

[0016] All references cited herein, including patents, patent applications and publications, are hereby incorporated by reference in their entirety.

SUMMARY

[0017] The present disclosure is generally directed to Siglec-7 agents, such as anti-Siglec-7 antibodies, and methods of using such Siglec-7 agents. The methods provided herein find use in preventing, reducing risk, or treating an individual having dementia, frontotemporal dementia, Alzheimer's disease, vascular dementia, mixed dementia, Creutzfeldt-Jakob disease, normal pressure hydrocephalus, amyotrophic lateral sclerosis, Huntington's disease, taupathy disease, Nasu-Hakola disease, stroke, acute trauma, chronic trauma, lupus, acute and chronic colitis, rheumatoid arthritis, wound healing, Crohn's disease, inflammatory bowel disease, ulcerative colitis, obesity, malaria, essential tremor, central nervous system lupus, Behcet's disease, Parkinson's disease, dementia with Lewy bodies, multiple system atrophy, Shy-Drager syndrome, progressive supranuclear palsy, cortical basal ganglionic degeneration, acute disseminated encephalomyelitis, granulomatous disorders, sarcoidosis, diseases of aging, seizures, spinal cord injury, traumatic brain injury, age related macular degeneration, glaucoma, retinitis pigmentosa, retinal degeneration, respiratory tract infection, sepsis, eye infection, systemic infection, lupus, arthritis, multiple sclerosis, low bone density, osteoporosis, osteogenesis, osteopetrotic disease, Paget's disease of bone, solid and blood cancer, bladder cancer, brain cancer, breast cancer, colon cancer, rectal cancer, endometrial cancer, kidney cancer, renal cell cancer, renal pelvis cancer, leukemia, lung cancer, melanoma, non-Hodgkin's lymphoma, pancreatic cancer, prostate cancer, ovarian cancer, fibrosarcoma, acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL), chronic myeloid leukemia (CML), multiple myeloma, polycythemia vera, essential thrombocytosis, primary or idiopathic myelofibrosis, primary or idiopathic myelosclerosis, myeloid-derived tumors, tumors that express Siglec-7 and/or Siglec-7 ligands, thyroid cancer, infections, CNS herpes, parasitic infections, Trypanosome infection, Cruzi infection, *Pseudomonas aeruginosa* infection, *Leishmania donovani* infection, group B *Streptococcus* infection, *Campylobacter jejuni* infection, *Neisseria meningitidis* infection, type I HIV, and Haemophilus influenza. The methods provided herein also find use in inducing or promoting the survival, maturation, functionality, migration, or proliferation of one or more immune cells in an individual in need thereof. The methods provided herein find further use in decreasing the activity, functionality, or survival of regulatory T cells, tumor-imbedded immunosuppressor dendritic cells, tumor-imbedded immunosuppressor macrophages, neutrophils, natural killer (NK) cells, myeloid-derived suppressor cells, tumor-associated macrophages, neutrophils, NK cells, acute myeloid leukemia (AML) cells, chronic lymphocytic leukemia (CLL) cell, or chronic myeloid leukemia (CML) cell in an individual in need thereof.

[0018] Certain examples of the present disclosure are based, at least in part, on the identification of anti-Siglec-7 antibodies that are capable of decreasing cell surface levels of Siglec-7 on human primary immune cells and Siglec-7-expressing cell lines and/or that are capable of inhibiting the binding of Siglec-7 ligands to Siglec-7 (*see, e.g.*, **Examples 3-5**).

[0019] Accordingly, certain examples of the present disclosure relate to an isolated monoclonal anti-Siglec-7 antibody, wherein the anti-Siglec-7 antibody decreases cellular levels of Siglec-7. In some examples, the anti-Siglec-7 antibody decreases cellular levels of Siglec-7 without inhibiting interaction between Siglec-7 and one or more Siglec-7 ligands. In some examples, the antibody further inhibits interaction between Siglec-7 and one or more Siglec-7 ligands.

[0019a] In one aspect, the present invention provides an isolated monoclonal anti-Siglec-7 antibody, wherein the anti-Siglec-7 antibody decreases cell surface levels of Siglec-7, as determined by a fluorescence-activated cell sorting (FACS) assay using a threshold value of 21% or higher reduction of Siglec-7 cell surface levels to indicate a decrease, and does not inhibit interaction between Siglec-7 and sialic acid-containing glycoproteins, as determined by a red blood cell solid adhesion assay using a threshold value of 80% or higher of RBC binding to Siglec-7 to indicate non-inhibition.

