

antibodies with variant light chains that have been engineered to remove potential liabilities, such as residues that may be modified by deamidation or glycation, resulting in antibodies with more desirable characteristics for manufacturing, storage, and/or drug development.

[0010] In certain examples, the present disclosure provides antibodies (*e.g.*, isolated antibodies) that bind an extracellular domain of a human SIRP- α polypeptide, where the antibodies comprise: a heavy chain comprising a heavy chain variable (VH) domain that comprises the amino acid sequence of SEQ ID NO:26; and a light chain comprising a light chain variable (VL) domain that comprises an amino acid sequence according to the formula

SYELTQPPSVSVSPGQTARITCSGGSYSSYYYAWYQQKPGQAPVTLIYSDDKRPSNI
PERFSGSSSGTTVTLTISGVQAEDEADYYCGGYDQSSYTNPF₁GT₂X₃TVL (SEQ
ID NO:71), wherein X₁ is G or T; X₂ is K, Q, or R; and X₃ is L or V, and wherein the VL domain does not comprise the sequence of SEQ ID NO:25.

[0010a] In one aspect, the present disclosure refers to an isolated antibody that binds an extracellular domain of a human SIRP- α polypeptide, wherein the antibody comprises: (a) a heavy chain comprising a heavy chain variable (VH) domain that comprises the amino acid sequence of SEQ ID NO:26; and (b) a light chain comprising a light chain variable (VL) domain that comprises an amino acid sequence according to the formula

SYELTQPPSVSVSPGQTARITCSGGSYSSYYYAWYQQKPGQAPVTLIYSDDKRPSNI
PERFSGSSSGTTVTLTISGVQAEDEADYYCGGYDQSSYTNPF₁GT₂X₃TVL (SEQ
ID NO:71), wherein X₁ is G or T; X₂ is K, Q, or R; and X₃ is L or V, and wherein the VL domain does not comprise the sequence of SEQ ID NO:25.

[0011] In some examples, the VL domain comprises an amino acid sequence selected from the group consisting of SEQ ID NOs:39-41. In some examples, the light chain further comprises a light chain constant (CL) domain sequence that comprises an amino acid sequence according to the formula

GQPKANPTVTLFPPSSEELQANKATLVCLISDFYPGAVTVAWKADGSPVKAGVETT
KPSKQ₄X₅KYAASSYLSLTPEQWKSHRSYSCQVTHEGSTVEKTVAPTECS (SEQ
ID NO:72), wherein X₄X₅ is ND, DN, DS, or SD. In some examples, the light chain further comprises a light chain constant (CL) domain sequence that comprises an amino acid sequence selected from the group consisting of SEQ ID NOs:43-46. In some examples, the light chain further comprises a kappa light chain constant (CL) domain. In some examples, the light chain comprises the amino acid sequence of SEQ ID NO:36. In some examples, the light chain further comprises a lambda light chain constant (CL) domain. In some examples, the light chain comprises the amino acid sequence of SEQ ID NO:37 or SEQ ID NO:38. In some examples, the light chain comprises an amino acid sequence selected from the group consisting of SEQ ID NOs:48-57.

[0012] In some examples, the antibody is a scFv-Fc, single domain antibody, single heavy chain antibody, or single light chain antibody. In some examples, the antibody is a monoclonal antibody. In some examples, the antibody comprises a heavy chain

comprising a heavy chain constant domain that comprises an Fc region. In some examples, the Fc region is a human Fc region selected from the group consisting of an IgG1 Fc region, an IgG2 Fc region, and an IgG4 Fc region. In some examples, the Fc region is a human IgG1 Fc region. In some examples, the Fc region is a human IgG1 Fc region comprising L234A, L235A, and G237A substitutions, amino acid position numbering according to EU. In some examples, the Fc region is a human IgG2 Fc region. In some examples, the Fc region is a human IgG2 Fc region comprising A330S and P331S substitutions, amino acid position numbering according to EU. In some examples, the Fc region further comprises an N297A substitution, amino acid position numbering according to EU. In some examples, the Fc region is a human IgG2 Fc region comprising an N297A substitution, amino acid position numbering according to EU. In some examples, the Fc region is a human IgG4 Fc region, and wherein the heavy chain comprises an S228P substitution, amino acid position numbering according to EU. In some examples, the heavy chain comprises a heavy chain constant domain that comprises an amino acid sequence selected from the group consisting of SEQ ID NOs:31-35. In some examples, the heavy chain comprises a heavy chain constant domain that comprises an amino acid sequence selected from the group consisting of SEQ ID NOs:33, 34, and 137. In some examples, the heavy chain comprises a heavy chain constant domain that comprises an amino acid sequence selected from the group consisting of SEQ ID NOs:132-139.

[0013] In some examples, the heavy chain comprises an amino acid sequence selected from the group consisting of SEQ ID NOs:58-62. In some examples, the heavy chain comprises an amino acid sequence selected from the group consisting of SEQ ID NOs:60, 61, and 129. In some examples, the heavy chain comprises an amino acid sequence selected from the group consisting of SEQ ID NOs:124-131.

