Clin Immunol., 2012, 130(3):563-71). There is currently a need for therapies that can control the activity of immune cells involved in inflammation, such as the activity of eosinophils and mast cells.

[0006] Previous studies have demonstrated that eosinophils undergo apoptosis when Siglec-8 is crosslinked with specific murine antibodies raised against the extracellular portion of Siglec-8 (Nutku et al., *Blood*, 2003, 336:918-24). These antibodies are described in U.S. Pat. No. 8,207,305, U.S. Pat. No. 8,197,811, U.S. Pat. No. 7,871,612, and U.S. Pat. No. 7,557,191. However, there remains a need for developing humanized anti-Siglec-8 antibodies that recognize human Siglec-8 with high affinity and specificity. Discovery of such anti-Siglec-8 antibodies may allow for the development of treatment for diseases mediated by the activity of eosinophils and/or mast cells.

[0007] All references cited herein, including patent applications, patent publications, and scientific literature, are herein incorporated by reference in their entirety, as if each individual reference were specifically and individually indicated to be incorporated by reference.

SUMMARY ~~OF THE INVENTION~~

[0008] Provided herein are anti-Siglec-8 antibodies (including humanized anti-Siglec-8 antibodies), compositions comprising thereof, and methods of using the same.

[0009] ~~In one aspect, p~~Provided herein is a humanized antibody that specifically binds to a human Siglec-8, wherein the binding affinity and/or binding avidity of the humanized antibody to a human Siglec-8 are higher than the binding affinity and/or binding avidity of antibody 2E2 and/or antibody 2C4 to the human Siglec-8. In one aspect, provided herein is a humanized antibody that binds to a human Siglec-8, wherein the binding affinity or avidity of the humanized antibody to the human Siglec-8 is higher than the binding affinity or avidity of antibody 2E2 or 2C4 to the human Siglec-8. In some embodiments, the human Siglec-8 is a dimer. In some embodiments, the human Siglec-8 comprises an extracellular domain human Siglec-8 fused to a Fc region of an immunoglobulin. In some embodiments, the Fc region is a human IgG1 Fc region. In some embodiments, the Fc region is a human IgG4 Fc region. In some embodiments, the human Siglec-8 comprises the amino acid sequence of SEQ ID NO:74.

[0010] In some embodiments, the humanized antibody comprises a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO:61, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO:62, and (iii) HVR-H3 comprising the amino acid sequence of SEQ ID NO:63; and/or wherein the light chain variable region comprises (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO:64, (ii) HVR-L2 comprising the amino acid sequence of SEQ ID NO:65, and (iii) HVR-L3 comprising the amino acid sequence of SEQ ID NO:66. In some embodiments, the antibody comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:6; and/or a light chain variable region comprising the

amino acid sequence selected from SEQ ID NOs:16 or 21. In any of the embodiments herein, the antibody may comprise a heavy chain Fc region comprising a human IgG Fc region. In further embodiments, the human IgG Fc region comprises a human IgG1 or IgG4. In some embodiments, the human IgG1 comprises the amino acid sequence of SEQ ID NO:78. In some embodiments, the human IgG4 comprises the amino acid sequence of SEQ ID NO:79. In any of the embodiments herein, the antibody may comprise a heavy chain comprising the amino acid sequence of SEQ ID NO:75; and/or a light chain comprising the amino acid sequence selected from SEQ ID NOs:76 or 77. In some embodiments, the human IgG4 comprises the amino acid substitution S228P, wherein the amino acid residues are numbered according to the EU index as in Kabat. In any of the embodiments herein, the antibody may comprise a heavy chain comprising the amino acid sequence of SEQ ID NO:87; and/or a light chain comprising the amino acid sequence of SEQ ID NO:76. In some embodiments, the antibody has been engineered to improve antibody-dependent cell-mediated cytotoxicity (ADCC) activity. In some embodiments, the antibody comprises two heavy chains and wherein at least one of the two or both heavy chains of the antibody is non-fucosylated.

[0011] ~~In another aspect, p~~Provided herein is a humanized antibody that specifically binds to a human Siglec-8, wherein the antibody has a Tm of at least about 70°C to at least about 72°C in a thermal shift assay. In one aspect, provided herein is a humanized antibody that binds to a human Siglec-8, wherein the antibody has a Tm of at least about 70°C in a thermal shift assay. In some embodiments, the antibody has a Tm at about 70°C, at about 71°C, or at about 72°C in a thermal shift assay. In some embodiments, the antibody has the same or higher Tm as compared to a chimeric 2C4 antibody. In some embodiments, the antibody has the same or higher Tm as compared to an antibody having a heavy chain comprising the amino acid sequence of SEQ ID NO:84 and a light chain comprising the amino acid sequence of SEQ ID NO:85.

[0012] In some embodiments, the antibody comprises a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO:61, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO:62, and (iii) HVR-H3 comprising the amino acid sequence of SEQ ID NO:63; and/or wherein the light chain variable region comprises (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO:64, (ii) HVR-L2 comprising the amino acid sequence of SEQ ID NO:65, and (iii) HVR-L3 comprising the amino acid sequence of SEQ ID NO:66. In some embodiments, the antibody comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:6; and/or a light chain variable region comprising the amino acid sequence selected from SEQ ID NOs:16 or 21. In any of the embodiments herein, the antibody may comprise a heavy chain Fc region comprising a human IgG Fc region. In further embodiments, the human IgG Fc region comprises a human IgG1 or IgG4. In some

embodiments, the human IgG1 comprises the amino acid sequence of SEQ ID NO:78. In some embodiments, the human IgG4 comprises the amino acid sequence of SEQ ID NO:79. In any of the embodiments herein, the antibody may comprise a heavy chain comprising the amino acid sequence of SEQ ID NO:75; and/or a light chain comprising the amino acid sequence selected from SEQ ID NOs:76 or 77. In some embodiments, the human IgG4 comprises the amino acid substitution S228P, wherein the amino acid residues are numbered according to the EU index as in Kabat. In any of the embodiments herein, the antibody may comprise a heavy chain comprising the amino acid sequence of SEQ ID NO:87; and/or a light chain comprising the amino acid sequence of SEQ ID NO:76. In some embodiments, the antibody has been engineered to improve antibody-dependent cell-mediated cytotoxicity (ADCC) activity. In some embodiments, at least one or two of the heavy chains of the antibody is non-fucosylated.

[0013] ~~In yet another aspect, p~~Provided herein is a humanized antibody that specifically binds to a human Siglec-8, wherein the antibody comprises a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO:61, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO:62, and (iii) HVR-H3 comprising the amino acid sequence selected from SEQ ID NOs:63 and 67-70; and/or wherein the light chain variable region comprises (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO:64, (ii) HVR-L2 comprising the amino acid sequence of SEQ ID NO:65, and (iii) HVR-L3 comprising the amino acid sequence of SEQ ID NO:66 or 71. In one aspect, provided herein is a humanized antibody that binds to human Siglec-8, wherein the antibody comprises: (a) a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO:61, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO:62, and (iii) HVR-H3 comprising the amino acid sequence selected from SEQ ID NOs:67-70; and/or wherein the light chain variable region comprises (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO:64, (ii) HVR-L2 comprising the amino acid sequence of SEQ ID NO:65, and (iii) HVR-L3 comprising the amino acid sequence of SEQ ID NO:71; or (b) a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO:61, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO:62, and (iii) HVR-H3 comprising the amino acid sequence of SEQ ID NO:63; and/or wherein the light chain variable region comprises (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO:64, (ii) HVR-L2 comprising the amino acid sequence of SEQ ID NO:65, and (iii) HVR-L3 comprising the amino acid sequence of SEQ ID NO:66. In some embodiments, the antibody comprises a heavy

chain variable region comprising the amino acid sequence selected from SEQ ID NOs:11-14; and/or a light chain variable region comprising the amino acid sequence selected from SEQ ID NOs:23-24. In some embodiments, the heavy chain variable region comprises (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO:61, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO:62, and (iii) HVR-H3 comprising the amino acid sequence selected from SEQ ID NO:63; and/or the light chain variable region comprises (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO:64, (ii) HVR-L2 comprising the amino acid sequence of SEQ ID NO:65, and (iii) HVR-L3 comprising the amino acid sequence of SEQ ID NO:66. In some embodiments, the antibody comprises a heavy chain variable region comprising the amino acid sequence selected from SEQ ID NO:6; and/or a light chain variable region comprising the amino acid sequence selected from SEQ ID NO:16 or 21. In any of the embodiments herein, the antibody may comprise a heavy chain Fc region comprising a human IgG Fc region. In further embodiments, the human IgG Fc region comprises a human IgG1 or IgG4. In some embodiments, the human IgG1 comprises the amino acid sequence of SEQ ID NO:78. In some embodiments, the human IgG4 comprises the amino acid sequence of SEQ ID NO:79. In some

embodiments, the human IgG4 comprises the amino acid substitution S228P, wherein the amino acid residues are numbered according to the EU index as in Kabat. In some embodiments, the antibody has been engineered to improve antibody-dependent cell-mediated cytotoxicity (ADCC) activity. In some embodiments, at least one or two of the heavy chains of the antibody is non-fucosylated.

