

Siglec-7 ligands, and/or reduce one or more Siglec-7 activities in order to treat one or more diseases, disorders, and conditions associated with undesired Siglec-7 activity.

[0011] All references cited herein, including patents, patent applications and publications, are hereby incorporated by reference in their entirety.

SUMMARY

[0012] The present disclosure is generally directed to compositions that include antibodies, *e.g.*, monoclonal, chimeric, humanized antibodies, antibody fragments, *etc.*, that specifically bind human Siglec-7, and to methods of using such compositions.

[0013] Certain examples of the present disclosure are based, at least in part, on the identification of anti-Siglec-7 antibodies with improved and/or enhanced functional characteristics (*e.g.*, relative to an anti-Siglec-7 antibody with a heavy chain variable region comprising the sequence of SEQ ID NO: 61 and a light chain variable region comprising the sequence SEQ ID NO: 62). Certain examples of the present disclosure are based, at least in part, on the identification of anti-Siglec-7 antibodies with improved and/or enhanced functional characteristics (*e.g.*, relative to an anti-Siglec-7 antibody with a heavy chain variable region comprising the sequence of SEQ ID NO: 38 and a light chain variable region comprising the sequence SEQ ID NO: 50), including, for example, improved and/or enhanced capabilities of decreasing cell surface levels of Siglec-7 on human primary immune cells, and/or have improved and/or enhanced binding kinetics. In some examples, anti-Siglec-7 antibodies of the present disclosure have a K_D for human Siglec-7 that is at least 100-fold lower than an anti-Siglec-7 antibody having a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 38 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 50. In some examples, anti-Siglec-7 antibodies of the present disclosure have a K_D for human Siglec-7 that is at least 5.3-fold lower than an anti-Siglec-7 antibody having a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 38 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 50.

[0014] In some examples, anti-Siglec-7 antibodies of the present disclosure reduce cell surface levels of Siglec-7 *in vitro* with an EC_{50} that is at least about 50% lower than an anti-Siglec-7 antibody having a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 61 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 62. In some examples, anti-Siglec-7 antibodies of the present disclosure reduce cell surface levels of Siglec-7 *in vitro* with an EC_{50} that is at least about 10% lower than an anti-Siglec-7 antibody having a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 38 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 50, as measured by flow cytometry. In some examples, the antibody is at least 4.2-fold more potent than an anti-Siglec-7 antibody comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 61 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 62; or at

least 1.4-fold more potent than an anti-Siglec-7 antibody comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 38 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 50, as measured by flow cytometry. Advantageously, the anti-Siglec-7 antibodies decrease cellular levels of Siglec-7 *in vitro* with a half-maximal effective concentration (EC₅₀) that ranges from about 33.2 pM to about 25.4 nM, bind to human cells (such as human primary dendritic cells), and have a dissociation constant (K_D) for human Siglec-7 that ranges from about 124 nM to about 1 pM.

[0015] Accordingly, in one example, the present disclosure relates to an antibody that binds to a Siglec-7 protein, wherein the antibody comprises a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises: an HVR-H1 comprising a sequence according to Formula I: GYAFTX₁X₂WMN (SEQ ID NO: 6), wherein X₁ is E, M, G, or A, and X₂ is T, A, or Y; an HVR-H2 comprising a sequence according to Formula II: RIFPGX₁GHTN (SEQ ID NO: 9), wherein X₁ is L or Y; and an HVR-H3 comprising the sequence of DYSDYYFDY (SEQ ID NO: 10).

[0016] In another example, the present disclosure relates to an antibody that binds to a Siglec-7 protein, wherein the antibody comprises a heavy chain variable region and a light chain variable region, wherein the light chain variable region comprises: an HVR-L1 comprising a sequence according to Formula III: RX₁SX₂DX₃NTYLN (SEQ ID NO: 15), wherein X₁ is G or A, X₂ is Q or E, and X₃ is I, T, or A; an HVR-L2 comprising the sequence of YTSRLHS (SEQ ID NO: 16); and an HVR-L3 comprising a sequence according to Formula IV: QX₁GX₂X₃X₄PWT (SEQ ID NO: 24), wherein X₁ is Q or G, X₂ is N or G, X₃ is L, T, V, or I, and X₄ is L or K; and wherein the antibody is not an antibody comprising a light chain variable region comprising an HVR-L1 comprising the sequence of RASQDINTYLN (SEQ ID NO: 65), an HVR-L2 comprising the sequence of YTSRLHS (SEQ ID NO: 16), and an HVR-L3 comprising the sequence of QQGNTLPWT (SEQ ID NO: 20).

[0017] In another aspect, the present disclosure relates to an antibody that binds to a Siglec-7 protein, wherein the antibody comprises a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises: an HVR-H1 comprising a sequence according to Formula I: GYAFTX₁X₂WMN (SEQ ID NO: 6), wherein X₁ is E, M, G, or A, and X₂ is T, A, or Y; an HVR-H2 comprising a sequence according to Formula II: RIFPGX₁GHTN (SEQ ID NO: 9), wherein X₁ is L or Y; and an HVR-H3 comprising the sequence of DYSDYYFDY (SEQ ID NO: 10); and the light chain variable region comprises: an HVR-L1 comprising a sequence according to Formula III: RX₁SX₂DX₃NTYLN (SEQ ID NO: 15), wherein X₁ is G or A, X₂ is Q or E, and X₃ is I, T, or A; an HVR-L2 comprising the sequence of YTSRLHS (SEQ ID NO: 16); and an HVR-L3 comprising a sequence according to Formula IV: QX₁GX₂X₃X₄PWT (SEQ ID NO: 24), wherein X₁ is Q or G, X₂ is N or G, X₃ is L, T, V, or I, and X₄ is L or K.