[0014] In certain examples, the present disclosure provides antibodies (*e.g.*, isolated antibodies) that bind an extracellular domain of a human SIRP- α polypeptide, wherein: the heavy chain comprises the amino acid sequence of SEQ ID NO:62, and the light chain comprises the amino acid sequence of SEQ ID NO:52; the heavy chain comprises the amino acid sequence of SEQ ID NO:62, and the light chain comprises the amino acid sequence of SEQ ID NO:53; the heavy chain comprises the amino acid sequence of SEQ ID NO:62, and the light chain comprises the amino acid sequence of SEQ ID NO:54; the heavy chain comprises the amino acid sequence of SEQ ID NO:62, and the light chain comprises

the amino acid sequence of SEQ ID NO:55; the heavy chain comprises the amino acid sequence of SEQ ID NO:62, and the light chain comprises the amino acid sequence of SEQ ID NO:56; or the heavy chain comprises the amino acid sequence of SEQ ID NO:62, and the light chain comprises the amino acid sequence of SEQ ID NO:57.

[0015] In certain examples, the present disclosure provides antibodies (*e.g.*, isolated antibodies) that bind an extracellular domain of a human SIRP- α polypeptide, wherein: the heavy chain comprises the amino acid sequence of SEQ ID NO:58, and the light chain comprises the amino acid sequence of SEQ ID NO:52; the heavy chain comprises the amino acid sequence of SEQ ID NO:59, and the light chain comprises the amino acid sequence of SEQ ID NO:52; the heavy chain comprises the amino acid sequence of SEQ ID NO:60, and the light chain comprises the amino acid sequence of SEQ ID NO:52; the heavy chain comprises the amino acid sequence of SEQ ID NO:61, and the light chain comprises the amino acid sequence of SEQ ID NO:52; the heavy chain comprises the amino acid sequence of SEQ ID NO:58, and the light chain comprises the amino acid sequence of SEQ ID NO:53; the heavy chain comprises the amino acid sequence of SEQ ID NO:59, and the light chain comprises the amino acid sequence of SEQ ID NO:53; the heavy chain comprises the amino acid sequence of SEQ ID NO:60, and the light chain comprises the amino acid sequence of SEQ ID NO:53; the heavy chain comprises the amino acid sequence of SEQ ID NO:61, and the light chain comprises the amino acid sequence of SEQ ID NO:53; the heavy chain comprises the amino acid sequence of SEQ ID NO:58, and the light chain comprises the amino acid sequence of SEQ ID NO:54; the heavy chain comprises the amino acid sequence of SEQ ID NO:59, and the light chain comprises the amino acid sequence of SEQ ID NO:54; the heavy chain comprises the amino acid sequence of SEQ ID NO:60, and the light chain comprises the amino acid sequence of SEQ ID NO:54; the heavy chain comprises the amino acid sequence of SEQ ID NO:61, and the light chain comprises the amino acid sequence of SEQ ID NO:54; the heavy chain comprises the amino acid sequence of SEQ ID NO:58, and the light chain comprises the amino acid sequence of SEQ ID NO:55; the heavy chain comprises the amino acid sequence of SEQ ID NO:59, and the light chain comprises the amino acid sequence of SEQ ID NO:55; the heavy chain comprises the amino acid sequence of SEQ ID NO:60, and the light chain comprises the amino acid sequence of SEQ ID NO:55; the heavy chain comprises the amino acid sequence of SEQ ID NO:61, and the light chain comprises the amino acid sequence of SEQ ID NO:55; the heavy chain comprises the amino acid

sequence of SEQ ID NO:58, and the light chain comprises the amino acid sequence of SEQ ID NO:56; the heavy chain comprises the amino acid sequence of SEQ ID NO:59, and the light chain comprises the amino acid sequence of SEQ ID NO:56; the heavy chain comprises the amino acid sequence of SEQ ID NO:60, and the light chain comprises the amino acid sequence of SEQ ID NO:56; the heavy chain comprises the amino acid sequence of SEQ ID NO:61, and the light chain comprises the amino acid sequence of SEQ ID NO:56; the heavy chain comprises the amino acid sequence of SEQ ID NO:58, and the light chain comprises the amino acid sequence of SEQ ID NO:57; the heavy chain comprises the amino acid sequence of SEQ ID NO:59, and the light chain comprises the amino acid sequence of SEQ ID NO:57; the heavy chain comprises the amino acid sequence of SEQ ID NO:60, and the light chain comprises the amino acid sequence of SEQ ID NO:57; the heavy chain comprises the amino acid sequence of SEQ ID NO:61, and the light chain comprises the amino acid sequence of SEQ ID NO:57; the heavy chain comprises the amino acid sequence of SEQ ID NO:60, and the light chain comprises the amino acid sequence of SEQ ID NO:55; the heavy chain comprises the amino acid sequence of SEQ ID NO:61, and the light chain comprises the amino acid sequence of SEQ ID NO:55; the heavy chain comprises the amino acid sequence of SEQ ID NO:129, and the light chain comprises the amino acid sequence of SEQ ID NO:55; the heavy chain comprises the amino acid sequence of SEQ ID NO:124, and the light chain comprises the amino acid sequence of SEQ ID NO:52; or the heavy chain comprises the amino acid sequence of SEQ ID NO:124, and the light chain comprises the amino acid sequence of SEQ ID NO:55.

[0016] In some examples, the antibody enhances phagocytosis by a macrophage expressing a human SIRP- α polypeptide. In some examples, the antibody enhances activation of a dendritic cell expressing a human SIRP- α polypeptide. In some examples, the antibody inhibits *in vivo* growth of a tumor that expresses CD47.

[0017] In some examples, the antibody is conjugated to an agent, *e.g.*, a cytotoxic agent, label, or moiety that modulates the immune system.

