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; and 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 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); or

(B) 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 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). In some embodiments, the antibody binds an extracellular domain of a human SIRP-α v1 polypeptide comprising the amino acid sequence of EEELQVIQPDKSVLVAAGETATLRCTATSLIPVGPIQWFRGAGPGRELIYNQKEGHFPRVTT VSDLTKRNNMDFSIRIGNITPADAGTYYCVKFRKGSPDDVEFKSGAGTELSVRAKPS (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 EEELQVIQPDKSVSVAAGESAILHCTVTSLIPVGPIQWFRGAGPARELIYNQKEGHFPRVTTV SESTKRENMDFSISISNITPADAGTYYCVKFRKGSPDTEFKSGAGTELSVRAKPS (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 EEELQVIQPDKSVLVAAGETATLRCTATSLIPVGPIQWFRGAGPGRELIYNQKEGHFPRVTT VSDLTKRNNMDFSIRIGNITPADAGTYYCVKFRKGSPDDVEFKSGAGTELSVRAKPS (SEQ ID NO:5) and binds an extracellular domain of a human SIRP-α v2 polypeptide comprising the amino acid sequence of EEELQVIQPDKSVSVAAGESAILHCTVTSLIPVGPIQWFRGAGPARELIYNQKEGHFPRVTTV SESTKRENMDFSISISNITPADAGTYYCVKFRKGSPDTEFKSGAGTELSVRAKPS (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

NO:166, 172, 178, or 184. In some embodiments, the antibody comprises a VH domain comprising the amino acid sequence of SEQ ID NO:141 and/or a VL domain comprising an HVR-L1 comprising the amino acid sequence of SEQ ID NO:164, 170, 176, or 182; an HVR-L2 comprising the amino acid sequence of SEQ ID NO:165, 171, 177, or 183; and an HVR-L3 comprising the amino acid sequence of SEQ ID NO:166, 172, 178, or 184. In some embodiments, one, two, three, four, five, or six of the HVR sequences are defined by Kabat. In some embodiments, one, two, three, four, five, or six of the HVR sequences are defined by Chothia. In some embodiments, one, two, three, four, five, or six of the HVR sequences are defined by IMGT. In some embodiments, the antibody comprises HVR sequences as defined by two or more of Kabat, Chothia, and IMGT (*e.g.*, the antibody comprises one or more HVR sequences as defined by one delineation and one or more HVR sequences as defined by a different delineation).

[0012] In other examples, 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 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). In some embodiments, 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. In some embodiments, 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; 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; 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; 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; 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; 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; 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 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.

[0013] In other examples, 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 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). In some embodiments, 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. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:127, and the VL domain comprises the amino acid sequence of SEQ ID NO:104; 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; 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; 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; the VH domain comprises the amino acid sequence of SEQ ID NO:127, and the VL domain comprises the amino acid sequence of SEQ ID NO:248; 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; 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 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.

[0014] In other examples, 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 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). In some embodiments, 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). In some embodiments, 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. In some embodiments, 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; 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; 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; 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; 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; 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; 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; 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; 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; 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; 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 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.

[0015] In other examples, 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 comprises: a heavy chain variable (VH) domain comprising: 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); 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 an HVR-H3 sequence comprising the amino acid sequence of ETWNHLFDY (SEQ ID NO:193); and/or a light chain variable (VL) domain comprising: 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); 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 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). In other examples, 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 comprises: a heavy chain variable (VH) domain comprising: a heavy chain variable (VH) domain comprising: 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); 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 an HVR-H3 sequence comprising the amino acid sequence of ETWNHLFDY (SEQ ID NO:193); and/or a light chain variable (VL) domain comprising: an HVR-L1 sequence comprising the amino acid sequence of $SGGX_1YSSYYYA$, wherein X_1 is S or A (SEQ ID NO:304); an HVR-L2 sequence comprising the amino acid sequence of SDDKRPS (SEQ ID NO:336); and an HVR-L3 sequence comprising the amino acid sequence of GGYDQSSYTNP (SEQ ID NO:172). In some embodiments, 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). In some embodiments, 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. In some embodiments, 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). In some embodiments, 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. In some embodiments, 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). In

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; 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; 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; 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; 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; 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; 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; 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; 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; 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; 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; 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; 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; 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; 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 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.

