEQ ID NO:2. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has a V_L region that comprises at least one CDR, or at least two CDRs, of a light chain variable region sequence of SEQ ID NO:16. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has a V_L region that comprises a CDR3 of a light chain variable region sequence of SEQ ID NO:16. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has a V_L region that comprises a CDR1, CDR2, and CDR3 of a light chain variable region sequence of SEQ ID NO:16. In some ~~embodiment~~examples, the antibody has six CDRs of antibody 2G12 as designated in Figures 1 and 2.

[0007] In some ~~embodiment~~examples, the anti-Siglec-7 antibody for use in the method has internalization activity, does not block ligand binding to Siglec-7, and competes with antibody S7.7, but not with antibody QA79 or antibody Z176 for binding to Siglec-7. In some ~~embodiment~~examples, the antibody competes with an antibody comprising the V_H and V_L of 8A2 as designated in Figures 1 and 2 for binding to Siglec-7. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has a V_H region that comprises at least one CDR, or at least two CDRs, of a heavy chain variable region sequence of SEQ ID NO:4. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has a V_H region that comprises a CDR3 of a heavy chain variable region sequence of

SEQ ID NO:4. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has a V_H region that comprises a CDR1, CDR2, and CDR3 of a heavy chain variable region sequence of SEQ ID NO:4. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has a V_L region that comprises at least one CDR, or at least two CDRs, of a light chain variable region sequence of SEQ ID NO:18. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has a V_L region that comprises a CDR3 of a light chain variable region sequence of SEQ ID NO:18. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has a V_L region that comprises a CDR1, CDR2, and CDR3 of a light chain variable region sequence of SEQ ID NO:18. In some emodiments, the anti-Siglec-7 antibody has six CDRs of the antibody designated as 8A2 in Figures 1 and 2.

[0008] In some ~~embodiment~~examples, the anti-Siglec-7 antibody for use in the method, has internalization activity, does not block ligand binding to Siglec-7, and competes with antibody Z176, but not with QA79 or S7.7 for binding to Siglec-7. In some ~~embodiment~~examples, the anti-Siglec-7 antibody competes with an antibody comprising the V_H andV_L of the antibody designated as 5D1 for binding to Siglec-7. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has a V_H region that comprises at least one CDR, or at least two CDRs, of a heavy chain variable region sequence of SEQ ID NO:3. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has a V_H region that comprises a CDR3 of a heavy chain variable region sequence of SEQ ID NO:3. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has a V_H region that comprises a CDR1, CDR2, and CDR3 of a heavy chain variable region sequence of SEQ ID NO:3. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has a V_L region that comprises at least one CDR, or at least two CDRs, of a light chain variable region sequence of SEQ ID NO:17. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has a V_L region that comprises a CDR3 of a light chain variable region sequence of SEQ ID NO:17. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has a VL region that comprises a CDR1, CDR2, and CDR3 of a light chain variable region sequence of SEQ ID NO:17. In some ~~embodiment~~examples, the antibody has six CDRs of the antibody designated as 5D1 in Figures 1 and 2.

[0009] In some ~~embodiment~~examples, the anti-Siglec-7 antibody for use in the method has internalization activity, does not block ligand binding to Siglec-7, and does not compete with antibody Z176, QA79, or S7.7 for binding to Siglec-7. In some ~~embodiment~~examples, the antibody competes with an antibody comprising a V_H and V_L of the antibody designated as 4B12 in Figures 1 and 2 for binding to Siglec-7. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has a VH region that comprises at least one CDR, or at least two CDRs, of a heavy chain variable region sequence of SEQ ID NO:11. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has a

VH region that comprises a CDR3 of a heavy chain variable region sequence of SEQ ID NO:11. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has a VH region that comprises a CDR1, CDR2, and CDR3 of a heavy chain variable region sequence of SEQ ID NO:11. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has a VL region that comprises at least one CDR, or at least two CDRs, of a light chain variable region sequence of SEQ ID NO:25. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has a VL region that comprises a CDR3 of a light chain variable region sequence of SEQ ID NO:25. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has a VL region that comprises a CDR1, CDR2, and CDR3 of a light chain variable region sequence of SEQ ID NO:25. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has six CDRs of the antibody designated as 4B12 in Figures 1 and 2.

[0010] In any of the foregoing ~~embodiment~~examples, the antibody may be in a monovalent format or may be in an Fv, Fab, Fab', scFv, diabody, or $F(ab')_2$ fragment. In some ~~embodiment~~examples, such an antibody is PEGylated.

[0011] In some ~~embodiment~~examples, the patient that is administered the antibody has a solid tumor, such as melanoma, lung cancer, or colorectal cancer.

[0012] In a further ~~aspect~~example, the disclosure provide an anti-Siglec-7 antibody that blocks binding of ligand to Siglec-7 and competes with antibody QA79 produced from the hybridoma deposited under accession number ICLC PD99003 for binding to Siglec-7, but does not compete with antibody Z176 or antibody S7.7 for binding to Siglec-7. In some ~~embodiment~~examples, the antibody competes with an antibody comprising the V_H and V_L of 2G12 as designated in Figures 1 and 2 for binding to Siglec-7. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has a V_H region that comprises at least one CDR, or at least two CDRs, of a heavy chain variable region sequence of SEQ ID NO:2. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has a V_H region that comprises a CDR3 of a heavy chain variable region sequence of SEQ ID NO:2. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has a V_H region that comprises a CDR1, CDR2, and CDR3 of a heavy chain variable region sequence of SEQ ID NO:2. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has a V_L region that comprises at least one CDR, or at least two CDRs, of a light chain variable region sequence of SEQ ID NO:16. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has a V_L region that comprises a CDR3 of a light chain variable region sequence of SEQ ID NO:16. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has a V_L region that comprises a CDR1, CDR2, and CDR3 of a light chain variable region sequence of SEQ ID

NO:16. In some ~~embodiment~~examples, the antibody has six CDRs of antibody 2G12 as designated in Figures 1 and 2.

[0013] In another ~~aspect~~example, the disclosure provides an anti-Siglec-7 antibody that has internalization activity, does not block ligand binding to Siglec-7, and competes with antibody S7.7, but not with antibody QA79 or antibody Z176 for binding to Siglec-7. In some ~~embodiment~~examples, the antibody competes with an antibody comprising the V_H and V_L of 8A2 as designated in Figures 1 and 2 for binding to Siglec-7. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has a V_H region that comprises at least one CDR, or at least two CDRs, of a heavy chain variable region sequence of SEQ ID NO:4, SEQ ID NO:104, or SEQ ID NO:106. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has a V_H region that comprises a CDR3 of a heavy chain variable region sequence of SEQ ID NO:4, SEQ ID NO:104, or SEQ ID NO:106. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has a V_H region that comprises a CDR1, CDR2, and CDR3 of a heavy chain variable region sequence of SEQ ID NO:4, SEQ ID NO:104, or SEQ ID NO:106. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has a V_L region that comprises at least one CDR, or at least two CDRs, of a light chain variable region sequence of SEQ ID NO:18, SEQ ID NO:105, or SEQ ID NO:107. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has a V_L region that comprises a CDR3 of a light chain variable region sequence of SEQ ID NO:18, SEQ ID NO:105, or SEQ ID NO:107. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has a V_L region that comprises a CDR1, CDR2, and CDR3 of a light chain variable region sequence of SEQ ID NO:18. SEQ ID NO:105, or SEQ ID NO:107. In some emodiments, the anti-Siglec-7 antibody has six CDRs of the antibody designated as 8A2 in Figures 1 and 2.

[0014] In still another ~~aspect~~example, the disclosure provides an anti-Siglec-7 antibody that has internalization activity, does not block ligand binding to Siglec-7, and competes with antibody Z176, but not with QA79 or S7.7 for binding to Siglec-7. In some ~~embodiment~~examples, the anti-Siglec-7 antibody competes with an antibody comprising the V_H andV_L of the antibody designated as 5D1 for binding to Siglec-7. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has a V_H region that comprises at least one CDR, or at least two CDRs, of a heavy chain variable region sequence of SEQ ID NO:3. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has a V_H region that comprises a CDR3 of a heavy chain variable region sequence of SEQ ID NO:3. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has a V_H region that comprises a CDR1, CDR2, and CDR3 of a heavy chain variable region sequence of SEQ ID NO:3. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has a V_L region that comprises at least one

CDR, or at least two CDRs, of a light chain variable region sequence of SEQ ID NO:17. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has a V_L region that comprises a CDR3 of a light chain variable region sequence of SEQ ID NO:17. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has a VL region that comprises a CDR1, CDR2, and CDR3 of a light chain variable region sequence of SEQ ID NO:17. In some ~~embodiment~~examples, the antibody has six CDRs of the antibody designated as 5D1 in Figures 1 and 2.