[0018] In some embodiments, the antibody is a bispecific antibody. In some examples, the antibody comprises a first antigen binding domain that binds an extracellular domain of a human SIRP- α polypeptide and a second antigen binding domain that binds an antigen expressed by a cancer cell. In some

examples, the antigen expressed by the cancer cell is selected from the group consisting of CD19, CD20, CD22, CD30, CD33, CD38, CD52, CD56, CD70, CD74, CD79b, CD123, CD138, CS1/SLAMF7, Trop-2, 5T4, EphA4, BCMA, Mucin 1, Mucin 16, PD-L1, PTK7, STEAP1, Endothelin B Receptor, mesothelin, EGFRvIII, ENPP3, SLC44A4, GNMB, nectin 4, NaPi2b, LIV-1A, Guanylyl cyclase C, DLL3, EGFR, HER2, VEGF, VEGFR, integrin α V β 3, integrin α 5 β 1, MET, IGF1R, TRAILR1, TRAILR2, RANKL, FAP, Tenascin, Le^y, EpCAM, CEA, gpA33, PSMA, TAG72, a mucin, CAIX, EPHA3, folate receptor α , GD2, GD3, and an MHC/peptide complex comprising a peptide from NY-ESO-1/LAGE, SSX-2, a MAGE family protein, MAGE-A3, gp100/pmel17, Melan-A/MART-1, gp75/TRP1, tyrosinase, TRP2, CEA, PSA, TAG-72, immature laminin receptor, MOK/RAGE-1, WT-1, SAP-1, BING-4, EpCAM, MUC1, PRAME, survivin, BRCA1, BRCA2, CDK4, CML66, MART-2, p53, Ras, β -catenin, TGF- β RII, HPV E6, or HPV E7. In some examples, the antibody comprises a first antigen binding domain that binds an extracellular domain of a human SIRP- α polypeptide and a second antigen binding domain that binds an antigen expressed by an immune cell. In some examples, the antigen expressed by the immune cell is selected from the group consisting of BDCA2, BDCA4, ILT7, LILRB1, LILRB2, LILRB3, LILRB4, LILRB5, Siglec-3, Siglec-7, Siglec-9, Siglec-15, FGL-1, CD200, CD200R, CSF-1R, CD40, CD40L, CD163, CD206, DEC205, CD47, CD123, arginase, IDO, TDO, AhR, EP2, COX-2, CCR2, CCR-7, CXCR1, CX3CR1, CXCR2, CXCR3, CXCR4, CXCR7, TGF- β RI, TGF- β RII, c-Kit, CD244, L-selectin/CD62L, CD11b, CD11c, CD68, 41BB, CTLA4, PD1, PD-L1, PD-L2, TIM-3, BTLA, VISTA, LAG-3, CD28, OX40, GITR, CD137, CD27, HVEM, CCR4, CD25, CD103, KIRg1, Nrp1, CD278, Gpr83, TIGIT, CD154, CD160, TNFR2, PVRIG, DNAM, and ICOS. In some examples, the antibody comprises a first antigen binding domain that binds an extracellular domain of a human SIRP- α polypeptide and a second antigen binding domain that binds an antigen expressed by a natural killer (NK) cell. In some examples, the antigen expressed by the NK cell is selected from the group consisting of NKR-P1A, CD94, KLRG1, KIR2DL5A, KIR2DL5B, KIR2DL1, KIR2DL2, KIR2DL3, KIR2DS2, KIR2DS3, KIR2DS4, KIR2DS5, KIR3DS1, KIR2DS1, CD94, NKG2D, CD160, CD16, NKp46, NKp30, NKp44, DNAM1, CRTAM, CD27, NTB-A, PSGL1, CD96, CD100, NKp80, SLAMF7, and CD244.

[0019] In certain aspects, the present disclosure refers to a polynucleotide encoding any one of the antibodies as disclosed herein. In certain aspects, the present

disclosure refers to a vector comprising the polynucleotide as disclosed herein. In certain aspects, the present disclosure refers to a host cell comprising the polynucleotide or vector as disclosed herein. In certain aspects, the present disclosure refers to a method of producing an antibody, the method comprising culturing the host cell as disclosed herein such that the antibody is produced. In some examples, the method further comprises recovering the antibody from the host cell.

[0019a] In one aspect, the present disclosure refers to use of any one of the antibodies as disclosed herein in the manufacture of a medicament for treating or delaying progression of cancer in an individual.

[0020] In certain examples, the present disclosure provides a method of treating or delaying progression of cancer in an individual, the method comprising administering to the individual an effective amount of the antibody according to any one of the above examples.

