polypeptide. In some embodiments, the antibody binds the extracellular domain (e.g., the D1 domain) of a human SIRP-α v1 polypeptide, the extracellular domain (e.g., the D1 domain) of a human SIRP-α v2 polypeptide, or both. In one aspect, there is provided an isolated antibody that binds an extracellular domain of a human SIRP-α polypeptide, wherein the antibody binds the extracellular domain of a human SIRP-α v1 polypeptide, the extracellular domain of a human SIRP-α v2 polypeptide, or both. In some embodiments, the antibody binds an extracellular domain of a human SIRP-α v1 polypeptide comprising the amino acid sequence of EEELQVIQPDKSVLVAAGETATLRCTATSLIPVGPIQWFRGAGPGRELIYNQKEGHF PRVTTVSDLTKRNNMDFSIRIGNITPADAGTYYCVKFRKGSPDDVEFKSGAGTELS VRAKPS (SEQ ID NO:5). In some embodiments, the antibody binds an extracellular domain of a human SIRP-α v2 polypeptide comprising the amino acid sequence of EEELQVIQPDKSVSVAAGESAILHCTVTSLIPVGPIQWFRGAGPARELIYNQKEGHFP RVTTVSESTKRENMDFSISISNITPADAGTYYCVKFRKGSPDTEFKSGAGTELSVRA KPS (SEQ ID NO:6). In some embodiments, the antibody binds an extracellular domain of a human SIRP-α v1 polypeptide comprising the amino acid sequence of EEELQVIQPDKSVLVAAGETATLRCTATSLIPVGPIQWFRGAGPGRELIYNQKEGHF PRVTTVSDLTKRNNMDFSIRIGNITPADAGTYYCVKFRKGSPDDVEFKSGAGTELS VRAKPS (SEQ ID NO:5) and binds an extracellular domain of a human SIRP-α v2 polypeptide comprising the amino acid sequence of EEELQVIQPDKSVSVAAGESAILHCTVTSLIPVGPIQWFRGAGPARELIYNQKEGHFP RVTTVSESTKRENMDFSISISNITPADAGTYYCVKFRKGSPDTEFKSGAGTELSVRA KPS (SEQ ID NO:6). In some embodiments, the antibody binds the extracellular domains (e.g., the D1 domains) of three, four, five, six, seven, eight, nine or ten different human SIRP-α variant polypeptides. In some embodiments, each of the three, four, five, six, seven, eight, nine or ten different human SIRP-α variant polypeptides comprises an extracellular domain comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 5, 6, and 76-83. In some embodiments, the antibody binds an extracellular domain (e.g., the D1 domain) of a monkey SIRP-α polypeptide. In some embodiments, the monkey SIRP-α polypeptide is a cynomolgus SIRP-α polypeptide. In some embodiments, the antibody binds the extracellular domains (e.g., the D1 domains) of at least two different monkey SIRP-α variant polypeptides. In some embodiments, the antibody binds an extracellular domain of a cynomolgus SIRP-α polypeptide comprising the amino acid sequence of SEQ ID NO:11, an extracellular domain of a cynomolgus SIRP-α polypeptide comprising the amino acid sequence of SEQ ID NO:12, or both. In some embodiments, the antibody binds an extracellular domain (e.g., the D1 domain) of a murine SIRP-α

ID NO:296. In some embodiments, the antibody further binds to the human SIRP-α v1 polypeptide at one or more amino acid positions selected from the group consisting of L30, P32, E54, T62, N71, M72, F74, and R95, according to SEQ ID NO:296. In some embodiments, the antibody further binds to the human SIRP-α v1 polypeptide at L30, P32, E54, T62, N71, M72, F74, and R95, according to SEQ ID NO:296.

[0017] In other aspects, provided herein is an isolated antibody that binds an extracellular domain of a human SIRP-α polypeptide (e.g., the D1 domain), wherein the antibody binds to a human SIRP-α v1 polypeptide at one or more amino acid positions selected from the group consisting of I7, P9, D10, K11, S12, A42, A108, and E111, according to SEQ ID NO:296. In some embodiments, the antibody binds to the human SIRP-α v1 polypeptide at K11, A42, A108, and E111, according to SEQ ID NO:296. In some embodiments, the antibody binds to the human SIRP-α v1 polypeptide at I7, P9, D10, K11, S12, A108, and E111, according to SEQ ID NO:296. In some embodiments, the antibody further binds to the human SIRP-α v1 polypeptide at one or more amino acid positions selected from the group consisting of L14, T26, T28, T88, Y90, S106, S113, and A116, according to SEQ ID NO:296. In some embodiments, the antibody further binds to the human SIRP-α v1 polypeptide at L14, T88, Y90, S106, S113, and A116 of human SIRP-α v1, according to SEQ ID NO:296. In some embodiments, the antibody further binds to the human SIRP-α v1 polypeptide at L14, T26, and T28, according to SEQ ID NO:296.

[0018] Disclosed is an isolated antibody that binds an extracellular domain of a human SIRP-α polypeptide (e.g., the D1 domain), wherein the antibody binds to a human SIRP-α v1 polypeptide at one or more amino acid positions selected from the group consisting of E47, L48, P58, R59, T82, and A84, according to SEQ ID NO:296. In some embodiments, the antibody binds to the human SIRP-α v1 polypeptide at E47, L48, P58, R59, T82, and A84, according to SEQ ID NO:296. In some embodiments, the antibody further binds to the human SIRP-α v1 polypeptide at one or more amino acid positions selected from the group consisting of A17, P44, G45, I49, E54, G55, H56, F57, and P83, according to SEQ ID NO:296. In some embodiments, the antibody further binds to the human SIRP-α v1 polypeptide at A17, P44, G45, I49, E54, G55, H56, F57, and P83 of human SIRP-α v1, according to SEQ ID NO:296.

[0019] In other aspects, provided herein is an isolated antibody that binds an extracellular domain of a human SIRP-α polypeptide (e.g., the D1 domain), wherein the

antibody binds the extracellular domain of a human SIRP-α v1 polypeptide with a dissociation constant (K_D) of less than 100nM, and wherein the antibody blocks binding between an extracellular domain of a human SIRP-α polypeptide and an IgSF domain of a human CD47 polypeptide. In some embodiments, the antibody binds the extracellular domain of a human SIRP-α v2 polypeptide with a dissociation constant (K_D) of less than 100nM. In some embodiments, the antibody binds the D1 domain of a human SIRP-α v1 polypeptide and the D1 domain of a human SIRP-α v2 polypeptide. In some embodiments, the antibody binds an extracellular domain of a cynomolgus SIRP-α polypeptide. In some embodiments, the antibody binds an extracellular domain of a human SIRP-β polypeptide. In some embodiments, the antibody binds an extracellular domain of a human SIRP-γ polypeptide. In some embodiments, the antibody binds an extracellular domain of a murine SIRP-α polypeptide.

[0020] In other aspects, provided herein is an isolated antibody that binds an extracellular domain of a human SIRP-α polypeptide (e.g., the D1 domain), wherein the antibody binds the D1 domain of a human SIRP-α polypeptide, and wherein the antibody does not block binding between an extracellular domain of a human SIRP-α polypeptide and an IgSF domain of a human CD47 polypeptide. In some embodiments, the antibody binds the D1 domain of a human SIRP-α with a dissociation constant (K_D) of less than 100nM. In some embodiments, the antibody binds the D1 domain of a human SIRP-α v1 polypeptide with a dissociation constant (K_D) of less than 100nM and/or binds the D1 domain of a human SIRP-α v2 polypeptide with a dissociation constant (K_D) of less than 100nM. In some embodiments, the antibody binds the D1 domain of a human SIRP-α v1 polypeptide and the D1 domain of a human SIRP-α v2 polypeptide. In some embodiments, the antibody binds an extracellular domain of a cynomolgus SIRP-α polypeptide. In some embodiments, the antibody binds an extracellular domain of a human SIRP-β polypeptide. In some embodiments, the antibody binds an extracellular domain of a murine SIRP-α polypeptide.

[0021] In other aspects, provided herein is an isolated antibody that binds an extracellular domain of a human SIRP-α polypeptide (e.g., the D1 domain), wherein the antibody competes for binding the extracellular domain of the human SIRP-α polypeptide with a reference anti-SIRP-α antibody comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain of an antibody selected from the group consisting of antibodies 119, 120, 121, 122, 21, 25, 27, 66, and 135. Disclosed is

an isolated antibody that binds an extracellular domain of a human SIRP-α polypeptide (e.g., the D1 domain), wherein the antibody competes for binding the extracellular domain of the human SIRP-α polypeptide with a reference anti-SIRP-α antibody comprising: (a) a heavy chain variable (VH) domain comprising the amino acid sequence of SEQ ID NO:120 and a light chain variable (VL) domain comprising the amino acid sequence of SEQ ID NO:97; (b) a heavy chain variable (VH) domain comprising the amino acid sequence of SEQ ID NO:121 and a light chain variable (VL) domain comprising the amino acid sequence of SEQ ID NO:98; (c) a heavy chain variable (VH) domain comprising the amino acid sequence of SEQ ID NO:130 and a light chain variable (VL) domain comprising the amino acid sequence of SEQ ID NO:107; (d) a heavy chain variable (VH) domain comprising the amino acid sequence of SEQ ID NO:122 and a light chain variable (VL) domain comprising the amino acid sequence of SEQ ID NO:99; (e) a heavy chain variable (VH) domain comprising the amino acid sequence of SEQ ID NO:135 and a light chain variable (VL) domain comprising the amino acid sequence of SEQ ID NO:136; (f) a heavy chain variable (VH) domain comprising the amino acid sequence of SEQ ID NO:137 and a light chain variable (VL) domain comprising the amino acid sequence of SEQ ID NO:138; (g) a heavy chain variable (VH) domain comprising the amino acid sequence of SEQ ID NO:139 and a light chain variable (VL) domain comprising the amino acid sequence of SEQ ID NO:140; (h) a heavy chain variable (VH) domain comprising the amino acid sequence of SEQ ID NO:141 and a light chain variable (VL) domain comprising the amino acid sequence of SEQ ID NO:142; or (i) a heavy chain variable (VH) domain comprising the amino acid sequence of SEQ ID NO:127 and a light chain variable (VL) domain comprising the amino acid sequence of SEQ ID NO:104.

[0022] In other aspects, provided herein is an isolated antibody that binds an extracellular domain of a human SIRP-α polypeptide (e.g., the D1 domain), wherein the antibody competes for binding the extracellular domain of the human SIRP-α polypeptide with a reference anti-SIRP-α antibody comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain of an antibody selected from the group consisting of antibodies 136 and 137. Disclosed is an isolated antibody that binds an extracellular domain of a human SIRP-α polypeptide (e.g., the D1 domain), wherein the antibody competes for binding the extracellular domain of the human SIRP-α polypeptide with a reference anti-SIRP-α antibody comprising: (a) a heavy chain variable (VH) domain comprising the amino acid sequence of SEQ ID NO:133 and a light chain variable (VL)

domain comprising the amino acid sequence of SEQ ID NO:134; or (b) a heavy chain variable (VH) domain comprising the amino acid sequence of SEQ ID NO:128 and a light chain variable (VL) domain comprising the amino acid sequence of SEQ ID NO:105.