[0015] In a further ~~aspect~~example, the disclosure provide an anti-Siglec-7 antibody that has internalization activity, does not block ligand binding to Siglec-7, and does not compete with antibody Z176, QA79, or S7.7 for binding to Siglec-7. In some ~~embodiment~~examples, the antibody competes with an antibody comprising a V_H and V_L of the antibody designated as 4B12 in Figures 1 and 2 for binding to Siglec-7. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has a VH region that comprises at least one CDR, or at least two CDRs, of a heavy chain variable region sequence of SEQ ID NO:11. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has a VH region that comprises a CDR3 of a heavy chain variable region sequence of SEQ ID NO:11. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has a VH region that comprises a CDR1, CDR2, and CDR3 of a heavy chain variable region sequence of SEQ ID NO:11. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has a VL region that comprises at least one CDR, or at least two CDRs, of a light chain variable region sequence of SEQ ID NO:25. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has a VL region that comprises a CDR3 of a light chain variable region sequence of SEQ ID NO:25. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has a VL region that comprises a CDR1, CDR2, and CDR3 of a light chain variable region sequence of SEQ ID NO:25. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has six CDRs of the antibody designated as 4B12 in Figures 1 and 2.

[0016] The disclosure additionally provides an anti-Siglec-7 antibody having a V_H region that comprises at least one CDR, or at least two CDRs, of a V_H region sequence set forth in Figure 1; or an anti-Siglec-7 antibody having a V_H region that comprises a CDR1, CDR2, and CDR3 of one of the heavy chain variable region sequences set forth in Figure 1.

[0017] The disclosure further provides an anti-Siglec-7 antibody having a V_L region that comprises at least one CDR, or at least two CDRs, of a V_L region sequence set forth in Figure 2; or an anti-Siglec-7 antibody having a V_L region that comprises a CDR1, CDR2, and CDR3 of one of the light chain variable region sequences set forth in Figure 2.

[0018] In some ~~aspect~~examples, the ~~invention~~disclosure provides an anti-Siglec-7 antibody comprising a V_H region that comprises at least one CDR, or at least two CDRs, of a V_H region sequence set forth in Figure 1; and a V_L region that comprises at least one CDR, or at least two CDRs, of a V_L region sequence set forth in Figure 2, where the V_L sequence in Figure 2 has the same antibody designation as the V_H sequence in Figure 1.

[0019] In some ~~embodiment~~example an anti-Siglec-7 antibody of the disclosure comprises a V_H region that comprises a CDR1, CDR2, and CDR3 of a heavy chain variable region sequences set forth in Figure 1; and a V_L region that comprises a CDR1, CDR2, and CDR3 of a light chain variable region sequence set forth in Figure 2, where the V_L sequence in Figure 2 has the same antibody designation as the VH sequence in Figure 1.

[0020] In another ~~aspect~~example, provided herein is an anti-Siglec-7 antibody that competes with an antibody having a variable heavy chain sequence of SEQ ID NO:1 and a variable light chain sequence of SEQ ID NO:15 for binding to Siglec-7. In some ~~embodiment~~examples, the antibody comprises a heavy chain variable region comprising a CDR3 having a sequence as set forth in any one of SEQ ID NOS:29-31, 33, and 35-61, in which 1, 2, or 3 amino acids are substituted; or comprises a heavy chain variable region comprising a CDR3 as set forth in any one of SEQ ID NOS:29-31, 33, and 35-61. In some ~~embodiment~~examples, the heavy chain variable region comprises a CDR1 having a sequence as set forth in any one of SEQ ID NOS:29-31, 33, and 35-61 in which 1, 2, or 3 amino acids are substituted; and/or a CDR2 having a sequence as set forth in any one of SEQ ID NOS:29-31, 33, and 35-61 in which 1, 2, or 3 amino acids are substituted. In some ~~embodiment~~examples, the heavy chain variable region comprises a CDR1 having a sequence as set forth in any one of SEQ ID NOS:29-31, 33, and 35-61 and a CDR2 having a sequence as set forth in any one of SEQ ID NOS:29-31, 33, and 35-61. In some emodiments, which can be combined with any of the preceding ~~embodiment~~examples in this paragraph, the anti-Siglec-7 antibody comprises a light chain variable region comprising a CDR3 having a sequence as set forth in any one of SEQ ID NOS:62 and 64-78 in which 1, 2, or 3 amino acids are substituted; or comprises a light chain variable region comprising a CDR3 as set forth in any one of SEQ ID NOS:62 and 64-78. In some ~~embodiment~~examples, the light chain variable region comprises a CDR1 having a sequence as set forth in any one of SEQ ID NOS:62 and 64-78 in which 1, 2, or 3 amino acids are substituted; and/or a CDR2 having a sequence as set forth in any one of SEQ ID NOS:62 and 64-78 in which 1, 2, or 3 amino acids are substituted. In some ~~embodiment~~examples, the light chain variable region comprises a CDR1 having a sequence as set forth in any one of SEQ ID NOS:62 and 64-78 and a CDR2 having a sequence as set forth in any

one of SEQ ID NOS:62 and 64-78. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has ligand blocking activity; and/or has a K_D of less than about 100 pM when measured as a monovalent Fab; and/or has an internalization activity of less than about 100 pM. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has a K_D of less than about 75 pM when measured as a monovalent Fab. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has an internalization activity of about 70 pM or less. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has an internalization activity of less than about 25 pM.

[0021] In another ~~aspect~~example, provided herein is an anti-Siglec-7 antibody that comprises a heavy chain variable region having at least 80%, or at least 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the amino acid sequence of a heavy chain variable region of any one of SEQ ID NOS:29-31, 33, and 35-61; and/or a light chain variable region having at least 80%, or at least 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the amino acid sequence of a light chain variable region of any one of SEQ ID NOS:62 and 64-78. In some ~~embodiment~~examples, the anti-Siglec-7 antibody comprises a heavy chain variable region having at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the amino acid sequence of a heavy chain variable region of any of SEQ ID NOS:41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 57, 58, 59, 60 or 61; and a light chain variable region having at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the amino acid sequence of a light chain variable region of SEQ ID NO:69, 70, 71, 72, 73, 74, 75, 76, 77, or 78. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has ligand blocking activity; and/or has a K_D of less than about 100 pM when measured as a monovalent Fab; and/or has an internalization activity of less than about 100 pM. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has a K_D of less than about 75 pM when measured as a monovalent Fab. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has an internalization activity of about 70 pM or less. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has an internalization activity of less than about 25 pM.

[0022] In a further ~~aspect~~example, provided herein is an anti-Siglec-7 antibody comprises a heavy chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in a heavy chain variable region sequence selected from SEQ ID NO:43, 45, 46, 47, 48, 49, 50, 51, 54, 55, 57, and 58; and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences of SEQ ID NO:69. Additionally provided herein is an anti-Siglec-7 antibody that comprises a heavy chain variable region comprising the CDR1, CDR2, and CDR3 sequences

as set forth in a heavy chain variable region sequence selected from SEQ ID NO:53, 54, 51, 55, 58, and 59; and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences of SEQ ID NO:78. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has ligand blocking activity; and/or has a K_D of less than about 100 pM when measured as a monovalent Fab; and/or has an internalization activity of less than about 100 pM. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has a K_D of less than about 75 pM when measured as a monovalent Fab. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has an internalization activity of about 70 pM or less. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has an internalization activity of less than about 25 pM.

[0023] In a further ~~aspect~~example, provided herein is an anti-Siglec-7 antibody that comprises:

a) a heavy chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:43, and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:69;

(b) a heavy chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:45, and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:69;

(c) a heavy chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:46, and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:69;

(d) a heavy chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:47, and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:69;

(e) a heavy chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:48, and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:69;

(f) a heavy chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:49, and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:69;

(g) a heavy chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:50, and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:69;

(h) a heavy chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:51, and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:69;

(i) CDR1, CDR2, and CDR3 sequences as set forth in a heavy chain variable region sequence SEQ ID NO:54, and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:69;

(j) a heavy chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:55, and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:69;

(k) a heavy chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:57, and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:69; or

(l) a heavy chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:58, and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:69. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has ligand blocking activity; and/or has a K_D of less than about 100 pM when measured as a monovalent Fab; and/or has an internalization activity of less than about 100 pM. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has a K_D of less than about 75 pM when measured as a monovalent Fab. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has an internalization activity of about 70 pM or less. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has an internalization activity of less than about 25 pM.

