

SUMMARY

[0003] The disclosure provides Fc-containing antibodies that are specific for one or more of SIRP α and SIRP β 1, and is also specific for SIRP γ , wherein binding of the antibody to one or more of SIRP α , SIRP β 1, and SIRP γ on a cell induces depletion of the cell.

[0003a] In one aspect, the present disclosure refers to an antibody that is specific for one or more of SIRP α and SIRP β 1, and is also specific for SIRP γ , wherein binding of the antibody to one or more of SIRP α , SIRP β 1, and SIRP γ does not disrupt the interaction between CD47 and SIRP α , and/or the interaction between CD47 and SIRP γ .

[0004] The disclosure provides antibodies that are specific for one or more of SIRP α and SIRP β 1, and antibodies specific for SIRP γ , wherein the antibody comprises a heavy chain variable region and a light chain variable region, and wherein the heavy chain variable region comprises: (i) a complementarity determining region 1 (CDR-H1) sequence selected from the group consisting of SEQ ID NOS: 54, 56, and 59-65; (ii) a CDR-H2 sequence selected from the group consisting of SEQ ID NOS: 70, 72, and 75-81; and (iii) a CDR-H3 sequence selected from the group consisting of SEQ ID NOS: 86, 88-89, and 92-99; and/or wherein the light chain variable region comprises: (i) a light chain CDR 1 (CDR-L1) sequence selected from the group consisting of SEQ ID NOS: 5, 7-8, and 11-18; (ii) a CDR-L2 sequence selected from the group consisting of SEQ ID NOS: 23-24, and 27-33; and (iii) a CDR-H3 sequence selected from the group consisting of SEQ ID NOS: 36, 38-39, and 42-49.

[0005] In some ~~embodiment~~examples of the antibodies of disclosure, the antibody comprises the heavy and light variable chain CDR sequence combination selected from the group consisting of: (a) SEQ ID NO: 5, SEQ ID NO: 23, SEQ ID NO: 36, SEQ ID NO: 54, SEQ ID NO: 70, and SEQ ID NO: 86; (b) SEQ ID NO: 7, SEQ ID NO: 24, SEQ ID NO: 38, SEQ ID NO: 54, SEQ ID NO: 72, and SEQ ID NO: 88; (c) SEQ ID NO: 8, SEQ ID NO: 24, SEQ ID NO: 39, SEQ ID NO: 56, SEQ ID NO: 72, and SEQ ID NO: 89; (d) SEQ ID NO: 11, SEQ ID NO: 27, SEQ ID NO: 42, SEQ ID NO: 59, SEQ ID NO: 75, and SEQ ID NO: 92; (e) SEQ ID NO: 12, SEQ ID NO: 28, SEQ ID NO: 43, SEQ ID NO: 60, SEQ ID NO: 76, and SEQ ID NO: 93; (f) SEQ ID NO: 13, SEQ ID NO: 29, SEQ ID NO: 44, SEQ ID NO: 61, SEQ ID NO: 76, and SEQ ID NO: 94; (g) SEQ ID NO: 13, SEQ ID NO: 30, SEQ ID NO: 45, SEQ ID NO: 62, SEQ ID NO: 77, and SEQ ID NO: 95; (h) SEQ ID NO: 14, SEQ ID NO: 31, SEQ ID NO: 46, SEQ ID NO: 63, SEQ ID NO: 78, and SEQ ID NO: 96; (i) SEQ ID NO: 15, SEQ ID NO: 31, SEQ ID NO: 47, SEQ ID NO: 62, SEQ ID NO: 79, and SEQ ID NO: 97; (j) SEQ ID NO: 16, SEQ ID NO: 31, SEQ ID NO: 47, SEQ ID NO: 62, SEQ ID NO: 79, and SEQ ID NO: 97; (k) SEQ ID NO: 17, SEQ ID NO: 32, SEQ ID NO: 48, SEQ ID NO: 64, SEQ ID NO: 80, and SEQ ID NO: 98; and (l) SEQ ID NO: 18, SEQ ID NO: 33, SEQ ID NO: 49, SEQ ID NO: 65, SEQ ID NO: 81, and SEQ ID

NO: 99. In some embodimentexamples, the heavy chain variable region comprises a sequence selected from the group consisting of SEQ ID NOS: 104, 106-107, and 110-118. In some embodimentexamples, the light chain variable region comprises a sequence selected from the group consisting of SEQ ID NOS: 123, 125-126, and 129-137.