[0023] Disclosed is an isolated antibody that binds an extracellular domain of a human SIRP-α polypeptide (e.g., the D1 domain), wherein the antibody competes for binding the extracellular domain of the human SIRP-α polypeptide with a reference anti-SIRP-α antibody comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain of an antibody selected from the group consisting of antibodies 3, 213, 173, and 209. Disclosed is an isolated antibody that binds an extracellular domain of a human SIRP-α polypeptide (e.g., the D1 domain), wherein the antibody competes for binding the extracellular domain of the human SIRP-α polypeptide with a reference anti-SIRP-α antibody comprising: (a) a heavy chain variable (VH) domain comprising the amino acid sequence of SEQ ID NO:242 and a light chain variable (VL) domain comprising the amino acid sequence of SEQ ID NO:243; (b) a heavy chain variable (VH) domain comprising the amino acid sequence of SEQ ID NO:275 and a light chain variable (VL) domain comprising the amino acid sequence of SEQ ID NO:276; (c) a heavy chain variable (VH) domain comprising the amino acid sequence of SEQ ID NO:278 and a light chain variable (VL) domain comprising the amino acid sequence of SEQ ID NO:279; or (d) a heavy chain variable (VH) domain comprising the amino acid sequence of SEQ ID NO:280 and a light chain variable (VL) domain comprising the amino acid sequence of SEQ ID NO:281.

[0024] Disclosed is an isolated antibody that binds an extracellular domain of a human SIRP-α polypeptide (e.g., the D1 domain), wherein the antibody competes for binding the extracellular domain of the human SIRP-α polypeptide with a reference anti-SIRP-α antibody comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain of an antibody selected from the group consisting of antibodies 115, 116, 117, 118, and 132. Disclosed is an isolated antibody that binds an extracellular domain of a human SIRP-α polypeptide (e.g., the D1 domain), wherein the antibody competes for binding the extracellular domain of the human SIRP-α polypeptide with a reference anti-SIRP-α antibody comprising: (a) a heavy chain variable (VH) domain comprising the amino acid sequence of SEQ ID NO:116 and a light chain variable (VL) domain comprising the amino acid sequence of SEQ ID NO:93; (b) a heavy chain variable (VH) domain comprising the amino acid sequence of SEQ ID NO:117

and a light chain variable (VL) domain comprising the amino acid sequence of SEQ ID NO:94; (c) a heavy chain variable (VH) domain comprising the amino acid sequence of SEQ ID NO:118 and a light chain variable (VL) domain comprising the amino acid sequence of SEQ ID NO:95; (d) a heavy chain variable (VH) domain comprising the amino acid sequence of SEQ ID NO:119 and a light chain variable (VL) domain comprising the amino acid sequence of SEQ ID NO:96; or (e) a heavy chain variable (VH) domain comprising the amino acid sequence of SEQ ID NO:282 and a light chain variable (VL) domain comprising the amino acid sequence of SEQ ID NO:283.

[0025] In other aspects, provided herein is an isolated antibody that binds an extracellular domain of a human SIRP-α polypeptide (e.g., the D1 domain), wherein the antibody competes for binding the extracellular domain of the human SIRP-α polypeptide with a reference anti-SIRP-α antibody comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain of an antibody selected from the group consisting of antibodies 218, 123, 149, 161, 162, and 194. Disclosed is an isolated antibody that binds an extracellular domain of a human SIRP-α polypeptide (e.g., the D1 domain), wherein the antibody competes for binding the extracellular domain of the human SIRP-α polypeptide with a reference anti-SIRP-α antibody comprising: (a) a heavy chain variable (VH) domain comprising the amino acid sequence of SEQ ID NO:284 and a light chain variable (VL) domain comprising the amino acid sequence of SEQ ID NO:285; (b) a heavy chain variable (VH) domain comprising the amino acid sequence of SEQ ID NO:123 and a light chain variable (VL) domain comprising the amino acid sequence of SEQ ID NO:100; (c) a heavy chain variable (VH) domain comprising the amino acid sequence of SEQ ID NO:286 and a light chain variable (VL) domain comprising the amino acid sequence of SEQ ID NO:287; (d) a heavy chain variable (VH) domain comprising the amino acid sequence of SEQ ID NO:288 and a light chain variable (VL) domain comprising the amino acid sequence of SEQ ID NO:289; (e) a heavy chain variable (VH) domain comprising the amino acid sequence of SEQ ID NO:290 and a light chain variable (VL) domain comprising the amino acid sequence of SEQ ID NO:291; or (f) a heavy chain variable (VH) domain comprising the amino acid sequence of SEQ ID NO:292 and a light chain variable (VL) domain comprising the amino acid sequence of SEQ ID NO:293.

[0026] In other aspects, provided herein is an isolated antibody that binds an extracellular domain of a human SIRP-α polypeptide (e.g., the D1 domain), wherein the antibody competes for binding the extracellular domain of the human SIRP-α polypeptide

with a reference anti-SIRP-α antibody comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain of antibody 45. Disclosed is an isolated antibody that binds an extracellular domain of a human SIRP-α polypeptide (e.g., the D1 domain), wherein the antibody competes for binding the extracellular domain of the human SIRP-α polypeptide with a reference anti-SIRP-α antibody comprising a heavy chain variable (VH) domain comprising the amino acid sequence of SEQ ID NO:244 and a light chain variable (VL) domain comprising the amino acid sequence of SEQ ID NO:245.

[0027] In some embodiments of any of the above embodiments, the antibody enhances phagocytosis by a macrophage expressing a human SIRP-α polypeptide. In some embodiments, the antibody enhances activation of a dendritic cell expressing a human SIRP-α polypeptide. In some embodiments, the antibody inhibits *in vivo* growth of a tumor that expresses CD47. In some embodiments, the antibody does not prevent interactions between a CD47-expressing cell and a T cell.

[0028] In some embodiments of any of the above embodiments, the antibody is a monoclonal antibody. In some embodiments, the antibody is a scFv-Fc, single domain antibody, single heavy chain antibody, or single light chain antibody. In some embodiments, the antibody comprises a light chain constant region comprising the amino acid sequence of SEQ ID NO:325, 326, or 426. In some embodiments, the antibody comprises an amino acid sequence selected from the group consisting of SEQ ID NOs:320-324. In some embodiments, the antibody comprises an Fc region. In some embodiments, 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 embodiments, the Fc region comprises a human IgG1 Fc region comprising one or more mutations selected from the group consisting of L234A, L235A, L235E, G237A, and N297A, according to EU numbering. In some embodiments, the Fc region comprises a human IgG2 Fc region comprising one or more mutations selected from the group consisting of A330S, P331S and N297A, according to EU numbering. In some embodiments, the Fc region comprises a human IgG4 Fc region comprising one or more mutations selected from the group consisting of S228P, E233P, F234V, L235A, L235E, delG236, and N297A, according to EU numbering. In some embodiments, the antibody is an antibody fragment selected from the group consisting of a Fab, F(ab')2, Fab'-SH, Fv, and scFv fragment. In some embodiments, the antibody is conjugated to a cytotoxic agent or label.

[0029] In some embodiments, the antibody is a bispecific antibody. In some embodiments, the antibody comprises a first antigen binding domain that binds an extracellular domain (e.g., the D1 domain) of a human SIRP-α polypeptide and a second antigen binding domain that binds an antigen expressed by a cancer cell. In some embodiments, 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 αVβ3, integrin α5β1, 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-βRII, HPV E6, or HPV E7. In some embodiments, the antibody is a chicken, humanized, chimeric, or human antibody. In some embodiments, the antibody is generated by or derived from a chicken.

[0030] In other aspects, provided herein are polynucleotides comprising the antibody according to any one of the above embodiments. In other aspects, provided herein are vectors comprising the polynucleotide according to any one of the above embodiments. In other aspects, provided herein are host cells comprising the polynucleotide or vector according to any one of the above embodiments. In other aspects, provided herein are methods of producing an antibody, comprising culturing the host cell according to any one of the above embodiments such that the antibody is produced. In some embodiments, the methods further include recovering the antibody from the host cell.

[0031] Further provided herein are methods of treating or delaying progression of cancer in an individual, the methods comprising administering to the individual an effective amount of the antibody according to any one of the above embodiments. In another aspect, there is provided use of an effective amount of the antibody disclosed herein in the manufacture of a medicament for treating or delaying progression of cancer in an individual. In some embodiments, the methods further comprise administering to the individual an effective amount of a second antibody. In some embodiments, the second antibody binds an antigen expressed by a cancer cell. In some embodiments, the antigen expressed by the cancer cell

block binding between an extracellular domain of a human SIRP-α polypeptide and an IgSF domain of a human CD47 polypeptide, and wherein the second antibody binds to PD-L1. In some embodiments, the individual is a human.

[0032] Further provided herein are methods of treating or delaying progression of an autoimmune disease or an inflammatory disease in an individual, the methods comprising administering to the individual an effective amount of the antibody according to any one of the above embodiments. In another aspect, there is provide use of an effective amount of the antibody disclosed herein in the manufacture of a medicament for treating or delaying progression of an autoimmune disease or an inflammatory disease in an individual. In some embodiments, 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, asthma, atopic dermatitis, acute respiratory distress syndrome (ARDS), vasculitis, and inflammatory autoimmune myositis. In some embodiments, the individual is a human.