[0018] In another aspect, the present disclosure relates to an antibody that binds to a Siglec-7 protein, wherein the antibody comprises a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises: an HVR-H1 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 1-5; an HVR-H2 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 7-8; and an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 10; and the light chain variable region comprises: an HVR-L1 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 11-14; an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 16; and an HVR-L3 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 17-23. In some examples, an anti-Siglec-7 antibody comprises the HVR-H1 comprising the amino acid sequence GYAFTMAWMN (SEQ ID NO: 2), the HVR-H2 comprising the amino acid sequence RIFPGYGHTN (SEQ ID NO: 8), the HVR-H3 comprising the amino acid sequence DYSDYYFDY (SEQ ID NO: 10), the HVR-L1 comprising the amino acid sequence RGSQDINTYLN (SEQ ID NO: 11), the HVR-L2 comprising the amino acid sequence YTSRLHS (SEQ ID NO: 16), and the HVR-L3 comprising the amino acid sequence QQGNLLPWT (SEQ ID NO: 17). In some examples, an anti-Siglec-7 antibody comprises the HVR-H1 comprising the amino acid sequence GYAFTGYWMN (SEQ ID NO: 3), the HVR-H2 comprising the amino acid sequence RIFPGLGHTN (SEQ ID NO: 7), the HVR-H3 comprising the amino acid sequence DYSDYYFDY (SEQ ID NO: 10), the HVR-L1 comprising the amino acid sequence RGSQDTNTYLN (SEQ ID NO: 12), the HVR-L2 comprising the amino acid sequence YTSRLHS (SEQ ID NO: 16), and the HVR-L3 comprising the amino acid sequence QQGNTLPWT (SEQ ID NO: 20). In some examples, an anti-Siglec-7 antibody comprises the HVR-H1 comprising the amino acid sequence GYAFTGYWMN (SEQ ID NO: 3), the HVR-H2 comprising the amino acid sequence RIFPGLGHTN (SEQ ID NO: 7), the HVR-H3 comprising the amino acid sequence DYSDYYFDY (SEQ ID NO: 10), the HVR-L1 comprising the amino acid sequence RGSQDINTYLN (SEQ ID NO: 11), the HVR-L2 comprising the amino acid sequence YTSRLHS (SEQ ID NO: 16), and the HVR-L3 comprising the amino acid sequence QQGNILPWT (SEQ ID NO: 23). In some examples, an anti-Siglec-7 antibody comprises the HVR-H1 comprising the amino acid sequence GYAFTAAWMN (SEQ ID NO: 4), the HVR-H2 comprising the amino acid sequence RIFPGLGHTN (SEQ ID NO: 7), the HVR-H3 comprising the amino acid sequence DYSDYYFDY (SEQ ID NO: 10), the HVR-L1 comprising the amino acid sequence RGSQDINTYLN (SEQ ID NO: 11), the HVR-L2 comprising the amino acid sequence YTSRLHS (SEQ ID NO: 16), and the HVR-L3 comprising the amino acid sequence QQGNILPWT (SEQ ID NO: 23).

[0018a] In one aspect, the present disclosure relates to an antibody that binds to a Siglec-7 protein, wherein the antibody comprises a heavy chain variable region and a light chain variable region, wherein: the heavy chain variable region comprises an HVR-H1 comprising the amino acid sequence GYAFTMAWMN (SEQ ID NO: 2), an HVR-H2 comprising the amino acid sequence RIFPGYGHTN (SEQ ID NO: 8), and an HVR-H3 comprising the amino acid sequence DYSDYYFDY (SEQ ID NO: 10), and the light chain variable region comprises an HVR-L1 comprising the amino acid sequence RGSQDINTYLN (SEQ ID NO: 11), an HVR-L2 comprising the amino acid sequence YTSRLHS (SEQ ID NO: 16), and an HVR-L3 comprising the amino acid sequence QQGNLLPWT (SEQ ID NO: 17).

[0018b] In one aspect, the present disclosure relates to an antibody that binds to a Siglec-7 protein, wherein the antibody comprises a heavy chain variable region and a light chain variable region, wherein: the heavy chain variable region comprises an HVR-H1 comprising the amino acid sequence GYAFTGYWMN (SEQ ID NO: 3), an HVR-H2 comprising the amino acid sequence RIFPGLGHTN (SEQ ID NO: 7), and an HVR-H3 comprising the amino acid sequence DYSDYYFDY (SEQ ID NO: 10), and the light chain variable region comprises an HVR-L1 comprising the amino acid sequence RGSQDTNTYLN (SEQ ID NO: 12), an HVR-L2 comprising the amino acid sequence YTSRLHS (SEQ ID NO: 16), and an HVR-L3 comprising the amino acid sequence QQGNTLPWT (SEQ ID NO: 20).

[0018c] In one aspect, the present disclosure relates to an antibody that binds to a Siglec-7 protein, wherein the antibody comprises a heavy chain variable region and a light chain variable region, wherein: the heavy chain variable region comprises an HVR-H1 comprising the amino acid sequence GYAFTGYWMN (SEQ ID NO: 3), an HVR-H2 comprising the amino acid sequence RIFPGLGHTN (SEQ ID NO: 7), and an HVR-H3 comprising the amino acid sequence DYSDYYFDY (SEQ ID NO: 10), and the light chain variable region comprises an HVR-L1 comprising the amino acid sequence RGSQDINTYLN (SEQ ID NO: 11), an HVR-L2 comprising the amino acid sequence YTSRLHS (SEQ ID NO: 16), and an HVR-L3 comprising the amino acid sequence QQGNILPWT (SEQ ID NO: 23).

[0018d] In one aspect, the present disclosure relates to an antibody that binds to a Siglec-7 protein, wherein the antibody comprises a heavy chain variable region and a light chain variable region, wherein: the heavy chain variable region comprises an HVR-H1 comprising the amino acid sequence GYAFTAAWMN (SEQ ID NO: 4), an HVR-H2 comprising the amino acid sequence RIFPGLGHTN (SEQ ID NO: 7), and an HVR-H3 comprising the amino acid sequence DYSDYYFDY (SEQ ID NO: 10), and the light chain variable region comprises an HVR-L1 comprising the amino acid sequence RGSQDINTYLN (SEQ ID NO: 11), an HVR-L2 comprising the amino acid sequence YTSRLHS (SEQ ID NO: 16), and an HVR-L3 comprising the amino acid sequence QQGNILPWT (SEQ ID NO: 23).

[0019] Other examples of the present disclosure relate to an antibody that binds to a Siglec-7 protein, wherein the antibody comprises a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises Kabat CDRs; and/or the light chain variable region

comprises Kabat CDRs. In some examples, the heavy chain variable region comprises a CDR-H1 comprising the sequence of GYAFTAAWMN (SEQ ID NO: 4), a CDR-H2 comprising the sequence of RIFPGLGHTN (SEQ ID NO: 7); and a CDR-H3 comprising the sequence of DYSDYYFDY (SEQ ID NO: 10). In some examples, the light chain variable region comprises a CDR-L1 comprising the sequence of RGSQDINTYLN (SEQ ID NO: 11), a CDR-L2 comprising the sequence of YTSRLHS (SEQ ID NO: 16); and a CDR-L3 comprising the sequence of QQGNILPWT (SEQ ID NO: 23). In some examples, the heavy chain variable region comprises a CDR-H1 comprising the sequence of GYAFTAAWMN (SEQ ID NO: 4), a CDR-H2 comprising the sequence of RIFPGLGHTN (SEQ ID NO: 7); and a CDR-H3 comprising the sequence of DYSDYYFDY (SEQ ID NO: 10); and the light chain variable region comprises a CDR-L1 comprising the sequence of RGSQDINTYLN (SEQ ID NO: 11), a CDR-L2 comprising the sequence of YTSRLHS (SEQ ID NO: 16); and a CDR-L3 comprising the sequence of QQGNILPWT (SEQ ID NO: 23).