In some examples, the method further comprises administering to the individual an effective amount of a second antibody that binds an antigen expressed by the cancer. In some examples, the antigen expressed by the cancer is selected from the group consisting of CD19, CD20, CD22, CD30, CD33, CD38, CD52, CD56, CD70, CD74, CD79b, CD123, CD138, CS1/SLAMF7, Trop-2, 5T4, EphA4, BCMA, Mucin 1, Mucin 16, PTK7, STEAP1, Endothelin B Receptor, mesothelin, EGFRvIII, ENPP3, SLC44A4, GNMB, nectin 4, NaPi2b, LIV-1A, Guanylyl cyclase C, DLL3, EGFR, HER2, VEGF, VEGFR, integrin α V β 3, integrin α 5 β 1, MET, IGF1R, TRAILR1, TRAILR2, RANKL, FAP, Tenascin, Le^y, EpCAM, CEA, gpA33, PSMA, TAG72, a mucin, CAIX, EPHA3, folate receptor α , GD2, GD3, and an MHC/peptide complex comprising a peptide from NY-ESO-1/LAGE, SSX-2, a MAGE family protein, MAGE-A3, gp100/pmel17, Melan-A/MART-1, gp75/TRP1, tyrosinase, TRP2, CEA, PSA, TAG-72, immature laminin receptor, MOK/RAGE-1, WT-1, SAP-1, BING-4, EpCAM, MUC1, PRAME, survivin, BRCA1, BRCA2, CDK4, CML66, MART-2, p53, Ras, β -catenin, TGF- β RII, HPV E6, or HPV E7. In some examples, the method further comprises administering to the individual an effective amount of an immunotherapeutic agent. In some examples, the immunotherapeutic agent comprises a second antibody. In some examples, the second antibody binds to an antigen selected from the group consisting of BDCA2, BDCA4, ILT7, LILRB1, LILRB2, LILRB3, LILRB4, LILRB5, Siglec-3, Siglec-7, Siglec-9, Siglec-15, FGL-1, CD200, CD200R, CSF-1R, CD40, CD40L, CD163, CD206, DEC205, CD47, CD123, arginase, IDO, TDO, AhR, EP2, COX-2, CCR2, CCR-7, CXCR1, CX3CR1, CXCR2, CXCR3, CXCR4, CXCR7, TGF- β RI, TGF- β RII, c-Kit, CD244, L-selectin/CD62L, CD11b, CD11c, CD68, 41BB, CTLA4, PD1, PD-L1, PD-L2, TIM-3,

BTLA, VISTA, LAG-3, CD28, OX40, GITR, CD137, CD27, HVEM, CCR4, CD25, CD103, KIRg1, Nrp1, CD278, Gpr83, TIGIT, CD154, CD160, TNFR2, PVRIG, DNAM, and ICOS. In some examples, the second antibody binds to PD-1. In some examples, the second antibody binds to PD-L1. In some examples, the immunotherapeutic agent comprises a vaccine, oncolytic virus, adoptive cell therapy, cytokine, or small molecule. In some examples, the method further comprises administering to the individual an effective amount of a second antibody that binds an antigen expressed by a natural killer (NK) cell. In some examples, the antigen expressed by the NK cell is selected from the group consisting of NKR-P1A, CD94, KLRG1, KIR2DL5A, KIR2DL5B, KIR2DL1, KIR2DL2, KIR2DL3, KIR2DS2, KIR2DS3, KIR2DS4, KIR2DS5, KIR3DS1, KIR2DS1, CD94, NKG2D, CD160, CD16, NKp46, NKp30, NKp44, DNAM1, CRTAM, CD27, NTB-A, PSGL1, CD96, CD100, NKp80, SLAMF7, and CD244. In some examples, the method further comprises administering to the individual an effective amount of a chemotherapeutic agent or small molecule anti-cancer agent. In some examples, the method further comprises administering to the individual an effective amount of a targeted small molecule inhibitor. In some examples, the targeted small molecule inhibitor is a VEGFR and/or PDGFR inhibitor, EGFR inhibitor, ALK inhibitor, CDK4/6 inhibitor, PARP inhibitor, mTOR inhibitor, KRAS inhibitor, TRK inhibitor, BCL2 inhibitor, IDH inhibitor, PI3K inhibitor, DNA damage response (DDR) inhibitor, or hypomethylation agent.

[0020a] In one aspect, the present disclosure refers to use of any one of the antibodies as disclosed herein in the manufacture of a medicament for treating or delaying progression of an autoimmune disease or an inflammatory disease in an individual.

[0021] In certain examples, the present disclosure provides a method of treating or delaying progression of an autoimmune disease or an inflammatory disease in an individual, the method comprising administering to the individual an effective amount of the antibody according to any one of the above examples. In some examples, the autoimmune disease or inflammatory disease is selected from the group consisting of multiple sclerosis, rheumatoid arthritis, a spondyloarthropathy, systemic lupus erythematosus, an antibody-mediated inflammatory or autoimmune disease, graft versus host disease, sepsis, diabetes, psoriasis, psoriatic arthritis, atherosclerosis, Sjogren's syndrome, progressive systemic sclerosis, scleroderma, acute coronary syndrome, ischemic reperfusion, Crohn's Disease, ulcerative colitis, endometriosis, glomerulonephritis, IgA nephropathy, polycystic kidney disease, myasthenia gravis, idiopathic pulmonary fibrosis, fibrotic disease (*e.g.*, pulmonary fibrosis, liver cirrhosis, atrial fibrosis, endomyocardial

fibrosis, myelofibrosis, or retroperitoneal fibrosis), asthma, atopic dermatitis, acute respiratory distress syndrome (ARDS), vasculitis, and inflammatory autoimmune myositis.

[0022] It is to be understood that one, some, or all of the properties of the various examples described herein may be combined to form other examples of the present disclosure. These and other aspects of the disclosure will become apparent to one of skill in the art. These and other examples of the disclosure are further described by the detailed description that follows.

BRIEF DESCRIPTION OF THE DRAWINGS

[0023] **FIG. 1** shows the results of an *in vivo* syngeneic mouse colon carcinoma model to assess single agent activity. MC38 cells were implanted subcutaneously in C57BL/6 mice and randomized into groups (8 mice/group). Mice were treated with vehicle (PBS), CD47 blocking anti-SIRP- α antibody AB27b, CD47 blocking anti-SIRP- α antibody AB25b, or CD47 blocking anti-SIRP- α antibody AB25c. Treatment was initiated when tumors were an average of 60mm³, day 7 post implant. Mice were dosed intraperitoneally (IP) at 10 mg/kg twice a week for three weeks with anti-SIRP α antibodies. Animals were sacrificed when tumors reached a volume of ~2000mm³.