[0033] In other aspects, provided herein are methods of identifying an antigen binding domain that binds an extracellular domain (e.g., the D1 domain) of a human SIRP-α polypeptide and does not block binding between human CD47 and the human SIRP-α polypeptide, the methods comprising (a) providing an antigen binding domain that binds the extracellular domain (e.g., the D1 domain) of a human SIRP-α polypeptide; (b) assembling a complex comprising a SIRP-α D1 variant bound to a polypeptide comprising an IgSF domain of CD47, wherein the SIRP-α D1 variant is a non-naturally occurring high affinity SIRP-α D1 domain, and wherein the SIRP-α D1 variant binds to human CD47 with an affinity that is at least 10-fold greater than the affinity of a naturally occurring SIRP-α D1 domain binding to human CD47; (c) contacting the antigen binding domain with the assembled complex; and (d) detecting binding of the antigen binding domain to the complex, wherein binding of the antigen binding domain to the complex indicates that the antigen binding domain does not block binding between human CD47 and the human SIRP-α polypeptide. Further provided herein are methods of identifying an antibody or antigen binding domain that binds an extracellular domain (e.g., the D1 domain) of a human SIRP-α polypeptide and does not block binding between human CD47 and the human SIRP-α polypeptide, the methods comprising contacting an antibody or antigen binding domain that binds the extracellular

domain (e.g., the D1 domain) of a human SIRP-α polypeptide with a complex comprising a SIRP-α D1 variant bound to a polypeptide comprising an IgSF domain of CD47, wherein the SIRP-α D1 variant is a non-naturally occurring high affinity SIRP-α D1 domain, and wherein the SIRP-α D1 variant binds to human CD47 with an affinity that is at least 10-fold greater than the affinity of a naturally occurring SIRP-α D1 domain binding to human CD47; and detecting binding of the antigen binding domain to the complex, wherein binding of the antigen binding domain to the complex indicates that the antigen binding domain does not block binding between human CD47 and the human SIRP-α polypeptide. In other aspects, provided herein are methods of identifying an antigen binding domain that binds an extracellular domain (e.g., the D1 domain) of a human SIRP-α polypeptide and blocks binding between human CD47 and the human SIRP-α polypeptide, the methods comprising (a) providing an antigen binding domain that binds the extracellular domain (e.g., the D1 domain) of a human SIRP-α polypeptide; (b) assembling a complex comprising a SIRP-α D1 variant bound to a polypeptide comprising an IgSF domain of CD47, wherein the SIRP-α D1 variant is a non-naturally occurring high affinity SIRP-α D1 domain, and wherein the SIRP-α D1 variant binds to human CD47 with an affinity that is at least 10-fold greater than the affinity of a naturally occurring SIRP-α D1 domain binding to human CD47; (c) contacting the antigen binding domain with the assembled complex; and (d) detecting binding of the antigen binding domain to the complex, wherein a lack of binding of the antigen binding domain to the complex indicates that the antigen binding domain blocks binding between human CD47 and the human SIRP-α polypeptide. Further provided herein are methods of identifying an antibody or antigen binding domain that binds an extracellular domain (e.g., the D1 domain) of a human SIRP-α polypeptide and blocks binding between human CD47 and the human SIRP-α polypeptide, the methods comprising contacting an antibody or antigen binding domain that binds the extracellular domain (e.g., the D1 domain) of a human SIRP-α polypeptide with a complex comprising a SIRP-α D1 variant bound to a polypeptide comprising an IgSF domain of CD47, wherein the SIRP-α D1 variant is a non-naturally occurring high affinity SIRP-α D1 domain, and wherein the SIRP-α D1 variant binds to human CD47 with an affinity that is at least 10-fold greater than the affinity of a naturally occurring SIRP-α D1 domain binding to human CD47; and (d) detecting binding of the antigen binding domain to the complex, wherein a lack of binding of the antigen binding domain to the complex indicates that the antigen binding domain blocks binding between human CD47 and the human SIRP-α polypeptide. In some

embodiments, the SIRP-α D1 variant comprises an amino acid sequence selected from the group consisting of SEQ ID NOs:17-52. In some embodiments, the IgSF domain of CD47 comprises the amino acid sequence of SEQ ID NO:16. In some embodiments, the polypeptide comprising the IgSF domain of CD47 comprises a human CD47 extracellular domain. In some embodiments, the polypeptide comprising the IgSF domain of CD47 further comprises an antibody Fc region.

[0034] In another aspect, there is provided a method of producing an anti-SIRP-α antibody that binds the extracellular domain of a human SIRP-α polypeptide, the method comprising: detecting binding between the antibody obtained from an antibody-producing cell and the extracellular domains of a human SIRP-α polypeptide, wherein binding between the antibody and the extracellular domain of the human SIRP-α polypeptide indicates that the antibody is an anti-SIRP-α antibody that binds the extracellular domain of a human SIRP-α variant polypeptide, and wherein the antibody-producing cell is to be obtained from a chicken that has been immunized with a peptide comprising at least a portion of a human SIRP-α extracellular domain. Further provided herein are methods of producing an anti-SIRP-α antibody that binds the extracellular domain (e.g., the D1 domain) of a human SIRP-α polypeptide, the methods comprising: (a) immunizing a chicken with a peptide comprising at least a portion of a human SIRP-α extracellular domain (e.g., the D1 domain); (b) obtaining an antibody from an antibody-producing cell from the immunized chicken; and (c) detecting binding between the antibody obtained from the cell and the extracellular domains (e.g., the D1 domains) of a human SIRP-α polypeptide, wherein binding between the antibody and the extracellular domain (e.g., the D1 domain) of the human SIRP-α polypeptide indicates that the antibody is an anti-SIRP-α antibody that binds the extracellular domain (e.g., the D1 domain) of a human SIRP-α variant polypeptide. In some embodiments, the antibody is a chicken, humanized, chimeric, or human antibody. In some embodiments, the antibody binds the extracellular domain (e.g., the D1 domain) of a human SIRP-α v1 polypeptide, the extracellular domain (e.g., the D1 domain) of a human SIRP-α v2 polypeptide, or both. In some embodiments, the antibody binds an extracellular domain (e.g., the D1 domain) of a human SIRP-α v1 polypeptide comprising the amino acid sequence of
EEELQVIQPDKSVLVAAGETATLRCTATSLIPVGPIQWFRGAGPGRELIYNQKEGHF
PRVTTVSDLTKRNNMDFSIRIGNITPADAGTYYCVKFRKGSPDDVEFKSGAGTELS
VRAKPS (SEQ ID NO:5). In some embodiments, the antibody binds an extracellular domain (e.g., the D1 domain) of a human SIRP-α v2 polypeptide comprising the amino acid sequence of
EEELQVIQPDKSVSVAAGESAILHCTVTSLIPVGPIQWFRGAGPARELIYNQKEGHFP
RVTTVSESTKRENMDFSISISNITPADAGTYYCVKFRKGSPDTEFKSGAGTELSVRA
KPS (SEQ ID NO:6). In some embodiments, the antibody binds an extracellular domain(e.g., the D1 domain) of a human SIRP-α v1 polypeptide comprising the amino acid sequence of
EEELQVIQPDKSVLVAAGETATLRCTATSLIPVGPIQWFRGAGPGRELIYNQKEGHF
PRVTTVSDLTKRNNMDFSIRIGNITPADAGTYYCVKFRKGSPDDVEFKSGAGTELS

(e.g., the D1 domain) of a human SIRP-α polypeptide reduces affinity of the human SIRP-α polypeptide for binding an IgSF domain of a human CD47 polypeptide. In some embodiments, binding of the antibody to an extracellular domain (e.g., the D1 domain) of a human SIRP-α polypeptide expressed on the surface of a first cell reduces affinity of the human SIRP-α polypeptide for binding an IgSF domain of a human CD47 polypeptide expressed on the surface of a second cell. In some embodiments, binding of the antibody to an extracellular domain (e.g., the D1 domain) of a human SIRP-α polypeptide increases k_{off} of the human SIRP-α polypeptide for binding an IgSF domain of a human CD47 polypeptide. In some embodiments, binding of the antibody to an extracellular domain (e.g., the D1 domain) of a human SIRP-α polypeptide expressed on the surface of a first cell increases k_{off} of the human SIRP-α polypeptide for binding an IgSF domain of a human CD47 polypeptide expressed on the surface of a second cell. In some embodiments, the antibody modulates SIRP-α signaling in a cell expressing a human SIRP-α polypeptide. In some embodiments, the cell is a leukocyte selected from the group consisting of a macrophage, a dendritic cell, a neutrophil, an eosinophil, and a myeloid-derived suppressor cell (MDSC). In some embodiments, the antibody inhibits SIRP-α signaling in a macrophage expressing a human SIRP-α polypeptide. In some embodiments, the antibody enhances phagocytosis by a macrophage expressing a human SIRP-α polypeptide.

[0035] 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 disclosure. These and other aspects of the disclosure will become apparent to one of skill in the art. These and other embodiments of the disclosure are further described by the detailed description that follows.

BRIEF DESCRIPTION OF THE DRAWINGS

[0036] **FIG. 1A** shows an alignment among the D1 domains of 10 different human SIRP-α variant polypeptides. Sequences shown correspond to SEQ ID NOs: 5, 6, and 76-83 (from top to bottom). Amino acid differences are indicated by asterisks.

[0037] **FIG. 1B** shows an alignment between human v1, human v2, cynomolgus monkey, and 129 mouse SIRP-α D1 domains. Sequences shown correspond to SEQ ID NOs: 5, 6, 11, and 7 (from top to bottom). Amino acid differences are indicated by asterisks.

[0038] **FIG. 1C** shows alignments between various human and mouse SIRP-α D1 domains, with R1, R2 and R3 loops indicated. Shown is an alignment between human v1,

CLAIMS

What is claimed is:

1. An isolated antibody that binds an extracellular domain of a human SIRP-α polypeptide, wherein the antibody binds the extracellular domain of a human SIRP-α v1 polypeptide, the extracellular domain of a human SIRP-α v2 polypeptide, or both.

2. The antibody of claim 1, wherein the antibody binds an extracellular domain of a human SIRP-α v1 polypeptide comprising the amino acid sequence of EEELQVIQPDKSVLVAAGETATLRCTATSLIPVGPIQWFRGAGPGRELIYNQKEGHFPRV TTVSDLTKRNNMDFSIRIGNITPADAGTYYCVKFRKGSPDDVEFKSGAGTELSVRAKPS (SEQ ID NO:5).

3. The antibody of claim 1, wherein the antibody binds an extracellular domain of a human SIRP-α v2 polypeptide comprising the amino acid sequence of EEELQVIQPDKSVSVAAGESAILHCTVTSLIPVGPIQWFRGAGPARELIYNQKEGHFPRVT TVSESTKRENMDFSISISNITPADAGTYYCVKFRKGSPDTEFKSGAGTELSVRAKPS (SEQ ID NO:6).

4. The antibody of any one of claims 1-3, wherein the antibody binds an extracellular domain of a human SIRP-α v1 polypeptide comprising the amino acid sequence of EEELQVIQPDKSVLVAAGETATLRCTATSLIPVGPIQWFRGAGPGRELIYNQKEGHFPRV TTVSDLTKRNNMDFSIRIGNITPADAGTYYCVKFRKGSPDDVEFKSGAGTELSVRAKPS (SEQ ID NO:5) and binds an extracellular domain of a human SIRP-α v2 polypeptide comprising the amino acid sequence of EEELQVIQPDKSVSVAAGESAILHCTVTSLIPVGPIQWFRGAGPARELIYNQKEGHFPRVT TVSESTKRENMDFSISISNITPADAGTYYCVKFRKGSPDTEFKSGAGTELSVRAKPS (SEQ ID NO:6).

5. The antibody of any one of claims 1-4, wherein the antibody binds an extracellular domain of a monkey SIRP-α polypeptide.

6. The antibody of claim 5, wherein the monkey SIRP-α polypeptide is a cynomolgus SIRP-α polypeptide.

7. The antibody of claim 5 or claim 6, wherein the antibody binds the extracellular domains of at least two different monkey SIRP-α variant polypeptides.

8. The antibody of claim 6 or claim 7, wherein the antibody binds an extracellular domain of a cynomolgus SIRP-α polypeptide comprising the amino acid sequence of SEQ ID NO:11, an extracellular domain of a cynomolgus SIRP-α polypeptide comprising the amino acid sequence of SEQ ID NO:12, or both.

9. The antibody of any one of claims 1-8, wherein the antibody binds an extracellular domain of a murine SIRP-α polypeptide.

10. The antibody of claim 9, wherein the antibody binds the extracellular domains of two or more different murine SIRP-α variant polypeptides.