[0020] In some examples that may be combined with any of the preceding examples, the heavy chain variable region comprises one, two, three, or four framework regions selected from VH FR1, VH FR2, VH FR3, and VH FR4, wherein: VH FR1 comprises the sequence of QVQLVQSGAEVKKPGASVKVSCKAS (SEQ ID NO: 25); VH FR2 comprises a sequence according to Formula V: WVRQAX1GQX2LEWIG (SEQ ID NO: 29), wherein X1 is P or R, and X2 is G or R; VH FR3 the sequence of YAQKFQGRATLTEDTSTSTAYMELSSLRSEDTAVYYCAR (SEQ ID NO: 30); and VH FR4 comprises the sequence WGQGTSLTVSS (SEQ ID NO: 31); and/or the light chain comprises one, two, three, or four framework regions selected from VL FR1, VL FR2, VL FR3, and VL FR4, wherein: VL FR1 comprises the sequence of DIQMTQSPSSLSASVG DRVTITC (SEQ ID NO: 32); VL FR2 comprises the sequence of WYQQKPGKAPKLLIY (SEQ ID NO: 33); VL FR3 comprises the sequence of GVPSRFSGSGSGTDYTLTISSLQPEDFATYYC (SEQ ID NO: 34); and VL FR4 comprises the sequence of FGQGTKLEIK (SEQ ID NO: 35). In some examples that may be combined with any of the preceding examples, the heavy chain variable region comprises one, two, three, or four framework regions selected from VH FR1, VH FR2, VH FR3, and VH FR4, wherein: VH FR1 comprises the sequence of SEQ ID NO: 25; VH FR2 comprises a sequence selected from the group consisting of SEQ ID NOs: 26-28; VH FR3 comprises the sequence of SEQ ID NO: 30; and VH FR4 comprises the sequence of SEQ ID NO: 31; and/or the light chain comprises one, two, three, or four framework regions selected from VL FR1, VL FR2, VL FR3, and VL FR4, wherein: VL FR1 comprises the sequence of SEQ ID NO: 32; VL FR2 comprises the sequence of SEQ ID NO: 33; VL FR3 comprises the sequence of SEQ ID NO: 34; and VL FR4 comprises the sequence of SEQ ID NO: 35.

[0021] In some examples that may be combined with any of the preceding examples, the antibody comprises a heavy chain variable region comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 36-48; and/or a light chain variable region comprises an amino

acid sequence selected from the group consisting of SEQ ID NOs: 49-60. In some examples, an anti-Siglec-7 antibody of the present disclosure comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 41 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 52; a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 42 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 55; a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 42 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 60; or 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: 60.

[0022] In one aspect, the present disclosure relates to an antibody that binds to a Siglec-7 protein, wherein the antibody comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 41 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 52. In one aspect, the present disclosure relates to an antibody that binds to a Siglec-7 protein, wherein the antibody comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 42 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 55. In one aspect, the present disclosure relates to an antibody that binds to a Siglec-7 protein, wherein the antibody comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 42 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 60. In one aspect, the present disclosure relates to an antibody that binds to a Siglec-7 protein, wherein the antibody comprises 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: 60.

[0023] In some examples that may be combined with any of the preceding examples, the antibody is of the IgG class the IgM class, or the IgA class. In some examples, the antibody is of the IgG class and has an IgG1, IgG2, IgG3, or IgG4 isotype.

[0024] In some examples, the Fc region comprises an amino acid substitution at position P331S, wherein the numbering of the residue position is according to EU numbering. In some examples, the Fc region comprises an amino acid substitution at positions L234A, L235A, and P331S, wherein the numbering of the residue position is according to EU numbering; the Fc region comprises an amino acid substitution at position N297A, wherein the numbering of the residue position is according to EU numbering; or the Fc region comprises an amino acid substitution at positions S267E and L328F, wherein the numbering of the residue position is according to EU numbering.

[0025] In some examples that may be combined with any of the preceding examples, the Siglec-7 protein is a non-human primate Siglec-7 protein or a human protein. In some examples, the Siglec-7 protein is a wild-type protein. In some examples, the Siglec-7 protein is a naturally

occurring variant. In some examples that may be combined with any of the preceding examples, the Siglec-7 protein is expressed on one or more cells selected from the group consisting of human dendritic cells, human macrophages, human monocytes, human osteoclasts, human neutrophils, human natural killer (NK) cells, human T cells, human T helper cell, human cytotoxic T cells, human granulocytes, and human microglia.

[0026] In some examples that may be combined with any of the preceding examples, the antibody binds specifically to a human Siglec-7 protein. In some examples, the antibody binds to a human Siglec-7 protein and does not cross-react with a Siglec-7 ortholog or homolog from another species. In some examples that may be combined with any of the preceding examples, the antibody is an antibody fragment that binds to an epitope comprising amino acid residues on a non-human primate Siglec-7 protein or a human Siglec-7 protein. In some examples that may be combined with any of the preceding examples, the antibody is an antibody fragment that binds to one or more human proteins selected from the group consisting of human Siglec-7, a naturally occurring variant of human Siglec-7, and a disease variant of human Siglec-7. In some examples, the antibody fragment is cross-linked to a second antibody fragment that binds to one or more human proteins selected from the group consisting of human Siglec-7, a naturally occurring variant of human Siglec-7, and a disease variant of human Siglec-7. In some examples, the fragment is an Fab, Fab', Fab'-SH, F(ab')₂, Fv, or scFv fragment.

