

comprises the step of formulating the antibody or antigen-binding fragment thereof into a pharmaceutical composition. Also provided herein are pharmaceutical formulations comprising an anti-SIRP α antibody or an antigen-binding fragment thereof as disclosed herein.

[0073a] In one aspect, the present disclosure relates to an anti-human SIRP α antibody or an antigen-binding fragment thereof comprising: a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 33 (H-CDR1); the amino acid sequence of SEQ ID NO: 34 (H-CDR2); and the amino acid sequence of SEQ ID NO: 35 (H-CDR3), and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 36 or SEQ ID NO: 37 (L-CDR1); the amino acid sequence of SEQ ID NO: 38 (L-CDR2); and the amino acid sequence of SEQ ID NO: 39 (L-CDR3).

[0073b] In another aspect, the present disclosure relates to the anti-SIRP α antibody or antigen-binding fragment thereof as disclosed herein for use as a medicament.

[0073c] In another aspect, the present disclosure relates to a pharmaceutical composition comprising an antibody or antigen-binding fragment as disclosed herein and a pharmaceutically acceptable carrier.

[0073d] In another aspect, the present disclosure relates to a use of the anti-SIRP α antibody or antigen-binding fragment as disclosed herein, or a pharmaceutical composition as disclosed herein, in manufacture of a medicament for treating a disease, wherein the disease is selected from cancer, inflammatory disease, autoimmune disease, respiratory disease, infectious disease or fibrosis.

[0073e] In another aspect, the present disclosure relates to an isolated polynucleotide encoding a heavy chain variable region and/or a light chain variable region as disclosed herein.

[0073f] In another aspect, the present disclosure relates to a vector comprising a polynucleotide as disclosed herein, preferably an expression vector, more preferred a vector comprising the polynucleotide according to the invention in functional association with an expression control sequence.

[0073g] In another aspect, the present disclosure relates to a host cell comprising a polynucleotide as disclosed herein.

[0073h] In another aspect, the present disclosure relates to a method for the production of an anti-SIRP α antibody or antigen-binding fragment as disclosed herein, comprising the steps: (a) cultivating the host cell under conditions allowing the expression of the anti-SIRP α antibody or antigen-binding fragment; and (b) recovering the anti-SIRP α antibody or antigen-binding fragment.

[0073i] In another aspect, the present disclosure relates to a method of manufacturing an antibody comprising the steps of: a) culturing a host cell comprising an expression vector comprising an isolated polynucleotide encoding a heavy chain variable region as disclosed herein and comprising a polynucleotide encoding a light chain variable region as disclosed herein under conditions that allow formation of an antibody; and b) recovering said antibody.

[0073j] In another aspect, the present disclosure relates to a method of manufacturing an antibody comprising the steps of: a) culturing a host cell comprising an expression vector comprising an isolated polynucleotide encoding a heavy chain as disclosed herein and a polynucleotide encoding a light chain as disclosed herein under conditions that allow formation of an antibody; and b) recovering said antibody.

[0073k] In another aspect, the present disclosure relates to an anti-SIRP α antibody or antigen-binding fragment thereof, wherein the anti-SIRP α antibody or antigen-binding fragment thereof comprises: a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 113; and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 125.

[0073l] In another aspect, the present disclosure relates to an anti-SIRP α antibody, wherein the anti-SIRP α antibody comprises: a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 113; and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 125.

[0073m] In another aspect, the present disclosure relates to anti-SIRP α antibody or antigen-binding fragment thereof, wherein the anti-SIRP α antibody or antigen-binding fragment thereof comprises: a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 111; and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 126.

[0073n] In another aspect, the present disclosure relates to an anti-SIRP α antibody, wherein the anti-SIRP α antibody comprises: a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 111; and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 126.

[0073o] In another aspect, the present disclosure relates to an anti-SIRP α antibody, wherein the anti-SIRP α antibody comprises: a heavy chain comprising the amino acid sequence of SEQ ID NO: 141; and a light chain comprising the amino acid sequence of SEQ ID NO: 184.

[0073p] In another aspect, the present disclosure relates to an anti-SIRP α antibody, wherein the anti-SIRP α antibody comprises: a heavy chain comprising the amino acid sequence of SEQ ID NO: 147; and a light chain comprising the amino acid sequence of SEQ ID NO: 190.

[0073q] In another aspect, the present disclosure relates to an anti-SIRP α antibody, wherein the anti-SIRP α antibody comprises: a heavy chain comprising the amino acid sequence of SEQ ID NO: 217; and a light chain comprising the amino acid sequence of SEQ ID NO: 218.

[0073r] In another aspect, the present disclosure relates to a pharmaceutical composition comprising the anti-SIRP α antibody as disclosed herein and a pharmaceutically acceptable carrier.