11. The antibody of claim 9 or claim 10, wherein the antibody binds an extracellular domain of one or more murine SIRP-α polypeptides, and wherein the one or more murine SIRP-α polypeptides each comprise an amino acid sequence selected from the group consisting of SEQ ID NOs: 7-10.

12. The antibody of any one of claims 1-11, wherein the antibody binds an extracellular domain of a human SIRP-β polypeptide.

13. The antibody of any one of claims 1-12, wherein the antibody binds an extracellular domain of a human SIRP-γ polypeptide.

14. The antibody of any one of claims 1-12, wherein the antibody does not bind an extracellular domain of a human SIRP-γ polypeptide.

15. The antibody of any one of claims 12-14, wherein the antibody binds the extracellular domain of a human SIRP-β polypeptide comprising the amino acid sequence of SEQ ID NO:13.

16. The antibody of any one of claims 12-15, wherein the antibody binds the extracellular domain of a human SIRP-γ polypeptide comprising the amino acid sequence of SEQ ID NO:15.

17. The antibody of any one of claims 1-16, wherein the antibody modulates SIRP-α signaling in a cell expressing a human SIRP-α polypeptide.

18. The antibody of claim 17, wherein the cell is a leukocyte selected from the group consisting of a macrophage, a dendritic cell, a neutrophil, an eosinophil, and a myeloid-derived suppressor cell (MDSC).

19. The antibody of claim 18, wherein the antibody inhibits SIRP-α signaling in a macrophage expressing a human SIRP-α polypeptide.

20. The antibody of any one of claims 17-19, wherein the antibody enhances phagocytosis by a macrophage expressing a human SIRP-α polypeptide.

21. The antibody of any one of claims 1-20, wherein the antibody blocks binding between an extracellular domain of a human SIRP-α polypeptide and an IgSF domain of a human CD47 polypeptide.

22. The antibody of claim 21, wherein the antibody does not bind a complex comprising a SIRP-α D1 variant bound to an IgSF domain of CD47, wherein the SIRP-α D1 variant is a non-naturally occurring high affinity SIRP-α D1 domain, and wherein the SIRP-α D1 variant binds to human CD47 with an affinity that is at least 10-fold greater than the affinity of a naturally occurring SIRP-α D1 domain binding to human CD47.

23. The antibody of any one of claims 1-20, wherein the antibody does not block binding between an extracellular domain of a human SIRP-α polypeptide and an IgSF domain of a human CD47 polypeptide.

24. The antibody of claim 23, wherein the antibody binds a complex comprising a SIRP-α D1 variant bound to an IgSF domain of CD47, wherein the SIRP-α D1 variant is a non-naturally occurring high affinity SIRP-α D1 domain, and wherein the SIRP-α D1 variant binds to human

CD47 with an affinity that is at least 10-fold greater than the affinity of a naturally occurring SIRP-α D1 domain binding to human CD47.

25. The antibody of claim 1, wherein the antibody binds the extracellular domain of a human SIRP-α v1 polypeptide, the extracellular domain of a human SIRP-α v2 polypeptide, or both; wherein the antibody binds the extracellular domain of a monkey SIRP-α polypeptide; and wherein the antibody does not block binding between an extracellular domain of a human SIRP-α polypeptide and an IgSF domain of a human CD47 polypeptide.

26. The antibody of claim 1, wherein the antibody binds the extracellular domain of a human SIRP-α v1 polypeptide, the extracellular domain of a human SIRP-α v2 polypeptide, or both; wherein the antibody binds the extracellular domain of a monkey SIRP-α polypeptide; and wherein the antibody blocks binding between an extracellular domain of a human SIRP-α polypeptide and an IgSF domain of a human CD47 polypeptide.

27. The antibody of claim 1, wherein the antibody binds the extracellular domain of a human SIRP-α v1 polypeptide, the extracellular domain of a human SIRP-α v2 polypeptide, or both; wherein the antibody binds the extracellular domain of a monkey SIRP-α polypeptide; wherein the antibody binds the extracellular domain of a murine SIRP-α polypeptide; and wherein the antibody does not block binding between an extracellular domain of a human SIRP-α polypeptide and an IgSF domain of a human CD47 polypeptide.

28. The antibody of claim 1, wherein the antibody binds the extracellular domain of a human SIRP-α v1 polypeptide, the extracellular domain of a human SIRP-α v2 polypeptide, or both; wherein the antibody binds the extracellular domain of a monkey SIRP-α polypeptide; wherein the antibody binds the extracellular domain of a murine SIRP-α polypeptide; and wherein the antibody blocks binding between an extracellular domain of a human SIRP-α polypeptide and an IgSF domain of a human CD47 polypeptide.

29. The antibody of claim 1, wherein the antibody binds the extracellular domain of a human SIRP-α v1 polypeptide, the extracellular domain of a human SIRP-α v2 polypeptide, or both; wherein the antibody binds the extracellular domain of a murine SIRP-α polypeptide; and

wherein the antibody does not block binding between an extracellular domain of a human SIRP-α polypeptide and an IgSF domain of a human CD47 polypeptide.

30. The antibody of claim 1, wherein the antibody binds the extracellular domain of a human SIRP-α v1 polypeptide, the extracellular domain of a human SIRP-α v2 polypeptide, or both; wherein the antibody binds the extracellular domain of a murine SIRP-α polypeptide; and wherein the antibody blocks binding between an extracellular domain of a human SIRP-α polypeptide and an IgSF domain of a human CD47 polypeptide.

31. The antibody of claim 1, wherein the antibody binds the extracellular domains of two or more different human SIRP-α variant polypeptides, a murine SIRP-α polypeptide, a monkey SIRP-α polypeptide, and at least one of an extracellular domain of a human SIRP-β polypeptide and an extracellular domain of a human SIRP-γ polypeptide; and wherein the antibody blocks binding between the extracellular domain of the human SIRP-α polypeptide and an IgSF domain of a human CD47 polypeptide.

32. The antibody of claim 31, wherein the antibody comprises one, two, three, four, five, or six CDR sequences; a heavy chain variable (VH) domain sequence; and/or a light chain variable (VL) domain sequence from an antibody selected from the group consisting of S8, S13, S14 and S121.

33. The antibody of claim 1, wherein the antibody binds the extracellular domains of two or more different human SIRP-α variant polypeptides, a murine SIRP-α polypeptide, and a monkey SIRP-α polypeptide; wherein the antibody does not bind, or binds with reduced affinity to, at least one of an extracellular domain of a human SIRP-β polypeptide and an extracellular domain of a human SIRP-γ polypeptide; and wherein the antibody does not block binding between the extracellular domain of the human SIRP-α polypeptide and an IgSF domain of a human CD47 polypeptide.

34. The antibody of claim 33, wherein the antibody comprises one, two, three, four, five, or six CDR sequences; a heavy chain variable domain sequence; and/or a light chain variable domain sequence from antibody S137.

35. The antibody of claim 1, wherein the antibody binds the extracellular domains of two or more different human SIRP-α variant polypeptides, a monkey SIRP-α polypeptide, and at least one of an extracellular domain of a human SIRP-β polypeptide and an extracellular domain of a human SIRP-γ polypeptide; wherein the antibody does not bind a murine SIRP-α polypeptide; and wherein the antibody blocks binding between the extracellular domain of the human SIRP-α polypeptide and an IgSF domain of a human CD47 polypeptide.

36. The antibody of claim 35, wherein the antibody comprises one, two, three, four, five, or six CDR sequences; a heavy chain variable domain sequence; and/or a light chain variable domain sequence from an antibody selected from the group consisting of S9, S11, S119, S120, S122, and S135.

37. The antibody of claim 1, wherein the antibody comprises:

(a) an HVR-H1 sequence comprising the amino acid sequence of $GFSFSX_1X_2AMX_3$, wherein X_1 is N or I; X_2 is F or Y; and X_3 is T or S (SEQ ID NO:185);

(b) an HVR-H2 sequence comprising the amino acid sequence of $TIGX_4X_5DTYYADSVKG$, wherein X_4 is S or A and X_5 is G or D (SEQ ID NO:186);

(c) an HVR-H3 sequence comprising the amino acid sequence of $DSTVX_6WSGDFFDY$, wherein X_6 is S or G (SEQ ID NO:187);

(d) an HVR-L1 sequence comprising the amino acid sequence of $RASQNVX_7X_8DX_9A$, wherein X_7 is K or R; X_8 is N or S; and X_9 is L or I (SEQ ID NO:188);

(e) an HVR-L2 sequence comprising the amino acid sequence of $AAX_{10}X_{11}RX_{12}T$, wherein X_{10} is R or S; X_{11} is I or S; and X_{12} is E or D (SEQ ID NO:189); and

(f) an HVR-L3 sequence comprising the amino acid sequence of QQYYDWPPFT (SEQ ID NO:148).

38. The antibody of claim 1, wherein the antibody comprises (a) a VH domain comprising an HVR-H1 comprising the amino acid sequence of SEQ ID NO:143, 202, 204, or 205, an HVR-H2 comprising the amino acid sequence of SEQ ID NO:144, 203, or 206, and an HVR-H3

comprising the amino acid sequence of SEQ ID NO:145 or 207; and/or (b) a VL domain comprising an HVR-L1 comprising the amino acid sequence of SEQ ID NO:146 or 208, an HVR-L2 comprising the amino acid sequence of SEQ ID NO:147 or 209, and an HVR-L3 comprising the amino acid sequence of SEQ ID NO:148 or 210.

39. The antibody of claim 1, wherein the antibody comprises a VH domain comprising the amino acid sequence of SEQ ID NO:120 and/or a VL domain comprising the amino acid sequence of SEQ ID NO:97.

40. The antibody of claim 1, wherein the antibody comprises (a) a VH domain comprising an HVR-H1 comprising the amino acid sequence of SEQ ID NO:149, 211, 213, or 214, an HVR-H2 comprising the amino acid sequence of SEQ ID NO:150, 212, or 215, and an HVR-H3 comprising the amino acid sequence of SEQ ID NO:151 or 216; and/or (b) a VL domain comprising an HVR-L1 comprising the amino acid sequence of SEQ ID NO:152 or 217, an HVR-L2 comprising the amino acid sequence of SEQ ID NO:153 or 218, and an HVR-L3 comprising the amino acid sequence of SEQ ID NO:148.

41. The antibody of claim 1, wherein the antibody comprises a VH domain comprising the amino acid sequence of SEQ ID NO:127 and/or a VL domain comprising the amino acid sequence of SEQ ID NO:104.

42. The antibody of claim 1, wherein the antibody comprises (a) a VH domain comprising an HVR-H1 comprising the amino acid sequence of SEQ ID NO:155, 219, 221, or 222, an HVR-H2 comprising the amino acid sequence of SEQ ID NO:156, 220, or 223, and an HVR-H3 comprising the amino acid sequence of SEQ ID NO:157 or 224; and/or (b) a VL domain comprising an HVR-L1 comprising the amino acid sequence of SEQ ID NO:158 or 225, an HVR-L2 comprising the amino acid sequence of SEQ ID NO:159 or 226, and an HVR-L3 comprising the amino acid sequence of SEQ ID NO:160.