[0014] In yet another aspect, provided herein is a humanized antibody that ~~specifically~~ binds to human Siglec-8, wherein the antibody comprises a heavy chain variable region comprising the amino acid sequence selected from SEQ ID NOs:2-14; and/or a light chain variable region comprising the amino acid sequence selected from SEQ ID NOs:16-24. In some embodiments, the antibody has been engineered to improve antibody-dependent cell-mediated cytotoxicity (ADCC) activity. In some embodiments, at least one or two of the heavy chains of the antibody is non-fucosylated.

[0015] ~~In yet another aspect, p~~Provided herein is a humanized antibody that specifically binds to human Siglec-8, wherein the antibody comprises a heavy chain variable region comprising the amino acid sequence selected from SEQ ID NOs:2-10; and/or a light chain variable region comprising the amino acid sequence selected from SEQ ID NOs:16-22. In some embodiments, the antibody has been engineered to improve antibody-dependent cell-mediated cytotoxicity (ADCC) activity. In some embodiments, at least one or two of the heavy chains of the antibody is non-fucosylated.

[0016] In another aspect, provided herein is a humanized antibody that ~~specifically~~ binds to a human Siglec-8, wherein the antibody comprises: ~~a heavy chain variable region and a light chain variable region, wherein~~ (a) ~~the~~ heavy chain variable region comprise~~s~~ing: (1) an HC-FR1 comprising the amino acid sequence selected from SEQ ID NOs:26-29; (2) an HVR-H1 comprising the amino acid sequence of SEQ ID NO:61; (3) an HC-FR2 comprising the amino acid sequence selected from SEQ ID NOs:31-36; (4) an HVR-H2 comprising the amino acid sequence of SEQ ID NO:62; (5) an HC-FR3 comprising the amino acid sequence selected from SEQ ID NOs:38-43; (6) an HVR-H3 comprising the amino acid sequence of SEQ ID NO:63; and (7) an HC-FR4 comprising the amino acid sequence selected from SEQ ID NOs:45-46, and/or (b) ~~the~~ a light chain variable region comprise~~s~~ing: (1) an ~~H~~LC-FR1 comprising the amino acid sequence selected from SEQ ID NOs:48-49; (2) an HVR-~~H~~L1 comprising the amino acid sequence of SEQ ID NO:64; (3) an ~~H~~LC-FR2 comprising the amino acid sequence selected from SEQ ID NOs:51-53; (4) an HVR-~~H~~L2 comprising the amino acid sequence of SEQ ID NO:65; (5) an ~~H~~LC-FR3 comprising the amino acid sequence selected from SEQ ID NOs:55-58; (6) an HVR-~~H~~L3 comprising the amino acid sequence of SEQ ID NO:66; and (7) an ~~H~~LC-FR4 comprising the amino acid sequence of SEQ ID NO:60. In some embodiments, the antibody has been

engineered to improve antibody-dependent cell-mediated cytotoxicity (ADCC) activity. In some embodiments, at least one or two of the heavy chains of the antibody is non-fucosylated.

[0017] ~~In yet another aspect, p~~Provided herein is an isolated antibody that binds a human Siglec-8 and kills mast cells expressing Siglec-8 by ADCC activity. In some embodiments, the antibody kills mast cells expressing Siglec-8 *in vitro* (e.g., measured in a cell culture assay as described in Example 2). In some embodiments, the antibody depletes mast cells expressing Siglec-8 in a subject when a therapeutically effective amount is administered. In a further embodiment, the antibody depletes at least about 20% (e.g. ,at least of the mast cells expressing Siglec-8 in a sample obtained from the subject as compared to a baseline level before treatment. In any of the embodiments herein, the sample can be a tissue sample or a biological fluid sample. In some embodiments, the tissue sample is one or more selected from the group consisting of: skin, lung, bone marrow, and nasal polyps. In some embodiments, the biological fluid sample is one or more selected from the group consisting of: blood, bronchoalveolar lavage, and nasal lavage. In any of the embodiments herein, the antibody can be engineered to improve antibody-dependent cell-mediated cytotoxicity (ADCC) activity. In some embodiments, at least one or two of the heavy chains of the antibody is non-fucosylated. In further embodiments, the antibody may be produced in a cell line having a alpha1,6-fucosyltransferase (Fut8) knockout. In some further embodiments, the antibody may be produced in a cell line overexpressing β1,4-N-acetylglycosminyltransferase III (GnT-III). In further embodiments, the cell line additionally overexpresses Golgi μ-mannosidase II (ManII). In any of the embodiments herein, the antibody may comprise at least one amino acid substitution in the Fc region that improves ADCC activity. In any of the embodiments herein, the antibody may be a humanized antibody, a chimeric antibody or a human antibody. In some embodiments, the antibody is a human IgG1 antibody. In some embodiments, the antibody is a murine antibody. In any of the embodiments herein, the antibody may comprise a heavy chain variable region comprising (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO:88, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO:91, and (iii) HVR-H3 comprising the amino acid sequence of SEQ ID NO:94; and/or a light chain variable region comprising (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO:97, (ii) HVR-L2 comprising the amino acid sequence of SEQ ID NO:100, and (iii) HVR-L3 comprising the amino acid sequence of SEQ ID NO:103. In a further embodiment, the antibody comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:106; and/or a light chain variable region comprising the amino acid sequence of SEQ ID NO:109. In any of the embodiments herein, the antibody may comprise a heavy chain variable region comprising a heavy chain variable region comprising (i) HVR-H1 comprising the amino acid sequence of

HVR-H1 comprising the amino acid sequence of SEQ ID NO:89, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO:92, and (iii) HVR-H3 comprising the amino acid sequence of SEQ ID NO:95; and/or a light chain variable region comprising (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO:98, (ii) HVR-L2 comprising the amino acid sequence of SEQ ID NO:101, and (iii) HVR-L3 comprising the amino acid sequence of SEQ ID NO:104. In a further embodiment, the antibody comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:107; and/or a light chain variable region comprising the amino acid sequence of SEQ ID NO:110. In any of the embodiments herein, the antibody may comprise a heavy chain variable region comprising a heavy chain variable region comprising a heavy chain variable region comprising (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO:90, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO:93, and (iii) HVR-H3 comprising the amino acid sequence of SEQ ID NO:96; and/or a light chain variable region comprising (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO:99, (ii) HVR-L2 comprising the amino acid sequence of SEQ ID NO:102, and (iii) HVR-L3 comprising the amino acid sequence of SEQ ID NO:105. In a further embodiment, the antibody comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:108; and/or a light chain variable region comprising the amino acid sequence of SEQ ID NO:111. In any of the embodiments herein, the antibody may bind to an epitope in Domain 1 of human Siglec-8 (e.g., Domain 1 that comprises the amino acid sequence of SEQ ID NO:112). In any of the embodiments herein, the antibody may bind to an epitope in Domain 3 of human Siglec-8 (e.g., Domain 3 that comprises the amino acid sequence of SEQ ID NO:114). In any of the embodiments herein, the antibody may bind to an epitope in Domain 2 of human Siglec-8 (e.g., Domain 2 that comprises the amino acid sequence of SEQ ID NO:113). In any of the embodiments herein, the antibody may be a humanized antibody, a chimeric antibody or a human antibody. In some embodiments, the antibody is a murine antibody. In some embodiments, the antibody is an IgG1 or IgG4 antibody (*e.g.*, human IgG1 or IgG4).

[0019] ~~In another aspect, p~~Provided herein is an anti-human Siglec 8 antibody that binds to a fusion protein comprising the amino acid of SEQ ID NO:116 but not to a fusion protein comprising the amino acid of SEQ ID NO:115. In some embodiments, the antibody described herein binds to a fusion protein comprising the amino acid of SEQ ID NO:117 but not to a fusion protein comprising the amino acid of SEQ ID NO:115. In some embodiments, the antibody described herein binds to a fusion protein comprising the amino acid of SEQ ID NO:117 but not to a fusion protein comprising the amino acid of SEQ ID NO:116. In some embodiments herein, the antibody may comprise a heavy chain variable region comprising (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO:88, (ii) HVR-H2 comprising the

amino acid sequence of SEQ ID NO:91, and (iii) HVR-H3 comprising the amino acid sequence of SEQ ID NO:94; and/or a light chain variable region comprising (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO:97, (ii) HVR-L2 comprising the amino acid sequence of SEQ ID NO:100, and (iii) HVR-L3 comprising the amino acid sequence of SEQ ID NO:103. In a further embodiment, the antibody comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:106; and/or a light chain variable region comprising the amino acid sequence of SEQ ID NO:109. In some embodiments herein, the antibody may comprise a heavy chain variable region comprising a heavy chain variable region comprising (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO:89, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO:92, and (iii) HVR-H3 comprising the amino acid sequence of SEQ ID NO:95; and/or a light chain variable region comprising (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO:98, (ii) HVR-L2 comprising the amino acid sequence of SEQ ID NO:101, and (iii) HVR-L3 comprising the amino acid sequence of SEQ ID NO:104. In a further embodiment, the antibody comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:107; and/or a light chain variable region comprising the amino acid sequence of SEQ ID NO:110. In some embodiments herein, the antibody may comprise a heavy chain variable region comprising a heavy chain variable region comprising a heavy chain variable region comprising (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO:90, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO:93, and (iii) HVR-H3 comprising the amino acid sequence of SEQ ID NO:96; and/or a light chain variable region comprising (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO:99, (ii) HVR-L2 comprising the amino acid sequence of SEQ ID NO:102, and (iii) HVR-L3 comprising the amino acid sequence of SEQ ID NO:105. In a further embodiment, the antibody comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:108; and/or a light chain variable region comprising the amino acid sequence of SEQ ID NO:111.