[0027] In some examples that may be combined with any of the preceding examples, the antibody is a humanized antibody, a bispecific antibody, a monoclonal antibody, a multivalent antibody, a conjugated antibody, or a chimeric antibody. In some examples, the antibody is a monoclonal antibody. In some examples, the antibody is a bispecific antibody recognizing a first antigen and a second antigen. In some examples, the first antigen is Siglec-7 and the second antigen is: an antigen facilitating transport across the blood-brain-barrier; an antigen facilitating transport across the blood-brain-barrier selected from the group consisting of transferrin receptor (TR), insulin receptor (HIR), insulin-like growth factor receptor (IGFR), low-density lipoprotein receptor related proteins 1 and 2 (LPR-1 and 2), diphtheria toxin receptor, CRM197, a llama single domain antibody, TMEM 30(A), a protein transduction domain, TAT, Syn-B, penetratin, a poly-arginine peptide, an angiopep peptide, and ANG1005; a disease-causing agent selected from the group consisting of disease-causing peptides or proteins and disease-causing nucleic acids, wherein the disease-causing peptides or proteins are selected from the group consisting of amyloid beta, oligomeric amyloid beta, amyloid beta plaques, amyloid precursor protein or fragments thereof, Tau, IAPP, alpha-synuclein, TDP-43, FUS protein, C9orf72 (chromosome 9 open reading frame 72), c9RAN protein, prion protein, PrPSc, huntingtin, calcitonin, superoxide dismutase, ataxin, ataxin 1, ataxin 2, ataxin 3, ataxin 7, ataxin 8, ataxin 10, Lewy body, atrial natriuretic factor, islet amyloid polypeptide, insulin, apolipoprotein AI, serum amyloid A, super oxide dismutase (SOD), medin,

prolactin, transthyretin, lysozyme, beta 2 microglobulin, gelsolin, keratoepithelin, cystatin, immunoglobulin light chain AL, S-IBM protein, Repeat-associated non-ATG (RAN) translation products, DiPeptide repeat (DPR) peptides, glycine-alanine (GA) repeat peptides, glycine-proline (GP) repeat peptides, glycine-arginine (GR) repeat peptides, proline-alanine (PA) repeat peptides, ubiquitin, and proline-arginine (PR) repeat peptides, and the disease-causing nucleic acids are antisense GGCCCC (G2C4) repeat-expansion RNA; a ligand and/or a proteins expressed on immune cells, wherein the ligand and/or the protein is selected from the group consisting of CD33, CD40, OX40, ICOS, CD28, CD137/4-1BB, CD27, GITR, PD-L1, CTLA4, PD-L2, PD-1, B7-H3, B7-H4, HVEM, LIGHT, BTLA, CD38, TIGIT, VISTA, KIR, GAL9, TIM1, TIM3, TIM4, A2AR, LAG3, DR5, CD39, CD70, CD73, TREM1, TREM2, Siglec-5, Siglec-9, Siglec-11, SirpA, CD47, CSF1-receptor, and phosphatidylserine; or a protein, a lipid, a polysaccharide, or a glycolipid expressed on one or more tumor cells.

[0028] In some examples that may be combined with any of the preceding examples, the antibody is used in combination with one or more antibodies that specifically bind a disease-causing agent selected from the group consisting of disease-causing peptides, disease-causing proteins, amyloid beta, oligomeric amyloid beta, amyloid beta plaques, amyloid precursor protein or fragments thereof, Tau, IAPP, alpha-synuclein, TDP-43, FUS protein, C9orf72 (chromosome 9 open reading frame 72), prion protein, PrPSc, huntingtin, calcitonin, superoxide dismutase, ataxin, ataxin 1, ataxin 2, ataxin 3, ataxin 7, ataxin 8, ataxin 10, Lewy body, atrial natriuretic factor, islet amyloid polypeptide, insulin, apolipoprotein AI, serum amyloid A, medin, prolactin, transthyretin, lysozyme, beta 2 microglobulin, gelsolin, keratoepithelin, cystatin, immunoglobulin light chain AL, super oxide dismutase (SOD), S-IBM protein, Repeat-associated non-ATG (RAN) translation products, DiPeptide repeat (DPR) peptides, glycine-alanine (GA) repeat peptides, glycine-proline (GP) repeat peptides, glycine-arginine (GR) repeat peptides, proline-alanine (PA) repeat peptides, ubiquitin, and proline-arginine (PR) repeat peptides, and any combination thereof; or with one or more antibodies that bind an immunomodulatory protein selected from the group consisting of: CD33, CD40, OX40, ICOS, CD28, CD137/4-1BB, CD27, GITR, PD-L1, CTLA4, PD-L2, PD-1, B7-H3, B7-H4, HVEM, LIGHT, BTLA, CD38, TIGIT, VISTA, KIR, GAL9, TIM1, TIM3, TIM4, A2AR3, DR5, CD39, CD70, CD73, LAG3, TREM1, TREM2, Siglec-5, Siglec-9, Siglec-11, SirpA, CD47, CSF1-receptor, phosphatidylserine, disease-causing nucleic acids, antisense GGCCCC (G2C4) repeat-expansion RNA, and any combination thereof.

[0029] In some examples that may be combined with any of the preceding examples, the antibody has a dissociation constant (K_D) for human Siglec-7 that is at least 4-fold lower than an anti-Siglec-7 antibody comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 61 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 62; or at least 1-fold lower than an anti-Siglec-7 antibody comprising a heavy chain variable region

comprising the amino acid sequence of SEQ ID NO: 38 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 50, wherein the K_D is determined by BioLayer Interferometry. In some examples that may be combined with any of the preceding examples, the antibody has a dissociation constant (K_D) for human Siglec-7 that ranges from about 124 nM to about 1 pM, or less than about 1 pM, and wherein the K_D is determined by BioLayer Interferometry.

[0030] In some examples that may be combined with any of the preceding examples, the antibody reduces cell surface levels of Siglec-7. In some examples, the Siglec-7 is expressed on the surface of human dendritic cells. In some examples, the antibody reduces cell surface levels of Siglec-7 *in vitro*. In some examples, the antibody reduces cell surface levels of Siglec-7 *in vitro* with a half maximal effective concentration (EC_{50}) that is less than 150 pM, as measured by flow cytometry. In some examples, the antibody reduces cell surface levels of Siglec-7 *in vitro* with an EC_{50} that is at least 50% lower than an anti-Siglec-7 antibody comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 61 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 62; or at least 10% lower than an anti-Siglec-7 antibody comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 38 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 50, as measured by flow cytometry. In some examples, cell surface levels of Siglec-7 are reduced to at least 20%. In some examples, the antibody is at least 4.2-fold more potent than an anti-Siglec-7 antibody comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 61 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 62; or at least 1.4-fold more potent than an anti-Siglec-7 antibody comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 38 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 50, as measured by flow cytometry.