43. The antibody of claim 1, wherein the antibody comprises a VH domain comprising the amino acid sequence of SEQ ID NO:133 and/or a VL domain comprising the amino acid sequence of SEQ ID NO:134.

44. The antibody of claim 1, wherein the antibody comprises (a) a VH domain comprising an HVR-H1 comprising the amino acid sequence of SEQ ID NO:161, 191, or 194, an HVR-H2 comprising the amino acid sequence of SEQ ID NO:162, 192, or 195, and an HVR-H3 comprising the amino acid sequence of SEQ ID NO:163 or 193; and/or (b) a VL domain comprising an HVR-L1 comprising the amino acid sequence of SEQ ID NO:164, an HVR-L2 comprising the amino acid sequence of SEQ ID NO:165, and an HVR-L3 comprising the amino acid sequence of SEQ ID NO:166.

45. The antibody of claim 1, wherein the antibody comprises a VH domain comprising the amino acid sequence of SEQ ID NO:135 and/or a VL domain comprising the amino acid sequence of SEQ ID NO:136.

46. The antibody of claim 1, wherein the antibody comprises (a) a VH domain comprising an HVR-H1 comprising the amino acid sequence of SEQ ID NO:161, 191, or 194, an HVR-H2 comprising the amino acid sequence of SEQ ID NO:168, 196, or 197, and an HVR-H3 comprising the amino acid sequence of SEQ ID NO:163 or 193; and/or (b) a VL domain comprising an HVR-L1 comprising the amino acid sequence of SEQ ID NO:170, an HVR-L2 comprising the amino acid sequence of SEQ ID NO:171, and an HVR-L3 comprising the amino acid sequence of SEQ ID NO:172.

47. The antibody of claim 1, wherein the antibody comprises a VH domain comprising the amino acid sequence of SEQ ID NO:137 and/or a VL domain comprising the amino acid sequence of SEQ ID NO:138.

48. The antibody of claim 1, wherein the antibody comprises (a) a VH domain comprising an HVR-H1 comprising the amino acid sequence of SEQ ID NO:173, 198, or 200, an HVR-H2 comprising the amino acid sequence of SEQ ID NO:174, 199, or 201, and an HVR-H3 comprising the amino acid sequence of SEQ ID NO:163 or 193; and/or (b) a VL domain comprising an HVR-L1 comprising the amino acid sequence of SEQ ID NO:176, an HVR-L2 comprising the amino acid sequence of SEQ ID NO:177, and an HVR-L3 comprising the amino acid sequence of SEQ ID NO:178.

49. The antibody of claim 1, wherein the antibody comprises a VH domain comprising the amino acid sequence of SEQ ID NO:139 and/or a VL domain comprising the amino acid sequence of SEQ ID NO:140.

50. The antibody of claim 1, wherein the antibody comprises (a) a VH domain comprising an HVR-H1 comprising the amino acid sequence of SEQ ID NO:179, an HVR-H2 comprising the amino acid sequence of SEQ ID NO:162, and an HVR-H3 comprising the amino acid sequence of SEQ ID NO:163; and/or (b) a VL domain comprising an HVR-L1 comprising the amino acid sequence of SEQ ID NO:182, an HVR-L2 comprising the amino acid sequence of SEQ ID NO:183, and an HVR-L3 comprising the amino acid sequence of SEQ ID NO:184.

51. The antibody of claim 1, wherein the antibody comprises a VH domain comprising the amino acid sequence of SEQ ID NO:141 and/or a VL domain comprising the amino acid sequence of SEQ ID NO:142.

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

(a) a heavy chain variable (VH) domain comprising (i) an HVR-H1 sequence comprising the amino acid sequence of NFAMT (SEQ ID NO:175), NFAVT (SEQ ID NO:204), or NFALT (SEQ ID NO:305), (ii) an HVR-H2 sequence comprising the amino acid sequence of TIGSGDTYYADSVKG (SEQ ID NO:144), and (iii) an HVR-H3 sequence comprising the amino acid sequence of DSTVSWSGDFFDY (SEQ ID NO:145); and/or

(b) a light chain variable (VL) domain comprising (i) an HVR-L1 sequence comprising the amino acid sequence of RASQNVKNDLA (SEQ ID NO:146), (ii) an HVR-L2 sequence comprising the amino acid sequence of AARIRET (SEQ ID NO:147), and (iii) an HVR-L3 sequence comprising the amino acid sequence of QQYYDWPPFT (SEQ ID NO:148).

53. The antibody of claim 52, wherein the VH domain comprises an amino acid sequence that is at least 90% identical to the amino acid sequence of SEQ ID NO:120, 335, 246, 258, or 327; and/or the VL domain comprises an amino acid sequence that is at least 90% identical to the amino acid sequence of SEQ ID NO:97 or 312.

54. The antibody of claim 53, wherein

(a) the VH domain comprises the amino acid sequence of SEQ ID NO:246, and the VL domain comprises the amino acid sequence of SEQ ID NO:97;

(b) the VH domain comprises the amino acid sequence of SEQ ID NO:258, and the VL domain comprises the amino acid sequence of SEQ ID NO:97;

(c) the VH domain comprises the amino acid sequence of SEQ ID NO:335, and the VL domain comprises the amino acid sequence of SEQ ID NO:97;

(d) the VH domain comprises the amino acid sequence of SEQ ID NO:327, and the VL domain comprises the amino acid sequence of SEQ ID NO:97;

(e) the VH domain comprises the amino acid sequence of SEQ ID NO:246, and the VL domain comprises the amino acid sequence of SEQ ID NO:312;

(f) the VH domain comprises the amino acid sequence of SEQ ID NO:258, and the VL domain comprises the amino acid sequence of SEQ ID NO:312;

(g) the VH domain comprises the amino acid sequence of SEQ ID NO:335, and the VL domain comprises the amino acid sequence of SEQ ID NO:312; or

(h) the VH domain comprises the amino acid sequence of SEQ ID NO:327, and the VL domain comprises the amino acid sequence of SEQ ID NO:312.

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

(a) a heavy chain variable (VH) domain comprising (i) an HVR-H1 sequence comprising the amino acid sequence of IYAMS (SEQ ID NO:269), IYAVS (SEQ ID NO:213), or IYALS (SEQ ID NO:306), (ii) an HVR-H2 sequence comprising the amino acid sequence of TIGADDTYYADSVKG (SEQ ID NO:150), and (iii) an HVR-H3 sequence comprising the amino acid sequence of DSTVGWSGDFFDY (SEQ ID NO:151); and/or

(b) a light chain variable (VL) domain comprising (i) an HVR-L1 sequence comprising the amino acid sequence of RASQNVRSDIA (SEQ ID NO:152), (ii) an HVR-L2 sequence comprising the amino acid sequence of AASSRDT (SEQ ID NO:153), and (iii) an HVR-L3 sequence comprising the amino acid sequence of QQYYDWPPFT (SEQ ID NO:148).

56. The antibody of claim 55, wherein the VH domain comprises an amino acid sequence that is at least 90% identical to the amino acid sequence of SEQ ID NO:341, 247, 259, or 328; and/or the VL domain comprises an amino acid sequence that is at least 90% identical to the amino acid sequence of SEQ ID NO:104 or 248.

57. The antibody of claim 56, wherein

(a) the VH domain comprises the amino acid sequence of SEQ ID NO:341, and the VL domain comprises the amino acid sequence of SEQ ID NO:104;

(b) the VH domain comprises the amino acid sequence of SEQ ID NO:247, and the VL domain comprises the amino acid sequence of SEQ ID NO:104;

(c) the VH domain comprises the amino acid sequence of SEQ ID NO:259, and the VL domain comprises the amino acid sequence of SEQ ID NO:104;

(d) the VH domain comprises the amino acid sequence of SEQ ID NO:328, and the VL domain comprises the amino acid sequence of SEQ ID NO:104;

(e) the VH domain comprises the amino acid sequence of SEQ ID NO:341, and the VL domain comprises the amino acid sequence of SEQ ID NO:248;

(f) the VH domain comprises the amino acid sequence of SEQ ID NO:247, and the VL domain comprises the amino acid sequence of SEQ ID NO:248;

(g) the VH domain comprises the amino acid sequence of SEQ ID NO:259, and the VL domain comprises the amino acid sequence of SEQ ID NO:248; or

(g) the VH domain comprises the amino acid sequence of SEQ ID NO:328, and the VL domain comprises the amino acid sequence of SEQ ID NO:248.

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

(a) a heavy chain variable (VH) domain comprising:

(i) an HVR-H1 sequence comprising the amino acid sequence of $X_1X_2DX_3N$, wherein X_1 is S or T; X_2 is Y or S; and X_3 is M, L, or V (SEQ ID NO:307);

(ii) an HVR-H2 sequence comprising the amino acid sequence of $LISGSGEIX_1YYADSVKG$, wherein X_1 is I or T (SEQ ID NO:308); and

(iii) an HVR-H3 sequence comprising the amino acid sequence of $EX_1X_2X_3YRFFDX_4$, wherein X_1 is N or D; X_2 is N or D; X_3 is R or M; and X_4 is D or Y (SEQ ID NO:309); and/or

(b) a light chain variable (VL) domain comprising:

(i) an HVR-L1 sequence comprising the amino acid sequence of RAX_1QSVYX_2YLA, wherein X_1 is S or D; and X_2 is T or S (SEQ ID NO:310);

(ii) an HVR-L2 sequence comprising the amino acid sequence of $X_1AX_2X_3RAX_4$, wherein X_1 is G, A, or D; X_2 is S or R; X_3 is S, N, or T; and X_4 is T or A (SEQ ID NO:311); and

(iii) an HVR-L3 sequence comprising the amino acid sequence of QQYYDRPPLT (SEQ ID NO:160).

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

(a) a heavy chain variable (VH) domain comprising (i) an HVR-H1 sequence comprising the amino acid sequence of SYDMN (SEQ ID NO:270), SYDVN (SEQ ID NO:221), or SYDLN (SEQ ID NO:313), (ii) an HVR-H2 sequence comprising the amino acid sequence of LISGSGEIIYYADSVKG (SEQ ID NO:156), and (iii) an HVR-H3 sequence comprising the amino acid sequence of ENNRYRFFDD (SEQ ID NO:157); and/or

(b) a light chain variable (VL) domain comprising (i) an HVR-L1 sequence comprising the amino acid sequence of RASQSVYTYLA (SEQ ID NO:158), (ii) an HVR-L2 sequence

comprising the amino acid sequence of GASSRAT (SEQ ID NO:159), and (iii) an HVR-L3 sequence comprising the amino acid sequence of QQYYDRPPLT (SEQ ID NO:160).

60. The antibody of claim 58 or claim 59, wherein the VH domain comprises an amino acid sequence that is at least 90% identical to the amino acid sequence of SEQ ID NO: 249, 133, 260, or 329; and/or the VL domain comprises an amino acid sequence that is at least 90% identical to the amino acid sequence of SEQ ID NO:134, 250, or 251.