[0024] In an additional ~~aspect~~example, provided herein is an anti-Siglec-7 antibody that comprises:

a) a heavy chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:53; and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:78;

(b) heavy chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:54; and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:78;

(c) heavy chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:51; and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:78;

(d) heavy chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:55; and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:78;

(e) heavy chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:58; and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:78; or

(f) heavy chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:59; and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:78. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has ligand blocking activity; and/or has a K_D of less than about 100 pM when measured as a monovalent Fab; and/or has an internalization activity of less than about 100 pM. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has a K_D of less than about 75 pM when measured as a monovalent Fab. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has an internalization activity of about 70 pM or less. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has an internalization activity of less than about 25 pM.

[0025] In a further ~~aspect~~example, provided herein is an anti-Siglec-7 antibody that comprises:

a) a heavy chain variable region comprising the amino acid sequence SEQ ID NO:43 and a light chain variable region comprising the amino acid sequence of SEQ ID NO:69;

(b) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:45 and a light chain variable region comprising the amino acid sequence of SEQ ID NO:69;

(c) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:46 and a light chain variable region comprising the amino acid sequence of SEQ ID NO:69;

(d) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:47 and a light chain variable region comprising the amino acid sequence of SEQ ID NO:69;

(e) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:48 and a light chain variable region comprising the amino acid sequence of SEQ ID NO:69;

(f) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:49 and a light chain variable region comprising the amino acid sequence of SEQ ID NO:69;

(g) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:50 and a light chain variable region comprising the amino acid sequence of SEQ ID NO:69;

(h) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:51 and a light chain variable region comprising the amino acid sequence of SEQ ID NO:69;

(i) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:54 and a light chain variable region comprising the amino acid sequence of SEQ ID NO:69;
(j) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:55 and a light chain variable region comprising the amino acid sequence of SEQ ID NO:69;
(k) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:57 and a light chain variable region comprising the amino acid sequence of SEQ ID NO:69; or
(l) a heavy chain variable comprising the amino acid sequence of SEQ ID NO:58 and a light chain variable region comprising the amino acid sequence of SEQ ID NO:69. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has ligand blocking activity; and/or has a K_D of less than about 100 pM when measured as a monovalent Fab; and/or has an internalization activity of less than about 100 pM. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has a K_D of less than about 75 pM when measured as a monovalent Fab. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has an internalization activity of about 70 pM or less. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has an internalization activity of less than about 25 pM.

[0026] In an additional ~~aspect~~example, provided herein is an anti-Siglec-7 antibody that comprises:
a) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:53 and a light chain variable region comprising the amino acid sequence of SEQ ID NO:78;
(b) heavy chain variable region comprising the amino acid sequence of SEQ ID NO:54 and a light chain variable region comprising the amino acid sequence of SEQ ID NO:78;
(c) heavy chain variable region comprising the amino acid sequence of SEQ ID NO:51 and a light chain variable region comprising the amino acid sequence of SEQ ID NO:78;
(d) heavy chain variable region comprising the amino acid sequence of SEQ ID NO:55 and a light chain variable region comprising the amino acid sequence of SEQ ID NO:78;
(e) heavy chain variable region comprising the amino acid sequence of SEQ ID NO:58 and a light chain variable region comprising the amino acid sequence of SEQ ID NO:78; or
(f) heavy chain variable region comprising the amino acid sequence of SEQ ID NO:59 and a light chain variable region comprising the amino acid sequence of SEQ ID NO:78. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has ligand blocking activity; and/or has a K_D of less than about 100 pM when measured as a monovalent Fab; and/or has an internalization activity of less than about 100 pM. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has a K_D of less than about 75 pM when measured as a monovalent Fab. In some ~~embodiment~~examples, the anti-Siglec-7 antibody has an internalization activity of about 70 pM or less. In some

~~embodiment~~examples, the anti-Siglec-7 antibody has an internalization activity of less than about 25 pM.

[0027] In some ~~embodiment~~examples, the anti-Siglec-7 antibody of the disclosure as described in the foregoing paragraphs is in a monovalent format, or an antibody fragment format, such as an Fv, Fab, Fab', scFv, diabody, or $F(ab')_2$ fragment.

[0028] In some emodiments, the anti-Siglec-7 antibody of the disclosure as described in the foregoing paragraphs is a multivalent form or bivalent form. In some ~~embodiment~~examples, the antibody isn IgG, such as an IgG1, IgG2, IgG3, or IgG4.

[0029] In a further ~~aspect~~example, the ~~invention~~disclosure provides a bispecific or multi-specific antibody that comprises an antibody of any one of the foregoing ~~embodiment~~examples.

[0030] In an additional ~~aspect~~example, the ~~invention~~disclosure provides a method of inhibiting proliferation of tumor cells, the method comprising administering a therapeutically effective amount of an antibody of any of the antibodies described in the foregoing paragraphs, or a bispecific or multi-specific antibody comprising such an antibody, to a patient that has a tumor that expresses sialylated Siglec-7 ligands. In some ~~embodiment~~examples, the tumor expresses sialylated Siglec-7 ligands in an amount above that which is detected in normal cells of the corresponding cell type. In some ~~embodiment~~examples, the tumor comprises an elevated level of CD8+ infiltrating T cells that express Siglec-7.

[0031] In a further ~~aspect~~example, the ~~invention~~disclosure provides a method of identifying a patient that is a candidate for treatment with an anti-Siglec-7 antibody, the method comprising determining the proportion of CD8+ T cells that have infiltrated a tumor, or a metastatic lesion, that express detectable Siglec-7 on the cell surface. In some ~~embodiment~~examples, a patient that has a tumor that is a candidate for treatment with an anti-Siglec-7 antibody, has at least 10% or at least 20%, or greater of tumor-infiltrating CD8+ T cells in the tumor or a metastatic lesion that express detectable Siglec-7 on the cell surface. In some ~~embodiment~~examples, the level of Siglec-7 expression is determined using an anti-Siglec-7 antibody. In some ~~embodiment~~examples, the level of expression is determined by flow cytometry or immunohistochemistry.

[0032] The disclosure additionally provides a method of identifying a patient that has a tumor that is a candidate for treatment with an anti-Siglec-7 antibody, the method comprising determining the proportion of CD8+ infiltrating T cells in a tumor or metastatic lesion that express detectable Siglec-7, wherein a patient that has a tumor or metastatic lesion in which at

least 10%, or at least 20%, of infiltrating CD8+ T express Siglec-7 is a candidate for treatment with an anti-Siglec-7 antibody. In some ~~embodiment~~example, the level of Siglec-7 expression is determined using an anti-Siglec-7 antibody. In some ~~embodiment~~example, the level of expression is determined by flow cytometry or immunohistochemistry.

[0033] In a further ~~aspect~~example, the disclosure provides a method of inhibiting proliferation of tumor cells, the method comprising administering a therapeutically effective amount of an anti-Siglec-7 antibody to a patient that has cancer, wherein the patient has a primary tumor or metastatic lesion that comprises an elevated level of CD8+ infiltrating-T cells that express Siglec-7; and further, wherein the tumor or metastatic lesion comprises cancer cells that express sialylated Siglec-7 ligands, *e.g.,* express sialyated Siglec-7 ligands at a level higher than normal tissue. In some ~~embodiment~~example, the anti-Siglec-7 antibody has a K_D of 70 pM or less when measured as a monovalent Fab.

[0034] In a further ~~aspect~~example, the disclosure futher provides use of an anti-Siglec-7 antibody as described herein in a method of treating a cancer as described herein.

BRIEF DESCRIPTION OF THE DRAWINGS

[0035] Figure 1 provides illustrative heavy chain variable region sequences of anti-Siglec-7 antibodies of the invention. The CDRs as defined by Kabat are underlined.

[0036] Figure 2 provides illustrative heavy chain variable region sequences of anti-Siglec-7 antibodies of the invention. The CDRs as defined by Chothia are underlined.

[0037] Figure 3 provides illustrative light chain variable region sequences of anti-Siglec-7 antibodies of the invention. The CDRs as defined by both Kabat and Chothia are underlined.

[0038] Figure 4 provides illustrative data showing that Siglec-7 is detected on a high percentage of tumor-infiltrating CD8+ cells in fresh primary tumors.

[0039] Figure 5 provides data illustrating that CD8+ T cells isolated from subsets of tumors have a high level of Siglec-7.

[0040] Figure 6 data illustrating that Siglec-7 ligands are expressed on subsets of tumors.