[0016] In other examples, 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 I31, V33, Q52, K53, T67, R69, N70, and K96, according to SEQ ID NO:296. In some embodiments, 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. 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 examples, 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 examples, 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 examples, 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 examples, 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 examples, 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)

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 examples, 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 examples, 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

[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 any one of the antibodies as disclosed herein. In other aspects, provided herein are vectors comprising any one of the polynucleotides as disclosed herein. In other aspects, provided herein are host cells comprising any one of the polynucleotides or vectors as disclosed herein. In other aspects, provided herein are methods of producing an antibody, comprising culturing any one of the host cells as disclosed herein 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 examples, 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 examples, 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 example, 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

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; and 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 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); or

(B) 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 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).

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 6, wherein the antibody binds an extracellular domain of a cynomolgus SIRP-α polypeptide comprising the amino acid sequence of SEQ ID NO:11.

8. The antibody of any one of claims 1-7, wherein the antibody binds an extracellular domain of a human SIRP-β polypeptide.

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

10. The antibody of any one of claims 8-9, wherein the antibody binds the extracellular domain of a human SIRP-β polypeptide comprising the amino acid sequence of SEQ ID NO:13.

11. The antibody of any one of claims 8-10, wherein the antibody binds the extracellular domain of a human SIRP-γ polypeptide comprising the amino acid sequence of SEQ ID NO:15.

12. The antibody of any one of claims 1-11, wherein the antibody modulates SIRP-α signaling in a cell expressing a human SIRP-α polypeptide.

13. The antibody of claim 12, 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).

14. The antibody of claim 13, wherein the antibody inhibits SIRP-α signaling in a macrophage expressing a human SIRP-α polypeptide.

15. The antibody of any one of claims 12-14 wherein the antibody enhances phagocytosis by a macrophage expressing a human SIRP-α polypeptide.

16. The antibody of any one of claims 1-15, wherein the antibody blocks binding between an extracellular domain of a human SIRP-α polypeptide and an IgSF domain of a human CD47 polypeptide.

17. The antibody of claim 1, 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 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.

18. The antibody of claim 17, 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.

19. The antibody of claim 1, 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 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.

20. The antibody of claim 19, 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.

21. The antibody of claim 1, 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.

22. The antibody of claim 21, 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.

23. The antibody of claim 21 or claim 22, 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.

24. The antibody of claim 23, 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.

25. The antibody of any one of claims 1-24, wherein the antibody is a monoclonal antibody.

26. The antibody of any one of claims 1-24, wherein the antibody is a scFv-Fc, single domain antibody, single heavy chain antibody, or single light chain antibody.

27. The antibody of any one of claims 1-24, wherein the antibody comprises a light chain constant region comprising the amino acid sequence of SEQ ID NO:325, 326, or 426.

28. The antibody of any one of claims 1-27, wherein the antibody comprises an Fc region.

29. The antibody of claim 28, wherein the antibody comprises an amino acid sequence selected from the group consisting of SEQ ID NOs:320-324.

30. The antibody of claim 28, 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.

31. The antibody of claim 28, 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.

32. The antibody of claim 28, 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.

33. The antibody of claim 28, 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.

34. The antibody of claim 1, wherein the antibody is an antibody fragment selected from the group consisting of a Fab, F(ab')2, Fab'-SH, Fv, and scFv fragment.

35. The antibody of any one of claims 1-34, wherein the antibody is conjugated to a cytotoxic agent or label.

36. The antibody of any one of claims 1-34, wherein the antibody is a bispecific antibody.

37. The antibody of claim 36, 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.

38. The antibody of claim 37, 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.

39. The antibody of any one of claims 1-38, wherein the antibody is a chicken, humanized, chimeric, or human antibody.

40. The antibody of any one of claims 1-39, wherein the antibody is generated by or derived from a chicken.

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

42. A vector comprising the polynucleotide of claim 41.

43. A host cell comprising the polynucleotide of claim 41 or the vector of claim 42.

44. A method of producing an antibody, the method comprising culturing the host cell of claim 43 such that the antibody is produced.

45. The method of claim 44, further comprising recovering the antibody from the host cell.

46. Use of an effective amount of the antibody of any one of claims 1-40 in the manufacture of a medicament for treating or delaying progression of cancer in an individual.

47. The use of claim 46, wherein the medicament is to be administered with an effective amount of a second antibody that binds an antigen expressed by the cancer.

48. The use of claim 47, 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.

49. The use of claim 46, wherein the medicament is to be administered with an effective amount of an immunotherapeutic agent.

50. The use of claim 49, wherein the immunotherapeutic agent comprises a second antibody.

51. The use of claim 50, 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.

52. The use of claim 50, 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.

53. The use of claim 50, 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.

54. Use of an effective amount of the antibody of any one of claims 1-40 in the manufacture of a medicament for treating or delaying progression of an autoimmune disease or an inflammatory disease in an individual.

55. The use of claim 54, 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.