[0024] **FIG. 2** compares expression yield and binding affinity of antibodies having the AB21 human heavy chain and the indicated humanized light chains. The antibodies were produced by expression in FreeStyle™ 293-FS cells (Thermo Fisher).

[0025] **FIGS. 3A & 3B** show the results of *in vitro* phagocytosis assays using EGFR(+) DLD-1 cells as the target and M2 macrophages as the phagocytosing cell. Anti-SIRP- α antibodies were tested at the indicated concentrations in combination with the anti-EGFR antibody cetuximab. Phagocytosis was measured by percentage of CFSE+ cells.

[0026] **FIGS. 4A & 4B** show the results of *in vivo* dendritic cell activation assays with the indicated anti-SIRP- α antibodies. Mice were intravenously injected with the indicated antibody at 10 mg/kg, and spleens were harvested five hours after injection. Activation markers CD86, MHCII and CCR7 on CD4+ dendritic cells were measured by flow cytometry.

[0027] **FIG. 5** shows the results of an *in vivo* syngeneic mouse colon carcinoma model to assess activity of combining anti-SIRP- α treatment with PD-L1/PD-1 pathway inhibition. CT26 cells were implanted subcutaneously in BALBc mice and randomized into groups (8 mice/group). Mice were treated with vehicle (PBS), anti-PD-L1 antibody, CD47 blocking anti-SIRP- α antibody AB25b, or AB25b and PD-L1. Treatment was initiated when tumors

CLAIMS

What is claimed is:

1. An isolated antibody that binds an extracellular domain of a human SIRP- α polypeptide, wherein the antibody comprises:

(a) a heavy chain comprising a heavy chain variable (VH) domain that comprises the amino acid sequence of SEQ ID NO:26; and

(b) a light chain comprising a light chain variable (VL) domain that comprises an amino acid sequence according to the formula
SYELTQPPSVSVSPGQTARITCSGGSYSSYYAWYQQKPGQAPVTLIYSDDKRPSNIP
ERFSGSSSGTTVTLTISGVQAEDEADYYCGGYDQSSYTNPFGX₁GTX₂X₃TVL (SEQ ID NO:71), wherein X₁ is G or T; X₂ is K, Q, or R; and X₃ is L or V, and wherein the VL domain does not comprise the sequence of SEQ ID NO:25.

2. The antibody of claim 1, wherein the VL domain comprises an amino acid sequence selected from the group consisting of SEQ ID NOs:39-41.

3. The antibody of claim 1 or claim 2, wherein the light chain further comprises a light chain constant (CL) domain sequence that comprises an amino acid sequence according to the formula
GQPKANPTVTLFPPSSEELQANKATLVCLISDFYPGAVTVAWKADGSPVKAGVETTK
PSKQSX₄X₅KYAASSYLSLTPEQWKSHRSYSCQVTHEGSTVEKTVAPTECS (SEQ ID NO:72), wherein X₄X₅ is ND, DN, DS, or SD.

4. The antibody of claim 1 or claim 2, wherein the light chain further comprises a light chain constant (CL) domain sequence that comprises an amino acid sequence selected from the group consisting of SEQ ID NOs:43-46.

5. The antibody of claim 1 or claim 2, wherein the light chain further comprises a kappa light chain constant (CL) domain.

6. The antibody of claim 5, wherein the light chain comprises the amino acid sequence of SEQ ID NO:36.

7. The antibody of claim 1 or claim 2, wherein the light chain further comprises a lambda light chain constant (CL) domain.
8. The antibody of claim 7, wherein the light chain comprises the amino acid sequence of SEQ ID NO:37 or SEQ ID NO:38.
9. The antibody of claim 1, wherein the light chain comprises an amino acid sequence selected from the group consisting of SEQ ID NOs:48-57.
10. The antibody of any one of claims 1-9, wherein the antibody is a scFv-Fc, single domain antibody, single heavy chain antibody, or single light chain antibody.
11. The antibody of any one of claims 1-9, wherein the antibody is a monoclonal antibody.
12. The antibody of any one of claims 1-9, wherein the heavy chain comprises a heavy chain constant domain that comprises an Fc region.
13. The antibody of claim 12, wherein the Fc region is a human Fc region selected from the group consisting of an IgG1 Fc region, an IgG2 Fc region, and an IgG4 Fc region.
14. The antibody of claim 12, wherein the Fc region is a human IgG1 Fc region.
15. The antibody of claim 12, wherein the Fc region is a human IgG1 Fc region comprising L234A, L235A, and G237A substitutions, amino acid position numbering according to EU.
16. The antibody of claim 15, wherein the Fc region further comprises an N297A substitution, amino acid position numbering according to EU.
17. The antibody of claim 12, wherein the Fc region is a human IgG2 Fc region.
18. The antibody of claim 12, wherein the Fc region is a human IgG2 Fc region comprising A330S and P331S substitutions, amino acid position numbering according to EU.
19. The antibody of claim 17 or claim 18, wherein the Fc region further comprises an N297A substitution, amino acid position numbering according to EU.