[0041] Figure 7 provides data showing anti-Siglec-7 antibodies of the present disclosure that have improved K_D values compared to antibodies Z176, S7.7, or QA79.

WHAT IS CLAIMED IS:

~~1. A method of inhibiting proliferation of tumor cells, the method comprising administering a therapeutically effective amount of an anti-Siglec-7 antibody to a patient that has cancer, wherein the patient has a primary tumor or metastatic lesion that comprises an elevated level of CD8+ infiltrating T cells that express Siglec-7, and further, wherein the tumor or metastatic lesion comprises cancer cells that express sialylated Siglec-7 ligands.~~

~~2. The method of claim 1, wherein the anti-Siglec-7 antibody has a bivalent avidity of 50 pM or less.~~

~~3. The method of claim 1 or 2, wherein the anti-Siglec-7 antibody blocks ligand binding at an IC_{50} of less than about 4000 pM.~~

~~4. The method of claim 1 or 2, wherein the anti-Siglec-7 antibody blocks ligand binding at an IC_{50} of less than about 3500 pM.~~

~~5. The method of claim 1 or 2, wherein the anti-Siglec-7 antibody has an internalization activity of less than about 70 pM.~~

~~6. The method of claim 1 or 2, wherein the anti-Siglec-7 antibody has an internalization activity of less than about 25 pM.~~

~~7. The method of claim 5 or 6, wherein the anti-Siglec-7 antibody does not block ligand binding.~~

~~8. The method of claim 1 or 2, wherein the anti-Siglec-7 antibody competes with an antibody having a variable heavy chain sequence of SEQ ID NO:1 and a variable light chain sequence of SEQ ID NO:15 for binding to Siglec-7.~~

~~9. The method of claim 8, wherein the anti-Siglec-7 antibody has a V_H region that comprises at least one CDR, or at least two CDRs, of a heavy chain variable region sequence of SEQ ID NO:1.~~

~~10. The method of claim 8, wherein the anti-Siglec-7 antibody has a V_H region that comprises a CDR3 of a heavy chain variable region sequence of SEQ ID NO:1.~~

~~11. The method of claim 8, wherein the anti-Siglec-7 antibody has a V_H region that comprises a CDR1, CDR2, and CDR3 of a heavy chain variable region sequence of SEQ ID NO:1.~~

~~12. The method of any one of claims 8 to 11, wherein the anti-Siglec-7 antibody has a V_L region that comprises at least one CDR, or at least two CDRs, of a light chain variable region sequence of SEQ ID NO:15.~~

~~13. The method of any one of claims 8 to 11, wherein the anti-Siglec-7 antibody has a V_L region that comprises a CDR3 of a light chain variable region sequence of SEQ ID NO:15.~~

~~14. The method of any one of claims 8 to 11, wherein the anti-Siglec-7 antibody has a V_L region that comprises a CDR1, CDR2, and CDR3 of a light chain variable region sequence of SEQ ID NO:15.~~

~~15. The method of claim 8, wherein the anti-Siglec-7 antibody comprises a heavy chain variable region comprising a CDR3 having a sequence as set forth in any one of SEQ ID NOS:29-31, 33, and 35-61 in which 1, 2, or 3 amino acids are substituted.~~

~~16. The method of claim 8, wherein the anti-Siglec-7 antibody comprises a heavy chain variable region comprising a CDR3 as set forth in any one of SEQ ID NOS:29-31, 33, and 35-61.~~

~~17. The method of claim 15 or 16, where the heavy chain variable region comprises a CDR1 having a sequence as set forth in any one of SEQ ID NOS:29-31, 33, and 35-61 in which 1, 2, or 3 amino acids are substituted; and/or a CDR2 having a sequence as set forth in any one of SEQ ID NOS:29-31, 33, and 35-61 in which 1, 2, or 3 amino acids are substituted.~~

~~18. The method of claim 15 or 16, where the heavy chain variable region comprises a CDR1 having a sequence as set forth in any one of SEQ ID NOS:29-31, 33, and 35-61 and a CDR2 having a sequence as set forth in any one of SEQ ID NOS:29-31, 33, and 35-61.~~

19. The method of any one of claims 8, and 15-18, wherein the anti-Siglec-7 antibody comprises a light chain variable region comprising a CDR3 having a sequence as set forth in any one of SEQ ID NOS:62 and 64-78 in which 1, 2, or 3 amino acids are substituted.

20. The method of any one of claims 8, and 15-18, wherein the anti-Siglec-7 antibody comprises a light chain variable region comprising a CDR3 as set forth in any one of SEQ ID NOS:62 and 64-78.

21. The method of claim 19 or 20, where the light chain variable region comprises a CDR1 having a sequence as set forth in any one of SEQ ID NOS:62 and 64-78 in which 1, 2, or 3 amino acids are substituted; and/or a CDR2 having a sequence as set forth in any one of SEQ ID NOS:62 and 64-78 in which 1, 2, or 3 amino acids are substituted.

22. The method of claim 19 or 20, where the light chain variable region comprises a CDR1 having a sequence as set forth in any one of SEQ ID NOS:62 and 64-78 and a CDR2 having a sequence as set forth in any one of SEQ ID NOS:62 and 64-78.

23. The method of claim 8, wherein the anti-Siglec-7 antibody comprises a heavy chain variable region having at least 80%, or at least 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the amino acid sequence of a heavy chain variable region of any one of SEQ ID NOS:29-31, 33, and 35-61.

24. The method of claim 8 or 23, wherein the anti-Siglec-7 antibody comprises a light chain variable region having at least 80%, or at least 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the amino acid sequence of a light chain variable region of any one of SEQ ID NOS:62 and 64-78.

25. The method of claim 8, wherein the anti-Siglec-7 antibody comprises a heavy chain variable region having at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the amino acid sequence of a heavy chain variable region of any of SEQ ID NOS:41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 57, 58, 59, 60 or 61; and a light chain variable region having at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the amino

~~acid sequence of a light chain variable region of SEQ ID NO:69, 70, 71, 72, 73, 74, 75, 76, 77, or 78.~~

~~26. The method of claim 8, wherein the anti-Siglec-7 antibody comprises a heavy chain variable region comprising CDR1, CDR2, and CDR3 sequences as set forth in a heavy chain variable region sequence selected from SEQ ID NO:43, 45, 46, 47, 48, 49, 50, 51, 54, 55, 57, and 58; and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences of SEQ ID NO:69.~~

~~27. The method of claim 8, wherein the anti-Siglec-7 antibody comprises a heavy chain variable region comprising CDR1, CDR2, and CDR3 sequences as set forth in a heavy chain variable region sequence selected from SEQ ID NO:53, 54, 51, 55, 58, and 59; and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences of SEQ ID NO:78.~~

~~28. The method of claim 8, wherein the anti-Siglec-7 antibody comprises:~~

~~a) a heavy chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:43, and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:69;~~

~~(b) a heavy chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:45, and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:69;~~

~~(c) a heavy chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:46, and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:69;~~

~~(d) a heavy chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:47, and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:69;~~

~~(e) a heavy chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:48, and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:69;~~

~~(f) a heavy chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:49, and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:69;~~

(g) a heavy chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:50, and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:69;

(h) a heavy chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:51, and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:69;

(i) CDR1, CDR2, and CDR3 sequences as set forth in a heavy chain variable region sequence SEQ ID NO:54, and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:69;

(j) a heavy chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:55, and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:69;

(k) a heavy chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:57, and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:69; or

(l) a heavy chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:58, and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:69.

29. The method of claim 8, wherein the anti-Siglec-7 antibody comprises:

a) a heavy chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:53; and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:78;

(b) heavy chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:54; and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:78;

(c) heavy chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:51; and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:78;

(d) heavy chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:55; and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:78;

(e) heavy chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:58; and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:78; or

(f) heavy chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:59; and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:78.

30. The method of claim 1, wherein the anti-Siglec-7 antibody blocks binding of ligand to Siglec-7 and competes with an antibody QA79 produced from the hybridoma deposited under accession number ICLC PD99003 for binding to Siglec-7, but does not compete with antibody Z176 or antibody S7.7 for binding to Siglec-7.

31. The method of claim 30, wherein the anti-Siglec-7 antibody competes with an antibody comprising a V_H sequence and V_L sequence designated as 2G12 in Figures 1 and 2 for binding to Siglec-7.

32. The method of claim 30, wherein the anti-Siglec-7 antibody has a V_H region that comprises at least one CDR, or at least two CDRs, of a heavy chain variable region sequence of SEQ ID NO:2.