[0020] ~~In another aspect, p~~Provided herein is a humanized antibody that binds to a human Siglec-8, wherein the EC_{50} in depleting activated human eosinophils is less than the EC_{50} of antibody 2E2 or 2C4 to the human Siglec-8. In some embodiments, the EC_{50} of the humanized antibody is about 85% or less than the EC_{50} of antibody 2E2 or 2C4 to the human Siglec-8. In some embodiments, the EC_{50} of the humanized antibody is about 85%, about 80%, about 70%, about 65%, about 60%, about 55%, about 50%, about 45%, about 40%, about 35%, about 30%, about 25%, about 20%, about 15%, about 10% or about 5% or less than the EC_{50} of antibody 2E2 or 2C4 to the human Siglec-8. In any of the embodiments herein, the humanized antibody may comprise a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises (i) HVR-H1 comprising the amino acid sequence of SEQ ID

comprising the amino acid sequence of SEQ ID NO:99, (ii) HVR-L2 comprising the amino acid sequence of SEQ ID NO:102, and (iii) HVR-L3 comprising the amino acid sequence of SEQ ID NO:105. In any of the embodiments herein, the antibody may comprise a heavy chain Fc region comprising a human IgG Fc region. In further embodiments, the human IgG Fc region comprises a human IgG1 or IgG4. In some embodiments, the human IgG1 comprises the amino acid sequence of SEQ ID NO:78. In some embodiments, the human IgG4 comprises the amino acid sequence of SEQ ID NO:79. In any of the embodiments herein, the antibody may comprise a heavy chain comprising the amino acid sequence of SEQ ID NO:75; and/or a light chain comprising the amino acid sequence selected from SEQ ID NOs:76 or 77. In some embodiments, the human IgG4 comprises the amino acid substitution S228P, wherein the amino acid residues are numbered according to the EU index as in Kabat. In any of the embodiments herein, the antibody may comprise a heavy chain comprising the amino acid sequence of SEQ ID NO:87; and/or a light chain comprising the amino acid sequence of SEQ ID NO:76.

[0021] In another aspect, provided herein is a nucleic acid encoding any antibody described above and herein. In yet another aspect, provided herein is a vector comprising a nucleic acid described herein. In one embodiment, the vector is an expression vector. In yet another aspect, provided herein is a host cell comprising a nucleic acid described herein. In some embodiments, the host cell expresses and produces the antibody.

[0022] In another aspect, provided herein is a method of producing an antibody comprising culturing a host cell comprising one or more nucleic acids encoding an antibody described herein under a condition that produces the antibody. In some embodiments, the method further comprises recovering the antibody produced by the host cell. In one aspect, ~~Also~~ provided herein is an anti-Siglec-8 antibody produced by the method described herein. Also provided herein is an antigen-binding fragment of an anti-Siglec-8 antibody described herein.

[0023] In another aspect, provided herein is a pharmaceutical composition comprising an antibody described above and herein ~~or an antigen-binding fragment thereof~~ and a pharmaceutically acceptable carrier. In yet another aspect, provided herein is a kit comprising an antibody described above and herein or a composition described above and herein.

[0024] In another aspect, provided herein is a composition comprising an antibody ~~or fragment thereof~~ that specifically binds to human Siglec-8, wherein the antibody comprises a Fc region and N-glycoside-linked carbohydrate chains linked to the Fc region, wherein less than 50% of the N-glycoside-linked carbohydrate chains ~~in the composition~~ contain a fucose residue. In some embodiments, substantially none of the N-glycoside-linked carbohydrate chains contain a fucose residue. In some embodiments, the antibody is a humanized antibody, a chimeric antibody or a human antibody. In some embodiments, the antibody comprises a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region

comprises (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO:61, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO:62, and (iii) HVR-H3 comprising the amino acid sequence of SEQ ID NO:63; and/or wherein the light chain variable region comprises (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO:64, (ii) HVR-L2 comprising the amino acid sequence of SEQ ID NO:65, and (iii) HVR-L3 comprising the amino acid sequence of SEQ ID NO:66. In some embodiments, the antibody comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NOs:2-10; and/or a light chain variable region comprising the amino acid sequence of SEQ ID NOs:16-22. In some embodiments, the antibody comprises a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO:61, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO:62, and (iii) HVR-H3 comprising the amino acid sequence selected from SEQ ID NOs:67-70; and/or wherein the light chain variable region comprises (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO:64, (ii) HVR-L2 comprising the amino acid sequence of SEQ ID NO:65, and (iii) HVR-L3 comprising the amino acid sequence of SEQ ID NO:71. In some embodiments, the antibody comprises a heavy chain variable region comprising the amino acid sequence selected from SEQ ID NOs:11-14; and/or a light chain variable region comprising the amino acid sequence selected from SEQ ID NOs:23-24. In some embodiments, the antibody comprises a heavy chain variable region comprising the amino acid sequence selected from SEQ ID NOs:2-14; and/or a light chain variable region comprising the amino acid sequence selected from SEQ ID NOs:16-24. In any of the embodiments herein, the composition may further comprise a pharmaceutically acceptable carrier. In any of the embodiments herein, the binding affinity and/or binding avidity of the antibody to a human Siglec-8 can be higher than the binding affinity and/or binding avidity of antibody 2E2 or 2C4 to the human Siglec-8. In any of the embodiments herein, the antibody may have a Tm of at least about 70°C to at least about 72°C in a thermal shift assay. In some embodiments, the antibody has a Tm of about 70°C, about 71°C, or about 72°C. In some embodiments, the antibody has the same or higher Tm as compared to a chimeric 2C4 antibody. In some embodiments, the antibody has the same or higher Tm as compared to an antibody having a heavy chain comprising the amino acid sequence of SEQ ID NO:84 and a light chain comprising the amino acid sequence of SEQ ID NO:85.

[0025] ~~In another aspect, p~~Provided herein is a method of treating or preventing a disease mediated by cells expressing Siglec-8 in a subject, the method comprising administering to the subject an effective amount of an antibody described herein or an antigen-binding fragment thereof or a composition described herein. In one aspect, provided herein is an antibody described herein or a composition described herein for use in the treatment or prevention of a disease mediated by cells expressing Siglec-8 in a subject. In some embodiments, the disease is an eosinophil mediated-disease. In some embodiments, the disease is a mast cell mediated-disease. In some

embodiments, the disease is selected from the group consisting of asthma, allergic rhinitis, nasal polyposis, atopic dermatitis, chronic urticaria, mastocytosis, eosinophilic leukemia, and hypereosinophilic syndrome. In some embodiments, the disease is selected from the group consisting of pauci granulocytic asthma, acute or chronic airway hypersensitivity, eosinophilic esophagitis, Churg-Strauss syndrome, inflammation associated with a cytokine, inflammation associated with cells expressing Siglec-8, malignancy associated with cells expressing Siglec-8, physical urticaria, cold urticaria, pressure-urticaria, bullous pemphigoid, food allergy, and allergic bronchopulmonary aspergillosis (ABPA). In some embodiments, the antibody inhibits one or more symptoms of an allergic reaction. In some embodiments, the allergic reaction is a Type I hypersensitivity reaction. In any of the embodiments herein, the subject may be suffering from asthma that is not adequately controlled by an inhaled corticosteroid, a short acting β2 agonist, a long acting β2 agonist, or a combination thereof.

[0026] ~~In another aspect, p~~Provided herein is a method of depleting mast cells expressing Siglec-8 in a subject comprising administering to the subject an effective amount of an antibody that binds to human Siglec-8, wherein the antibody kills mast cells expressing Siglec-8 by ADCC activity. In one aspect, provided herein is an antibody that binds to human Siglec-8 for use in depleting mast cells expressing Siglec-8 in a subject, wherein the antibody kills mast cells expressing Siglec-8 by ADCC activity. In some embodiments, the antibody kills mast cells expressing Siglec-8 *in vitro* (e.g., measured in a cell culture assay as described in Example 2). In some embodiments, the antibody depletes at least about 20% of the mast cells expressing Siglec-8 in a sample obtained from the subject as compared to a baseline level before treatment. In any of the embodiments herein, the sample can be a tissue sample or a biological fluid sample. In some embodiments, the tissue sample is one or more selected from the group consisting of: skin, lung, bone marrow, and nasal polyps. In some embodiments, the biological fluid sample is one or more selected from the group consisting of: blood, bronchoalveolar lavage, and nasal lavage. In any of the embodiments herein, the antibody can be engineered to improve antibody-dependent cell-mediated cytotoxicity (ADCC) activity. In any of the embodiments herein, the antibody may comprise two heavy chains and wherein at least one of the two or both heavy chains of the antibody is non-fucosylated. In further embodiments, the antibody may be produced in a cell line having a alpha1,6-fucosyltransferase (Fut8) knockout. In some further embodiments, the antibody may be produced in a cell line overexpressing β1,4-N-acetylglycosminyltransferase III (GnT-III). In further embodiments, the cell line additionally overexpresses Golgi μ-mannosidase II (ManII). In any of the embodiments herein, the antibody may comprise at least one amino acid substitution in the Fc region that improves ADCC activity. In any of the embodiments herein, the antibody may be a humanized antibody, a chimeric antibody or a human antibody. In some embodiments, the antibody is a human IgG1 antibody. In any of the embodiments herein, the antibody may comprise a heavy chain variable region comprising (i)