20. The antibody of claim 12, wherein the Fc region is a human IgG4 Fc region, and wherein the heavy chain comprises an S228P substitution, amino acid position numbering according to EU.
21. The antibody of claim 12, wherein the heavy chain constant domain comprises an amino acid sequence selected from the group consisting of SEQ ID NOs:31-35.
22. The antibody of claim 12, wherein the heavy chain constant domain comprises an amino acid sequence selected from the group consisting of SEQ ID NOs:33, 34, and 137.
23. The antibody of claim 12, wherein the heavy chain constant domain comprises an amino acid sequence selected from the group consisting of SEQ ID NOs:132-139.
24. The antibody of claim 1, wherein the heavy chain comprises an amino acid sequence selected from the group consisting of SEQ ID NOs:58-62.
25. The antibody of claim 1, wherein the heavy chain comprises an amino acid sequence selected from the group consisting of SEQ ID NOs:60, 61, and 129.
26. The antibody of claim 1, wherein:
- (a) the heavy chain comprises the amino acid sequence of SEQ ID NO:62, and the light chain comprises the amino acid sequence of SEQ ID NO:52;
 - (b) the heavy chain comprises the amino acid sequence of SEQ ID NO:62, and the light chain comprises the amino acid sequence of SEQ ID NO:53;
 - (c) the heavy chain comprises the amino acid sequence of SEQ ID NO:62, and the light chain comprises the amino acid sequence of SEQ ID NO:54;
 - (d) the heavy chain comprises the amino acid sequence of SEQ ID NO:62, and the light chain comprises the amino acid sequence of SEQ ID NO:55;
 - (e) the heavy chain comprises the amino acid sequence of SEQ ID NO:62, and the light chain comprises the amino acid sequence of SEQ ID NO:56; or
 - (f) the heavy chain comprises the amino acid sequence of SEQ ID NO:62, and the light chain comprises the amino acid sequence of SEQ ID NO:57.

27. The antibody of claim 1, wherein:

(a) the heavy chain comprises the amino acid sequence of SEQ ID NO:58, and the light chain comprises the amino acid sequence of SEQ ID NO:52;

(b) the heavy chain comprises the amino acid sequence of SEQ ID NO:59, and the light chain comprises the amino acid sequence of SEQ ID NO:52;

(c) the heavy chain comprises the amino acid sequence of SEQ ID NO:60, and the light chain comprises the amino acid sequence of SEQ ID NO:52;

(d) the heavy chain comprises the amino acid sequence of SEQ ID NO:61, and the light chain comprises the amino acid sequence of SEQ ID NO:52;

(e) the heavy chain comprises the amino acid sequence of SEQ ID NO:58, and the light chain comprises the amino acid sequence of SEQ ID NO:53;

(f) the heavy chain comprises the amino acid sequence of SEQ ID NO:59, and the light chain comprises the amino acid sequence of SEQ ID NO:53;

(g) the heavy chain comprises the amino acid sequence of SEQ ID NO:60, and the light chain comprises the amino acid sequence of SEQ ID NO:53;

(h) the heavy chain comprises the amino acid sequence of SEQ ID NO:61, and the light chain comprises the amino acid sequence of SEQ ID NO:53;

(i) the heavy chain comprises the amino acid sequence of SEQ ID NO:58, and the light chain comprises the amino acid sequence of SEQ ID NO:54;

(j) the heavy chain comprises the amino acid sequence of SEQ ID NO:59, and the light chain comprises the amino acid sequence of SEQ ID NO:54;

(k) the heavy chain comprises the amino acid sequence of SEQ ID NO:60, and the light chain comprises the amino acid sequence of SEQ ID NO:54;

(l) the heavy chain comprises the amino acid sequence of SEQ ID NO:61, and the light chain comprises the amino acid sequence of SEQ ID NO:54;

(m) the heavy chain comprises the amino acid sequence of SEQ ID NO:58, and the light chain comprises the amino acid sequence of SEQ ID NO:55;

(n) the heavy chain comprises the amino acid sequence of SEQ ID NO:59, and the light chain comprises the amino acid sequence of SEQ ID NO:55;

(o) the heavy chain comprises the amino acid sequence of SEQ ID NO:60, and the light chain comprises the amino acid sequence of SEQ ID NO:55;

(p) the heavy chain comprises the amino acid sequence of SEQ ID NO:61, and the light chain comprises the amino acid sequence of SEQ ID NO:55;

(q) the heavy chain comprises the amino acid sequence of SEQ ID NO:58, and the light chain comprises the amino acid sequence of SEQ ID NO:56;

(r) the heavy chain comprises the amino acid sequence of SEQ ID NO:59, and the light chain comprises the amino acid sequence of SEQ ID NO:56;

(s) the heavy chain comprises the amino acid sequence of SEQ ID NO:60, and the light chain comprises the amino acid sequence of SEQ ID NO:56;

(t) the heavy chain comprises the amino acid sequence of SEQ ID NO:61, and the light chain comprises the amino acid sequence of SEQ ID NO:56;

(u) the heavy chain comprises the amino acid sequence of SEQ ID NO:58, and the light chain comprises the amino acid sequence of SEQ ID NO:57;

(v) the heavy chain comprises the amino acid sequence of SEQ ID NO:59, and the light chain comprises the amino acid sequence of SEQ ID NO:57;

(w) the heavy chain comprises the amino acid sequence of SEQ ID NO:60, and the light chain comprises the amino acid sequence of SEQ ID NO:57; or

(x) the heavy chain comprises the amino acid sequence of SEQ ID NO:61, and the light chain comprises the amino acid sequence of SEQ ID NO:57.