33. The method of claim 30, wherein the anti-Siglec-7 antibody has a V_H region that comprises a CDR3 of a heavy chain variable region sequence of SEQ ID NO:2.

34. The method of claim 30, wherein the anti-Siglec-7 antibody has a V_H region that comprises a CDR1, CDR2, and CDR3 of a heavy chain variable region sequence of SEQ ID NO:2.

35. The method of any one of claims 30 to 34, wherein the anti-Siglec-7 antibody has a V_L region that comprises at least one CDR, or at least two CDRs, of a light chain variable region sequence of SEQ ID NO:16.

36. The method of any one of claims 30 to 34, wherein the anti-Siglec-7 antibody has a V_L region that comprises a CDR3 of a light chain variable region sequence of SEQ ID NO:16.

37. The method of any one of claims 30 to 34, wherein the anti-Siglec-7 antibody has a V_L region that comprises a CDR1, CDR2, and CDR3 of a light chain variable region sequence of SEQ ID NO:16.

38. The method of claim 1, wherein the anti-Siglec-7 antibody has internalization activty, does not block ligand binding to Siglec-7, and competes with antibody S7.7, but not with antibody QA79 or antibody Z176 for binding to Siglec-7.

39. The method of claim 38, wherein the anti-Siglec-7 antibody competes with an antibody comprising a V_H sequence and V_L sequence designated as 8A2 in Figures 1 and 2.

40. The method of claim 38, wherein the anti-Siglec-7 antibody has a V_H region that comprises at least one CDR, or at least two CDRs, as set forth in a heavy chain variable region sequence of SEQ ID NO:4, SEQ ID NO:104, or SEQ ID NO:106.

41. The method of claim 38, wherein the anti-Siglec-7 antibody has a V_H region that comprises a CDR3 as set forth in a heavy chain variable region sequence of SEQ ID NO:4, SEQ ID NO:104, or SEQ ID NO:106.

42. The method of claim 38, wherein the anti-Siglec-7 antibody has a V_H region that comprises a CDR1, CDR2, and CDR3 as set forth in a heavy chain variable region sequence of SEQ ID NO:4, SEQ ID NO:104, or SEQ ID NO:106.

43. The method of any one of claims 38 to 42, wherein the anti-Siglec-7 antibody has a V_L region that comprises at least one CDR, or at least two CDRs, as set forth in a light chain variable region sequence of SEQ ID NO:18, SEQ ID NO:105, or SEQ ID NO:107.

44. The method of any one of claims 38 to 42, wherein the anti-Siglec-7 antibody has a V_L region that comprises a CDR3 as set forth in a light chain variable region sequence of SEQ ID NO:18, SEQ ID NO:105, or SEQ ID NO:107.

45. The method of any one of claims 38 to 42, wherein the anti-Siglec-7 antibody has a V_L region that comprises a CDR1, CDR2, and CDR3 as set forth in a light chain variable region sequence of SEQ ID NO:18, SEQ ID NO:105, or SEQ ID NO:107.

~~46. The method of claim 1, wherein the anti-Siglec-7 antibody has internalization activity, does not block ligand binding to Siglec-7, and competes with antibody Z176, but not with QA79 or S7.7 for binding to Siglec-7.~~

~~47. The method of claim 46, wherein the anti-Siglec-7 antibody competes with an antibody comprising a V_H sequence and V_L sequence designated as 5D1 in Figures 1 and 2.~~

~~48. The method of claim 46, wherein the anti-Siglec-7 antibody has a V_H region that comprises at least one CDR, or at least two CDRs, of a heavy chain variable region sequence of SEQ ID NO:3.~~

~~49. The method of claim 46, wherein the anti-Siglec-7 antibody has a V_H region that comprises a CDR3 of a heavy chain variable region sequence of SEQ ID NO:3.~~

~~50. The method of claim 46, wherein the anti-Siglec-7 antibody has a V_H region that comprises a CDR1, CDR2, and CDR3 of a heavy chain variable region sequence of SEQ ID NO:3.~~

~~51. The method of any one of claims 46 to 50, wherein the anti-Siglec-7 antibody has a V_L region that comprises at least one CDR, or at least two CDRs, of a light chain variable region sequence of SEQ ID NO:17.~~

~~52. The method of any one of claims 46 to 50, wherein the anti-Siglec-7 antibody has a V_L region that comprises a CDR3 of a light chain variable region sequence of SEQ ID NO:17.~~

~~53. The method of any one of claims 46 to 50, wherein the anti-Siglec-7 antibody has a V_L region that comprises a CDR1, CDR2, and CDR3 of a light chain variable region sequence of SEQ ID NO:17.~~

~~54. The method of claim 1, wherein the anti-Siglec-7 antibody has internalization activity, does not block ligand binding to Siglec-7, and does not compete with antibody Z176, QA79, or S7.7 for binding to Siglec-7.~~

~~55. The method of claim 54, wherein the anti-Siglec-7 antibody competes with an antibody comprising a V_H sequence and V_L sequence designated as 4B12 in Figures 1 and 2.~~

~~56. The method of claim 54, wherein the anti-Siglec-7 antibody has a V_H region that comprises at least one CDR, or at least two CDRs, of a heavy chain variable region sequence of SEQ ID NO:11.~~

~~57. The method of claim 54, wherein the anti-Siglec-7 antibody has a V_H region that comprises a CDR3 of a heavy chain variable region sequence of SEQ ID NO:11.~~

~~58. The method of claim 54, wherein the anti-Siglec-7 antibody has a V_H region that comprises a CDR1, CDR2, and CDR3 of a heavy chain variable region sequence of SEQ ID NO:11.~~

~~59. The method of any one of claims 54 to 58, wherein the anti-Siglec-7 antibody has a V_L region that comprises at least one CDR, or at least two CDRs, of a light chain variable region sequence of SEQ ID NO:25.~~

~~60. The method of any one of claims 54 to 58, wherein the anti-Siglec-7 antibody has a V_L region that comprises a CDR3 of a light chain variable region sequence of SEQ ID NO:25.~~

~~61. The method of any one of claims 54 to 58, wherein the anti-Siglec-7 antibody has a V_L region that comprises a CDR1, CDR2, and CDR3 of a light chain variable region sequence of SEQ ID NO:25.~~

~~62. The method of any one of claims 1 to 61, wherein the antibody is in a monovalent format or a fragment format.~~

~~63. The method of claim 62, wherein the antibody is PEGylated.~~

~~64. The method of any one of claims 1 to 63, wherein the patient has melanoma, lung cancer, or colorectal cancer.~~

~~65. An anti-Siglec-7 antibody that competes with an antibody having a variable heavy chain sequence of SEQ ID NO:1 and a variable light chain sequence of SEQ ID NO:15 for binding to Siglec-7.~~

~~66. The anti-Siglec-7 antibody of claim 65, wherein the antibody comprises a heavy chain variable region comprising a CDR3 having a sequence as set forth in any one of SEQ ID NOS:29-31, 33, and 35-61 in which 1, 2, or 3 amino acids are substituted.~~

~~67. The anti-Siglec-7 antibody of claim 65, wherein the anti-Siglec-7 antibody comprises a heavy chain variable region comprising a CDR3 as set forth in any one of SEQ ID NOS:29-31, 33, and 35-61.~~

~~68. The anti-Siglec-7 antibody of claim 66 or 67, where the heavy chain variable region comprises a CDR1 having a sequence as set forth in any one of SEQ ID NOS:29-31, 33, and 35-61 in which 1, 2, or 3 amino acids are substituted; and/or a CDR2 having a sequence as set forth in any one of SEQ ID NOS:29-31, 33, and 35-61 in which 1, 2, or 3 amino acids are substituted.~~

~~69. The anti-Siglec-7 antibody of claim 66 or 67, where the heavy chain variable region comprises a CDR1 having a sequence as set forth in any one of SEQ ID NOS:29-31, 33, and 35-61 and a CDR2 having a sequence as set forth in any one of SEQ ID NOS:29-31, 33, and 35-61.~~

~~70. The anti-Siglec-7 antibody of any one of claims 65 to 69, wherein the anti-Siglec-7 antibody comprises a light chain variable region comprising a CDR3 having a sequence as set forth in any one of SEQ ID NOS:62 and 64-78 in which 1, 2, or 3 amino acids are substituted.~~

~~71. The anti-Siglec-7 antibody of any one of claims 65 to 69, wherein the anti-Siglec-7 antibody comprises a light chain variable region comprising a CDR3 as set forth in any one of SEQ ID NOS:62 and 64-78.~~