[0006] In some embodimentexamples of the antibodies of the disclosure, the heavy chain variable region sequence and the light chain variable region sequence are selected from the group consisting of: (a) SEQ ID NO: 104 and SEQ ID NO: 123; (b) SEQ ID NO: 106 and SEQ ID NO: 125; (c) SEQ ID NO: 107 and SEQ ID NO: 126; (d) SEQ ID NO: 110 and SEQ ID NO: 129; (e) SEQ ID NO: 111 and SEQ ID NO: 130; (f) SEQ ID NO: 112 and SEQ ID NO: 131; (g) SEQ ID NO: 113 and SEQ ID NO: 132; (h) SEQ ID NO: 114 and SEQ ID NO: 133; (i) SEQ ID NO: 115 and SEQ ID NO: 134; (j) SEQ ID NO: 116 and SEQ ID NO: 135; (k) SEQ ID NO: 117 and SEQ ID NO: 136; and (l) SEQ ID NO: 118 and SEQ ID NO: 137.

[0007] In some embodimentexamples of the antibodies of the disclosure, the heavy chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 104 or an amino acid sequence with at least 80% sequence identity thereto; and/or wherein the light chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 123, or an amino acid sequence with at least 80% sequence identity thereto. In some embodimentexamples, the heavy chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 106 or an amino acid sequence with at least 80% sequence identity thereto; and/or wherein the light chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 125, or an amino acid sequence with at least 80% sequence identity thereto. In some embodimentexamples, the heavy chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 107 or an amino acid sequence with at least 80% sequence identity thereto; and/or wherein the light chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 126, or an amino acid sequence with at least 80%, sequence identity thereto. In some embodimentexamples, the heavy chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 110 or an amino acid sequence with at least 80% sequence identity thereto; and/or wherein the light chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 129, or an amino acid sequence with at least 80% sequence identity thereto. In some embodimentexamples, the heavy chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 111 or an amino acid sequence with at least 80% sequence

[0008] In some embodimentexamples of the antibodies of the disclosure, the antibody is an Fc-containing antibody, and the binding of the antibody to one or more of SIRP α , SIRP β 1, and SIRP γ on a cell induces depletion of the cell. In some embodimentexamples, the cell depletion involves antibody dependent cellular phagocytosis (ADCP). In some embodimentexamples, the cell depletion involves antibody dependent cellular cytotoxicity (ADCC). In some embodimentexamples, the cell depletion involves depletion of SIRP γ positive cells. In some embodimentexamples, the SIRP γ cells are lymphocytes. In some embodimentexamples, the lymphocytes are T cells or NK cells. In some embodimentexamples, the T cells are cytotoxic T cells, helper T cells, memory T cells, regulatory T cells, natural killer T cells, mucosal associated invariant T cells, gamma delta T cells, or a combination thereof. In some embodimentexamples, the cell depletion involves depletion of SIRP γ positive cells and SIRP α and/or SIRP β 1 positive cells. In some embodimentexamples, the SIRP α and/or SIRP β 1 cells are myeloid cells or myeloid progenitor cells. In some embodimentexamples, the SIRP α and/or SIRP β 1 cells are selected from the group consisting of monocytes, macrophages, dendritic cells, basophils, eosinophils, neutrophils, and mast cells.

[0009] In some embodimentexamples of the antibodies of the disclosure, the antibody is a monoclonal antibody. In some embodimentexamples, the antibody is an antibody fragment. In some embodimentexamples, the antibody is a human antibody. In some embodimentexamples, the antibody is a humanized antibody. In some embodimentexamples, the antibody is a chimeric antibody. In some embodimentexamples, the antibody is a full-length antibody.