[0031] In some examples, an anti-Siglec-7 antibody of the present disclosure competes with an antibody comprising the heavy chain variable domain and the light chain variable domain of an antibody selected from the group consisting of S7AB-H1, S7AB-H2, S7AB-H3, S7AB-H4, S7AB-H5, S7AB-H6, S7AB-H7, S7AB-H8, S7AB-H9, S7AB-H10, S7AB-H11, S7AB-H12, S7AB-H8.1, S7AB-H8.2, S7AB-H8.3, S7AB-H8.4, S7AB-H8.5, S7AB-H8.6, S7AB-H8.7, S7AB-H8.8, S7AB-H8.9, S7AB-H8.10, S7AB-H8.11, S7AB-H8.12, S7AB-H8.13, S7AB-H8.14, S7AB-H8.15, S7AB-H8.16, S7AB-H8.17, S7AB-H8.18, S7AB-H8.19, S7AB-H8.20, S7AB-H8.21, S7AB-H8.22, S7AB-H8.23, S7AB-H8.24, S7AB-H8.25, S7AB-H8.26, S7AB-H8.27, S7AB-H8.28, S7AB-H8.29, S7AB-H8.30, S7AB-H8.31, S7AB-H8.32, S7AB-H8.33, S7AB-H8.34, S7AB-H8.35, S7AB-H8.36, S7AB-H8.37, S7AB-H8.38, S7AB-H8.39, S7AB-H8.40, S7AB-H8.41, S7AB-H8.42, S7AB-H8.43, S7AB-H8.44, S7AB-H8.45, S7AB-H8.9.1, S7AB-H8.9.2, S7AB-H8.10.1, S7AB-H8.10.2, S7AB-H8.29.1, S7AB-H8.29.2, S7AB-H8.30.1, S7AB-H8.30.2, S7AB-H8.34.1, S7AB-H8.34.2, S7AB-H8.35.1,

S7AB-H8.35.2, S7AB-H8.44.1, S7AB-H8.44.2, S7AB-H8.45.1, S7AB-H8.45.2, and any combination thereof for binding to Siglec-7.

[0032] In some examples, an anti-Siglec-7 antibody of the present disclosure binds essentially the same Siglec-7 epitope as an antibody comprising the heavy chain variable domain and the light chain variable domain of an antibody selected from the group consisting of S7AB-H1, S7AB-H2, S7AB-H3, S7AB-H4, S7AB-H5, S7AB-H6, S7AB-H7, S7AB-H8, S7AB-H9, S7AB-H10, S7AB-H11, S7AB-H12, S7AB-H8.1, S7AB-H8.2, S7AB-H8.3, S7AB-H8.4, S7AB-H8.5, S7AB-H8.6, S7AB-H8.7, S7AB-H8.8, S7AB-H8.9, S7AB-H8.10, S7AB-H8.11, S7AB-H8.12, S7AB-H8.13, S7AB-H8.14, S7AB-H8.15, S7AB-H8.16, S7AB-H8.17, S7AB-H8.18, S7AB-H8.19, S7AB-H8.20, S7AB-H8.21, S7AB-H8.22, S7AB-H8.23, S7AB-H8.24, S7AB-H8.25, S7AB-H8.26, S7AB-H8.27, S7AB-H8.28, S7AB-H8.29, S7AB-H8.30, S7AB-H8.31, S7AB-H8.32, S7AB-H8.33, S7AB-H8.34, S7AB-H8.35, S7AB-H8.36, S7AB-H8.37, S7AB-H8.38, S7AB-H8.39, S7AB-H8.40, S7AB-H8.41, S7AB-H8.42, S7AB-H8.43, S7AB-H8.44, S7AB-H8.45, S7AB-H8.9.1, S7AB-H8.9.2, S7AB-H8.10.1, S7AB-H8.10.2, S7AB-H8.29.1, S7AB-H8.29.2, S7AB-H8.30.1, S7AB-H8.30.2, S7AB-H8.34.1, S7AB-H8.34.2, S7AB-H8.35.1, S7AB-H8.35.2, S7AB-H8.44.1, S7AB-H8.44.2, S7AB-H8.45.1, and S7AB-H8.45.2.

[0033] In another aspect, the present disclosure relates to isolated nucleic acids comprising a nucleic acid sequence encoding any of the antibodies described herein.

[0034] In another aspect, the present disclosure relates to vectors comprising any of the nucleic acids described herein. In some examples, the vector is an expression vector and/or a display vector.

[0035] In another example, the present disclosure relates to isolated host cells comprising any of the nucleic acids or vectors described herein. In one aspect, the present disclosure relates to isolated host cells comprising any of the vectors described herein.

[0036] In another aspect, the present disclosure relates to a method of producing an antibody that binds to Siglec-7 comprising culturing any of the host cells described herein so that the antibody is produced. In some examples, the method further comprises recovering the antibody produced by the cell.

[0037] In another aspect, the present disclosure relates to an antibody produced by any of the methods described herein.

[0038] In another aspect, the present disclosure relates to pharmaceutical compositions comprising any of the antibodies described herein and a pharmaceutically acceptable carrier. In some examples, the present disclosure relates to the use of any of the antibodies described herein for the preparation of a medicament.

[0039] In another aspect, the present disclosure relates to use of any of the antibodies described herein in the manufacture of a medicament for preventing, reducing risk for, or treating cancer. Also described herein is a method of preventing, reducing risk for, or treating a disease, disorder, or injury selected from the group consisting of dementia, frontotemporal dementia, Alzheimer's disease, vascular dementia, mixed dementia, tauopathy disease,

infections, and cancer, comprising administering to an individual in need thereof a therapeutically effective amount of any of the antibodies described herein. In some examples, the disease, disorder, or injury is cancer. In some examples, the cancer is selected from the group consisting of 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), and multiple myeloma. In some examples, the present disclosure relates to the use of any of the antibodies described herein for the preparation of a medicament useful for preventing, reducing risk, or treating a disease, disorder, or injury selected from the group consisting of dementia, frontotemporal dementia, Alzheimer's disease, vascular dementia, mixed dementia, taupathy disease, infections, and cancer. In some examples, the disease, disorder, or injury is cancer. In some examples, the cancer is selected from the group consisting of 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), and multiple myeloma. In some examples, the cancer expresses increased or high levels of Siglec-7 ligand. In some examples, the Siglec-7 ligand is one or more of alpha-2,3-linked sialic acid and alpha-2,6-linked sialic acid, disialogalactosyl globoside, disialyl lactotetraosylceramide and/or disialyl GalNAc lactotetraosylceramide. In some examples, the cancer has increased or high levels of tumor infiltrating NK cells.

BRIEF DESCRIPTION OF THE DRAWINGS

[0040] FIG. 1 depicts results from a flow cytometry assay measuring binding of humanized Siglec-7 antibodies to primary human monocyte-derived dendritic cells.

[0041] FIG. 2 depicts flow cytometry results measuring binding of affinity matured humanized Siglec-7 antibodies to primary human monocyte-derived dendritic cells.

[0042] FIG. 3 depicts results from a flow cytometry assay measuring Siglec-7 levels on the surface of primary human dendritic cells after treatment with affinity matured Siglec-7 antibodies.