comprising the amino acid sequence of SEQ ID NO:61, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO:62, and (iii) HVR-H3 comprising the amino acid sequence selected from SEQ ID NOs:67-70; and/or wherein the light chain variable region comprises (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO:64, (ii) HVR-L2 comprising the amino acid sequence of SEQ ID NO:65, and (iii) HVR-L3 comprising the amino acid sequence of SEQ ID NO:71. In any of the embodiments herein, the subject has a disease mediated by cells expressing Siglec-8. In some embodiments, the disease is selected from the group consisting of asthma, allergic rhinitis, nasal polyposis, atopic dermatitis, chronic urticaria, mastocytosis, eosinophilic leukemia, and hypereosinophilic syndrome. In some embodiments, the disease is selected from the group consisting of pauci granulocytic asthma, acute or chronic airway hypersensitivity, eosinophilic esophagitis, Churg-Strauss syndrome, inflammation associated with a cytokine, inflammation associated with cells expressing Siglec-8, malignancy associated with cells expressing Siglec-8, physical urticaria, cold urticaria, pressure-urticaria, bullous pemphigoid, food allergy, and allergic bronchopulmonary aspergillosis (ABPA). In some embodiments, the antibody inhibits one or more symptoms of an allergic reaction. In some embodiments, the allergic reaction is a Type I hypersensitivity reaction. In any of the embodiments herein, the subject may be suffering from asthma that is not adequately controlled by an inhaled corticosteroid, a short acting β2 agonist, a long acting β2 agonist, or a combination thereof. In any of the embodiments herein, the subject can be a human.

[0027] It is to be understood that one, some, or all of the properties of the various embodiments described herein may be combined to form other embodiments of the present ~~invention~~disclosure. These and other aspects of the invention will become apparent to one of skill in the art. These and other embodiments of the ~~invention~~ disclosure are further described by the detailed description that follows.

BRIEF DESCRIPTION OF THE DRAWINGS

[0028] **FIG. 1** is a sequence alignment showing the comparison of heavy chain sequences of humanized antibodies. Framework residues within 4Å of the CDRs in the molecular model of mouse 2E2 antibody are represented by a *; residues within 4Å of the CDRs and VCI residues that were different in the acceptor human framework are highlighted in ^, back-mutations of these residues in the acceptor human framework to mouse are indicated by @; Somatic mutations from human germline are indicated by °; if those residues were different from the AF471521 FW and mou2E2 (*i.e.*, mouse 2E2) or different from the AF471521 framework and identical to the mou2E2 (*i.e.*, mouse 2E2) the corresponding residues in the acceptor human framework were back-mutated to human germline and are indicated by +. Sequences highlighted

CLAIMS

WHAT IS CLAIMED IS:

1. A humanized antibody that binds to a human Siglec-8, wherein the binding affinity or avidity of the humanized antibody to the human Siglec-8 is higher than the binding affinity or avidity of antibody 2E2 or 2C4 to the human Siglec-8.

2. A humanized antibody that binds to a human Siglec-8, wherein the antibody has a Tm of at least about 70°C in a thermal shift assay.

3. The antibody of claim 2, wherein the antibody has a Tm of at least about 70°C to at least about 72°C in a thermal shift assay.

4. The antibody of any one of claims 1-3, wherein the antibody comprises a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO:61, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO:62, and (iii) HVR-H3 comprising the amino acid sequence of SEQ ID NO:63; and/or wherein the light chain variable region comprises (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO:64, (ii) HVR-L2 comprising the amino acid sequence of SEQ ID NO:65, and (iii) HVR-L3 comprising the amino acid sequence of SEQ ID NO:66.

5. The antibody of any one of claims 1-4, wherein the antibody comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:6; and/or a light chain variable region comprising the amino acid sequence selected from SEQ ID NOs:16 or 21.

6. The antibody of any one of claims 1-5, wherein the antibody comprises a heavy chain Fc region comprising a human IgG Fc region.

7. The antibody of claim 6, wherein the human IgG Fc region comprises a human IgG1 or a human IgG4.

8. The antibody of claim 7, wherein the human IgG4 comprises the amino acid substitution S228P, and wherein the amino acid residues are numbered according to the EU index as in Kabat.

9. The antibody of any one of claims 1-7, wherein the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:75; and/or a light chain comprising the amino acid sequence selected from SEQ ID NOs:76 or 77.

10. The antibody of any one of claims 1-7, wherein the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:87; and/or a light chain comprising the amino acid sequence of SEQ ID NO:76.

11. The antibody of any one of claims 1-9, wherein the antibody has been engineered to improve antibody-dependent cell-mediated cytotoxicity (ADCC) activity.

12. The antibody of any one of claims 1-11, wherein at least one or two of the heavy chains of the antibody is non-fucosylated.

13. A humanized antibody that binds to human Siglec-8, wherein the antibody comprises:

(a) a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO:61, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO:62, and (iii) HVR-H3 comprising the amino acid sequence selected from SEQ ID NOs:67-70; and/or wherein the light chain variable region comprises (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO:64, (ii) HVR-L2 comprising the amino acid sequence of SEQ ID NO:65, and (iii) HVR-L3 comprising the amino acid sequence of SEQ ID NO:71; or

(b) a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO:61, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO:62, and (iii) HVR-H3 comprising the amino acid sequence of SEQ ID NO:63; and/or wherein the light chain variable region comprises (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO:64, (ii) HVR-L2 comprising the amino acid sequence of SEQ ID NO:65, and (iii) HVR-L3 comprising the amino acid sequence of SEQ ID NO:66.

14. The antibody of claim 13, wherein the antibody comprises a heavy chain variable region comprising the amino acid sequence selected from SEQ ID NOs:11-14; and/or a light chain variable region comprising the amino acid sequence selected from SEQ ID NOs:23-24.

15. A humanized antibody that binds to a human Siglec-8, wherein the antibody comprises a heavy chain variable region comprising the amino acid sequence selected from SEQ ID NOs:2-14; and/or a light chain variable region comprising the amino acid sequence selected from SEQ ID NOs:16-24.

16. A humanized antibody that binds to a human Siglec-8, wherein the antibody comprises a heavy chain variable region comprising the amino acid sequence selected from SEQ ID NOs:2-10; and/or a light chain variable region comprising the amino acid sequence selected from SEQ ID NOs:16-22.

17. A humanized antibody that binds to a human Siglec-8, wherein the antibody comprises:
(a) heavy chain variable region comprising:
(1) an HC-FR1 comprising the amino acid sequence selected from SEQ ID NOs:26-29;
(2) an HVR-H1 comprising the amino acid sequence of SEQ ID NO:61;
(3) an HC-FR2 comprising the amino acid sequence selected from SEQ ID NOs:31-36;
(4) an HVR-H2 comprising the amino acid sequence of SEQ ID NO:62;
(5) an HC-FR3 comprising the amino acid sequence selected from SEQ ID NOs:38-43;
(6) an HVR-H3 comprising the amino acid sequence of SEQ ID NO:63; and
(7) an HC-FR4 comprising the amino acid sequence selected from SEQ ID NOs:45-46, and/or
(b) a light chain variable region comprising:
(1) an LC-FR1 comprising the amino acid sequence selected from SEQ ID NOs:48-49;
(2) an HVR-L1 comprising the amino acid sequence of SEQ ID NO:64;
(3) an LC-FR2 comprising the amino acid sequence selected from SEQ ID NOs:51-53;
(4) an HVR-L2 comprising the amino acid sequence of SEQ ID NO:65;
(5) an LC-FR3 comprising the amino acid sequence selected from SEQ ID NOs:55-58;
(6) an HVR-L3 comprising the amino acid sequence of SEQ ID NO:66; and
(7) an LC-FR4 comprising the amino acid sequence of SEQ ID NO:60.

18. The humanized antibody of claim 17, wherein the antibody comprises:
(a) heavy chain variable region comprising:
(1) an HC-FR1 comprising the amino acid sequence of SEQ ID NO:26;
(2) an HVR-H1 comprising the amino acid sequence of SEQ ID NO:61;
(3) an HC-FR2 comprising the amino acid sequence of SEQ ID NO:34;
(4) an HVR-H2 comprising the amino acid sequence of SEQ ID NO:62;
(5) an HC-FR3 comprising the amino acid sequence of SEQ ID NO:38;

(6) an HVR-H3 comprising the amino acid sequence of SEQ ID NO:63; and

(7) an HC-FR4 comprising the amino acid sequence of SEQ ID NOs:45;

and/or

(b) a light chain variable region comprising:

(1) an LC-FR1 comprising the amino acid sequence of SEQ ID NO:48;

(2) an HVR-L1 comprising the amino acid sequence of SEQ ID NO:64;

(3) an LC-FR2 comprising the amino acid sequence of SEQ ID NO:51;

(4) an HVR-L2 comprising the amino acid sequence of SEQ ID NO:65;

(5) an LC-FR3 comprising the amino acid sequence of SEQ ID NO:55;

(6) an HVR-L3 comprising the amino acid sequence of SEQ ID NO:66; and

(7) an LC-FR4 comprising the amino acid sequence of SEQ ID NO:60.