28. The antibody of claim 1, wherein:

(a) the heavy chain comprises the amino acid sequence of SEQ ID NO:60, and the light chain comprises the amino acid sequence of SEQ ID NO:55;

(b) the heavy chain comprises the amino acid sequence of SEQ ID NO:61, and the light chain comprises the amino acid sequence of SEQ ID NO:55;

(c) the heavy chain comprises the amino acid sequence of SEQ ID NO:129, and the light chain comprises the amino acid sequence of SEQ ID NO:55;

(d) the heavy chain comprises the amino acid sequence of SEQ ID NO:124, and the light chain comprises the amino acid sequence of SEQ ID NO:52; or

(e) the heavy chain comprises the amino acid sequence of SEQ ID NO:124, and the light chain comprises the amino acid sequence of SEQ ID NO:55.

29. The antibody of any one of claims 1-28, wherein the antibody enhances phagocytosis by a macrophage expressing a human SIRP- α polypeptide.

30. The antibody of any one of claims 1-28, wherein the antibody enhances activation of a dendritic cell expressing a human SIRP- α polypeptide.

31. The antibody of any one of claims 1-30, wherein the antibody inhibits *in vivo* growth of a tumor that expresses CD47.

32. The antibody of any one of claims 1-31, wherein the antibody is conjugated to an agent.

33. The antibody of any one of claims 1-31, wherein the antibody is a bispecific antibody.

34. The antibody of claim 33, wherein the antibody comprises a first antigen binding domain that binds an extracellular domain of a human SIRP- α polypeptide and a second antigen binding domain that binds an antigen expressed by a cancer cell.

35. The antibody of claim 34, wherein the antigen expressed by the cancer cell is selected from the group consisting of CD19, CD20, CD22, CD30, CD33, CD38, CD52, CD56, CD70, CD74, CD79b, CD123, CD138, CS1/SLAMF7, Trop-2, 5T4, EphA4, BCMA, Mucin 1, Mucin 16, PD-L1, PTK7, STEAP1, Endothelin B Receptor, mesothelin, EGFRvIII, ENPP3, SLC44A4, GNMB, nectin 4, NaPi2b, LIV-1A, Guanylyl cyclase C, DLL3, EGFR, HER2,

VEGF, VEGFR, integrin α V β 3, integrin α 5 β 1, MET, IGF1R, TRAILR1, TRAILR2, RANKL, FAP, Tenascin, Le^y, EpCAM, CEA, gpA33, PSMA, TAG72, a mucin, CAIX, EPHA3, folate receptor α , GD2, GD3, and an MHC/peptide complex comprising a peptide from NY-ESO-1/LAGE, SSX-2, a MAGE family protein, MAGE-A3, gp100/pmel17, Melan-A/MART-1, gp75/TRP1, tyrosinase, TRP2, CEA, PSA, TAG-72, immature laminin receptor, MOK/RAGE-1, WT-1, SAP-1, BING-4, EpCAM, MUC1, PRAME, survivin, BRCA1, BRCA2, CDK4, CML66, MART-2, p53, Ras, β -catenin, TGF- β RII, HPV E6, or HPV E7.

36. The antibody of claim 33, wherein the antibody comprises a first antigen binding domain that binds an extracellular domain of a human SIRP- α polypeptide and a second antigen binding domain that binds an antigen expressed by an immune cell.

37. The antibody of claim 36, wherein the antigen expressed by the immune cell is selected from the group consisting of BDCA2, BDCA4, ILT7, LILRB1, LILRB2, LILRB3, LILRB4, LILRB5, Siglec-3, Siglec-7, Siglec-9, Siglec-15, FGL-1, CD200, CD200R, CSF-1R, CD40, CD40L, CD163, CD206, DEC205, CD47, CD123, arginase, IDO, TDO, AhR, EP2, COX-2, CCR2, CCR-7, CXCR1, CX3CR1, CXCR2, CXCR3, CXCR4, CXCR7, TGF- β RI, TGF- β RII, c-Kit, CD244, L-selectin/CD62L, CD11b, CD11c, CD68, 41BB, CTLA4, PD1, PD-L1, PD-L2, TIM-3, BTLA, VISTA, LAG-3, CD28, OX40, GITR, CD137, CD27, HVEM, CCR4, CD25, CD103, KIRg1, Nrp1, CD278, Gpr83, TIGIT, CD154, CD160, TNFR2, PVRIG, DNAM, and ICOS.

38. The antibody of claim 33, wherein the antibody comprises a first antigen binding domain that binds an extracellular domain of a human SIRP- α polypeptide and a second antigen binding domain that binds an antigen expressed by a natural killer (NK) cell.

39. The antibody of claim 38, wherein the antigen expressed by the NK cell is selected from the group consisting of NKR-P1A, CD94, KLRG1, KIR2DL5A, KIR2DL5B, KIR2DL1, KIR2DL2, KIR2DL3, KIR2DS2, KIR2DS3, KIR2DS4, KIR2DS5, KIR3DS1, KIR2DS1, CD94, NKG2D, CD160, CD16, NKp46, NKp30, NKp44, DNAM1, CRTAM, CD27, NTB-A, PSGL1, CD96, CD100, NKp80, SLAMF7, and CD244.