[0043] FIG. 4 depicts results from a flow cytometry assay measuring Siglec-7 levels on the surface of primary human dendritic cells after treatment with different concentrations of Siglec-7 antibodies containing different Fc regions.

[0044] FIG. 5A depicts flow cytometry results measuring human Siglec-7 levels on the surface of myeloid cells in human Siglec-7 transgenic mice that were injected with Siglec-7 antibodies. **FIG.**

CLAIMS

What is claimed is:

1. An antibody that binds to a Siglec-7 protein, wherein the antibody comprises a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises:
 - an HVR-H1 comprising a sequence according to Formula I: GYAFTX₁X₂WMN (SEQ ID NO: 6), wherein X₁ is E, M, G, or A, and X₂ is T, A, or Y;
 - an HVR-H2 comprising a sequence according to Formula II: RIFPGX₁GHTN (SEQ ID NO: 9), wherein X₁ is L or Y; and
 - an HVR-H3 comprising the sequence of DYSDYYFDY (SEQ ID NO: 10); andthe light chain variable region comprises:
 - an HVR-L1 comprising a sequence according to Formula III: RX₁SX₂DX₃NTYLN (SEQ ID NO: 15), wherein X₁ is G or A, X₂ is Q or E, and X₃ is I, T, or A;
 - an HVR-L2 comprising the sequence of YTSRLHS (SEQ ID NO: 16); and
 - an HVR-L3 comprising a sequence according to Formula IV: QX₁GX₂X₃X₄PWT (SEQ ID NO: 24), wherein X₁ is Q or G, X₂ is N or G, X₃ is L, T, V, or I, and X₄ is L or K.
2. An antibody that binds to a Siglec-7 protein, wherein the antibody comprises a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises:
 - an HVR-H1 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 1-5;
 - an HVR-H2 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 7-8; and
 - an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 10; andthe light chain variable region comprises:
 - an HVR-L1 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 11-14;
 - an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 16; and
 - an HVR-L3 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 17-23.
3. The antibody of any one of claims 1-2, wherein:
 - (a) the HVR-H1 comprises the amino acid sequence GYAFTMAWMN (SEQ ID NO: 2),
 - the HVR-H2 comprises the amino acid sequence RIFPGYGHTN (SEQ ID NO: 8),
 - the HVR-H3 comprises the amino acid sequence DYSDYYFDY (SEQ ID NO: 10),
 - the HVR-L1 comprises the amino acid sequence RGSQDINTYLN (SEQ ID NO: 11),

- the HVR-L2 comprises the amino acid sequence YTSRLHS (SEQ ID NO: 16), and the HVR-L3 comprises the amino acid sequence QQGNLLPWT (SEQ ID NO: 17);
- (b) the HVR-H1 comprises the amino acid sequence GYAFTGYWMN (SEQ ID NO: 3), the HVR-H2 comprises the amino acid sequence RIFPGLGHTN (SEQ ID NO: 7), the HVR-H3 comprises the amino acid sequence DYSDYYFDY (SEQ ID NO: 10), the HVR-L1 comprises the amino acid sequence RGSQDTNTYLN (SEQ ID NO: 12), the HVR-L2 comprises the amino acid sequence YTSRLHS (SEQ ID NO: 16), and the HVR-L3 comprises the amino acid sequence QQGNTLPWT (SEQ ID NO: 20);
- (c) the HVR-H1 comprises the amino acid sequence GYAFTGYWMN (SEQ ID NO: 3), the HVR-H2 comprises the amino acid sequence RIFPGLGHTN (SEQ ID NO: 7), the HVR-H3 comprises the amino acid sequence DYSDYYFDY (SEQ ID NO: 10), the HVR-L1 comprises the amino acid sequence RGSQDINTYLN (SEQ ID NO: 11), the HVR-L2 comprises the amino acid sequence YTSRLHS (SEQ ID NO: 16), and the HVR-L3 comprises the amino acid sequence QQGNILPWT (SEQ ID NO: 23); or
- (d) the HVR-H1 comprises the amino acid sequence GYAFTAAWMN (SEQ ID NO: 4), the HVR-H2 comprises the amino acid sequence RIFPGLGHTN (SEQ ID NO: 7), the HVR-H3 comprises the amino acid sequence DYSDYYFDY (SEQ ID NO: 10), the HVR-L1 comprises the amino acid sequence RGSQDINTYLN (SEQ ID NO: 11), the HVR-L2 comprises the amino acid sequence YTSRLHS (SEQ ID NO: 16), and the HVR-L3 comprises the amino acid sequence QQGNILPWT (SEQ ID NO: 23).

4. An antibody that binds to a Siglec-7 protein, wherein the antibody comprises a heavy chain variable region and a light chain variable region, wherein: the heavy chain variable region comprises an HVR-H1 comprising the amino acid sequence GYAFTMAWMN (SEQ ID NO: 2), an HVR-H2 comprising the amino acid sequence RIFPGYGHTN (SEQ ID NO: 8), and an HVR-H3 comprising the amino acid sequence DYSDYYFDY (SEQ ID NO: 10), and the light chain variable region comprises an HVR-L1 comprising the amino acid sequence RGSQDINTYLN (SEQ ID NO: 11), an HVR-L2 comprising the amino acid sequence YTSRLHS (SEQ ID NO: 16), and an HVR-L3 comprising the amino acid sequence QQGNLLPWT (SEQ ID NO: 17).

5. An antibody that binds to a Siglec-7 protein, wherein the antibody comprises a heavy chain variable region and a light chain variable region, wherein: the heavy chain variable region comprises an HVR-H1 comprising the amino acid sequence GYAFTGYWMN (SEQ ID NO: 3), an HVR-H2 comprising the amino acid sequence RIFPGLGHTN (SEQ ID NO: 7), and an HVR-H3 comprising the amino acid sequence DYSDYYFDY (SEQ ID NO: 10), and the light chain variable region

comprises an HVR-L1 comprising the amino acid sequence RGSQDTNTYLN (SEQ ID NO: 12), an HVR-L2 comprising the amino acid sequence YTSRLHS (SEQ ID NO: 16), and an HVR-L3 comprising the amino acid sequence QQGNTLPWT (SEQ ID NO: 20).