[0020] Other examples of the present disclosure relate to an isolated monoclonal anti-Siglec-7 antibody, wherein the anti-Siglec-7 antibody decreases cellular levels of Siglec-7 and inhibits interaction between Siglec-7 and one or more Siglec-7 ligands.

[0021] In some examples that may be combined with any of the preceding examples, the anti-Siglec-7 antibody decreases cell surface levels of Siglec-7, decreases intracellular levels of Siglec-7, decreases total levels of Siglec-7, or any combination thereof. In some examples that may be combined with any of the preceding examples, the anti-Siglec-7 antibody induces Siglec-7 degradation, Siglec-7 cleavage, Siglec-7 internalization, Siglec-7 shedding, downregulation of Siglec-7 expression, or any combination thereof. In some examples that may be combined with any of the preceding examples, antibody decreases cellular levels of Siglec-7 *in vivo*. In some examples that may be combined with any of the preceding examples, the anti-Siglec-7 antibody inhibits cell surface clustering of Siglec-7. In some examples that may be combined with any of the preceding examples, the anti-Siglec-7 antibody inhibits one or more Siglec-7 activities. In some examples that may be combined with any of the preceding examples, the one or more Siglec-7 activities are selected from: (a) Siglec-7 binding to one or more Siglec-7 ligands, optionally wherein the one or more Siglec-7 ligands are selected from sialic acid-containing glycoproteins, sialic acid-containing glycolipids, and any combination thereof; (b) Siglec-7 binding to SHP1 or SHP2; (c) phosphorylation of Tyr-437, Tyr-460, or both, induced by one or more SRC family tyrosine kinases, optionally, wherein the one or more SRC family tyrosine kinases are selected from Syk, LCK, FYM, and ZAP-70; (d) modulated expression of one or more pro-inflammatory cytokines, optionally wherein the one or more pro-inflammatory cytokines are

antibody comprises a light chain variable domain comprising an amino acid sequence selected from SEQ ID NOs: 189-318, 449-461, and 484-489; and/or a heavy chain variable domain comprising an amino acid sequence selected from SEQ ID NOs: 319-448, 462-474, and 490-496. In some examples that may be combined with any of the preceding examples, the anti-Siglec-7 antibody comprises a light chain variable domain of a monoclonal antibody selected from: 1A12, 1E8, 2G1, 2G4, 3E11, 4A1, 4D7, 4E3, 4E3H1, 4E3H2, 7A3, 7E11, 7F12, 10B5, 10B5L1, 10B5H1, and 10G8; and/or a heavy chain variable domain of a monoclonal antibody selected from: 1A12, 1E8, 2G1, 2G4, 3E11, 4A1, 4D7, 4E3, 4E3H1, 4E3H2, 7A3, 7E11, 7F12, 10B5, 10B5L1, 10B5H1, and 10G8.

[0022a] Disclosed is an isolated monoclonal anti-Siglec-7 antibody, wherein the anti-Siglec-7 antibody binds to one or more amino acid residues selected from the group consisting of M30, Q31, V44, R45, S47, F48, Y50, T103, K104, and T107 of SEQ ID NO: 1, or one or more amino acid residues on a mammalian Siglec-7 protein corresponding to an amino acid residue selected from the group consisting of M30, Q31, V44, R45, S47, F48, Y50, T103, K104, and T107 of SEQ ID NO: 1.

[0023] Other examples of the present disclosure relate to an isolated monoclonal anti-Siglec-7 antibody, wherein the anti-Siglec-7 antibody binds to one or more amino acids within amino acid residues 39-353, 39-149, 93-104, 95-105, 39-122, 123-149, 150-233, 240-336, 264-273, 295-306, 327-341, or 337-353 of SEQ ID NO: 1; or within amino acid residues on a mammalian Siglec-7 protein corresponding to amino acid residues 39-353, 39-149, 93-104, 95-105, 39-122, 123-149, 150-233, 240-336, 264-273, 295-306, 327-341, or 337-353 of SEQ ID NO: 1. In some examples that may be combined with any of the preceding examples, the anti-Siglec-7 antibody binds to one or more amino acids within amino acid residues selected from the group consisting of: i. amino acid residues 60-69 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-7 protein corresponding to amino acid residues 60-69 of SEQ ID NO: 1; ii. amino acid residues 60-69 and 84-95 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-7 protein corresponding to amino acid residues 60-69 and 84-95 of SEQ ID NO: 1; iii. amino acid residues 60-69 and 117-127 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-7 protein corresponding to amino acid residues 60-69 and 117-127 of SEQ ID NO: 1; iv. amino acid residues 68-78 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-7 protein corresponding to amino acid residues 68-78 of SEQ ID NO: 1; v. amino acid residues 84-95 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-7 protein corresponding to amino acid residues 84-95 of SEQ ID NO: 1; vi. amino acid residues 111-122 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-7 protein corresponding to amino acid residues 111-122 of SEQ ID NO: 1; vii. amino acid residues 111-122 and 282-291 of SEQ ID NO: 1, or amino acid residues on a