61. The antibody of claim58, wherein

(a) the VH domain comprises the amino acid sequence of SEQ ID NO:133, and the VL domain comprises the amino acid sequence of SEQ ID NO:134;

(b) the VH domain comprises the amino acid sequence of SEQ ID NO:260, and the VL domain comprises the amino acid sequence of SEQ ID NO:134;

(c) the VH domain comprises the amino acid sequence of SEQ ID NO:329, and the VL domain comprises the amino acid sequence of SEQ ID NO:134;

(d) the VH domain comprises the amino acid sequence of SEQ ID NO:133, and the VL domain comprises the amino acid sequence of SEQ ID NO:250;

(e) the VH domain comprises the amino acid sequence of SEQ ID NO:260, and the VL domain comprises the amino acid sequence of SEQ ID NO:250;

(f) the VH domain comprises the amino acid sequence of SEQ ID NO:329, and the VL domain comprises the amino acid sequence of SEQ ID NO:250;

(g) the VH domain comprises the amino acid sequence of SEQ ID NO:133, and the VL domain comprises the amino acid sequence of SEQ ID NO:251;

(h) the VH domain comprises the amino acid sequence of SEQ ID NO:260, and the VL domain comprises the amino acid sequence of SEQ ID NO:251;

(i) the VH domain comprises the amino acid sequence of SEQ ID NO:329, and the VL domain comprises the amino acid sequence of SEQ ID NO:251;

(j) the VH domain comprises the amino acid sequence of SEQ ID NO:249, and the VL domain comprises the amino acid sequence of SEQ ID NO:134;

(k) the VH domain comprises the amino acid sequence of SEQ ID NO:249, and the VL domain comprises the amino acid sequence of SEQ ID NO:250; or

(l) the VH domain comprises the amino acid sequence of SEQ ID NO:249, and the VL domain comprises the amino acid sequence of SEQ ID NO:251.

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

(a) a heavy chain variable (VH) domain comprising:

(i) an HVR-H1 sequence comprising the amino acid sequence of $X_1X_2AX_3S$, wherein X_1 is S or T; X_2 is N, Y, H, or D; and X_3 is M, L, or V (SEQ ID NO:297);

(ii) an HVR-H2 sequence comprising the amino acid sequence of $GISX_1X_2X_3X_4X_5X_6YYX_7X_8SX_9KG$, wherein X_1 is A or S; X_2 is G, S, or absent; X_3 is S, D or G; X_4 is G or S; X_5 is D, S, or G; X_6 is T or A; X_7 is P, G, V, I, A, or S; X_8 is A, D, or G; and X_9 is V or M (SEQ ID NO:298); and

(iii) an HVR-H3 sequence comprising the amino acid sequence of ETWNHLFDY (SEQ ID NO:193); and/or

(b) a light chain variable (VL) domain comprising:

(i) an HVR-L1 sequence comprising the amino acid sequence of $SGGX_1X_2$ $X_3SX_4YYX_5$, wherein X_1 is D, G, S, I, or absent; X_2 is S, W, G, Y, D, or absent; X_3 is S, Y, T, or D; X_4 is H, T, S, or Y; and X_5 is G or A (SEQ ID NO:299);

(ii) an HVR-L2 sequence comprising the amino acid sequence of $SDX_1X_2RPX_3$, wherein X_1 is D or N; X_2 is E, K, or Q; and X_3 is S or P (SEQ ID NO:300); and

(iii) an HVR-L3 sequence comprising the amino acid sequence of $X_1X_2YDX_3X_4X_5YX_6NX_7$, wherein X_1 is G or A; X_2 is G or A; X_3 is G, Y, Q, S, or A; X_4 is S, R, or T; X_5 is T or S; X_6 is A, I, V, L, or T; and X_7 is T, A, D, or P (SEQ ID NO:301).

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

(a) a heavy chain variable (VH) domain comprising:

(i) an HVR-H1 sequence comprising the amino acid sequence of SX_1AX_2S, wherein X_1 is N or Y; and wherein X_2 is M, L, or V (SEQ ID NO:302);

(ii) an HVR-H2 sequence comprising the amino acid sequence of $GISX_1GX_2X_3DTYYX_4X_5SVKG$, wherein X_1 is A or S; X_2 is G or absent; X_3 is S or G; X_4 is P, G, or V; and X_5 is A or D (SEQ ID NO:303); and

(iii) an HVR-H3 sequence comprising the amino acid sequence of ETWNHLFDY (SEQ ID NO:193); and/or

(b) a light chain variable (VL) domain comprising:

(i) an HVR-L1 sequence comprising the amino acid sequence of $SGGX_1YSSYYYA$, wherein X_1 is S or A (SEQ ID NO:304);

(ii) an HVR-L2 sequence comprising the amino acid sequence of SDDKRPS (SEQ ID NO:336); and

(iii) an HVR-L3 sequence comprising the amino acid sequence of GGYDQSSYTNP (SEQ ID NO:172).

64. The antibody of claim 62 or claim 63, wherein the VH domain comprises (i) an HVR-H1 sequence comprising the amino acid sequence of SNAMS (SEQ ID NO:194), SNAVS (SEQ ID NO:271), or SNALS (SEQ ID NO:318), (ii) an HVR-H2 sequence comprising the amino acid sequence of GISAGGSDTYYPASVKG (SEQ ID NO:195), and (iii) an HVR-H3 sequence comprising the amino acid sequence of ETWNHLFDY (SEQ ID NO:193).

65. The antibody of claim 64, wherein the VH domain comprises an amino acid sequence that is at least 90% identical to the amino acid sequence of SEQ ID NO:135, 263, 264, or 330.

66. The antibody of claim 62, wherein the VH domain comprises (i) an HVR-H1 sequence comprising the amino acid sequence of SNAMS (SEQ ID NO:194), SNAVS (SEQ ID NO:271), or SNALS (SEQ ID NO:318), (ii) an HVR-H2 sequence comprising the amino acid sequence of GISSGSDTYYGDSVKG (SEQ ID NO:197), and (iii) an HVR-H3 sequence comprising the amino acid sequence of ETWNHLFDY (SEQ ID NO:193).

67. The antibody of claim 66, wherein the VH domain comprises an amino acid sequence that is at least 90% identical to the amino acid sequence of SEQ ID NO:137, 265, 266, or 331.

68. The antibody of claim 62, wherein the VH domain comprises (i) an HVR-H1 sequence comprising the amino acid sequence of SYAMS (SEQ ID NO:200), SYAVS (SEQ ID NO:272), or SYALS (SEQ ID NO:319), (ii) an HVR-H2 sequence comprising the amino acid sequence of GISSGGDTYYVDSVKG (SEQ ID NO:201), and (iii) an HVR-H3 sequence comprising the amino acid sequence of ETWNHLFDY (SEQ ID NO:193).

69. The antibody of claim 68, wherein the VH domain comprises an amino acid sequence that is at least 90% identical to the amino acid sequence of SEQ ID NO:139, 267, 268, or 332.

70. The antibody of any one of claims 62-69, wherein the VL domain comprises the sequence FW1—HVR-L1—FW2—HVR-L2—FW3—HVR-L3—FW4 (N-terminus to C-terminus), wherein FW1 comprises the amino acid sequence SYELTQPPSVSVSPGQTARITC (SEQ ID NO:314), FW2 comprises the amino acid sequence WYQQKPGQAPVTLIY (SEQ ID NO:315), FW3 comprises the amino acid sequence NIPERFSGSSSGTTVTLTISGVQAEDEADYYC (SEQ ID NO:316), and FW4 comprises the amino acid sequence FGGGTKLTVL (SEQ ID NO:317).

71. The antibody of any one of claims 62-70, wherein the VL domain comprises (i) an HVR-L1 sequence comprising the amino acid sequence of SGGSYSSYYYA (SEQ ID NO:170), (ii) an HVR-L2 sequence comprising the amino acid sequence of SDDKRPS (SEQ ID NO:336), and

(iii) an HVR-L3 sequence comprising the amino acid sequence of GGYDQSSYTNP (SEQ ID NO:172).

72. The antibody of claim 71, wherein the VL domain comprises an amino acid sequence that is at least 90% identical to the amino acid sequence of SEQ ID NO:252.

73. The antibody of any one of claims 62-70, wherein the VL domain comprises (i) an HVR-L1 sequence comprising the amino acid sequence of SGGAYSSYYYA (SEQ ID NO:261), (ii) an HVR-L2 sequence comprising the amino acid sequence of SDDKRPS (SEQ ID NO:336), and (iii) an HVR-L3 sequence comprising the amino acid sequence of GGYDQSSYTNP (SEQ ID NO:172).

74. The antibody of claim 73, wherein the VL domain comprises an amino acid sequence that is at least 90% identical to the amino acid sequence of SEQ ID NO:262.

75. The antibody of claim 62, wherein

(a) the VH domain comprises the amino acid sequence of SEQ ID NO:263, and the VL domain comprises the amino acid sequence of SEQ ID NO:252;

(b) the VH domain comprises the amino acid sequence of SEQ ID NO:264, and the VL domain comprises the amino acid sequence of SEQ ID NO:252;

(c) the VH domain comprises the amino acid sequence of SEQ ID NO:330, and the VL domain comprises the amino acid sequence of SEQ ID NO:252;

(d) the VH domain comprises the amino acid sequence of SEQ ID NO:135, and the VL domain comprises the amino acid sequence of SEQ ID NO:252;

(e) the VH domain comprises the amino acid sequence of SEQ ID NO:137, and the VL domain comprises the amino acid sequence of SEQ ID NO:252;

(f) the VH domain comprises the amino acid sequence of SEQ ID NO:139, and the VL domain comprises the amino acid sequence of SEQ ID NO:252;

(g) the VH domain comprises the amino acid sequence of SEQ ID NO:265, and the VL domain comprises the amino acid sequence of SEQ ID NO:252;

(h) the VH domain comprises the amino acid sequence of SEQ ID NO:266, and the VL domain comprises the amino acid sequence of SEQ ID NO:252;

(i) the VH domain comprises the amino acid sequence of SEQ ID NO:331, and the VL domain comprises the amino acid sequence of SEQ ID NO:252;

(j) the VH domain comprises the amino acid sequence of SEQ ID NO:267, and the VL domain comprises the amino acid sequence of SEQ ID NO:252;

(k) the VH domain comprises the amino acid sequence of SEQ ID NO:268, and the VL domain comprises the amino acid sequence of SEQ ID NO:252;

(l) the VH domain comprises the amino acid sequence of SEQ ID NO:332, and the VL domain comprises the amino acid sequence of SEQ ID NO:252;

(j) the VH domain comprises the amino acid sequence of SEQ ID NO:263, and the VL domain comprises the amino acid sequence of SEQ ID NO:262;

(m) the VH domain comprises the amino acid sequence of SEQ ID NO:264, and the VL domain comprises the amino acid sequence of SEQ ID NO:262;

(n) the VH domain comprises the amino acid sequence of SEQ ID NO:330, and the VL domain comprises the amino acid sequence of SEQ ID NO:262;

(o) the VH domain comprises the amino acid sequence of SEQ ID NO:265, and the VL domain comprises the amino acid sequence of SEQ ID NO:262;

(p) the VH domain comprises the amino acid sequence of SEQ ID NO:266, and the VL domain comprises the amino acid sequence of SEQ ID NO:262;

(q) the VH domain comprises the amino acid sequence of SEQ ID NO:331, and the VL domain comprises the amino acid sequence of SEQ ID NO:262;

(r) the VH domain comprises the amino acid sequence of SEQ ID NO:267, and the VL domain comprises the amino acid sequence of SEQ ID NO:262;

(s) the VH domain comprises the amino acid sequence of SEQ ID NO:268, and the VL domain comprises the amino acid sequence of SEQ ID NO:262;

(t) the VH domain comprises the amino acid sequence of SEQ ID NO:332, and the VL domain comprises the amino acid sequence of SEQ ID NO:262;

(u) the VH domain comprises the amino acid sequence of SEQ ID NO:135, and the VL domain comprises the amino acid sequence of SEQ ID NO:262;

(v) the VH domain comprises the amino acid sequence of SEQ ID NO:137, and the VL domain comprises the amino acid sequence of SEQ ID NO:262; or

(w) the VH domain comprises the amino acid sequence of SEQ ID NO:139, and the VL domain comprises the amino acid sequence of SEQ ID NO:262.