~~72. The anti-Siglec-7 antibody of claim 70 or 71, where the light chain variable region comprises a CDR1 having a sequence as set forth in any one of SEQ ID NOS:62 and 64-78 in which 1, 2, or 3 amino acids are substituted; and/or a CDR2 having a~~

~~sequence as set forth in any one of SEQ ID NOS:62 and 64-78 in which 1, 2, or 3 amino acids are substituted.~~

~~73. The anti-Siglec-7 antibody of claim 70 or 71, where the light chain variable region comprises a CDR1 having a sequence as set forth in any one of SEQ ID NOS:62 and 64-78 and a CDR2 having a sequence as set forth in any one of SEQ ID NOS:62 and 64-78.~~

~~74. The anti-Siglec-7 antibody of claim 65, wherein the anti-Siglec-7 antibody comprises a heavy chain variable region having at least 80%, or at least 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the amino acid sequence of a heavy chain variable region of any one of SEQ ID NOS:29-31, 33, and 35-61.~~

~~75. The anti-Siglec-7 antibody of claim 65 or 74, wherein the anti-Siglec-7 antibody comprises a light chain variable region having at least 80%, or at least 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the amino acid sequence of a light chain variable region of any one of SEQ ID NOS:62 and 64-78.~~

1. An anti-Siglec-7 antibody that binds to Siglec-7 and comprises:
a heavy chain variable region comprising:
an HCDR1 sequence GYDFSNF (SEQ ID NO:79) or a variant HCDR1 sequence GYDFSNY (SEQ ID NO:89);
an HCDR2 sequence YPGDGE (SEQ ID NO:80); and
an HCDR3 sequence DDYLRAMDY (SEQ ID NO:81), or a variant HCDR3 sequence DDYLRAMDV (SEQ ID NO:91) or DDYLRAMDI (SEQ ID NO:92); and
a light chain variable region comprising:
an LCDR1 sequence RASGNIHNYLA (SEQ ID NO:93) or a variant LCDR1 sequence RASQNIHNYLA (SEQ ID NO:100);
an LCDR2 sequence SAKALAD or a variant LCDR2 sequence SAKRLES (SEQ ID NO:94), or SAKRLED (SEQ ID NO:103); and
an LCDR3 sequence QHFWSSPYT (SEQ ID NO:95).

2. The anti-Siglec-7 antibody of claim 1, where the antibody comprises:
an HCDR1 sequence GYDFSNF (SEQ ID NO:79) or GYDFSNY (SEQ ID NO:89);
an HCDR2 sequence YPGDGE (SEQ ID NO:80);

an HCDR3 sequence DDYLRAMDY (SEQ ID NO:81) or DDYLRAMDI (SEQ ID NO:92);
an LCDR1 sequence RASGNIHNYLA (SEQ ID NO:93) or RASQNIHNYLA (SEQ ID NO:100);
an LCDR2 sequence SAKRLES (SEQ ID NO:94); and
an LCDR3 sequence QHFWSSPYT (SEQ ID NO:95).

3. The anti-Siglec-7 antibody of claim 2, wherein the antibody comprises:
a) a heavy chain variable region comprising HCDR1 sequence GYDFSNF (SEQ ID NO:79), HCDR2 sequence YPGDGE (SEQ ID NO:80), and HCDR3 sequence DDYLRAMDY (SEQ ID NO:81); and a light chain variable region comprising LCDR1 sequence RASGNIHNYLA (SEQ ID NO:93), LCDR2 sequence SAKRLES (SEQ ID NO:94), and LCDR3 sequence QHFWSSPYT (SEQ ID NO:95);
b) a heavy chain variable region comprising HCDR1 sequence GYDFSNF (SEQ ID NO:79), HCDR2 sequence YPGDGE (SEQ ID NO:80), and HCDR3 sequence DDYLRAMDI (SEQ ID NO:92); and a light chain variable region comprising LCDR1 sequence RASGNIHNYLA (SEQ ID NO:93), LCDR2 sequence SAKRLES (SEQ ID NO:94), and LCDR3 sequence QHFWSSPYT (SEQ ID NO:95);
c) a heavy chain variable region comprising HCDR1 sequence GYDFSNY(SEQ ID NO:89), HCDR2 sequence YPGDGE (SEQ ID NO:80), and HCDR3 sequence DDYLRAMDI (SEQ ID NO:92); and a light chain variable region comprising LCDR1 sequence RASGNIHNYLA (SEQ ID NO:93), LCDR2 sequence SAKRLES (SEQ ID NO:94), and LCDR3 sequence QHFWSSPYT (SEQ ID NO:95); or
(d) a heavy chain variable region comprising, HCDR1 sequence GYDFSNY(SEQ ID NO:89), HCDR2 sequence YPGDGE (SEQ ID NO:80), and HCDR3 sequence DDYLRAMDY (SEQ ID NO:81); and a light chain variable region comprising LCDR1 sequence RASGNIHNYLA (SEQ ID NO:93), LCDR2 sequence SAKRLES (SEQ ID NO:94), and LCDR3 sequence QHFWSSPYT (SEQ ID NO:95).

4. The anti-Siglec-7 antibody of claim 2, wherein the antibody comprises:
a) a heavy chain variable region comprising HCDR1 sequence GYDFSNF (SEQ ID NO:79), HCDR2 sequence YPGDGE (SEQ ID NO:80), and HCDR3 sequence DDYLRAMDI (SEQ ID NO:92); and a light chain variable region comprising LCDR1 sequence

RASQNIHNYLA (SEQ ID NO:100), LCDR2 sequence SAKRLES (SEQ ID NO:94), and LCDR3 sequence QHFWSSPYT (SEQ ID NO:95);

b) a heavy chain variable region comprising CDR1 sequence GYDFSNY(SEQ ID NO:89), HCDR2 sequence YPGDGE (SEQ ID NO:80), and HCDR3 sequence DDYLRAMDY (SEQ ID NO:81); and a light chain variable region comprising LCDR1 sequence RASQNIHNYLA (SEQ ID NO:100), LCDR2 sequence SAKRLES (SEQ ID NO:94), and LCDR3 sequence QHFWSSPYT (SEQ ID NO:95);

(c) a heavy chain variable region comprising HCDR1 sequence GYDFSNY(SEQ ID NO:89), HCDR2 sequence YPGDGE (SEQ ID NO:80), and HCDR3 sequence DDYLRAMDI (SEQ ID NO:92); and a light chain variable region comprising LCDR1 sequence RASQNIHNYLA (SEQ ID NO:100), LCDR2 sequence SAKRLES (SEQ ID NO:94), and LCDR3 sequence QHFWSSPYT (SEQ ID NO:95); or

(d) a heavy chain variable region comprising GYDFSNF (SEQ ID NO:79), HCDR2 sequence YPGDGE (SEQ ID NO:80), and HCDR3 sequence DDYLRAMDY (SEQ ID NO:81); and a light chain variable region comprising LCDR1 sequence RASQNIHNYLA (SEQ ID NO:100), LCDR2 sequence SAKRLES (SEQ ID NO:94), and LCDR3 sequence QHFWSSPYT (SEQ ID NO:95).

5. The anti-Siglec-7 antibody that binds Siglec-7, wherein the antibody comprises:

a heavy chain variable region comprising 100 % identity in CDRs, and at least 90 % identity in the remaining regions to the amino acid sequence of any one of SEQ ID NOS:41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 57, 58, or 59; and a light chain variable region comprising 100 % identity in CDRs, and at least 90 % identity in the remaining regions to the amino acid sequence of any one of SEQ ID NOS:69, 70, 71, 76, 77, or 78.

6. The anti-Siglec-7 antibody of claim 5, wherein the antibody comprises:

a heavy chain variable region comprising the amino acid sequence of any one of SEQ ID NOS:41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 57, 58, or 59; and a light chain variable region comprising the amino acid sequence of any one of SEQ ID NOS:69, 70, 71, 76, 77, or 78.

7. The anti-Siglec-7 antibody of claim 5, wherein the antibody comprises:

a heavy chain variable region comprising 100 % identity in CDRs, and at least 90 % identity in the remaining regions to the amino acid sequence of any one of SEQ ID NOS:43, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 57, 58, or 59; and a light chain variable region comprising 100 % identity in CDRs, and at least 90 % identity in the remaining regions to the amino acid sequence of SEQ ID NO:69 or 78.

8. The anti-Siglec-7 antibody of claim 7, wherein the antibody comprises:
a heavy chain variable region comprising the amino acid sequence of any one of SEQ ID NOS:43, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 57, 58, or 59; and a light chain variable region comprising the amino acid sequence of SEQ ID NO:69 or 78.