anti-Siglec-7 antibody binds to one or more amino acids within amino acid residues 117-127 of human Siglec-7 (SEQ ID NO: 1), or within amino acid residues on a Siglec-7 homolog or ortholog corresponding to amino acid residues 117-127 of SEQ ID NO: 1. In some examples that may be combined with any of the preceding examples, the anti-Siglec-7 antibody binds to one or more amino acids within amino acid residues 282-291 of human Siglec-7 (SEQ ID NO: 1), or within amino acid residues on a Siglec-7 homolog or ortholog corresponding to amino acid residues 282-29 of SEQ ID NO: 1. Other examples of the present disclosure relate to an isolated monoclonal anti-Siglec-7 antibody, wherein the anti-Siglec-7 antibody binds to one or more amino acid residues selected from the group consisting of M30, Q31, V44, R45, S47, F48, Y50, I72, W74, N81, T103, K104, T107, and R124 of SEQ ID NO: 1, or one or more amino acid residues on a mammalian Siglec-7 protein corresponding to an amino acid residue selected from the group consisting of M30, Q31, V44, R45, S47, F48, Y50, I72, W74, N81, T103, K104, T107, and R124 of SEQ ID NO: 1.

[0024] Other examples of the present disclosure relate to an isolated monoclonal anti-Siglec-7 antibody, wherein the anti-Siglec-7 antibody comprises a light chain variable domain and a heavy chain variable domain, wherein the light chain variable domain, the heavy chain variable domain, or both comprise at least one, two, three, four, five, or six HVRs selected from HVR-L1, HVR-L2, HVR-L3, HVR-H1, HVR-H2, and HVR-H3 of a monoclonal antibody selected from: 1A12, 1E8, 2G1, 2G4, 3E11, 4A1, 4D7, 4E3, 4E3H1, 4E3H2, 7A3, 7E11, 7F12, 10B5, 10B5L1, 10B5H1, and 10G8.

[0024a] Disclosed is an isolated monoclonal anti-Siglec-7 antibody, wherein the anti-Siglec-7 antibody competes with one or more antibodies selected from the group consisting of 4D7, 7A3, 7E11, 10B5, 10G8, and any combination thereof for binding to Siglec-7.

[0024b] Disclosed is an isolated monoclonal anti-Siglec-7 antibody which binds essentially the same Siglec-7 epitope as a monoclonal antibody selected from the group consisting of: 4D7, 7A3, 7E11, 10B5, and 10G8.

[0025] In some examples that may be combined with any of the preceding examples: (a) the HVR-L1 comprises an amino acid sequence selected from SEQ ID NOs: 7-19 and 476; (b) the HVR-L2 comprises an amino acid sequence selected from SEQ ID NOs: 20-32 and 477; (c) the HVR-L3 comprises an amino acid sequence selected from SEQ ID NOs: 33-45 and 478; (d) the HVR-H1 comprises an amino acid sequence selected from SEQ ID NOs: 46-58 and 479; (e) the HVR-H2 comprises an amino acid sequence selected from SEQ ID NOs: 59-71 and 480-482; or (f) the HVR-H3 comprises an amino acid sequence selected from SEQ ID NOs: 72-84 and 483. In some examples that may be combined with any of the preceding

Other examples of the present disclosure relate to a vector comprising the nucleic acid of any of the preceding examples. Other examples of the present disclosure relate to an isolated host cell comprising the vector of any of the preceding examples. Other examples of the present disclosure relate to a method of producing an anti-Siglec-7 antibody, comprising culturing the host cell of any of the preceding examples so that the anti-Siglec-7 antibody is produced. In some examples, the method further comprises recovering the anti-Siglec-7 antibody produced by the host cell. Other examples of the present disclosure relate to an isolated anti-Siglec-7 antibody produced by the method of any of the preceding examples. Other examples of the present disclosure relate to a pharmaceutical composition comprising the anti-Siglec-7 antibody of any of the preceding examples, and a pharmaceutically acceptable carrier.