[0073s] In another aspect, the present disclosure relates to an isolated polynucleotide composition, the isolated polynucleotide composition comprising: a) a first isolated polynucleotide encoding the heavy chain variable region as disclosed herein; and/or b) a second isolated polynucleotide encoding the light chain variable region as disclosed herein.

[0073t] In another aspect, the present disclosure relates to an isolated polynucleotide composition, the isolated polynucleotide composition comprising: a) a first isolated polynucleotide encoding the heavy chain as disclosed herein; and/or b) a second isolated polynucleotide encoding the light chain as disclosed herein.

[0073u] In another aspect, the present disclosure relates to an expression vector composition, the composition comprising: a) a first expression vector comprising the first isolated polynucleotide as disclosed herein; and/or b) a second expression vector comprising the second isolated polynucleotide as disclosed herein.

[0073v] In another aspect, the present disclosure relates to a host cell comprising the isolated polynucleotide composition as disclosed herein.

[0073w] In another aspect, the present disclosure relates to a method for the production of an anti-SIRP α antibody, comprising the steps: a) cultivating the host cell of claim 37 under conditions for expression of the anti-SIRP α antibody; and b) recovering the anti-SIRP α antibody.

BRIEF DESCRIPTION OF THE DRAWINGS

[0074] The summary, as well as the following detailed description, is further understood when read in conjunction with the appended drawings. For the purpose of illustrating the disclosed compositions, methods, and kits there are shown in the drawings exemplary embodiments of methods and kits; however, these should not be limited to the specific embodiments disclosed.

[0075] Figures 1A-1C are series of graphs depicting the binding of antibodies to full-length human V1-SIRP α or V2-SIRP α expressed on CHO cells. Figure 1A. Antibody binding to parental CHO cells. Figure 1B. Antibody binding to CHO cells expressing full-length human SIRP α V1 (NP_542970.1). Figure 1C. Antibody binding to CHO cells expressing full-length human SIRP α V2-expressing CHO cells (CAA71403.1) .

[0076] Figures 2A-2B are series of graphs depicting the binding of antibodies to endogenous human V1-SIRP α or V2-SIRP α expressed on human monocytic cell lines. Figure 2A. Antibody binding to U-937 human monocytic cell line. Figure 2B. Antibody binding to THP-1 human monocytic cell line.

[0077] Figures 3A-3D are series of graphs depicting the binding of antibodies to endogenous human V1-SIRP α and/or V2-SIRP α expressed on primary human monocytes. Antibody binding to primary human CD14⁺ monocytes from donors homozygous for V1-SIRP α allele (Figures 3A-3D). Solid, dashed, and dotted lines indicate antibody molecules engineered on hIgG1 (LALA), hIgG4P, hIgG1 (K322A) backbones, respectively.

[0078] Figures 4A-4D are series of graphs depicting the binding of antibodies to endogenous human V1-SIRP α and/or V2-SIRP α expressed on primary human monocytes. Antibody binding to primary human CD14⁺ monocytes from donors heterozygous for V1- and V2-SIRP α alleles (Figures 4A-4D). Solid, dashed, and dotted lines indicate antibody molecules engineered on hIgG1 (LALA), hIgG4P, hIgG1 (K322A) backbones, respectively.

[0079] Figures 5A-5D are series of graphs depicting the binding of antibodies to endogenous human V1-SIRP α and/or V2-SIRP α expressed on primary human monocytes.

What is claimed is:

1. An anti-human SIRP α antibody or an antigen-binding fragment thereof comprising:
a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 33 (H-CDR1); the amino acid sequence of SEQ ID NO: 34 (H-CDR2); and the amino acid sequence of SEQ ID NO: 35 (H-CDR3), and

a light chain variable region comprising the amino acid sequence of SEQ ID NO: 36 or SEQ ID NO: 37 (L-CDR1); the amino acid sequence of SEQ ID NO: 38 (L-CDR2); and the amino acid sequence of SEQ ID NO: 39 (L-CDR3).

2. The anti-SIRP α antibody or antigen-binding fragment thereof according to claim 1, wherein the antibody or antigen-binding fragment thereof comprises:

- a) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 100;
and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 105;
or
- b) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 110;
and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 125;
or
- c) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 111;
and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 125;
or
- d) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 112;
and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 125;
or
- e) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 113;
and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 125;
or
- f) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 114;
and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 125;
or
- g) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 115;
and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 125;
or

- h) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 116;
and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 125;
or
- i) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 117;
and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 125;
or
- j) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 110;
and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 126;
or
- k) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 111;
and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 126;
or
- l) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 112;
and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 126;
or
- m) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 113;
and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 126;
or
- n) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 114;
and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 126;
or
- o) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 115;
and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 126;
or
- p) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 117;
and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 126.