76. An isolated antibody that binds an extracellular domain of a human SIRP-α polypeptide, wherein the antibody binds to a human SIRP-α v1 polypeptide at one or more amino acid positions selected from the group consisting of I31, V33, Q52, K53, T67, R69, N70, and K96, according to SEQ ID NO:296.

77. The antibody of claim 76, wherein the antibody binds to the human SIRP-α v1 polypeptide at I31, V33, Q52, K53, T67, R69, N70, and K96, according to SEQ ID NO:296.

78. The antibody of claim 76 or claim 77, wherein the antibody further binds to the human SIRP-α v1 polypeptide at one or more amino acid positions selected from the group consisting of L30, P32, E54, T62, N71, M72, F74, and R95, according to SEQ ID NO:296.

79. The antibody of claim 78, wherein the antibody further binds to the human SIRP-α v1 polypeptide at L30, P32, E54, T62, N71, M72, F74, and R95, according to SEQ ID NO:296.

80. An isolated antibody that binds an extracellular domain of a human SIRP-α polypeptide, wherein the antibody binds to a human SIRP-α v1 polypeptide at one or more amino acid

positions selected from the group consisting of I7, P9, D10, K11, S12, A42, A108, and E111, according to SEQ ID NO:296.

81. The antibody of claim 80, wherein the antibody binds to the human SIRP-α v1 polypeptide at K11, A42, A108, and E111, according to SEQ ID NO:296.

82. The antibody of claim 80 or 81, wherein the antibody further binds to the human SIRP-α v1 polypeptide at one or more amino acid positions selected from the group consisting of L14, T26, T28, T88, Y90, S106, S113, and A116, according to SEQ ID NO:296.

83. The antibody of claim 82, wherein the antibody further binds to the human SIRP-α v1 polypeptide at L14, T88, Y90, S106, S113, and A116 of human SIRP-α v1, according to SEQ ID NO:296.

84. An isolated antibody that binds an extracellular domain of a human SIRP-α polypeptide, wherein the antibody binds the extracellular domain of a human SIRP-α v1 polypeptide with a dissociation constant (K_D) of less than 100nM, and wherein the antibody blocks binding between an extracellular domain of a human SIRP-α polypeptide and an IgSF domain of a human CD47 polypeptide.

85. The antibody of claim 84, wherein the antibody binds the extracellular domain of a human SIRP-α v2 polypeptide with a dissociation constant (K_D) of less than 100nM.

86. The antibody of claim 84, wherein the antibody binds the D1 domain of a human SIRP-α v1 polypeptide and the D1 domain of a human SIRP-α v2 polypeptide.

87. The antibody of any one of claims 84-86, wherein the antibody binds an extracellular domain of a cynomolgus SIRP-α polypeptide.

88. The antibody of any one of claims 84-87, wherein the antibody binds an extracellular domain of a human SIRP-β polypeptide.

89. The antibody of any one of claims 84-88, wherein the antibody binds an extracellular domain of a human SIRP-γ polypeptide.

90. The antibody of any one of claims 84-89, wherein the antibody binds an extracellular domain of a murine SIRP-α polypeptide.

91. An isolated antibody that binds an extracellular domain of a human SIRP-α polypeptide, wherein the antibody binds the D1 domain of a human SIRP-α polypeptide, and wherein the antibody does not block binding between an extracellular domain of a human SIRP-α polypeptide and an IgSF domain of a human CD47 polypeptide.

92. The antibody of claim 91, wherein the antibody binds the D1 domain of a human SIRP-α with a dissociation constant (K_D) of less than 100nM.

93. The antibody of claim 91 or claim 92, wherein the antibody binds the D1 domain of a human SIRP-α v1 polypeptide with a dissociation constant (K_D) of less than 100nM and/or binds the D1 domain of a human SIRP-α v2 polypeptide with a dissociation constant (K_D) of less than 100nM.

94. The antibody of claim 91, wherein the antibody binds the D1 domain of a human SIRP-α v1 polypeptide and the D1 domain of a human SIRP-α v2 polypeptide.

95. The antibody of any one of claims 91-94, wherein the antibody binds an extracellular domain of a cynomolgus SIRP-α polypeptide.

96. The antibody of any one of claims 91-95, wherein the antibody binds an extracellular domain of a human SIRP-β polypeptide.

97. The antibody of any one of claims 91-96, wherein the antibody binds an extracellular domain of a murine SIRP-α polypeptide.

98. An isolated antibody that binds an extracellular domain of a human SIRP-α polypeptide, wherein the antibody competes for binding the extracellular domain of the human SIRP-α polypeptide with a reference anti-SIRP-α antibody comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain of an antibody selected from the group consisting of antibodies 119, 120, 121, 122, 21, 25, 27, 66, and 135.

99. An isolated antibody that binds an extracellular domain of a human SIRP-α polypeptide, wherein the antibody competes for binding the extracellular domain of the human SIRP-α polypeptide with a reference anti-SIRP-α antibody comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain of an antibody selected from the group consisting of antibodies 136 and 137.

100. An isolated antibody that binds an extracellular domain of a human SIRP-α polypeptide, wherein the antibody competes for binding the extracellular domain of the human SIRP-α polypeptide with a reference anti-SIRP-α antibody comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain of an antibody selected from the group consisting of antibodies 218, 123, 149, 161, 162, and 194.

101. An isolated antibody that binds an extracellular domain of a human SIRP-α polypeptide, wherein the antibody competes for binding the extracellular domain of the human SIRP-α polypeptide with a reference anti-SIRP-α antibody comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain of antibody 45.

102. The antibody of any one of claims 84-101, wherein the antibody enhances phagocytosis by a macrophage expressing a human SIRP-α polypeptide.

103. The antibody of any one of claims 84-102, wherein the antibody enhances activation of a dendritic cell expressing a human SIRP-α polypeptide.

104. The antibody of any one of claims 84-103, wherein the antibody inhibits *in vivo* growth of a tumor that expresses CD47.

105. The antibody of any one of claims 84-104, wherein the antibody does not prevent interactions between a CD47-expressing cell and a T cell.

106. The antibody of any one of claims 1-105, wherein the antibody is a monoclonal antibody.

107. The antibody of any one of claims 1-105, wherein the antibody is a scFv-Fc, single domain antibody, single heavy chain antibody, or single light chain antibody.

108. The antibody of any one of claims 1-105, wherein the antibody comprises a light chain constant region comprising the amino acid sequence of SEQ ID NO:325, 326, or 426.

109. The antibody of any one of claims 1-105 and 107, wherein the antibody comprises an Fc region.

110. The antibody of claim 109, wherein the antibody comprises an amino acid sequence selected from the group consisting of SEQ ID NOs:320-324.

111. The antibody of claim 109, 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.

112. The antibody of claim 109, wherein the Fc region comprises a human IgG1 Fc region comprising one or more mutations selected from the group consisting of L234A, L235A, G237A, and N297A, according to EU numbering.

113. The antibody of claim 109, wherein the Fc region comprises a human IgG2 Fc region comprising one or more mutations selected from the group consisting of A330S, P331S and N297A, according to EU numbering.

114. The antibody of claim 109, wherein the Fc region comprises a human IgG4 Fc region comprising one or more mutations selected from the group consisting of S228P, E233P, F234V, L235A, L235E, delG236, and N297A, according to EU numbering.

115. The antibody of any one of claims 1-22, 24, 26, 28, 30-57, 62-79, 84-90, and 98 wherein the antibody is an antibody fragment selected from the group consisting of a Fab, F(ab')2, Fab'-SH, Fv, and scFv fragment.

116. The antibody of any one of claims 1-115, wherein the antibody is conjugated to a cytotoxic agent or label.

117. The antibody of any one of claims 1-115, wherein the antibody is a bispecific antibody.

118. The antibody of claim 116, 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.

119. The antibody of claim 117, 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 αVβ3, integrin α5β1, 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-βRII, HPV E6, or HPV E7.

120. The antibody of any one of claims 1-119, wherein the antibody is a chicken, humanized, chimeric, or human antibody.

121. The antibody of any one of claims 1-120, wherein the antibody is generated by or derived from a chicken.

122. A polynucleotide encoding the antibody of any one of claims 1-121.

123. A vector comprising the polynucleotide of claim 122.

124. A host cell comprising the polynucleotide of claim 122 or the vector of claim 123.

125. A method of producing an antibody, the method comprising culturing the host cell of claim 124 such that the antibody is produced.

126. The method of claim 125, further comprising recovering the antibody from the host cell.

127. Use of an effective amount of the antibody of any one of claims 1-121 in the manufacture of a medicament for treating or delaying progression of cancer in an individual.

128. The use of claim 127, wherein the medicament is to be administered with an effective amount of a second antibody that binds an antigen expressed by the cancer.

129. The use of claim 128, 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 αVβ3, integrin α5β1, 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-βRII, HPV E6, or HPV E7.

130. The use of claim 127, wherein the medicament is to be administered with an effective amount of an immunotherapeutic agent.

131. The use of claim 130, wherein the immunotherapeutic agent comprises a second antibody.

132. The use of claim 131, wherein the second antibody binds to an antigen selected from the group consisting of PD-1, PD-L1, OX40, CTLA-4, CD137/4-1BB, TNFR2, B7-H3, FZD7, CD27, CCR4, CSF1R, CSF, TIM-3, LAG-3, VISTA, ICOS, CCR2, IDO, A2R, CD39, CD73, TIGIT, CD80, CD47, arginase, TDO, and PVRIG.

133. The use of claim 131, wherein the first antibody binds the extracellular domain of a human SIRP-α v1 polypeptide, the extracellular domain of a human SIRP-α v2 polypeptide, or the extracellular domains of both a human SIRP-α v1 polypeptide and a human SIRP-α v2

polypeptide with a dissociation constant (K_D) of less than 100nM, wherein the first antibody blocks binding between an extracellular domain of a human SIRP-α polypeptide and an IgSF domain of a human CD47 polypeptide, and wherein the second antibody binds to PD-1.