40. A polynucleotide encoding the antibody of any one of claims 1-39.

41. A vector comprising the polynucleotide of claim 40.

42. A host cell comprising the polynucleotide of claim 40 or the vector of claim 41.
43. A method of producing an antibody, the method comprising culturing the host cell of claim 42 such that the antibody is produced.
44. The method of claim 43, further comprising recovering the antibody from the host cell.
45. Use of the antibody of any one of claims 1-39 in the manufacture of a medicament for treating or delaying progression of cancer in an individual.
46. The use of claim 45, wherein an effective amount of a second antibody that binds an antigen expressed by the cancer is to be administered to the individual.
47. The use of claim 46, wherein the antigen expressed by the cancer is selected from the group consisting of CD19, CD20, CD22, CD30, CD33, CD38, CD52, CD56, CD70, CD74, CD79b, CD123, CD138, CS1/SLAMF7, Trop-2, 5T4, EphA4, BCMA, Mucin 1, Mucin 16, PTK7, STEAP1, Endothelin B Receptor, mesothelin, EGFRvIII, ENPP3, SLC44A4, GNMB, nectin 4, NaPi2b, LIV-1A, Guanylyl cyclase C, DLL3, EGFR, HER2, VEGF, VEGFR, integrin α V β 3, integrin α 5 β 1, MET, IGF1R, TRAILR1, TRAILR2, RANKL, FAP, Tenascin, Le^y, EpCAM, CEA, gpA33, PSMA, TAG72, a mucin, CAIX, EPHA3, folate receptor α , GD2, GD3, and an MHC/peptide complex comprising a peptide from NY-ESO-1/LAGE, SSX-2, a MAGE family protein, MAGE-A3, gp100/pmel17, Melan-A/MART-1, gp75/TRP1, tyrosinase, TRP2, CEA, PSA, TAG-72, immature laminin receptor, MOK/RAGE-1, WT-1, SAP-1, BING-4, EpCAM, MUC1, PRAME, survivin, BRCA1, BRCA2, CDK4, CML66, MART-2, p53, Ras, β -catenin, TGF- β RII, HPV E6, or HPV E7.
48. The use of any one of claims 45-47, wherein an effective amount of an immunotherapeutic agent is to be administered to the individual.
49. The use of claim 48, wherein the immunotherapeutic agent comprises a second antibody.
50. The use of claim 49, wherein the second antibody binds to an antigen selected from the group consisting of BDCA2, BDCA4, ILT7, LILRB1, LILRB2, LILRB3, LILRB4, LILRB5, Siglec-3, Siglec-7, Siglec-9, Siglec-15, FGL-1, CD200, CD200R, CSF-1R, CD40,

CD40L, CD163, CD206, DEC205, CD47, CD123, arginase, IDO, TDO, AhR, EP2, COX-2, CCR2, CCR-7, CXCR1, CX3CR1, CXCR2, CXCR3, CXCR4, CXCR7, TGF- β RI, TGF- β RII, c-Kit, CD244, L-selectin/CD62L, CD11b, CD11c, CD68, 41BB, CTLA4, PD1, PD-L1, PD-L2, TIM-3, BTLA, VISTA, LAG-3, CD28, OX40, GITR, CD137, CD27, HVEM, CCR4, CD25, CD103, KIRg1, Nrp1, CD278, Gpr83, TIGIT, CD154, CD160, TNFR2, PVRIG, DNAM, and ICOS.

51. The use of claim 50, wherein the second antibody binds to PD-1.
52. The use of claim 50, wherein the second antibody binds to PD-L1.
53. The use of claim 48, wherein the immunotherapeutic agent comprises a vaccine, oncolytic virus, adoptive cell therapy, cytokine, or small molecule agent.
54. The use of any one of claims 45-53, wherein an effective amount of a second antibody that binds an antigen expressed by a natural killer (NK) cell is to be administered to the individual.
55. The use of claim 54, wherein the antigen expressed by the NK cell is selected from the group consisting of NKR-P1A, CD94, KLRG1, KIR2DL5A, KIR2DL5B, KIR2DL1, KIR2DL2, KIR2DL3, KIR2DS2, KIR2DS3, KIR2DS4, KIR2DS5, KIR3DS1, KIR2DS1, CD94, NKG2D, CD160, CD16, NKp46, NKp30, NKp44, DNAM1, CRTAM, CD27, NTB-A, PSGL1, CD96, CD100, NKp80, SLAMF7, and CD244.
56. The use of any one of claims 45-55, wherein an effective amount of a chemotherapeutic agent or small molecule anti-cancer agent is to be administered to the individual.
57. The use of any one of claims 45-56, wherein an effective amount of a targeted small molecule inhibitor is to be administered to the individual.
58. The use of claim 57, wherein the targeted small molecule inhibitor is a VEGFR and/or PDGFR inhibitor, EGFR inhibitor, ALK inhibitor, CDK4/6 inhibitor, PARP inhibitor, mTOR inhibitor, KRAS inhibitor, TRK inhibitor, BCL2 inhibitor, IDH inhibitor, PI3K inhibitor, DNA damage response (DDR) inhibitor, or hypomethylation agent.

59. Use of the antibody of any one of claims 1-39 in the manufacture of a medicament for treating or delaying progression of an autoimmune disease or an inflammatory disease in an individual.

60. The use of claim 59, wherein the autoimmune disease or inflammatory disease is selected from the group consisting of multiple sclerosis, rheumatoid arthritis, a spondyloarthropathy, systemic lupus erythematosus, an antibody-mediated inflammatory or autoimmune disease, graft versus host disease, sepsis, diabetes, psoriasis, psoriatic arthritis, atherosclerosis, Sjogren's syndrome, progressive systemic sclerosis, scleroderma, acute coronary syndrome, ischemic reperfusion, Crohn's Disease, ulcerative colitis, endometriosis, glomerulonephritis, IgA nephropathy, polycystic kidney disease, myasthenia gravis, idiopathic pulmonary fibrosis, pulmonary fibrosis, liver cirrhosis, atrial fibrosis, endomyocardial fibrosis, myelofibrosis, retroperitoneal fibrosis, asthma, atopic dermatitis, acute respiratory distress syndrome (ARDS), vasculitis, and inflammatory autoimmune myositis.