[0010] In some embodimentexamples of the antibodies of the disclosure, the Fc domain is selected from the group consisting of human IgG1, IgG2, IgG3, and IgG4. In some embodimentexamples, the Fc domain comprises SEQ ID NO: 3, SEQ ID NO: 4 or SEQ ID NO: 26. In some embodimentexamples, the Fc domain comprises one or more amino acid substitutions relative to SEQ ID NO: 3, SEQ ID NO: 4 or SEQ ID NO: 26. In some embodimentexamples, the Fc domain of the antibody is human IgG1 and comprises at least one amino acid substitution at a position selected from the group consisting of: 214, 215, 221, 222, 228, 234, 235, 236, 239, 240, 241, 243, 244, 245, 247, 250, 252, 254, 256, 262, 263, 264, 265, 266, 267, 268, 269, 270, 292, 296, 297, 298, 299, 300, 305, 313, 324, 325, 326, 327, 328, 329, 330, 332, 333, 334, 345, 356, 358, 396, 428, 430, 433, 434, and 440 wherein the position numbers of the amino acid residues are of the EU numbering scheme. In some embodimentexamples, the IgG1 Fc comprises a sequence selected from the group consisting of: (a) SEQ ID NO: 19; (b) SEQ ID NO: 20, wherein X1 is V or A; (c) SEQ ID NO:

21, wherein X1 is V or A; X2 is G or A; X3 is S or D; and X4 is I or E; (d) SEQ ID NO: 22, wherein X1 is V or A; (e) SEQ ID NO: 25, wherein X1 is V or A; X2 is M or L; and X3 is N or S; and (f) SEQ ID NO: 26, wherein X1 is K or R; X2 is D or E; and X3 is L or M. In some embodimentexamples, the IgG4 Fc comprises a sequence of SEQ ID NO: 34, 35 or 37, wherein X1 in SEQ ID NO: 37 is S or P; and X2 in SEQ ID NO: 37 is L or E.

[0011] In some embodimentexamples of the antibodies of the disclosure, the binding of the antibody does not disrupt the interaction between CD47 and SIRP α , and/or the interaction between CD47 and SIRP γ . In some embodimentexamples, binding of the antibody disrupts the interaction between CD47 and SIRP α , and/or the interaction between CD47 and SIRP γ . In some embodimentexamples, the antibody binds SIRP α , SIRP β 1 and SIRP γ . In some embodimentexamples, the antibody binds SIRP α and SIRP γ and exhibits little or no binding to SIRP β 1. In some embodimentexamples, the antibody binds SIRP β 1 and SIRP γ and exhibits little or no binding to SIRP α .

[0012] In some embodimentexamples of the antibodies of the disclosure, the antibody comprises a binding affinity for SIRP α of about 100 pm, about 1 nM, about 5 nM, about 10 nM, about 50 nM, about 100 nM, about 500 nM, or about 1 μ M. In some embodimentexamples, the antibody comprises a binding affinity for SIRP β 1 of about 0.5 nM, about 0.1 nM, about 5 nM, about 10 nM, about 50 nM, about 100 nM, about 500 nM, about 1 μ M, about 5 μ M, or about 10 μ M. In some embodimentexamples, the antibody comprises a binding affinity for SIRP γ of about 0.0001 nM, about 0.0005 nM, about 0.001 nM, about 0.005 nM, about 0.1 nM, about 0.05 nM, about 0.1 nM, about 0.5 nM, about 1 nM, about 5 nM, about 10 nM, about 50 nM, about 100 nM, about 500 nM, about 1 μ M, about 2 μ M, or about 3 μ M.

[0013] The disclosure provides a pharmaceutical composition comprising an antibody of the disclosure, and optionally a pharmaceutically acceptable carrier.

[0013a] In one aspect, the present disclosure refers to a pharmaceutical composition comprising any one of the antibodies disclosed herein, and optionally a pharmaceutically acceptable carrier.

[0014] The disclosure provides a nucleic acid encoding for the antibody of the disclosure. In some embodimentexamples, the nucleic acid comprises nucleic acid sequence selected from the group consisting of SEQ ID NOS: 142, 144-145, 148-156, 161, 163-164, and 167-175. In some embodimentexamples, the heavy chain variable domain is encoded by the nucleic acid sequence of SEQ ID NO: 142, or a nucleic acid sequence with at least 80% sequence identity thereto; and/or wherein the light chain variable domain is encoded by the nucleic acid sequence of SEQ ID NO: 161, or a nucleic acid sequence with at least 80% sequence identity thereto. In some

embodimentexamples, the heavy chain variable domain is encoded by the nucleic acid sequence of SEQ ID NO: 154, or a nucleic acid sequence with at least 80% sequence identity thereto; and/or wherein the light chain variable domain is encoded by the nucleic acid sequence of SEQ ID NO: 173, or a nucleic acid sequence with at least 80% sequence identity thereto. In some embodimentexamples, the heavy chain variable domain is encoded by the nucleic acid sequence of SEQ ID NO: 155, or a nucleic acid sequence with at least 80% sequence identity thereto; and/or wherein the light chain variable domain is encoded by the nucleic acid sequence of SEQ ID NO: 174, or a nucleic acid sequence with at least 80% sequence identity thereto. In some embodimentexamples, the heavy chain variable domain is encoded by the nucleic acid sequence of SEQ ID NO: 156, or a nucleic acid sequence with at least 80% sequence identity thereto; and/or wherein the light chain variable domain is encoded by the nucleic acid sequence of SEQ ID NO: 175, or a nucleic acid sequence with at least 80% sequence identity thereto.