[0028a] In yet another aspect, the present invention provides an isolated nucleic acid comprising a nucleic acid sequence encoding the anti-Siglec-7 antibody described herein. In yet another aspect, the present invention provides a vector comprising the nucleic acid described herein. In yet another aspect, the present invention provides isolated host cell comprising the vector described herein. In yet another aspect, the present invention provides a method of producing an anti-Siglec-7 antibody, comprising culturing the host cell described herein so that the anti-Siglec-7 antibody is produced. In yet another aspect, the present invention provides a pharmaceutical composition comprising the anti-Siglec-7 antibody described herein, and a pharmaceutically acceptable carrier. In yet another aspect, the present invention provides use of an antibody as described herein in the manufacture of a medicament for preventing, reducing risk, or treating cancer.

[0029] Other examples of the present disclosure relate to a method of preventing, reducing risk, or treating a disease, disorder, or injury selected from dementia, frontotemporal dementia, Alzheimer's disease, vascular dementia, mixed dementia, Creutzfeldt-Jakob disease, normal pressure hydrocephalus, amyotrophic lateral sclerosis, Huntington's disease, tauopathy disease, Nasu-Hakola disease, stroke, acute trauma, chronic trauma, lupus, acute and chronic colitis, rheumatoid arthritis, wound healing, Crohn's disease, inflammatory bowel disease, ulcerative colitis, obesity, malaria, essential tremor, central nervous system lupus, Behcet's disease, Parkinson's disease, dementia with Lewy bodies, multiple system atrophy, Shy-Drager syndrome, progressive supranuclear palsy, cortical basal ganglionic degeneration, acute disseminated encephalomyelitis, granulomatous disorders, sarcoidosis, diseases of aging, seizures, spinal cord injury, traumatic brain injury, age related macular degeneration, glaucoma, retinitis pigmentosa, retinal degeneration,

CLAIMS

What is claimed is:

1. An isolated monoclonal anti-Siglec-7 antibody, wherein the anti-Siglec-7 antibody decreases cell surface levels of Siglec-7, as determined by a fluorescence-activated cell sorting (FACS) assay using a threshold value of 21% or higher reduction of Siglec-7 cell surface levels to indicate a decrease, and does not inhibit interaction between Siglec-7 and sialic acid-containing glycoproteins, as determined by a red blood cell solid adhesion assay using a threshold value of 80% or higher of RBC binding to Siglec-7 to indicate non-inhibition.
2. The anti-Siglec-7 antibody of claim 1, wherein the antibody decreases cell surface levels of Siglec-7 *in vivo*.
3. The anti-Siglec-7 antibody of claim 1 or claim 2, wherein the anti-Siglec-7 antibody inhibits one or more Siglec-7 activities.
4. The anti-Siglec-7 antibody of any one of claims 1-3, wherein the one or more Siglec-7 ligands are selected from the group consisting of Siglec-7 ligands expressed on red blood cells, Siglec-7 ligands expressed on bacterial cells, Siglec-7 ligands expressed on apoptotic cells, Siglec-7 ligands expressed on nerve cells, Siglec-7 ligands expressed on glial cells, Siglec-7 ligands expressed on microglia, Siglec-7 ligands expressed on astrocytes, Siglec-7 ligands expressed on tumor cells, Siglec-7 ligands expressed on viruses, Siglec-7 ligands expressed on dendritic cells, Siglec-7 ligands bound to beta amyloid plaques, Siglec-7 ligands bound to Tau tangles, Siglec-7 ligands on disease-causing proteins, Siglec-7 ligands on disease-causing peptides, Siglec-7 ligands expressed on macrophages, Siglec-7 ligands expressed on neutrophils, Siglec-7 ligands expressed on monocytes, Siglec-7 ligands expressed on natural killer cells, Siglec-7 ligands expressed on T cells, Siglec-7 ligands expressed on T helper cells, Siglec-7 ligands expressed on cytotoxic T cells, Siglec-7 ligands expressed on B cells, Siglec-7 ligands expressed on tumor-imbedded immunosuppressor dendritic cells, Siglec-7 ligands expressed on tumor-imbedded immunosuppressor macrophages, Siglec-7 ligands expressed on tumor-imbedded immunosuppressor neutrophils, Siglec-7 ligands expressed on tumor-imbedded immunosuppressor NK cells, Siglec-7 ligands expressed on myeloid-derived suppressor cells, Siglec-7 ligands expressed on regulatory T cells, secreted mucins, sialic acid, sialic acid-containing glycolipids, sialic acid-containing glycoproteins, alpha-2,8-disialyl containing glycolipids, branched alpha-2,6-linked sialic acid-containing glycoproteins, terminal alpha-2,6-linked sialic acid-containing glycolipids, terminal alpha-2,3-linked sialic acid-containing glycoproteins, and disialogangliosides.