6. An antibody that binds to a Siglec-7 protein, wherein the antibody comprises a heavy chain variable region and a light chain variable region, wherein: the heavy chain variable region comprises an HVR-H1 comprising the amino acid sequence GYAFTGYWMN (SEQ ID NO: 3), an HVR-H2 comprising the amino acid sequence RIFPGLGHTN (SEQ ID NO: 7), and an HVR-H3 comprising the amino acid sequence DYSDYYFDY (SEQ ID NO: 10), and the light chain variable region comprises an HVR-L1 comprising the amino acid sequence RGSQDINTYLN (SEQ ID NO: 11), an HVR-L2 comprising the amino acid sequence YTSRLHS (SEQ ID NO: 16), and an HVR-L3 comprising the amino acid sequence QQGNILPWT (SEQ ID NO: 23).

7. An antibody that binds to a Siglec-7 protein, wherein the antibody comprises a heavy chain variable region and a light chain variable region, wherein: the heavy chain variable region comprises an HVR-H1 comprising the amino acid sequence GYAFTAAMN (SEQ ID NO: 4), an HVR-H2 comprising the amino acid sequence RIFPGLGHTN (SEQ ID NO: 7), and an HVR-H3 comprising the amino acid sequence DYSDYYFDY (SEQ ID NO: 10), and the light chain variable region comprises an HVR-L1 comprising the amino acid sequence RGSQDINTYLN (SEQ ID NO: 11), an HVR-L2 comprising the amino acid sequence YTSRLHS (SEQ ID NO: 16), and an HVR-L3 comprising the amino acid sequence QQGNILPWT (SEQ ID NO: 23).

8. The antibody of any one of claims 1-7, wherein the antibody comprises a heavy chain variable region comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 36-48; and/or a light chain variable region comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 49-60.

9. The antibody of claim 8, wherein the antibody comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 41 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 52; a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 42 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 55; a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 42 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 60; or 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: 60.

10. An antibody that binds to a Siglec-7 protein, wherein the antibody comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 41 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 52.
11. An antibody that binds to a Siglec-7 protein, wherein the antibody comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 42 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 55.
12. An antibody that binds to a Siglec-7 protein, wherein the antibody comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 42 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 60.
13. An antibody that binds to a Siglec-7 protein, wherein the antibody comprises 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: 60.
14. The antibody of any one of claims 1-13, wherein the antibody is of the IgG class, the IgM class, or the IgA class.
15. The antibody of claim 14, wherein the antibody is of the IgG class and has an IgG1, IgG2, IgG3, or IgG4 isotype.
16. The antibody of claim 15, wherein:
 - (a) the Fc region comprises an amino acid substitution at position P331S, wherein the numbering of the residue position is according to EU numbering.
 - (b) the Fc region comprises an amino acid substitution at positions L234A, L235A, and P331S, wherein the numbering of the residue position is according to EU numbering;
 - (c) the Fc region comprises an amino acid substitution at position N297A, wherein the numbering of the residue position is according to EU numbering; or
 - (d) the Fc region comprises an amino acid substitution at positions S267E and L328F, wherein the numbering of the residue position is according to EU numbering.
17. The antibody of any one of claims 1-16, wherein the Siglec-7 protein is a non-human primate protein or a human protein.
18. The antibody of any one of claims 1-17, wherein the Siglec-7 protein is a wild-type protein.
19. The antibody of any one of claims 1-17, wherein the Siglec-7 protein is a naturally occurring variant.

20. The antibody of any one of claims 1-19, wherein the Siglec-7 protein is expressed on one or more cells selected from the group consisting of human dendritic cells, human macrophages, human monocytes, human osteoclasts, human neutrophils, human natural killer (NK) cells, human T cells, human T helper cell, human cytotoxic T cells, human granulocytes, and human microglia.
21. The antibody of any one of claims 1-20, wherein the antibody binds specifically to a human Siglec-7 protein.
22. The antibody of any one of claims 1-19, wherein the antibody is an antibody fragment that binds to an epitope comprising amino acid residues on a non-human primate Siglec-7 protein or a human Siglec-7 protein.
23. The antibody of any one of claims 1-21, wherein the antibody is an antibody fragment that binds to one or more human proteins selected from the group consisting of human Siglec-7, a naturally occurring variant of human Siglec-7, and a disease variant of human Siglec-7.
24. The antibody of claim 23, wherein the antibody fragment is cross-linked to a second antibody fragment that binds to one or more human proteins selected from the group consisting of human Siglec-7, a naturally occurring variant of human Siglec-7, and a disease variant of human Siglec-7.
25. The antibody of any one of claims 22-24, wherein the antibody fragment is an Fab, Fab', Fab'-SH, F(ab')₂, Fv, or scFv fragment.
26. The antibody of any one of claims 1-25, wherein the antibody is a humanized antibody, a bispecific antibody, a monoclonal antibody, a multivalent antibody, a conjugated antibody, or a chimeric antibody.
27. The antibody of any one of claims 1-26, wherein the antibody is a monoclonal antibody.
28. The antibody of any one of claims 1-26, wherein the antibody is a bispecific antibody recognizing a first antigen and a second antigen.
29. The antibody of claim 28, wherein the first antigen is Siglec-7 and the second antigen is:
- (a) a ligand and/or a protein expressed on immune cells, wherein the ligand and/or the protein is selected from the group consisting of CD33, CD40, OX40, ICOS, CD28, CD137/4-1BB, CD27, GITR, PD-L1, CTLA4, PD-L2, PD-1, B7-H3, B7-H4, HVEM, LIGHT, BTLA, CD38, TIGIT, VISTA, KIR, GAL9, TIM1, TIM3, TIM4, A2AR, LAG3, DR5, CD39, CD70, CD73, TREM1, TREM2, Siglec-5, Siglec-9, Siglec-11, SirpA, CD47, CSF1-receptor, and phosphatidylserine; or
 - (b) a protein, a lipid, a polysaccharide, or a glycolipid expressed on one or more tumor cells.

30. The antibody of any one of claims 1-29, wherein the antibody is used in combination with one or more antibodies that bind an immunomodulatory protein selected from the group consisting of: CD33, CD40, OX40, ICOS, CD28, CD137/4-1BB, CD27, GITR, PD-L1, CTLA4, PD-L2, PD-1, B7-H3, B7-H4, HVEM, LIGHT, BTLA, CD38, TIGIT, VISTA, KIR, GAL9, TIM1, TIM3, TIM4, A2AR3, DR5, CD39, CD70, CD73, LAG3, TREM1, TREM2, Siglec-5, Siglec-9, Siglec-11, SirpA, CD47, CSF1-receptor, phosphatidylserine, disease-causing nucleic acids, antisense GGCCCC (G2C4) repeat-expansion RNA, and any combination thereof.

31. The antibody of any one of claims 1-7, wherein the antibody has a dissociation constant (K_D) for human Siglec-7 that is at least 4-fold lower than an anti-Siglec-7 antibody comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 61 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 62; or at least 1-fold lower than an anti-Siglec-7 antibody comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 38 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 50, wherein the K_D is determined by BioLayer Interferometry.