19. The humanized antibody of claim 17, wherein the antibody comprises:

(a) heavy chain variable region comprising:

(1) an HC-FR1 comprising the amino acid sequence of SEQ ID NO:26;

(2) an HVR-H1 comprising the amino acid sequence of SEQ ID NO:61;

(3) an HC-FR2 comprising the amino acid sequence of SEQ ID NO:34;

(4) an HVR-H2 comprising the amino acid sequence of SEQ ID NO:62;

(5) an HC-FR3 comprising the amino acid sequence of SEQ ID NO:38;

(6) an HVR-H3 comprising the amino acid sequence of SEQ ID NO:63; and

(7) an HC-FR4 comprising the amino acid sequence of SEQ ID NOs:45;

and/or

(b) a light chain variable region comprising:

(1) an LC-FR1 comprising the amino acid sequence of SEQ ID NO:48;

(2) an HVR-L1 comprising the amino acid sequence of SEQ ID NO:64;

(3) an LC-FR2 comprising the amino acid sequence of SEQ ID NO:51;

(4) an HVR-L2 comprising the amino acid sequence of SEQ ID NO:65;

(5) an LC-FR3 comprising the amino acid sequence of SEQ ID NO:58;

(6) an HVR-L3 comprising the amino acid sequence of SEQ ID NO:66; and

(7) an LC-FR4 comprising the amino acid sequence of SEQ ID NO:60.

20. The antibody of any one of claims 13-19, wherein the antibody has been engineered to improve antibody-dependent cell-mediated cytotoxicity (ADCC) activity.

21. The antibody of any one of claims 13-20, wherein at least one or two of the heavy chains of the antibody is non-fucosylated.

22. A nucleic acid encoding the antibody of any one of claims 1-21.

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

24. The vector of claim 23, which is an expression vector.

25. A host cell comprising the nucleic acid of claim 22.

26. A method of producing an antibody comprising culturing the host cell of claim 25 under a condition that produces the antibody.

27. The method of claim 26, further comprising recovering the antibody produced by the host cell.

28. An anti-Siglec-8 antibody produced by the method of claim 26 or 27.

29. A pharmaceutical composition comprising the antibody of any one of claims 1-21 and 28 and a pharmaceutically acceptable carrier.

30. A composition comprising an antibody that specifically binds to human Siglec-8, wherein the antibody comprises a Fc region and N-glycoside-linked carbohydrate chains linked to the Fc region, wherein less than 50% of the N-glycoside-linked carbohydrate chains contain a fucose residue.

31. The composition of claim 30, wherein substantially none of the N-glycoside-linked carbohydrate chains contain a fucose residue.

32. The composition of claim 30 or 31, wherein the antibody is a humanized antibody, a chimeric antibody or a human antibody.

33. The composition of any one of claims 30-32, wherein the antibody comprises a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO:61, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO:62, and (iii) HVR-H3 comprising the amino acid sequence of SEQ ID NO:63; and/or wherein the light chain variable region comprises (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO:64, (ii) HVR-L2 comprising the amino acid sequence of SEQ ID NO:65, and (iii) HVR-L3 comprising the amino acid sequence of SEQ ID NO:66.

34. The composition of claim 33, wherein the antibody comprises a heavy chain variable region comprising the amino acid sequence selected from SEQ ID NOs:2-10; and/or a light chain variable region comprising the amino acid sequence selected from SEQ ID NOs:16-22.

35. The composition of any one of claims 30-32, wherein the antibody comprises a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO:61, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO:62, and (iii) HVR-H3 comprising the amino acid sequence selected from SEQ ID NOs:67-70; and/or wherein the light chain variable region comprises (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO:64, (ii) HVR-L2 comprising the amino acid sequence of SEQ ID NO:65, and (iii) HVR-L3 comprising the amino acid sequence of SEQ ID NO:71.

36. The composition of claim 35, wherein the antibody comprises a heavy chain variable region comprising the amino acid sequence selected from SEQ ID NOs:11-14; and/or a light chain variable region comprising the amino acid sequence selected from SEQ ID NOs:23-24.

37. The composition of any one of claims 30-32, wherein the antibody comprises a heavy chain variable region comprising the amino acid sequence selected from SEQ ID NOs:2-14; and/or a light chain variable region comprising the amino acid sequence selected from SEQ ID NOs:16-24.

38. The composition of any one of claims 30-37, further comprising a pharmaceutically acceptable carrier.

39. The composition of any one of claims 30-38, wherein the binding affinity or avidity of the antibody to a human Siglec-8 is higher than the binding affinity or avidity of antibody 2E2 or 2C4 to the human Siglec-8.

40. The composition of any one of claims 30-39, wherein the antibody has a Tm of at least about 70°C in a thermal shift assay.

41. The composition of claim 40, wherein the antibody has a Tm of at least about 70°C to at least about 72°C in a thermal shift assay.

42. An isolated antibody that binds a human Siglec-8 and kills mast cells expressing Siglec-8 by ADCC activity.

43. The antibody of claim 42, wherein the antibody depletes mast cells expressing Siglec-8 in a subject when a therapeutically effective amount is administered.

44. The antibody of claim 43, wherein the antibody depletes at least about 20% of the mast cells expressing Siglec-8 in a sample obtained from the subject as compared to a baseline level before treatment.

45. The antibody of claim 44, wherein the sample is a tissue sample or a biological fluid sample.

46. The antibody of claim 45, wherein the tissue sample is one or more selected from the group consisting of: skin, lung, bone marrow, and nasal polyps.

47. The antibody of claim 45, wherein the biological fluid sample is one or more selected from the group consisting of: blood, bronchoalveolar lavage, and nasal lavage.

48. The antibody of any one of claims 42-47, wherein the antibody has been engineered to improve antibody-dependent cell-mediated cytotoxicity (ADCC) activity.

49. The antibody of any one of claims 42-48, wherein at least one or two of the heavy chains of the antibody is non-fucosylated.

50. The antibody of claim 49, wherein the antibody is produced in a cell line having a alpha1,6-fucosyltransferase (Fut8) knockout.

51. The antibody of claim 49, wherein the antibody is produced in a cell line overexpressing β1,4-N-acetylglycosminyltransferase III (GnT-III).

52. The antibody of claim 51, wherein the cell line additionally overexpresses Golgi μ-mannosidase II (ManII).

53. The antibody of claim 48, wherein the antibody comprises at least one amino acid substitution in the Fc region that improves ADCC activity.

54. The antibody of any one of claims 42-53, wherein the antibody is a humanized antibody, a chimeric antibody or a human antibody.

55. The antibody of any one of claims 42-54, wherein the antibody is a human IgG1 antibody.

56. The antibody of any one of claims 42-53, wherein the antibody is a murine antibody.

57. The antibody of any one of claims 42-56, wherein the antibody comprises:

(a) a heavy chain variable region comprising (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO:88, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO:91, and (iii) HVR-H3 comprising the amino acid sequence of SEQ ID NO:94; and/or a light chain variable region comprising (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO:97, (ii) HVR-L2 comprising the amino acid sequence of SEQ ID NO:100, and (iii) HVR-L3 comprising the amino acid sequence of SEQ ID NO:103.

(b) a heavy chain variable region comprising (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO:89, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO:92, and (iii) HVR-H3 comprising the amino acid sequence of SEQ ID NO:95; and/or a light chain variable region comprising (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO:98, (ii) HVR-L2 comprising the amino acid sequence of SEQ ID NO:101, and (iii) HVR-L3 comprising the amino acid sequence of SEQ ID NO:104.

(c) a heavy chain variable region comprising (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO:90, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO:93, and (iii) HVR-H3 comprising the amino acid sequence of SEQ ID NO:96; and/or a light chain variable region comprising (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO:99, (ii) HVR-L2 comprising the amino acid sequence of SEQ ID NO:102, and (iii) HVR-L3 comprising the amino acid sequence of SEQ ID NO:105.

58. The antibody of claim 57, wherein the antibody comprises:

(a) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:106; and/or a light chain variable region comprising the amino acid sequence of SEQ ID NO:109.

(b) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:107; and/or a light chain variable region comprising the amino acid sequence of SEQ ID NO:110.

(c) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:108; and/or a light chain variable region comprising the amino acid sequence of SEQ ID NO:111.

59. The antibody of any one of claims 42-56, wherein the antibody comprises a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO:61, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO:62, and (iii) HVR-H3 comprising the amino acid sequence of SEQ ID NO:63; and/or wherein the light chain variable region comprises (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO:64, (ii) HVR-L2 comprising the amino acid sequence of SEQ ID NO:65, and (iii) HVR-L3 comprising the amino acid sequence of SEQ ID NO:66.

60. The antibody of any one of claims 42-56, wherein the antibody comprises a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO:61, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO:62, and (iii) HVR-H3 comprising the amino acid sequence selected from SEQ ID NOs:67-70; and/or wherein the light chain variable region comprises (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO:64, (ii) HVR-L2 comprising the amino acid sequence of SEQ ID NO:65, and (iii) HVR-L3 comprising the amino acid sequence of SEQ ID NO:71.