[0015] The disclosure provides vectors comprising the nucleic acid of the disclosure.

[0015a] In one aspect, the present disclosure refers to a nucleic acid encoding for the antibody disclosed herein, optionally wherein: a. the heavy chain variable domain is encoded by the nucleic acid sequence of SEQ ID NO: 142, or a nucleic acid sequence with at least 80% sequence identity thereto; and/or wherein the light chain variable domain is encoded by the nucleic acid sequence of SEQ ID NO: 161, or a nucleic acid sequence with at least 80% sequence identity thereto; b. the heavy chain variable domain is encoded by the nucleic acid sequence of SEQ ID NO: 153, or a nucleic acid sequence with at least 80% sequence identity thereto; and/or wherein the light chain variable domain is encoded by the nucleic acid sequence of SEQ ID NO: 172, or a nucleic acid sequence with at least 80% sequence identity thereto; c. the heavy chain variable domain is encoded by the nucleic acid sequence of SEQ ID NO: 154, or a nucleic acid sequence with at least 80% sequence identity thereto; and/or wherein the light chain variable domain is encoded by the nucleic acid sequence of SEQ ID NO: 173, or a nucleic acid sequence with at least 80% sequence identity thereto; or d. the heavy chain variable domain is encoded by the nucleic acid sequence of SEQ ID NO: 156, or a nucleic acid sequence with at least 80% sequence identity thereto; and/or wherein the light chain variable domain is encoded by the nucleic acid sequence of SEQ ID NO: 175, or a nucleic acid sequence with at least 80% sequence identity thereto.

[0015b] In one aspect, the present disclosure refers to a vector comprising the nucleic acid disclosed herein.

[0016] The disclosure provides methods of inducing the depletion of a population of cells, the methods comprising contacting the population of cells with the antibody of the disclosure.

[0017] In some embodimentexamples of the methods of the disclosure, at least a subset of the population of cells expresses SIRP γ . In some embodimentexamples, the population of cells that express SIRP γ comprise lymphocytes. In some embodimentexamples, the lymphocytes comprise T cells or NK cells. In some embodimentexamples, at least a subset of the population of cells expresses SIRP α and/or SIRP β 1. In some embodimentexamples, the population of cells that express SIRP α and/or SIRP β 1 comprise myeloid cells or myeloid progenitor cells. In some embodimentexamples, the population of cells that express SIRP α and/or SIRP β 1 comprise monocytes, macrophages, dendritic cells, basophils, eosinophils, neutrophils, or mast cells. In some embodimentexamples, the method is in vitro. In some embodimentexamples, the method is in vivo. In some embodimentexamples, the population of cells comprises tissue-resident cells. In some embodimentexamples, the population of cells comprises circulating cells.

[0018] In some embodimentexamples of the methods of the disclosure, the cell depletion involves ADCC. In some embodimentexamples the cell depletion involves ADCP. In some embodimentexamples, the cell depletion involves ADCC and ADCP.

[0019] The disclosure provides methods of treating a disease or condition in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of the antibody or pharmaceutical composition of the disclosure.

[0019a] In one aspect, the present disclosure refers to the antibody disclosed herein or the pharmaceutical composition disclosed herein, for use in therapy.

[0019b] In one aspect, the present disclosure refers to use of the antibody disclosed herein or the pharmaceutical composition disclosed herein, in the manufacture of a medicament for treating a disease or condition in a subject in need thereof.

[0020] In some embodimentexamples of the methods of treating a disease or condition of the disclosure, the disease or condition is characterized by overactivation and/or hyperproliferation of lymphocytes, and the antibody induces depletion of lymphocytes. In some embodimentexamples, the lymphocytes are T cells. In some embodimentexamples, the disease or condition comprises aplastic anemia, cell mediated rejection of solid organ transplant, graft failure post-HSCT (hematopoietic stem cell transplant), lymphocyte-variant hypereosinophilia, atopic dermatitis, lymphocytic myocarditis, axial spondyloarthritis, celiac disease, or Rasmussen's encephalitis.