5. The anti-Siglec-7 antibody of any one of claims 1-4, wherein the cell surface levels of Siglec-7 are measured on primary cells selected from the group consisting of dendritic cells, bone marrow-derived dendritic cells, monocytes, microglia, macrophages, neutrophils, and NK cells, or on cell lines, and wherein the cell surface levels of Siglec-7 are measured utilizing an *in vitro* cell assay.
6. The anti-Siglec-7 antibody of any one of claims 1-5, wherein the anti-Siglec-7 antibody does not reduce TREM2 expression.
7. The anti-Siglec-7 antibody of any one of claims 1-6, wherein the anti-Siglec-7 antibody binds to amino acid residues selected from the group consisting of:
 - i. amino acid residues 60-69 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-7 protein corresponding to amino acid residues 60-69 of SEQ ID NO: 1;
 - ii. amino acid residues 60-69 and 84-95 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-7 protein corresponding to amino acid residues 60-69 and 84-95 of SEQ ID NO: 1;
 - iii. amino acid residues 60-69 and 117-127 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-7 protein corresponding to amino acid residues 60-69 and 117-127 of SEQ ID NO: 1;
 - iv. amino acid residues 68-78 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-7 protein corresponding to amino acid residues 68-78 of SEQ ID NO: 1;
 - v. amino acid residues 84-95 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-7 protein corresponding to amino acid residues 84-95 of SEQ ID NO: 1;
 - vi. amino acid residues 113-123 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-7 protein corresponding to amino acid residues 113-123 of SEQ ID NO: 1;
 - vii. amino acid residues 117-127 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-7 protein corresponding to amino acid residues 117-127 of SEQ ID NO: 1.
8. The anti-Siglec-7 antibody of any one of claims 1-7, wherein the anti-Siglec-7 antibody binds to amino acid residues R45, S47, T103, K104, and T107 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-7 protein corresponding to amino acid residues R45, S47, T103, K104, and T107 of SEQ ID NO: 1.
9. The anti-Siglec-7 antibody of any one of claims 1-7, wherein the anti-Siglec-7 antibody binds to amino acid residue K104 of SEQ ID NO: 1, or to an amino acid residue on a mammalian Siglec-7 protein corresponding to amino acid residue K104 of SEQ ID NO: 1.

10. The anti-Siglec-7 antibody of any one of claims 1-9, wherein the anti-Siglec-7 antibody competes with one or more antibodies selected from the group consisting of 4D7, 7A3, 7E11, 10B5, 10G8, and any combination thereof for binding to Siglec-7.
11. The anti-Siglec-7 antibody of any one of claims 1-10, wherein the anti-Siglec-7 antibody comprises a light chain variable domain and a heavy chain variable domain, wherein:
- (a) the light chain variable domain comprises an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 13 or the amino acid sequence of SEQ ID NO: 13 having one or more conservative amino acid substitutions, an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 26 or the amino acid sequence of SEQ ID NO: 26 having one or more conservative amino acid substitutions, an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 39 or the amino acid sequence of SEQ ID NO: 39 having one or more conservative amino acid substitutions, and the heavy chain variable domain comprises an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 52 or the amino acid sequence of SEQ ID NO: 52 having one or more conservative amino acid substitutions, an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 65 or the amino acid sequence of SEQ ID NO: 65 having one or more conservative amino acid substitutions, and an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 78 or the amino acid sequence of SEQ ID NO: 78 having one or more conservative amino acid substitutions;
 - (b) the light chain variable domain comprises an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 15 or the amino acid sequence of SEQ ID NO: 15 having one or more conservative amino acid substitutions, an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 28 or the amino acid sequence of SEQ ID NO: 28 having one or more conservative amino acid substitutions, an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 41 or the amino acid sequence of SEQ ID NO: 41 having one or more conservative amino acid substitutions, and the heavy chain variable domain comprises an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 54 or the amino acid sequence of SEQ ID NO: 54 having one or more conservative amino acid substitutions, an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 67 or the amino acid sequence of SEQ ID NO: 67 having one or more conservative amino acid substitutions, and an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 80 or the amino acid sequence of SEQ ID NO: 80 having one or more conservative amino acid substitutions;