3. The anti-SIRP α antibody according to claim 1, wherein the antibody comprises

- a) a heavy chain comprising the amino acid sequence of SEQ ID NO: 131; and a light chain comprising the amino acid sequence of SEQ ID NO: 174; or
- b) a heavy chain comprising the amino acid sequence of SEQ ID NO: 138; and a light chain comprising the amino acid sequence of SEQ ID NO: 181; or
- c) a heavy chain comprising the amino acid sequence of SEQ ID NO: 139; and a light chain comprising the amino acid sequence of SEQ ID NO: 182; or

- d) a heavy chain comprising the amino acid sequence of SEQ ID NO: 140; and a light chain comprising the amino acid sequence of SEQ ID NO: 183; or
- e) a heavy chain comprising the amino acid sequence of SEQ ID NO: 141; and a light chain comprising the amino acid sequence of SEQ ID NO: 184; or
- f) a heavy chain comprising the amino acid sequence of SEQ ID NO: 142; and a light chain comprising the amino acid sequence of SEQ ID NO: 185; or
- g) a heavy chain comprising the amino acid sequence of SEQ ID NO: 143; and a light chain comprising the amino acid sequence of SEQ ID NO: 186; or
- h) a heavy chain comprising the amino acid sequence of SEQ ID NO: 144; and a light chain comprising the amino acid sequence of SEQ ID NO: 187; or
- i) a heavy chain comprising the amino acid sequence of SEQ ID NO: 145; and a light chain comprising the amino acid sequence of SEQ ID NO: 188; or
- j) a heavy chain comprising the amino acid sequence of SEQ ID NO: 146; and a light chain comprising the amino acid sequence of SEQ ID NO: 189; or
- k) a heavy chain comprising the amino acid sequence of SEQ ID NO: 147; and a light chain comprising the amino acid sequence of SEQ ID NO: 190; or
- l) a heavy chain comprising the amino acid sequence of SEQ ID NO: 148; and a light chain comprising the amino acid sequence of SEQ ID NO: 191; or
- m) a heavy chain comprising the amino acid sequence of SEQ ID NO: 149; and a light chain comprising the amino acid sequence of SEQ ID NO: 192; or
- n) a heavy chain comprising the amino acid sequence of SEQ ID NO: 150; and a light chain comprising the amino acid sequence of SEQ ID NO: 193; or
- o) a heavy chain comprising the amino acid sequence of SEQ ID NO: 151; and a light chain comprising the amino acid sequence of SEQ ID NO: 194; or
- p) a heavy chain comprising the amino acid sequence of SEQ ID NO: 152; and a light chain comprising the amino acid sequence of SEQ ID NO: 195; or
- q) a heavy chain comprising the amino acid sequence of SEQ ID NO: 217; and a light chain comprising the amino acid sequence of SEQ ID NO: 218.

4. The anti-SIRP α antibody or antigen-binding fragment thereof according to claim 1, wherein the antibody is a human antibody.

5. The anti-SIRP α antibody or antigen-binding fragment thereof according to any one of claims 1 to 4 for use as a medicament.

6. A pharmaceutical composition comprising an antibody or antigen-binding fragment according to any one of claims 1 to 4 and a pharmaceutically acceptable carrier.

7. An anti-SIRP α antibody or antigen-binding fragment according to any one of claims 1 to 4, or a pharmaceutical composition of claim 6, for use in treating a disease, wherein the disease is selected from cancer, inflammatory disease, autoimmune disease, respiratory disease, infectious disease or fibrosis.

8. Use of the anti-SIRP α antibody or antigen-binding fragment according to any one of claims 1 to 4, or a pharmaceutical composition of claim 6, in manufacture of a medicament for treating a disease, wherein the disease is selected from cancer, inflammatory disease, autoimmune disease, respiratory disease, infectious disease or fibrosis.

9. The anti-SIRP α antibody or antigen-binding fragment according to claim 7, or the use of the anti-SIRP α antibody or antigen-binding fragment according to claim 8, wherein the disease is cancer.

10. An isolated polynucleotide encoding a heavy chain variable region and/or a light chain variable region according to claim 2.

11. An isolated polynucleotide encoding a heavy chain and/or a light chain according to claim 3.

12. A vector comprising a polynucleotide according to any one of claims 10 or 11, preferably an expression vector, more preferred a vector comprising the polynucleotide according to the invention in functional association with an expression control sequence.

13. A host cell comprising a polynucleotide according to any one of claims 10 or 11.

14. A method for the production of an anti-SIRP α antibody or antigen-binding fragment according to any one of claims 1 to 4, comprising the steps:

(a) cultivating the host cell under conditions allowing the expression of the anti-SIRP α antibody or antigen-binding fragment; and

(b) recovering the anti-SIRP α antibody or antigen-binding fragment.