[0021] In some embodimentexamples of the methods of treating a disease or condition of the disclosure, the disease or condition is characterized by overactivation and/or hyperproliferation of myeloid cells, and the antibody induces depletion of myeloid cells. In some embodimentexamples, the myeloid cells comprise monocytes, macrophages, dendritic cells, basophils, eosinophils, neutrophils, or mast cells. In some embodimentexamples, the myeloid cells comprise eosinophils, and the disease or condition comprises acute eosinophilic pneumonia, chronic eosinophilic pneumonia, eosinophilic esophagitis, eosinophilic gastritis, eosinophilic gastroenteritis, eosinophilic enteritis, eosinophilic colitis, lymphocyte-variant hypereosinophilia, eosinophilic cardiomyopathy/Loeffler endocarditis, Löffler syndrome or episodic angioedema with eosinophilia/Gleich syndrome. In some embodimentexamples, the myeloid cells comprise mast cells, and the disease or condition comprises cutaneous mastocytosis, mastocytic enterocolitis, systemic mastocytosis, mast cell activation syndrome, hereditary alpha tryptasemia syndrome, chronic urticaria or severe allergic conjunctivitis. In some embodimentexamples, the myeloid cells comprise neutrophils, and the disease or condition comprises neutrophilic dermatoses, psoriatic arthritis, generalized pustular psoriasis, pyoderma gangrenosum, Sweet's syndrome, subcorneal pustular dermatosis, neutrophilic eccrine hidradenitis, bowel-associated dermatosis-arthritis syndrome (BADAS), rheumatoid neutrophilic dermatitis, or Behçet's disease.

[0022] In some embodimentexamples of the methods of treating a disease or condition of the disclosure, the disease or condition comprises a disease or disorder associated with both lymphocytes and myeloid cells. In some embodimentexamples, the disease or disorder comprises histiocytosis. In some embodimentexamples, the histiocytosis comprises hemophagocytic lymphohistiocytosis (HLH)

(including primary and secondary HLH), macrophage activation syndrome, Langerhans cell histiocytosis (LCH), indeterminate cell histiocytosis, Erdheim-Chester disease (ECD), mixed LCH/ECD, Rosai Dorfman disease, malignant histiocytosis, cutaneous non-LCH histiocytoses, juvenile xanthogranuloma, infection-associated HLH, or malignancy-triggered HLH. In some [embodimentexamples](#), the malignancy-triggered HLH includes an HLH triggered by a hematological malignancy or solid tumor. In some [embodimentexamples](#), the disease or disorder comprises a non-mendelian secondary HLH (secondary HLH, or sHLH). In some [embodimentexamples](#), the secondary HLH comprises an infection-associated HLH. In some [embodimentexamples](#), the infection-associated HLH comprises virus-associated HLH, bacteria-associated HLH, parasite-associated HLH, or fungal-associated (fungal induced) HLH. In some [embodimentexamples](#), the sHLH is associated with a rheumatologic condition. In some [embodimentexamples](#), the sHLH is associated with a kidney transplant or hematologic stem cell transplant.

[0023] In some [embodimentexamples](#) of the methods of treating a disease or condition of the disclosure, the disease or condition comprises sHLH or cytokine release syndrome (CRS). In some [embodimentexamples](#), the sHLH or CRS is associated with iatrogenic immune activation, infection, T cell therapy, chimeric antigen receptor – T cell therapy (CAR-T), T cell receptor T cell therapy (TCR-T), T cell activating bispecific antibody therapy, or iatrogenic immune suppression.

[0024] In some [embodimentexamples](#) of the methods of treating a disease or condition of the disclosure, the disease or condition comprises a granulomatous disease or condition, or a disease characterized by the presence of multinucleated giant cells. In some [embodimentexamples](#), the disease or condition comprises sarcoidosis, Crohn’s disease, Takayasu arteritis, giant cell arteritis, psoriatic arthritis, granulomatosis with polyangiitis (Wegener’s Granulomatosis), giant cell myocarditis, chronic granulomatous disease, eosinophilic granulomatosis with polyangiitis (Churg-Strauss Syndrome), or chronic beryllium disease (berylliosis).