- (c) the light chain variable domain comprises an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 16 or the amino acid sequence of SEQ ID NO: 16 having one or more conservative amino acid substitutions, an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 29 or the amino acid sequence of SEQ ID NO: 29 having one or more conservative amino acid substitutions, an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 42 or the amino acid sequence of SEQ ID NO: 42 having one or more conservative amino acid substitutions, and the heavy chain variable domain comprises an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 55 or the amino acid sequence of SEQ ID NO: 55 having one or more conservative amino acid substitutions, an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 68 or the amino acid sequence of SEQ ID NO: 68 having one or more conservative amino acid substitutions, and an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 81 or the amino acid sequence of SEQ ID NO: 81 having one or more conservative amino acid substitutions;
- (d) the light chain variable domain comprises an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 18 or the amino acid sequence of SEQ ID NO: 18 having one or more conservative amino acid substitutions, an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 31 or the amino acid sequence of SEQ ID NO: 31 having one or more conservative amino acid substitutions, an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 44 or the amino acid sequence of SEQ ID NO: 44 having one or more conservative amino acid substitutions, an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 57 or the amino acid sequence of SEQ ID NO: 57 having one or more conservative amino acid substitutions, an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 70 or the amino acid sequence of SEQ ID NO: 70 having one or more conservative amino acid substitutions, and an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 83 or the amino acid sequence of SEQ ID NO: 83 having one or more conservative amino acid substitutions; or
- (e) the light chain variable domain comprises an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 19 or the amino acid sequence of SEQ ID NO: 19 having one or more conservative amino acid substitutions, an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 32 or the amino acid sequence of SEQ ID NO: 32 having one or more conservative amino acid substitutions, an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 45 or the amino acid sequence of SEQ ID NO: 45 having one or more conservative amino acid substitutions, and the heavy chain variable domain comprises an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 58 or the amino acid sequence of SEQ ID NO: 58 having one or more conservative amino acid substitutions, an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 71 or the amino acid sequence of SEQ ID NO: 71 having one or more conservative amino acid substitutions, and an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 84 or the amino acid sequence of SEQ ID NO: 84 having one or more conservative amino acid substitutions;

NO: 45 having one or more conservative amino acid substitutions, and the heavy chain variable domain comprises an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 58 or the amino acid sequence of SEQ ID NO: 58 having one or more conservative amino acid substitutions, an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 71 or the amino acid sequence of SEQ ID NO: 71 having one or more conservative amino acid substitutions, and an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 84 or the amino acid sequence of SEQ ID NO: 84 having one or more conservative amino acid substitutions.

12. The anti-Siglec-7 antibody of any one of the preceding claims, wherein the antibody is of the IgG class, the IgM class, or the IgA class.