61. An antibody that binds to a human Siglec-8 and a non-human primate Siglec-8.

62. The antibody of claim 61, wherein the non-human primate is a baboon.

63. The antibody of claim 61 or 62, wherein the antibody comprises:

(a) a heavy chain variable region comprising (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO:89, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO:92, and (iii) HVR-H3 comprising the amino acid sequence of SEQ ID NO:95; and/or a light chain variable region comprising (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO:98, (ii) HVR-L2 comprising

the amino acid sequence of SEQ ID NO:101, and (iii) HVR-L3 comprising the amino acid sequence of SEQ ID NO:104.

(b) a heavy chain variable region comprising (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO:90, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO:93, and (iii) HVR-H3 comprising the amino acid sequence of SEQ ID NO:96; and/or a light chain variable region comprising (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO:99, (ii) HVR-L2 comprising the amino acid sequence of SEQ ID NO:102, and (iii) HVR-L3 comprising the amino acid sequence of SEQ ID NO:105.

64. The antibody of any one of claims 61-63, wherein the antibody binds to an epitope in Domain 1 of human Siglec-8, wherein Domain 1 comprises the amino acid sequence of SEQ ID NO:112.

65. The antibody of any one of claims 61-63, wherein the antibody binds to an epitope in Domain 3 of human Siglec-8, wherein Domain 3 comprises the amino acid sequence of SEQ ID NO:114.

66. The antibody of any one of claims 61-65, wherein the antibody is a humanized antibody, a chimeric antibody or a human antibody.

67. The antibody of any one of claims 61-66, wherein the antibody is a murine antibody.

68. The antibody of any one of claims 61-67, wherein the antibody is an IgG1 antibody.

69. The antibody of any one of claims 43-60, wherein the subject is a human.

70. A nucleic acid encoding the antibody of any one of claims 42-69.

71. A vector comprising the nucleic acid of claim 70.

72. The vector of claim 71, which is an expression vector.

73. A host cell comprising the nucleic acid of claim 70.

74. A method of producing an antibody comprising culturing the host cell of claim 73 under a condition that produces the antibody.

75. The method of claim 74, further comprising recovering the antibody produced by the host cell.

76. An anti-Siglec-8 antibody produced by the method of claim 74 or 75.

77. A method of treating or preventing a disease mediated by cells expressing Siglec-8 in a subject, the method comprising administering to the subject an effective amount of the antibody of any one of claims 1-22, 28, 42-69 and 76 or the composition of any one of claims 30-41.

78. The method of claim 77, wherein the disease is an eosinophil mediated-disease.

79. The method of claim 77, wherein the disease is a mast cell mediated-disease.

80. The method of claim 77, wherein the antibody inhibits one or more symptoms of an allergic reaction.

81. The method of claim 80, wherein the allergic reaction is a Type I hypersensitivity reaction.

82. The method of claim 77, wherein the disease is selected from the group consisting of: asthma, allergic rhinitis, nasal polyposis, atopic dermatitis, chronic urticaria, mastocytosis, eosinophilic leukemia, and hypereosinophilic syndrome.

83. The method of claim 77, wherein the disease is selected from the group consisting of: pauci granulocytic asthma, acute or chronic airway hypersensitivity, eosinophilic esophagitis, Churg-Strauss syndrome, inflammation associated with a cytokine, inflammation associated with cells expressing Siglec-8, malignancy associated with cells expressing Siglec-8, physical urticaria, cold urticaria, pressure-urticaria, bullous pemphigoid, food allergy, and allergic bronchopulmonary aspergillosis (ABPA).

84. The method of any one of claims 74-83, wherein the subject is suffering from asthma that is not adequately controlled by an inhaled corticosteroid, a short acting β2 agonist, a long acting β2 agonist, or a combination thereof.

85. A method of depleting mast cells expressing Siglec-8 in a subject comprising administering to the subject an effective amount of an antibody that binds to human Siglec-8, wherein the antibody kills mast cells expressing Siglec-8 by ADCC activity.

86. The method of claim 85, wherein the antibody depletes at least about 20% of the mast cells expressing Siglec-8 in a sample obtained from the subject as compared to a baseline level before treatment.

87. The method of claim 86, wherein the sample is a tissue sample or a biological fluid sample.

88. The method of claim 87, wherein the tissue sample is one or more selected from the group consisting of: skin, lung, bone marrow, and nasal polyps.

89. The method of claim 87, wherein the biological fluid sample is one or more selected from the group consisting of: blood, bronchoalveolar lavage, and nasal lavage.

90. The method of any one of claims 85-89, wherein the antibody has been engineered to improve antibody-dependent cell-mediated cytotoxicity (ADCC) activity.

91. The method of any one of claims 85-90, wherein at least one or two of the heavy chains of the antibody is non-fucosylated.

92. The method of claim 91, wherein the antibody is produced in a cell line having a alpha1,6-fucosyltransferase (Fut8) knockout.

93. The method of claim 91, wherein the antibody is produced in a cell line overexpressing β1,4-N-acetylglycosminyltransferase III (GnT-III).

94. The method of claim 93, wherein the cell line additionally overexpresses Golgi μ-mannosidase II (ManII).

95. The method of claim 90, wherein the antibody comprises at least one amino acid substitution in the Fc region that improves ADCC activity.

96. The method of any one of claims 85-95, wherein the antibody is a humanized antibody, a chimeric antibody or a human antibody.

97. The method of any one of claims 85-96, wherein the antibody is a human IgG1 antibody.

98. The method of any one of claims 85-97, wherein the antibody comprises:

(a) a heavy chain variable region comprising (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO:88, (ii) HVR-H2 comprising the amino acid sequence of

SEQ ID NO:91, and (iii) HVR-H3 comprising the amino acid sequence of SEQ ID NO:94; and/or a light chain variable region comprising (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO:97, (ii) HVR-L2 comprising the amino acid sequence of SEQ ID NO:100, and (iii) HVR-L3 comprising the amino acid sequence of SEQ ID NO:103.

(b) a heavy chain variable region comprising (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO:89, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO:92, and (iii) HVR-H3 comprising the amino acid sequence of SEQ ID NO:95; and/or a light chain variable region comprising (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO:98, (ii) HVR-L2 comprising the amino acid sequence of SEQ ID NO:10

(c) a heavy chain variable region comprising (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO:90, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO:93, and (iii) HVR-H3 comprising the amino acid sequence of SEQ ID NO:96; and/or a light chain variable region comprising (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO:99, (ii) HVR-L2 comprising the amino acid sequence of SEQ ID NO:102, and (iii) HVR-L3 comprising the amino acid sequence of SEQ ID NO:105.

99. The method of claim 98, wherein the antibody comprises:

(a) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:106; and/or a light chain variable region comprising the amino acid sequence of SEQ ID NO:109.

(b) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:107; and/or a light chain variable region comprising the amino acid sequence of SEQ ID NO:110.

(c) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:108; and/or a light chain variable region comprising the amino acid sequence of SEQ ID NO:111.

100. The method of any one of claims 85-97, wherein the antibody comprises a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO:61, (ii)

HVR-H2 comprising the amino acid sequence of SEQ ID NO:62, and (iii) HVR-H3 comprising the amino acid sequence of SEQ ID NO:63; and/or wherein the light chain variable region comprises (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO:64, (ii) HVR-L2 comprising the amino acid sequence of SEQ ID NO:65, and (iii) HVR-L3 comprising the amino acid sequence of SEQ ID NO:66.

101. The method of any one of claims 85-97, wherein the antibody comprises a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO:61, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO:62, and (iii) HVR-H3 comprising the amino acid sequence selected from SEQ ID NOs:67-70; and/or wherein the light chain variable region comprises (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO:64, (ii) HVR-L2 comprising the amino acid sequence of SEQ ID NO:65, and (iii) HVR-L3 comprising the amino acid sequence of SEQ ID NO:71.

102. The method of any one of claims 85-101, wherein the subject has a disease mediated by cells expressing Siglec-8.

103. The method of any one of claims 85-102, wherein the antibody inhibits one or more symptoms of an allergic reaction.

104. The method of claim 103, wherein the allergic reaction is a Type I hypersensitivity reaction.

105. The method of claim 102, wherein the disease is selected from the group consisting of: asthma, allergic rhinitis, nasal polyposis, atopic dermatitis, chronic urticaria, mastocytosis, eosinophilic leukemia, and hypereosinophilic syndrome.

106. The method of claim 102, wherein the disease is selected from the group consisting of: pauci granulocytic asthma, acute or chronic airway hypersensitivity, eosinophilic esophagitis, Churg-Strauss syndrome, inflammation associated with a cytokine, inflammation associated with cells expressing Siglec-8, malignancy associated with cells expressing Siglec-8, physical urticaria, cold urticaria, pressure-urticaria, bullous pemphigoid, food allergy, and allergic bronchopulmonary aspergillosis (ABPA).

107. The method of any one of claims 85-106, wherein the subject is suffering from asthma that is not adequately controlled by an inhaled corticosteroid, a short acting β2 agonist, a long acting β2 agonist, or a combination thereof.

108. A pharmaceutical composition comprising the antibody of any one of claims 42-69 and 76 and a pharmaceutically acceptable carrier.

109. A kit comprising the antibody of any one of claims 1-22, 28, 42-69 and 76 or the composition of any one of claims 30-41.

CLAIMS

WHAT IS CLAIMED IS:

1. A humanized antibody that binds to a human Siglec-8, wherein the binding affinity or avidity of the humanized antibody to the human Siglec-8 is higher than the binding affinity or avidity of antibody 2E2 or 2C4 to the human Siglec-8.