[0025] In some [embodimentexamples](#) of the methods of treating a disease or condition of the disclosure, the disease or condition comprises an autoimmune disorder or an inflammatory disorder. In some [embodimentexamples](#), the autoimmune disorder comprises presentation of self antigens by antigen presenting myeloid cells (e.g. dendritic cells) in germinal centers of secondary lymphoid tissue of the subject.

[0026] In some embodiment examples, the disease or condition comprises Guillain-Barre syndrome, chronic inflammatory demyelinating polyneuropathy (CIDP), Lambert-Eaton myasthenic syndrome (LEMS), myasthenia gravis (MG), neuromyelitis optica (NMO), bullous pemphigoid, epidermolysis bullosa acquisita, pemphigus foliaceus, pemphigus vulgaris, anti-glomerular basement membrane disease (Goodpasture Syndrome), membranous nephropathy, ankylosing spondylitis, rheumatoid arthritis, rheumatoid vasculitis, lupus nephritis, lupus vasculitis, systemic lupus erythematosus (SLE), scleroderma (systemic sclerosis), Behcet's disease, granulomatosis with polyangiitis (Wegener's Granulomatosis), eosinophilic granulomatosis with polyangiitis (Churg-Strauss Syndrome), microscopic polyangiitis (MPA), Kawasaki disease, anti-glomerular basement membrane disease (Goodpasture Syndrome), antiphospholipid syndrome and catastrophic antiphospholipid syndrome, Graves ophthalmopathy, Castleman disease, and antibody-mediated rejection (AMR), Sjögren's syndrome, multiple sclerosis, Hashimoto's thyroiditis, primary sclerosing cholangitis, primary biliary cirrhosis, autoimmune neutropenia, systemic juvenile idiopathic arthritis, axial spondyloarthritis, celiac disease, autoimmune hepatitis, or psoriatic arthritis.

[0027] In some embodiment examples, the disease or condition comprises disseminated encephalomyelitis, acute respiratory distress syndrome, Addison's disease, Adult-Onset Still's disease, ankylosing spondylitis, antibody-mediated rejection (AMR), anti-glomerular basement membrane disease (Goodpasture Syndrome), antiphospholipid syndrome, aplastic anemia, atopic dermatitis, autoimmune hemolytic anemia, autoimmune hepatitis, autoimmune lymphoproliferative syndrome, axial spondyloarthritis, Behcet's disease, bullous pemphigoid, Castleman disease, catastrophic antiphospholipid syndrome, celiac disease, cell mediated rejection of solid organ transplant, Chediak-Higashi syndrome, chronic inflammatory demyelinating polyneuropathy (CIDP), chronic neutrophilic leukemia, chronic urticaria, coronary artery disease (CAD)/ peripheral artery disease (PAD), COVID-19, cutaneous mastocytosis, eosinophilic cardiomyopathy/Loeffler endocarditis, epidermolysis bullosa acquisita, Evans syndrome, Felty's syndrome, general pustular psoriasis, giant cell myocarditis, graft failure post-HSCT (hematopoietic stem cell transplant), graft vs. host disease, Graves' disease, Graves ophthalmopathy, Guillain-Barre syndrome, Hashimoto's thyroiditis, hereditary alpha tryptasemia syndrome, hyper IgE syndrome, Idiopathic interstitial pneumonia, idiopathic pulmonary fibrosis, IgA nephropathy, immune/idiopathic thrombocytopenia purpura, inclusion body myositis, inflammatory bowel disease, Kawasaki disease, Lambert-Eaton myasthenic

syndrome (LEMS), linear IgA disease, Löffler syndrome, lupus nephritis, lupus vasculitis, mast cell activation syndrome, mastocytic enterocolitis, membranous nephropathy, microscopic polyangiitis (MPA), multiple sclerosis, myasthenia gravis, myelodysplastic syndromes, myelofibrosis, myocarditis, neuromyelitis optica (NMO), neutrophilic dermatoses, paraneoplastic syndrome, pemphigus foliaceus, pemphigus vulgaris, primary biliary cholangitis, primary sclerosing cholangitis, pyoderma gangrenosum, Rasmussen's encephalitis, rheumatoid arthritis, rheumatoid vasculitis, Schmidt syndrome, scleroderma (systemic sclerosis), severe allergic conjunctivitis, Sjogren syndrome, Susac syndrome, systemic inflammatory response syndrome, systemic juvenile idiopathic arthritis, systemic lupus erythematosus, systemic mastocytosis, type 1 diabetes, ulcerative colitis, uveitis, vitiligo or X-linked lymphoproliferative disease.