13. The anti-Siglec-7 antibody of claim 12, wherein the anti-Siglec-7 antibody has an IgG1, IgG2, IgG3, or IgG4 isotype.

14. The anti-Siglec-7 antibody of claim 13, wherein:

- (a) the anti-Siglec-7 antibody has a human or mouse IgG1 isotype and comprises one or more amino acid substitutions in the Fc region at a residue position selected from the group consisting of: N297A, D265A, D270A, L234A, L235A, G237A, P238D, L328E, E233D, G237D, H268D, P271G, A330R, C226S, C229S, E233P, L234V, L234F, L235E, P331S, S267E, L328F, A330L, M252Y, S254T, T256E, N297Q, P238S, P238A, A327Q, A327G, P329A, K322A, T394D, and any combination thereof, wherein the numbering of the residues is according to EU numbering, or comprises an amino acid deletion in the Fc region at a position corresponding to glycine 236;
- (b) the anti-Siglec-7 antibody has an IgG1 isotype and comprises an IgG2 isotype heavy chain constant domain 1(CH1) and hinge region, optionally wherein the IgG2 isotype CH1 and hinge region comprises the amino acid sequence of ASTKGPSVFP LAPCSRSTSE STAALGCLVK DYFPEPVTVS WNSGALTSGVHTFPAVLQSS GLYSLSSVVT VPSSNFGTQT YTCNVDPHKPS NTKVDKTVRKCCVECPPCP (SEQ ID NO: 475), and optionally wherein the antibody Fc region comprises a S267E amino acid substitution, a L328F amino acid substitution, or both, and/or a N297A or N297Q amino acid substitution, wherein the numbering of the residues is according to EU numbering;
- (c) the anti-Siglec-7 antibody has an IgG2 isotype and comprises one or more amino acid substitutions in the Fc region at a residue position selected from the group consisting of: P238S, V234A, G237A, H268A, H268Q, V309L, A330S, P331S, C214S, C232S,

C233S, S267E, L328F, M252Y, S254T, T256E, H268E, N297A, N297Q, A330L, and any combination thereof, wherein the numbering of the residues is according to EU numbering;

- (d) the anti-Siglec-7 antibody has a human or mouse IgG4 isotype and comprises one or more amino acid substitutions in the Fc region at a residue position selected from the group consisting of: L235A, G237A, S228P, L236E, S267E, E318A, L328F, M252Y, S254T, T256E, E233P, F234V, L234A/F234A, S228P, S241P, L248E, T394D, N297A, N297Q, L235E, and any combination thereof, wherein the numbering of the residues is according to EU numbering; or
- (e) the anti-Siglec-7 antibody has a hybrid IgG2/4 isotype, and optionally wherein the antibody comprises an amino acid sequence comprising amino acids 118 to 260 of human IgG2 and amino acids 261 to 447 of human IgG4, wherein the numbering of the residues is according to EU or, Kabat numbering.

15. The anti-Siglec-7 antibody of any one of the preceding claims, wherein the Siglec-7 protein is a mammalian protein or a human protein.

16. The anti-Siglec-7 antibody of any one of the preceding claims, wherein the anti-Siglec-7 antibody binds Siglec-7 in a pH dependent manner.

17. The anti-Siglec-7 antibody of any one of the preceding claims, wherein the anti-Siglec-7 antibody is an antibody fragment that binds to an epitope comprising amino acid residues on human Siglec-7 or a mammalian Siglec-7 protein.

18. The anti-Siglec-7 antibody of claim 17, wherein the fragment is an Fab, Fab', Fab'-SH, F(ab')₂, Fv, or scFv fragment.

19. The anti-Siglec-7 antibody of any one of the preceding claims, wherein the anti-Siglec-7 antibody is a murine antibody, a humanized antibody, a bispecific antibody, a monoclonal antibody, a multivalent antibody, a conjugated antibody, or a chimeric antibody.

20. The anti-Siglec-7 antibody of any one of the preceding claims, wherein the anti-Siglec-7 antibody has a dissociation constant (K_D) for human Siglec-7 that ranges from about 9.5 nM to about 17 pM, or less than 17 pM, wherein the K_D is determined at a temperature of approximately 25°C.

21. The anti-Siglec-7 antibody of any one of the preceding claims, wherein the anti-Siglec-7 antibody binds to human dendritic cells with an EC_{50} that ranges from 2 nM to 100 pM, wherein the EC_{50} is determined at a temperature of approximately 4°C.

22. The anti-Siglec-7 antibody of any one of the preceding claims, wherein the anti-Siglec-7 antibody decreases cell surface levels of Siglec-7 with an EC_{50} that ranges from 500 pM to 18 pM, wherein the EC_{50} is determined at a temperature of approximately 37°C.
23. An isolated nucleic acid comprising a nucleic acid sequence encoding the anti-Siglec-7 antibody of any one of the preceding claims.
24. A vector comprising the nucleic acid of claim 23.
25. An isolated host cell comprising the vector of claim 24.
26. A method of producing an anti-Siglec-7 antibody, comprising culturing the host cell of claim 25 so that the anti-Siglec-7 antibody is produced.
27. A pharmaceutical composition comprising the anti-Siglec-7 antibody of any one of claims 1-22, and a pharmaceutically acceptable carrier.
28. Use of an antibody of any one of claims 1-22 in the manufacture of a medicament for preventing, reducing risk, or treating cancer.