9. The anti-Siglec-7 antibody of claim 8, wherein the antibody comprises:
a heavy chain variable region comprising the amino acid sequence of any one of SEQ ID NOS:43, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 57, or 58; and a light chain variable region comprising the amino acid sequence of SEQ ID NO:69.

10. An anti-Siglec-7 antibody of claim 8, wherein the antibody comprises:
a heavy chain variable region comprising the amino acid sequence of any one of SEQ ID NOS:51, 52, 54, 55, 57, 58, or 59; and a light chain variable region comprising the amino acid sequence of SEQ ID NO:78.

11. The anti-Siglec-7 antibody of claim 8, wherein the antibody comprises:
(a) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:55 and a light chain variable region comprising the amino acid sequence of SEQ ID NO:69;
(b) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:57 and a light chain variable region comprising the amino acid sequence of SEQ ID NO:69;
(c) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:59 and a light chain variable region comprising the amino acid sequence of SEQ ID NO:78.

~~76. The anti-Siglec-7 antibody of claim 65, wherein the anti-Siglec-7 antibody comprises a heavy chain variable region having at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the amino acid~~

~~sequence of a heavy chain variable region of any of SEQ ID NOS:41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 57, 58, 59, 60 or 61; and a light chain variable region having at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the amino acid sequence of a light chain variable region of SEQ ID NO:69, 70, 71, 72, 73, 74, 75, 76, 77, or 78.~~

~~77. The anti-Siglec-7 antibody of claim 65, wherein the anti-Siglec-7 antibody comprises a heavy chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in a heavy chain variable region sequence selected from SEQ ID NO:43, 45, 46, 47, 48, 49, 50, 51, 54, 55, 57, and 58; and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences of SEQ ID NO:69.~~

~~78. The anti-Siglec-7 antibody of claim 65, wherein the anti-Siglec-7 antibody comprises a heavy chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in a heavy chain variable region sequence selected from SEQ ID NO:53, 54, 51, 55, 58, and 59; and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences of SEQ ID NO:78.~~

~~79. The method of claim 8, wherein the anti-Siglec-7 antibody comprises:~~

~~a) a heavy chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:43, and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:69;~~

~~(b) a heavy chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:45, and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:69;~~

~~(c) a heavy chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:46, and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:69;~~

~~(d) a heavy chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:47, and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:69;~~

~~(e) a heavy chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:48, and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:69;~~

(f) a heavy chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:49, and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:69;

(g) a heavy chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:50, and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:69;

(h) a heavy chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:51, and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:69;

(i) a heavy chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in a heavy chain variable region sequence SEQ ID NO:54, and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:69;

(j) a heavy chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:55, and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:69;

(k) a heavy chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:57, and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:69; or

(l) a heavy chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:58, and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:69.

80. The anti-Siglec-7 antibody of claim 65, wherein the anti-Siglec-7 antibody comprises:

a) a heavy chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:53; and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:78;

(b) heavy chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:54; and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:78;

(c) heavy chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:51; and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:78;

~~(d) heavy chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:55; and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:78;~~

~~(e) heavy chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:58; and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:78; or~~

~~(f) heavy chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:59; and a light chain variable region comprising the CDR1, CDR2, and CDR3 sequences as set forth in SEQ ID NO:78.~~

~~81. The method of claim 8, wherein the anti-Siglec-7 antibody comprises:~~

~~a) 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:69;~~

~~(b) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:45 and a light chain variable region comprising the amino acid sequence of SEQ ID NO:69;~~

~~(c) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:46 and a light chain variable region comprising the amino acid sequence of SEQ ID NO:69;~~

~~(d) a heavy chain variable region comprising the amino acid sequence of ID NO:47 and a light chain variable region comprising the amino acid sequence of SEQ ID NO:69;~~

~~(e) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:48 and a light chain variable region comprising the amino acid sequence of SEQ ID NO:69;~~

~~(f) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:49 and a light chain variable region comprising the amino acid sequence of SEQ ID NO:69;~~

~~(g) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:50 and a light chain variable region comprising the amino acid sequence of SEQ ID NO:69;~~

(h) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:51 and a light chain variable region comprising the amino acid sequence of SEQ ID NO:69;

(i) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:54 and a light chain variable region comprising the amino acid sequence of SEQ ID NO:69;

(j) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:55 and a light chain variable comprising the amino acid sequence of SEQ ID NO:69;

(k) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:57 and a light chain variable region comprising the amino acid sequence of SEQ ID NO:69; or

(l) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:58 and a light chain variable comprising the amino acid sequence of SEQ ID NO:69.

82. The anti-Siglec-7 antibody of claim 65, wherein the anti-Siglec-7 antibody comprises:

a) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:53 and a light chain variable region comprising the amino acid sequence of SEQ ID NO:78;

(b) heavy chain variable region comprising the amino acid sequence of SEQ ID NO:54 and a light chain variable region comprising the amino acid sequence of SEQ ID NO:78;

(c) heavy chain variable region comprising the amino acid sequence of SEQ ID NO:51 and a light chain variable region comprising the amino acid sequence of SEQ ID NO:78;

(d) heavy chain variable region comprising the amino acid sequence of SEQ ID NO:55 and a light chain variable region comprising the amino acid sequence of SEQ ID NO:78;

(e) heavy chain variable region comprising the amino acid sequence of SEQ ID NO:58 and a light chain variable region comprising the amino acid sequence of ; or

(f) heavy chain variable region comprising the amino acid sequence of SEQ ID NO:59 and a light chain variable region comprising the amino acid sequence of SEQ ID NO:78.

83. An anti-Siglec-7 antibody that blocks binding of ligand to Siglec-7 and competes with antibody QA79 produced from the hybridoma deposited under accession number ICLC PD99003 for binding to Siglec-7, but does not compete with antibody Z176 or antibody S7.7 for binding to Siglec-7.

84. The anti-Siglect antibody of claim 83, wherein the anti-Siglec-7 antibody competes with an antibody comprising a V_H sequence and V_L sequence designated as 2G12 in Figures 1 and 2.

85. The anti-Siglec-7 antibody of claim 83, wherein the anti-Siglec-7 antibody has a V_H region that comprises at least one CDR, or at least two CDRs, of a heavy chain variable region sequence of SEQ ID NO:2.

86. The anti-Siglec-7 antibody of claim 83, wherein the anti-Siglec-7 antibody has a V_H region that comprises a CDR3 of a heavy chain variable region sequence of SEQ ID NO:2.

87. The anti-Siglec-7 antibody of claim 83, wherein the anti-Siglec-7 antibody has a V_H region that comprises a CDR1, CDR2, and CDR3 of a heavy chain variable region sequence of SEQ ID NO:2.

88. The anti-Siglec-7 antibody of any one of claims 83 to 87, wherein the anti-Siglec-7 antibody has a V_L region that comprises at least one CDR, or at least two CDRs, of a ligh chain variable region sequence of SEQ ID NO:16.

89. The anti-Siglec-7 antibody of any one of claims 83 to 87, wherein the anti-Siglec-7 antibody has a V_L region that comprises a CDR3 of a light chain variable region sequence of SEQ ID NO:16.

90. The anti-Siglec-7 antibody of any one of claims 83 to 87, wherein the anti-Siglec-7 antibody has a V_L region that comprises a CDR1, CDR2, and CDR3 of a light chain variable region sequence of SEQ ID NO:16.

91. An anti-Siglec-7 antibody that has internalization activity, does not block ligand binding to Siglec-7, and competes with antibody S7.7, but not with antibody QA79 or antibody Z176, for binding to Siglec-7.

92. The anti-Siglec-7 antibody of claim 91, wherein the anti-Siglec-7 antibody competes with an antibody comprising a V_H sequence and V_L sequence designated as 8A2 in Figures 1 and 2.

93. The anti-Siglec-7 antibody of claim 91, wherein the anti-Siglec-7 antibody has a V_H region that comprises at least one CDR, or at least two CDRs, of a heavy chain variable region sequence of SEQ ID NO:4, SEQ ID NO:104, or SEQ ID NO:106.

94. The anti-Siglec-7 antibody of claim 91, wherein the anti-Siglec-7 antibody has a V_H region that comprises a CDR3 of a heavy chain variable region sequence of SEQ ID NO:4, SEQ ID NO:104, or SEQ ID NO:106.