32. The antibody of any one of claims 1-7, wherein the antibody has a dissociation constant (K_D) for human Siglec-7 that ranges from about 124 nM to about 1 pM, or less than about 1 pM, and wherein the K_D is determined by BioLayer Interferometry.

33. The antibody of any one of claims 1-7, wherein the antibody reduces cell surface levels of Siglec-7.

34. The antibody of claim 33, wherein the Siglec-7 is expressed on the surface of human dendritic cells.

35. The antibody of claim 33 or claim 34, wherein the antibody reduces cell surface levels of Siglec-7 *in vitro*.

36. The antibody of any one of claims 33-35, wherein the antibody reduces cell surface levels of Siglec-7 *in vitro* with a half maximal effective concentration (EC_{50}) that is less than 150 pM, as measured by flow cytometry.

37. The antibody of any one of claims 33-36, wherein the antibody reduces cell surface levels of Siglec-7 *in vitro* with an EC_{50} that is at least 50% lower than an anti-Siglec-7 antibody comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 61 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 62; or at least 10% lower than an anti-Siglec-7 antibody comprising a heavy chain variable region comprising the amino acid sequence

of SEQ ID NO: 38 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 50, as measured by flow cytometry.

38. The antibody of claim 33, wherein cell surface levels of Siglec-7 are reduced to at least 20%.

39. The antibody of claim 38, wherein the antibody is at least 4.2-fold more potent than an anti-Siglec-7 antibody comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 61 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 62; or at least 1.4-fold more potent than an anti-Siglec-7 antibody comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 38 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 50, as measured by flow cytometry.

40. The antibody of any one of claims 1-39, wherein the antibody competes with an antibody comprising the heavy chain variable domain and the light chain variable domain of an antibody selected from the group consisting of S7AB-H1, S7AB-H2, S7AB-H3, S7AB-H4, S7AB-H5, S7AB-H6, S7AB-H7, S7AB-H8, S7AB-H9, S7AB-H10, S7AB-H11, S7AB-H12, S7AB-H8.1, S7AB-H8.2, S7AB-H8.3, S7AB-H8.4, S7AB-H8.5, S7AB-H8.6, S7AB-H8.7, S7AB-H8.8, S7AB-H8.9, S7AB-H8.10, S7AB-H8.11, S7AB-H8.12, S7AB-H8.13, S7AB-H8.14, S7AB-H8.15, S7AB-H8.16, S7AB-H8.17, S7AB-H8.18, S7AB-H8.19, S7AB-H8.20, S7AB-H8.21, S7AB-H8.22, S7AB-H8.23, S7AB-H8.24, S7AB-H8.25, S7AB-H8.26, S7AB-H8.27, S7AB-H8.28, S7AB-H8.29, S7AB-H8.30, S7AB-H8.31, S7AB-H8.32, S7AB-H8.33, S7AB-H8.34, S7AB-H8.35, S7AB-H8.36, S7AB-H8.37, S7AB-H8.38, S7AB-H8.39, S7AB-H8.40, S7AB-H8.41, S7AB-H8.42, S7AB-H8.43, S7AB-H8.44, S7AB-H8.45, S7AB-H8.9.1, S7AB-H8.9.2, S7AB-H8.10.1, S7AB-H8.10.2, S7AB-H8.29.1, S7AB-H8.29.2, S7AB-H8.30.1, S7AB-H8.30.2, S7AB-H8.34.1, S7AB-H8.34.2, S7AB-H8.35.1, S7AB-H8.35.2, S7AB-H8.44.1, S7AB-H8.44.2, S7AB-H8.45.1, S7AB-H8.45.2, and any combination thereof for binding to Siglec-7.

41. The antibody of any one of claims 1-40, wherein the antibody binds essentially the same Siglec-7 epitope as an antibody comprising the heavy chain variable domain and the light chain variable domain of an antibody selected from the group consisting of S7AB-H1, S7AB-H2, S7AB-H3, S7AB-H4, S7AB-H5, S7AB-H6, S7AB-H7, S7AB-H8, S7AB-H9, S7AB-H10, S7AB-H11, S7AB-H12, S7AB-H8.1, S7AB-H8.2, S7AB-H8.3, S7AB-H8.4, S7AB-H8.5, S7AB-H8.6, S7AB-H8.7, S7AB-H8.8, S7AB-H8.9, S7AB-H8.10, S7AB-H8.11, S7AB-H8.12, S7AB-H8.13, S7AB-H8.14, S7AB-H8.15, S7AB-H8.16, S7AB-H8.17, S7AB-H8.18, S7AB-H8.19, S7AB-H8.20, S7AB-H8.21, S7AB-H8.22, S7AB-H8.23, S7AB-H8.24, S7AB-H8.25, S7AB-H8.26, S7AB-H8.27, S7AB-H8.28, S7AB-H8.29, S7AB-H8.30, S7AB-H8.31, S7AB-H8.32, S7AB-H8.33, S7AB-H8.34, S7AB-H8.35, S7AB-H8.36, S7AB-H8.37, S7AB-H8.38, S7AB-H8.39, S7AB-H8.40, S7AB-H8.41, S7AB-H8.42, S7AB-H8.43, S7AB-H8.44, S7AB-H8.45, S7AB-H8.9.1, S7AB-H8.9.2, S7AB-H8.10.1,

S7AB-H8.10.2, S7AB-H8.29.1, S7AB-H8.29.2, S7AB-H8.30.1, S7AB-H8.30.2, S7AB-H8.34.1, S7AB-H8.34.2, S7AB-H8.35.1, S7AB-H8.35.2, S7AB-H8.44.1, S7AB-H8.44.2, S7AB-H8.45.1, and S7AB-H8.45.2.

42. An isolated nucleic acid comprising a nucleic acid sequence encoding the antibody of any one of claims 1-41.

43. A vector comprising the nucleic acid of claim 42.

44. An isolated host cell comprising the vector of claim 43.

45. A method of producing an antibody that binds to Siglec-7, comprising culturing the cell of claim 44 so that the antibody is produced.

46. The method of claim 45, further comprising recovering the antibody produced by the cell.

47. An isolated antibody that binds to Siglec-7 produced by the method of claim 45 or claim 46.

48. A pharmaceutical composition comprising the antibody of any one of claims 1-41 and a pharmaceutically acceptable carrier.

49. Use of the antibody of any one of claims 1-41 in the manufacture of a medicament for preventing, reducing risk for, or treating cancer.

50. The use of claim 49, wherein the cancer is selected from the group consisting of 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), and multiple myeloma.