[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 disclosure refers to 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

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 disclosure refers to an isolated nucleic acid comprising a nucleic acid sequence encoding the anti-Siglec-7 antibody described herein. In yet another aspect, the present disclosure refers to a vector comprising the nucleic acid described herein. In yet another aspect, the present disclosure refers to anisolated host cell comprising the vector described herein. In yet another aspect, the present disclosure refers to 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 disclosure refers to a pharmaceutical composition comprising the anti-Siglec-7 antibody described herein, and a pharmaceutically acceptable carrier. In yet another aspect, the present disclosure refers to use of an antibody as described herein in the manufacture of a medicament for reducing risk of 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, 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, granulomartous 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 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.

5. The anti-Siglec-7 antibody of any one of claims 1-4, wherein the anti-Siglec-7 antibody does not reduce TREM2 expression.

6. The anti-Siglec-7 antibody of any one of claims 1-5, 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; and

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.

7. The anti-Siglec-7 antibody of any one of claims 1-6, 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.

8. The anti-Siglec-7 antibody of any one of claims 1-6, 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.

9. The anti-Siglec-7 antibody of any one of claims 1-8, 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.

10. The anti-Siglec-7 antibody of any one of claims 1-9, 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.

11. 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.

12. The anti-Siglec-7 antibody of claim 11, wherein the anti-Siglec-7 antibody has an IgG1, IgG2, IgG3, or IgG4 isotype.

13. The anti-Siglec-7 antibody of claim 12, 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 YTCNVDHKPS NTKVDKTVERKCCVECPPCP (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 numbering.

14. 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.

15. 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.

16. 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.

17. The anti-Siglec-7 antibody of claim 16, wherein the fragment is an Fab, Fab', Fab'-SH, F(ab')2, Fv, or scFv fragment.

18. 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.

19. 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 25ºC.

20. 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 4ºC.

21. 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 37ºC.

22. An isolated nucleic acid comprising a nucleic acid sequence encoding the anti-Siglec-7 antibody of any one of the preceding claims.

23. A vector comprising the nucleic acid of claim 22.

24. An isolated host cell comprising the vector of claim 23.

25. A method of producing an anti-Siglec-7 antibody, comprising culturing the host cell of claim 24 so that the anti-Siglec-7 antibody is produced.

26. A pharmaceutical composition comprising the anti-Siglec-7 antibody of any one of claims 1-21, and a pharmaceutically acceptable carrier.

27. Use of an antibody of any one of claims 1-21 in the manufacture of a medicament for reducing risk of or treating cancer.