95. The anti-Siglec-7 antibody of claim 91, wherein the anti-Siglec-7 antibody has a V_H region that comprises a CDR1, CDR2, and CDR3 of a heavy chain variable region sequence of SEQ ID NO:4, SEQ ID NO:104, or SEQ ID NO:106.

96. The anti-Siglec-7 antibody of any one of claims 91 to 95, wherein the anti-Siglec-7 antibody has a V_L region that comprises at least one CDR, or at least two CDRs, of a light chain variable region sequence of SEQ ID NO:18, SEQ ID NO:105, or SEQ ID NO:107.

97. The anti-Siglec-7 antibody of any one of claims 91 to 95, wherein the anti-Siglec-7 antibody has a V_L region that comprises a CDR3 of a light chain variable region sequence of SEQ ID NO:18, SEQ ID NO:105, or SEQ ID NO:107.

98. The anti-Siglec-7 antibody of any one of claims 91 to 95, wherein the anti-Siglec-7 antibody has a V_L region that comprises a CDR1, CDR2, and CDR3 of a light chain variable region sequence of SEQ ID NO:18, SEQ ID NO:105, or SEQ ID NO:107.

99. An anti-Siglec-7 antibody has internalization activity, does not block ligand binding to Siglec-7, and competes with antibody Z176, but not with antibody QA79 or antibody S7.7 for binding to Siglec-7.

100. The anti-Siglec antibody of claim 99, wherein the anti-Siglec-7 antibody competes with an antibody comprising a V_H sequence and V_L sequence designated as 5D1 in Figures 1 and 2.

101. The anti-Siglec-7 antibody of claim 99, wherein the anti-Siglec-7 antibody has a V_H region that comprises at least one CDR, or at least two CDRs, of a heavy chain variable region sequence of SEQ ID NO:3.

102. The anti-Siglec-7 antibody of claim 99, wherein the anti-Siglec-7 antibody has a V_H region that comprises a CDR3 of a heavy chain variable region sequence of SEQ ID NO:3.

103. The anti-Siglec-7 antibody of claim 99, wherein the anti-Siglec-7 antibody has a V_H region that comprises a CDR1, CDR2, and CDR3 of a heavy chain variable region sequence of SEQ ID NO:3.

104. The anti-Siglec-7 antibody of any one of claims 99 to 103, wherein the anti-Siglec-7 antibody has a V_L region that comprises at least one CDR, or at least two CDRs, of a light chain variable region sequence of SEQ ID NO:17.

105. The anti-Siglec-7 antibody of any one of claims 99 to 103, wherein the anti-Siglec-7 antibody has a V_L region that comprises a CDR3 of a light chain variable region sequence of SEQ ID NO:17.

106. The anti-Siglec-7 antibody of any one of claims 99 to 103, wherein the anti-Siglec-7 antibody has a V_L region that comprises a CDR1, CDR2, and CDR3 of a light chain variable region sequence of SEQ ID NO:17.

107. The anti-Siglec-7 antibody of claim 1, wherein the anti-Siglec-7 antibody has internalization activity, does not block ligand binding to Siglec-7, and does not compete with antibody Z176, antibody QA79, or antibody S7.7 for binding to Siglec-7.

108. The anti-Siglec-7 antibody of claim 107, wherein the anti-Siglec-7 antibody competes with an antibody comprising a V_H sequence and V_L sequence designated as 4B12 in Figures 1 and 2.

~~109. The anti-Siglec-7 antibody of claim 107, wherein the anti-Siglec-7 antibody has a V_H region that comprises at least one CDR, or at least two CDRs, of a heavy chain variable region sequence of SEQ ID NO:11.~~

~~110. The anti-Siglec-7 antibody of claim 107, wherein the anti-Siglec-7 antibody has a V_H region that comprises a CDR3 of a heavy chain variable region sequence of SEQ ID NO:11.~~

~~111. The anti-Siglec-7 antibody of claim 107, wherein the anti-Siglec-7 antibody has a V_H region that comprises a CDR1, CDR2, and CDR3 of a heavy chain variable region sequence of SEQ ID NO:11.~~

~~112. The anti-Siglec-7 antibody of any one of claims 107 to 111, wherein the anti-Siglec-7 antibody has a V_L region that comprises at least one CDR, or at least two CDRs, of a light chain variable region sequence of SEQ ID NO:25.~~

~~113. The anti-Siglec-7 antibody of any one of claims 107 to 111, wherein the anti-Siglec-7 antibody has a V_L region that comprises a CDR3 of a light chain variable region sequence of SEQ ID NO:25.~~

~~114. The anti-Siglec-7 antibody of any one of claims 107 to 111, wherein the anti-Siglec-7 antibody has a V_L region that comprises a CDR1, CDR2, and CDR3 of a light chain variable region sequence of SEQ ID NO:25.~~

~~115. An anti-Siglec-7 antibody having a V_H region that comprises at least one CDR, or at least two CDRs, of a V_H region sequence set forth in Figure 1.~~

~~116. An anti-Siglec-7 antibody having a V_H region that comprises a CDR1, CDR2, and CDR3 of one of the heavy chain variable region sequences set forth in Figure 1.~~

~~117. The anti-Siglec-7 antibody of claim 116, having a V_H region that comprises a heavy chain variable region sequence set forth in Figure 1.~~

~~118. An anti-Siglec-7 antibody having a V_L region that comprises at least one CDR, or at least two CDRs, of a V_L region sequence set forth in Figure 2.~~

~~119. An anti-Siglec-7 antibody having a V_H region that comprises a CDR1, CDR2, and CDR3 of one of the light chain variable region sequences set forth in Figure 2.~~

~~120. The anti-Siglec-7 antibody of claim 119, having a V_L region that comprises a light chain variable region sequence set forth in Figure 2.~~

~~121~~12. The anti-Siglec-7 antibody ~~of~~ as defined in any one of claims ~~83 to 120~~1-11, wherein the antibody:

(a) is in a monovalent form;~~.~~

~~122. The anti-Siglec-7 antibody of any one of claims 83 to 120, wherein the antibody~~ (b) is a multivalent Fab form~~.~~; or

~~123. The anti-Siglec-7 antibody of any one of claims 83 to 120, wherein the antibody~~ (c) is an IgG.

~~124~~13. A bispecific or multi-specific antibody that comprises an antibody ~~of~~ as defined in any one of claims ~~83 to 120~~1-11.

~~125. A method of inhibiting proliferation of tumor cells, the method comprising administering a therapeutically effective amount of an antibody of any one of claims 83 to 123, or a bispecific or multi-specific antibody of claim 124, to a patient that has a tumor that expresses sialylated Siglec-7 ligands.~~

~~126. The method of claim 125, wherein the tumor has an elevated number of CD8+ infiltrating T cells that express Siglec-7.~~

~~127. A method of identifying a patient that is a candidate for treatment with an anti-Siglec-7 antibody, the method comprising determining the proportion of CD8+ T cells that have infiltrated a tumor, or a metastatic lesion, that express Siglec-7.~~

~~128. A method of identifying a patient that has a tumor that is a candidate for treatment with an anti-Siglec-7 antibody, the method comprising determining that at least 10% of tumor-infiltrating CD8+ T cells in the tumor or a metastatic lesion, express Siglec-7.~~

~~129. A method of identifying a patient that has a tumor that is a candidate for treatment with an anti-Siglec-7 antibody, the method comprising determining the~~

~~proportion of CD8+ infiltrating T cells in a tumor or metastatic lesion that express Siglec-7, wherein a patient that has a tumor or metastatic lesion in which at least 10% of infiltrating CD8+ T express Siglec-7 is a candidate for treatment with an anti-Siglec-7 antibody.~~

~~130. The method of claim 127, 128, or 129, wherein the level of Siglec-7 expression is determined using an anti-Siglec-7 antibody.~~

~~131. The method of claim 130, wherein the level of expression is determined by flow cytometry or immunohistochemistry.~~

14. A pharmaceutical composition comprising an antibody as defined in any one of claims 1-11 or a bispecific or multi-specific antibody as defined in claim 13 for the treatment of a tumor that expresses sialylated Siglec-7 ligands.

15. The antibody as defined in any one of claims 1-11, the bispecific or multi-specific antibody as defined in claim 13, or the pharmaceutical composition as defined in claim 14 for use in therapy.

16. Use of the antibody as defined in any one of claims 1-11, the bispecific or multi-specific antibody as defined in claim 13, or the pharmaceutical composition as defined in claim 14 in the manufacture of a medicament for the treatment of a tumor that expresses sialylated Siglec-7 ligands.

17. The use of claim 16, wherein the tumor has an elevated number of CD8+ infiltrating T cells that express Siglec-7.`