2. A humanized antibody that binds to a human Siglec-8, wherein the antibody has a Tm of at least about 70°C in a thermal shift assay.

3. The antibody of claim 2, wherein the antibody has a Tm of at least about 70°C to at least about 72°C in a thermal shift assay.

4. The antibody of any one of claims 1-3, wherein the antibody comprises a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO:61, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO:62, and (iii) HVR-H3 comprising the amino acid sequence of SEQ ID NO:63; and/or wherein the light chain variable region comprises (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO:64, (ii) HVR-L2 comprising the amino acid sequence of SEQ ID NO:65, and (iii) HVR-L3 comprising the amino acid sequence of SEQ ID NO:66.

5. The antibody of any one of claims 1-4, wherein the antibody comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:6; and/or a light chain variable region comprising the amino acid sequence selected from SEQ ID NOs:16 or 21.

6. The antibody of any one of claims 1-5, wherein the antibody comprises a heavy chain Fc region comprising a human IgG Fc region.

7. The antibody of claim 6, wherein the human IgG Fc region comprises a human IgG1 or a human IgG4.

8. The antibody of claim 7, wherein the human IgG4 comprises the amino acid substitution S228P, and wherein the amino acid residues are numbered according to the EU index as in Kabat.

9. The antibody of any one of claims 1-7, wherein the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:75; and/or a light chain comprising the amino acid sequence selected from SEQ ID NOs:76 or 77.

10. The antibody of any one of claims 1-8, wherein the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:87; and/or a light chain comprising the amino acid sequence of SEQ ID NO:76.

11. A humanized antibody that binds to human Siglec-8, wherein the antibody comprises:

(a) a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO:61, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO:62, and (iii) HVR-H3 comprising the amino acid sequence selected from SEQ ID NOs:67-70; and/or wherein the light chain variable region comprises (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO:64, (ii) HVR-L2 comprising the amino acid sequence of SEQ ID NO:65, and (iii) HVR-L3 comprising the amino acid sequence of SEQ ID NO:71; or

(b) a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO:61, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO:62, and (iii) HVR-H3 comprising the amino acid sequence of SEQ ID NO:63; and/or wherein the light chain variable region comprises (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO:64, (ii) HVR-L2 comprising the amino acid sequence of SEQ ID NO:65, and (iii) HVR-L3 comprising the amino acid sequence of SEQ ID NO:66.

12. The antibody of claim 11, wherein the antibody comprises a heavy chain variable region comprising the amino acid sequence selected from SEQ ID NOs:11-14; and/or a light chain variable region comprising the amino acid sequence selected from SEQ ID NOs:23-24.

13. A humanized antibody that binds to a human Siglec-8, wherein the antibody comprises a heavy chain variable region comprising the amino acid sequence selected from SEQ ID NOs:2-14; and/or a light chain variable region comprising the amino acid sequence selected from SEQ ID NOs:16-24.

14. A humanized antibody that binds to a human Siglec-8, wherein the antibody comprises:

(a) heavy chain variable region comprising:

(1) an HC-FR1 comprising the amino acid sequence selected from SEQ ID NOs:26-29;

(2) an HVR-H1 comprising the amino acid sequence of SEQ ID NO:61;

(3) an HC-FR2 comprising the amino acid sequence selected from SEQ ID NOs:31-36;

(4) an HVR-H2 comprising the amino acid sequence of SEQ ID NO:62;

(5) an HC-FR3 comprising the amino acid sequence selected from SEQ ID NOs:38-43;

(6) an HVR-H3 comprising the amino acid sequence of SEQ ID NO:63; and

(7) an HC-FR4 comprising the amino acid sequence selected from SEQ ID NOs:45-46, and/or

(b) a light chain variable region comprising:

(1) an LC-FR1 comprising the amino acid sequence selected from SEQ ID NOs:48-49;

(2) an HVR-L1 comprising the amino acid sequence of SEQ ID NO:64;

(3) an LC-FR2 comprising the amino acid sequence selected from SEQ ID NOs:51-53;

(4) an HVR-L2 comprising the amino acid sequence of SEQ ID NO:65;

(5) an LC-FR3 comprising the amino acid sequence selected from SEQ ID NOs:55-58;

(6) an HVR-L3 comprising the amino acid sequence of SEQ ID NO:66; and

(7) an LC-FR4 comprising the amino acid sequence of SEQ ID NO:60.

15. The humanized antibody of claim 14, wherein the antibody comprises:

(a) heavy chain variable region comprising:

(1) an HC-FR1 comprising the amino acid sequence of SEQ ID NO:26;

(2) an HVR-H1 comprising the amino acid sequence of SEQ ID NO:61;

(3) an HC-FR2 comprising the amino acid sequence of SEQ ID NO:34;

(4) an HVR-H2 comprising the amino acid sequence of SEQ ID NO:62;

(5) an HC-FR3 comprising the amino acid sequence of SEQ ID NO:38;

(6) an HVR-H3 comprising the amino acid sequence of SEQ ID NO:63; and

(7) an HC-FR4 comprising the amino acid sequence of SEQ ID NOs:45;

and/or

(b) a light chain variable region comprising:

(1) an LC-FR1 comprising the amino acid sequence of SEQ ID NO:48;

(2) an HVR-L1 comprising the amino acid sequence of SEQ ID NO:64;

(3) an LC-FR2 comprising the amino acid sequence of SEQ ID NO:51;

(4) an HVR-L2 comprising the amino acid sequence of SEQ ID NO:65;

(5) an LC-FR3 comprising the amino acid sequence of SEQ ID NO:55;

(6) an HVR-L3 comprising the amino acid sequence of SEQ ID NO:66; and

(7) an LC-FR4 comprising the amino acid sequence of SEQ ID NO:60.

16. The humanized antibody of claim 14, wherein the antibody comprises:

(a) heavy chain variable region comprising:

(1) an HC-FR1 comprising the amino acid sequence of SEQ ID NO:26;

(2) an HVR-H1 comprising the amino acid sequence of SEQ ID NO:61;

(3) an HC-FR2 comprising the amino acid sequence of SEQ ID NO:34;

(4) an HVR-H2 comprising the amino acid sequence of SEQ ID NO:62;

(5) an HC-FR3 comprising the amino acid sequence of SEQ ID NO:38;

(6) an HVR-H3 comprising the amino acid sequence of SEQ ID NO:63; and

(7) an HC-FR4 comprising the amino acid sequence of SEQ ID NOs:45;

and/or

(b) a light chain variable region comprising:

(1) an LC-FR1 comprising the amino acid sequence of SEQ ID NO:48;

(2) an HVR-L1 comprising the amino acid sequence of SEQ ID NO:64;

(3) an LC-FR2 comprising the amino acid sequence of SEQ ID NO:51;

(4) an HVR-L2 comprising the amino acid sequence of SEQ ID NO:65;

(5) an LC-FR3 comprising the amino acid sequence of SEQ ID NO:58;

(6) an HVR-L3 comprising the amino acid sequence of SEQ ID NO:66; and

(7) an LC-FR4 comprising the amino acid sequence of SEQ ID NO:60.

17. A composition comprising an antibody that specifically binds to human Siglec-8, wherein the antibody comprises a Fc region and N-glycoside-linked carbohydrate chains linked to the Fc region, wherein less than 50% of the N-glycoside-linked carbohydrate chains contain a fucose residue.

18. The composition of claim 17, wherein substantially none of the N-glycoside-linked carbohydrate chains contain a fucose residue.

19. The composition of claim 17 or 18, wherein the antibody is a humanized antibody, a chimeric antibody or a human antibody.

20. The composition of any one of claims 17-19, wherein the antibody comprises a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO:61, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO:62, and (iii) HVR-H3

comprising the amino acid sequence of SEQ ID NO:63; and/or wherein the light chain variable region comprises (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO:64, (ii) HVR-L2 comprising the amino acid sequence of SEQ ID NO:65, and (iii) HVR-L3 comprising the amino acid sequence of SEQ ID NO:66.

21. The composition of claim 20, wherein the antibody comprises a heavy chain variable region comprising the amino acid sequence selected from SEQ ID NOs:2-10; and/or a light chain variable region comprising the amino acid sequence selected from SEQ ID NOs:16-22.

22. The composition of any one of claims 17-19, wherein the antibody comprises a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO:61, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO:62, and (iii) HVR-H3 comprising the amino acid sequence selected from SEQ ID NOs:67-70; and/or wherein the light chain variable region comprises (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO:64, (ii) HVR-L2 comprising the amino acid sequence of SEQ ID NO:65, and (iii) HVR-L3 comprising the amino acid sequence of SEQ ID NO:71.

23. The composition of claim 22, wherein the antibody comprises a heavy chain variable region comprising the amino acid sequence selected from SEQ ID NOs:11-14; and/or a light chain variable region comprising the amino acid sequence selected from SEQ ID NOs:23-24.

24. The composition of any one of claims 17-19, wherein the antibody comprises a heavy chain variable region comprising the amino acid sequence selected from SEQ ID NOs:2-14; and/or a light chain variable region comprising the amino acid sequence selected from SEQ ID NOs:16-24.

25. The composition of any one of claims 17-24, further comprising a pharmaceutically acceptable carrier.

26. The composition of any one of claims 17-25, wherein the binding affinity or avidity of the antibody to a human Siglec-8 is higher than the binding affinity or avidity of antibody 2E2 or 2C4 to the human Siglec-8.