134. The use of claim 131, wherein the first antibody binds the D1 domain of a human SIRP-α polypeptide, wherein the first antibody does not block binding between an extracellular domain of a human SIRP-α polypeptide and an IgSF domain of a human CD47 polypeptide, and wherein the second antibody binds to PD-1.

135. The use of claim 131, wherein the first antibody binds the extracellular domain of a human SIRP-α v1 polypeptide with a dissociation constant (K_D) of less than 100nM, wherein the first antibody blocks binding between an extracellular domain of a human SIRP-α polypeptide and an IgSF domain of a human CD47 polypeptide, and wherein the second antibody binds to PD-L1.

136. The use of claim 131, wherein the first antibody binds the D1 domain of a human SIRP-α polypeptide, wherein the first antibody does not block binding between an extracellular domain of a human SIRP-α polypeptide and an IgSF domain of a human CD47 polypeptide, and wherein the second antibody binds to PD-L1.

137. Use of an effective amount of the antibody of any one of claims 1-121 in the manufacture of a medicament for treating or delaying progression of an autoimmune disease or an inflammatory disease in an individual.

138. The use of claim 137, 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, asthma, atopic dermatitis, acute respiratory distress syndrome (ARDS), vasculitis, and inflammatory autoimmune myositis.

139. A method of identifying an antigen binding domain that binds an extracellular domain of a human SIRP-α polypeptide and does not block binding between human CD47 and the human SIRP-α polypeptide, the method comprising:

(a) providing an antigen binding domain that binds the extracellular domain of a human SIRP-α polypeptide;

(b) assembling a complex comprising a SIRP-α D1 variant bound to a polypeptide comprising an IgSF domain of CD47, wherein the SIRP-α D1 variant is a non-naturally occurring high affinity SIRP-α D1 domain, and wherein the SIRP-α D1 variant binds to human CD47 with an affinity that is at least 10-fold greater than the affinity of a naturally occurring SIRP-α D1 domain binding to human CD47;

(c) contacting the antigen binding domain with the assembled complex; and

(d) detecting binding of the antigen binding domain to the complex, wherein binding of the antigen binding domain to the complex indicates that the antigen binding domain does not block binding between human CD47 and the human SIRP-α polypeptide.

140. A method of identifying an antigen binding domain that binds an extracellular domain of a human SIRP-α polypeptide and blocks binding between human CD47 and the human SIRP-α polypeptide, the method comprising:

(a) providing an antigen binding domain that binds the extracellular domain of a human SIRP-α polypeptide;

(b) assembling a complex comprising a SIRP-α D1 variant bound to a polypeptide comprising an IgSF domain of CD47, wherein the SIRP-α D1 variant is a non-naturally occurring high affinity SIRP-α D1 domain, and wherein the SIRP-α D1 variant binds to human CD47 with an affinity that is at least 10-fold greater than the affinity of a naturally occurring SIRP-α D1 domain binding to human CD47;

(c) contacting the antigen binding domain with the assembled complex; and

(d) detecting binding of the antigen binding domain to the complex, wherein a lack of binding of the antigen binding domain to the complex indicates that the antigen binding domain blocks binding between human CD47 and the human SIRP-α polypeptide.

141. The method of claim 139 or claim 140, wherein the SIRP-α D1 variant comprises an amino acid sequence selected from the group consisting of SEQ ID NOs:17-52.

142. The method of any one of claims 139-141, wherein the IgSF domain of CD47 comprises the amino acid sequence of SEQ ID NO:16.

143. The method of any one of claims 139-142, wherein the polypeptide comprising the IgSF domain of CD47 comprises a human CD47 extracellular domain.

144. The method of any one of claims 139-143, wherein the polypeptide comprising the IgSF domain of CD47 further comprises an antibody Fc region.

145. A method of producing an anti-SIRP-α antibody that binds the extracellular domain of a human SIRP-α polypeptide, the method comprising:

detecting binding between the antibody obtained from an antibody-producing cell and the extracellular domains of a human SIRP-α polypeptide, wherein binding between the antibody and the extracellular domain of the human SIRP-α polypeptide indicates that the antibody is an anti-SIRP-α antibody that binds the extracellular domain of a human SIRP-α variant polypeptide, and wherein the antibody-producing cell is to be obtained from a chicken that has been immunized with a peptide comprising at least a portion of a human SIRP-α extracellular domain.

146. The method of claim 145, wherein the antibody is a chicken, humanized, chimeric, or human antibody.

147. The method of claim 145 or claim 146, wherein the antibody binds the extracellular domain of a human SIRP-α v1 polypeptide, the extracellular domain of a human SIRP-α v2 polypeptide, or both.

148. The method of claim 147, wherein the antibody binds an extracellular domain of a human SIRP-α v1 polypeptide comprising the amino acid sequence of EEELQVIQPDKSVLVAAGETATLRCTATSLIPVGPIQWFRGAGPGRELIYNQKEGHFPRV TTVSDLTKRNNMDFSIRIGNITPADAGTYYCVKFRKGSPDDVEFKSGAGTELSVRAKPS (SEQ ID NO:5).

149. The method of claim 146, wherein the antibody binds an extracellular domain of a human SIRP-α v2 polypeptide comprising the amino acid sequence of EEELQVIQPDKSVSVAAGESAILHCTVTSLIPVGPIQWFRGAGPARELIYNQKEGHFPRVT TVSESTKRENMDFSISISNITPADAGTYYCVKFRKGSPDTEFKSGAGTELSVRAKPS (SEQ ID NO:6).

150. The method of any one of claims 146-149, wherein the antibody binds an extracellular domain of a human SIRP-α v1 polypeptide comprising the amino acid sequence of EEELQVIQPDKSVLVAAGETATLRCTATSLIPVGPIQWFRGAGPGRELIYNQKEGHFPRV TTVSDLTKRNNMDFSIRIGNITPADAGTYYCVKFRKGSPDDVEFKSGAGTELSVRAKPS (SEQ ID NO:5) and binds an extracellular domain of a human SIRP-α v2 polypeptide comprising the amino acid sequence of EEELQVIQPDKSVSVAAGESAILHCTVTSLIPVGPIQWFRGAGPARELIYNQKEGHFPRVT TVSESTKRENMDFSISISNITPADAGTYYCVKFRKGSPDTEFKSGAGTELSVRAKPS (SEQ ID NO:6).

151. The method of any one of claims 146-149, wherein the antibody binds the extracellular domains of three, four, five, six, seven, eight, nine or ten different human SIRP-α variant polypeptides.

152. The method of claim 150, wherein each of the three, four, five, six, seven, eight, nine or ten different human SIRP-α variant polypeptides comprises an extracellular domain comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 5, 6, and 76-83.

153. The method of any one of claims 144-152, further comprising detecting binding between the antibody obtained from the cell and an extracellular domain of one or more SIRP-α

polypeptides selected from the group consisting of a monkey SIRP-α polypeptide, a murine SIRP-α polypeptide, a human SIRP-β polypeptide, and a human SIRP-γ polypeptide.

154. The method of claim 153, wherein the antibody binds an extracellular domain of a monkey SIRP-α polypeptide.

155. The method of claim 154, wherein the monkey SIRP-α polypeptide is a cynomolgus SIRP-α polypeptide.

156. The method of claim 154 or claim 155, wherein the antibody binds the extracellular domains of at least two different monkey SIRP-α variant polypeptides.

157. The method of claim 155 or claim156, wherein the antibody binds an extracellular domain of a cynomolgus SIRP-α polypeptide comprising the amino acid sequence of SEQ ID NO:11, an extracellular domain of a cynomolgus SIRP-α polypeptide comprising the amino acid sequence of SEQ ID NO:12, or both.

158. The method of any one of claims 153-157, wherein the antibody binds an extracellular domain of a murine SIRP-α polypeptide.

159. The method of claim 158, wherein the antibody binds the extracellular domains of two or more different murine SIRP-α variant polypeptides.

160. The method of claim 158 or claim 159, wherein the antibody binds an extracellular domain of one or more murine SIRP-α polypeptides, and wherein the one or more murine SIRP-α polypeptides each comprise an amino acid sequence selected from the group consisting of SEQ ID NOs: 7-10.

161. The method of any one of claims 153-160, wherein the antibody binds an extracellular domain of a human SIRP-β polypeptide.

162. The method of any one of claims 153-161, wherein the antibody binds an extracellular domain of a human SIRP-γ polypeptide.

163. The method of any one of claims 153-161, wherein the antibody does not bind an extracellular domain of a human SIRP-γ polypeptide.

164. The method of any one of claims 161-163, wherein the antibody binds the extracellular domain of a human SIRP-β polypeptide comprising the amino acid sequence of SEQ ID NO:13.

165. The method of any one of claims 161-164, wherein the antibody binds the extracellular domain of a human SIRP-γ polypeptide comprising the amino acid sequence of SEQ ID NO:15.

166. The method of any one of claims 144-165, further comprising detecting binding or a lack of binding between the antibody obtained from the cell and a complex comprising a SIRP-α D1 variant bound to an IgSF domain of CD47, wherein the SIRP-α D1 variant is a non-naturally occurring high affinity SIRP-α D1 domain, and wherein the SIRP-α D1 variant binds to human CD47 with an affinity that is at least 10-fold greater than the affinity of a naturally occurring SIRP-α D1 domain binding to human CD47.

167. The method of claim 166, wherein the antibody binds a complex comprising a SIRP-α D1 variant bound to an IgSF domain of CD47, wherein the SIRP-α D1 variant is a non-naturally occurring high affinity SIRP-α D1 domain, and wherein the SIRP-α D1 variant binds to human CD47 with an affinity that is at least 10-fold greater than the affinity of a naturally occurring SIRP-α D1 domain binding to human CD47.

168. The method of claim 167, wherein the antibody does not block binding between an extracellular domain of a human SIRP-α polypeptide and an IgSF domain of a human CD47 polypeptide.

169. The method of claim 166, wherein the antibody does not bind a complex comprising a SIRP-α D1 variant bound to an IgSF domain of CD47, wherein the SIRP-α D1 variant is a non-naturally occurring high affinity SIRP-α D1 domain, and wherein the SIRP-α D1 variant binds to human CD47 with an affinity that is at least 10-fold greater than the affinity of a naturally occurring SIRP-α D1 domain binding to human CD47.

170. The method of claim 169, wherein the antibody blocks binding between an extracellular domain of a human SIRP-α polypeptide and an IgSF domain of a human CD47 polypeptide.

171. The method of any one of claims 145-170, wherein the antibody modulates SIRP-α signaling in a cell expressing a human SIRP-α polypeptide.

172. The method of claim 171171, wherein the cell is a leukocyte selected from the group consisting of a macrophage, a dendritic cell, a neutrophil, an eosinophil, and a myeloid-derived suppressor cell (MDSC).

173. The method of claim 172, wherein the antibody inhibits SIRP-α signaling in a macrophage expressing a human SIRP-α polypeptide.

174. The method of any one of claims 171-172, wherein the antibody enhances phagocytosis by a macrophage expressing a human SIRP-α polypeptide.