[0028] In some [embodiment examples](#) of the methods of treating a disease or condition of the disclosure, the disease or disorder comprises a hematological malignancy. In some [embodiment examples](#), the hematological malignancy comprises acute lymphoblastic leukemia, acute myelogenous leukemia, chronic myelogenous leukemia, chronic myelomonocytic leukemia, chronic neutrophilic leukemia, juvenile myelomonocytic leukemia, chronic eosinophilic leukemia, large granular lymphocyte leukemia, T-cell prolymphocytic leukemia, hepatosplenic lymphoma, Hodgkin's lymphomas, T-cell lymphoblastic lymphoma or leukemia, T-cell non-lymphoblastic lymphoma, NK-cell lymphoma/leukemia, myeloid neoplasia, or chronic neutrophilic leukemia.

[0029] In some [embodiment examples](#) of the methods of treating a disease or condition of the disclosure, the disease or disorder comprises hemophagocytic lymphohistiocytosis (HLH) (including primary and secondary HLH), macrophage activation syndrome, Langerhans cell histiocytosis (LCH), indeterminate cell histiocytosis, Erdheim-Chester disease (ECD), mixed LCH/ECD, Rosai Dorfman disease, malignant histiocytosis, cutaneous non-LCH histiocytosis, juvenile xanthogranuloma, virus-associated HLH, bacteria-associated HLH, parasite-associated HLH, fungal-associated/fungal-induced HLH, malignancy-triggered HLH, HLH occurring during chemotherapy, HLH associated with systemic-onset juvenile idiopathic arthritis (SoJIA), HLH associated with adult-onset Still's disease, HLH associated with systemic lupus erythematosus (SLE), HLH associated with vasculitis, HLH associated with auto-immune conditions, HLH associated with a kidney transplant, HLH associated with hematologic stem cell transplants, sHLH or CRS associated with checkpoint inhibitors for the treatment of malignancies, sHLH or

mastocytosis, mastocytic enterocolitis, mast cell activation syndrome, IgA nephropathy, Chediak-Higashi syndrome, eosinophilic cardiomyopathy/Loeffler endocarditis, acute kidney injury, chronic kidney disease, coronary artery disease (CAD)/ peripheral artery disease (PAD), myelofibrosis, IgG4-related disease, Löffler syndrome, chronic neutrophilic leukemia, myocarditis, episodic angioedema with eosinophilia / Gleich syndrome, idiopathic interstitial pneumonia, hereditary alpha tryptasemia syndrome, chronic urticaria, severe allergic conjunctivitis, Adult-onset Still's, aplastic Anemia, cell mediated rejection of solid organ transplant, graft failure Post-hematopoietic stem cell transplant (HSCT), lymphocyte-variant hypereosinophilia, myelodysplastic syndromes, atopic dermatitis, axial spondyloarthritis, celiac disease, hyperthyroidism, Rasmussen's encephalitis, chronic beryllium disease (Berylliosis), Takayasu arteritis, autoimmune hepatitis, neutrophilic dermatoses, psoriatic arthritis, Corona Virus Disease 2019 (COVID-19), or general pustular psoriasis.

[0030] In some embodimentexamples of the methods of treating a disease or condition of the disclosure, the subject is human.

[0031] In some embodimentexamples of the methods of treating a disease or condition of the disclosure, the antibody or pharmaceutical composition is administered intravenously. In some embodimentexamples, the antibody or pharmaceutical composition is administered subcutaneously.

[0032] The disclosure provides cells expressing SIRP γ , wherein the cells are bound to an antibody of the disclosure, wherein the antibody is bound to the SIRP γ .

[0033] The disclosure provides kits or articles of manufacture comprising the antibodies or pharmaceutical compositions of the disclosure.

[0034] The disclosure provides use of the antibodies or the pharmaceutical compositions of the disclosure for the treatment of a disease or disorder in a subject in need thereof.

[0035] The disclosure provides use of the antibodies or the pharmaceutical compositions of the disclosure for the manufacture of a medicament for the treatment of a disease or disorder in a subject in need thereof.