27. An antibody that binds to a human Siglec-8 and a non-human primate Siglec-8.

28. The antibody of claim 27, wherein the non-human primate is a baboon.

29. The antibody of claim 27 or 28, wherein the antibody comprises:

(a) a heavy chain variable region comprising (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO:89, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO:92, and (iii) HVR-H3 comprising the amino acid sequence of SEQ ID NO:95; and/or a light chain variable region comprising (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO:98, (ii) HVR-L2 comprising the amino acid sequence of SEQ ID NO:101, and (iii) HVR-L3 comprising the amino acid sequence of SEQ ID NO:104.

(b) a heavy chain variable region comprising (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO:90, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO:93, and (iii) HVR-H3 comprising the amino acid sequence of SEQ ID NO:96; and/or a light chain variable region comprising (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO:99, (ii) HVR-L2 comprising the amino acid sequence of SEQ ID NO:102, and (iii) HVR-L3 comprising the amino acid sequence of SEQ ID NO:105.

30. The antibody of any one of claims 27-29, wherein the antibody binds to an epitope in Domain 1 of human Siglec-8, wherein Domain 1 comprises the amino acid sequence of SEQ ID NO:112.

31. The antibody of any one of claims 27-29, wherein the antibody binds to an epitope in Domain 3 of human Siglec-8, wherein Domain 3 comprises the amino acid sequence of SEQ ID NO:114.

32. The antibody of any one of claims 27-31, wherein the antibody is a humanized antibody, a chimeric antibody or a human antibody.

33. The antibody of any one of claims 27-31, wherein the antibody is a murine antibody.

34. The antibody of any one of claims 27-33, wherein the antibody is an IgG1 antibody.

35. A nucleic acid encoding the antibody of any one of claims 1-16 and 27-34.

36. A vector comprising the nucleic acid of claim 35.

37. The vector of claim 36, which is an expression vector.

38. A host cell comprising the nucleic acid of claim 35.

39. A method of producing an antibody comprising culturing the host cell of claim 38 under a condition that produces the antibody.

40. The method of claim 39, further comprising recovering the antibody produced by the host cell.

41. An anti-Siglec-8 antibody produced by the method of claim 39 or 40.

42. The antibody of any one of claims 1-16, 27-34 and 41 or the composition of any one of claims 17-26 for use in the treatment or prevention of a disease mediated by cells expressing Siglec-8 in a subject.

43. The antibody or composition of claim 42, wherein the disease is an eosinophil mediated-disease.

44. The antibody or composition of claim 42, wherein the disease is a mast cell mediated-disease.

45. An antibody that binds to human Siglec-8 for use in depleting mast cells expressing Siglec-8 in a subject, wherein the antibody kills mast cells expressing Siglec-8 by ADCC activity.

46. The antibody of claim 45, wherein the antibody depletes at least about 20% of the mast cells expressing Siglec-8 in a sample obtained from the subject as compared to a baseline level before treatment.

47. The antibody of claim 46, wherein the sample is a tissue sample or a biological fluid sample.

48. The antibody of claim 47, wherein the tissue sample is one or more selected from the group consisting of: skin, lung, bone marrow, and nasal polyps.

49. The antibody of claim 47, wherein the biological fluid sample is one or more selected from the group consisting of: blood, bronchoalveolar lavage, and nasal lavage.

50. The antibody of any one of claims 1-9, 11-16 and 45-49, wherein the antibody has been engineered to improve antibody-dependent cell-mediated cytotoxicity (ADCC) activity.

51. The antibody of any one of claims 1-16 and 45-50, wherein at least one or two of the heavy chains of the antibody is non-fucosylated.

52. The antibody of claim 51, wherein the antibody is produced in a cell line having a alpha1,6-fucosyltransferase (Fut8) knockout.

53. The antibody of claim 51, wherein the antibody is produced in a cell line overexpressing β1,4-N-acetylglycosminyltransferase III (GnT-III).

54. The antibody of claim 53, wherein the cell line additionally overexpresses Golgi μ-mannosidase II (ManII).

55. The antibody of claim 50, wherein the antibody comprises at least one amino acid substitution in the Fc region that improves ADCC activity.

56. The antibody of any one of claims 45-55, wherein the antibody is a humanized antibody, a chimeric antibody or a human antibody.

57. The antibody of any one of claims 45-56, wherein the antibody is a human IgG1 antibody.

58. The antibody of any one of claims 45-55, wherein the antibody is a murine antibody.

59. The antibody of any one of claims 45-58, wherein the antibody comprises:

(a) a heavy chain variable region comprising (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO:88, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO:91, and (iii) HVR-H3 comprising the amino acid sequence of SEQ ID NO:94; and/or a light chain variable region comprising (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO:97, (ii) HVR-L2 comprising the amino acid sequence of SEQ ID NO:100, and (iii) HVR-L3 comprising the amino acid sequence of SEQ ID NO:103.

(b) a heavy chain variable region comprising (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO:89, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO:92, and (iii) HVR-H3 comprising the amino acid sequence of SEQ

ID NO:95; and/or a light chain variable region comprising (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO:98, (ii) HVR-L2 comprising the amino acid sequence of SEQ ID NO:101, and (iii) HVR-L3 comprising the amino acid sequence of SEQ ID NO:104.

(c) a heavy chain variable region comprising (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO:90, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO:93, and (iii) HVR-H3 comprising the amino acid sequence of SEQ ID NO:96; and/or a light chain variable region comprising (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO:99, (ii) HVR-L2 comprising the amino acid sequence of SEQ ID NO:102, and (iii) HVR-L3 comprising the amino acid sequence of SEQ ID NO:105.

60. The antibody of claim 59, wherein the antibody comprises:

(a) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:106; and/or a light chain variable region comprising the amino acid sequence of SEQ ID NO:109.

(b) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:107; and/or a light chain variable region comprising the amino acid sequence of SEQ ID NO:110.

(c) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:108; and/or a light chain variable region comprising the amino acid sequence of SEQ ID NO:111.

61. The antibody of any one of claims 45-58, wherein the antibody comprises a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO:61, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO:62, and (iii) HVR-H3 comprising the amino acid sequence of SEQ ID NO:63; and/or wherein the light chain variable region comprises (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO:64, (ii) HVR-L2 comprising the amino acid sequence of SEQ ID NO:65, and (iii) HVR-L3 comprising the amino acid sequence of SEQ ID NO:66.

62. The antibody of any one of claims 45-58, wherein the antibody comprises a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region

comprises (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO:61, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO:62, and (iii) HVR-H3 comprising the amino acid sequence selected from SEQ ID NOs:67-70; and/or wherein the light chain variable region comprises (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO:64, (ii) HVR-L2 comprising the amino acid sequence of SEQ ID NO:65, and (iii) HVR-L3 comprising the amino acid sequence of SEQ ID NO:71.

63. The antibody of any one of claims 45-62, wherein the subject has a disease mediated by cells expressing Siglec-8.

64. The antibody of any one of claims 45-62 for use in the treatment or prevention of a disease mediated by cells expressing Siglec-8 in a subject.

65. The antibody of claim 64, wherein the disease is an eosinophil mediated-disease.

66. The antibody of claim 64, wherein the disease is a mast cell mediated-disease.

67. The antibody or composition of any one of claims 42 and 45-64, wherein the antibody inhibits one or more symptoms of an allergic reaction.

68. The antibody or composition of claim 67, wherein the allergic reaction is a Type I hypersensitivity reaction.

69. The antibody or composition of any one of claims 42, 63 and 64, wherein the disease is selected from the group consisting of: asthma, allergic rhinitis, nasal polyposis, atopic dermatitis, chronic urticaria, mastocytosis, eosinophilic leukemia, and hypereosinophilic syndrome.

70. The antibody or composition of any one of claims 42, 63 and 64, wherein the disease is selected from the group consisting of: pauci granulocytic asthma, acute or chronic airway hypersensitivity, eosinophilic esophagitis, Churg-Strauss syndrome, inflammation associated with a cytokine, inflammation associated with cells expressing Siglec-8, malignancy associated with cells expressing Siglec-8, physical urticaria, cold urticaria, pressure-urticaria, bullous pemphigoid, food allergy, and allergic bronchopulmonary aspergillosis (ABPA).

71. The antibody or composition of any one of claims 42-70, wherein the subject is suffering from asthma that is not adequately controlled by an inhaled corticosteroid, a short acting β2 agonist, a long acting β2 agonist, or a combination thereof.

72. The antibody of any one of claims 42-71, wherein the subject is a human.

73. A nucleic acid encoding the antibody of any one of claims 42-72.

74. A vector comprising the nucleic acid of claim 73.

75. The vector of claim 74, which is an expression vector.

76. A host cell comprising the nucleic acid of claim 73.

77. A method of producing an antibody comprising culturing the host cell of claim 76 under a condition that produces the antibody.

78. The method of claim 77, further comprising recovering the antibody produced by the host cell.

79. An anti-Siglec-8 antibody produced by the method of claim 77 or 78.

80. A pharmaceutical composition comprising the antibody of any one of claims 1-16, 27-34, 41-72 and 79 and a pharmaceutically acceptable carrier.

81. A kit comprising the antibody of any one of claims 1-16, 27-34, 41-72 and 79 or the composition of any one of claims 17-26, 42-44 and 67-71.