15. A method of manufacturing an antibody comprising the steps of:

a) culturing a host cell comprising an expression vector comprising an isolated polynucleotide encoding a heavy chain variable region according to claim 2 and comprising a polynucleotide encoding a light chain variable region according to claim 2 under conditions that allow formation of an antibody; and

b) recovering said antibody.

16. A method of manufacturing an antibody comprising the steps of:

a) culturing a host cell comprising an expression vector comprising an isolated polynucleotide encoding a heavy chain according to claim 3 and a polynucleotide encoding a light chain according to claim 3 under conditions that allow formation of an antibody; and

b) recovering said antibody.

17. The method of claim 15 or 16, further comprising the step of purifying said antibody.

18. The method of claim 15 or 16, further comprising the step of formulating said antibody into a pharmaceutical composition.

19. An anti-SIRP α antibody or antigen-binding fragment thereof, wherein the anti-SIRP α antibody or antigen-binding fragment thereof comprises:

a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 113; and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 125.

20. An anti-SIRP α antibody, wherein the anti-SIRP α antibody comprises:

a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 113; and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 125.

21. An anti-SIRP α antibody or antigen-binding fragment thereof, wherein the anti-SIRP α antibody or antigen-binding fragment thereof comprises:

a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 111; and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 126.

22. An anti-SIRP α antibody, wherein the anti-SIRP α antibody comprises:
a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 111;
and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 126.
23. An anti-SIRP α antibody, wherein the anti-SIRP α antibody comprises:
a heavy chain comprising the amino acid sequence of SEQ ID NO: 141; and a light chain
comprising the amino acid sequence of SEQ ID NO: 184.
24. An anti-SIRP α antibody, wherein the anti-SIRP α antibody comprises:
a heavy chain comprising the amino acid sequence of SEQ ID NO: 147; and a light chain
comprising the amino acid sequence of SEQ ID NO: 190.
25. An anti-SIRP α antibody, wherein the anti-SIRP α antibody comprises:
a heavy chain comprising the amino acid sequence of SEQ ID NO: 217; and a light chain
comprising the amino acid sequence of SEQ ID NO: 218.
26. A pharmaceutical composition comprising the anti-SIRP α antibody according to any
one of claims 20 or 22-25 and a pharmaceutically acceptable carrier.
27. An isolated polynucleotide composition, the isolated polynucleotide composition
comprising:
a) a first isolated polynucleotide encoding the heavy chain variable region according to
claim 20; and/or
b) a second isolated polynucleotide encoding the light chain variable region according to
claim 20.
28. An isolated polynucleotide composition, the isolated polynucleotide composition
comprising:
a) a first isolated polynucleotide encoding the heavy chain variable region according to
claim 22; and/or
b) a second isolated polynucleotide encoding the light chain variable region according to
claim 22.

29. An isolated polynucleotide composition, the isolated polynucleotide composition comprising:

- a) a first isolated polynucleotide encoding the heavy chain according to claim 23; and/or
- b) a second isolated polynucleotide encoding the light chain according to claim 23.

30. An isolated polynucleotide composition, the isolated polynucleotide composition comprising:

- a) a first isolated polynucleotide encoding the heavy chain according to claim 24; and/or
- b) a second isolated polynucleotide encoding the light chain according to claim 24.

31. An isolated polynucleotide composition, the isolated polynucleotide composition comprising:

- a) a first isolated polynucleotide encoding the heavy chain according to claim 25; and/or
- b) a second isolated polynucleotide encoding the light chain according to claim 25.

32. An expression vector composition, the composition comprising;

- a) a first expression vector comprising the first isolated polynucleotide of claim 27; and/or
- b) a second expression vector comprising the second isolated polynucleotide of claim 27.

33. An expression vector composition, the composition comprising;

- a) a first expression vector comprising the first isolated polynucleotide of claim 28; and/or
- b) a second expression vector comprising the second isolated polynucleotide of claim 28.

34. An expression vector composition, the composition comprising;

- a) a first expression vector comprising the first isolated polynucleotide of claim 29; and/or
- b) a second expression vector comprising the second isolated polynucleotide of claim 29.

35. An expression vector composition, the composition comprising;

- a) a first expression vector comprising the first isolated polynucleotide of claim 30; and/or
- b) a second expression vector comprising the second isolated polynucleotide of claim 30.

36. An expression vector composition, the composition comprising;

- a) a first expression vector comprising the first isolated polynucleotide of claim 31; and/or
- b) a second expression vector comprising the second isolated polynucleotide of claim 31.

37. A host cell comprising the isolated polynucleotide composition according to any one of claims 27-31.

38. A method for the production of an anti-SIRP α antibody, comprising the steps:

a) cultivating the host cell of claim 37 under conditions for expression of the anti-SIRP α antibody; and

b) recovering the anti-SIRP α antibody.