phagocytosis of the cancer cell and/or the infected cell. Thus, anti-CD47 agents can be used to treat and/or protect against a wide variety of conditions/disorders. In fact, anti-CD47 and anti-SIRPα blocking antibodies significantly increase phagocytosis of cancer cells *in vitro* and *in vivo*. They have been shown to be effective at treating mice engrafted with a wide range of human cancers, from leukemias to solid tumors. However, in some cases an initial high dose of an anti-CD47 agent can cause a dose-dependent loss of red blood cells (RBCs) in mice and non-human primate (NHP) models by binding to CD47 on the surface of the RBCs. The severity of this anemia can preclude the use of higher doses that are required to achieve sustained serum concentrations associated with therapeutic efficacy.

[0004] The present disclosure provides anti-SIRPα antibodies that block the interaction of CD47 on one cell (e.g., a cancer cell, an infected cell, etc.) with SIRPα on another cell (e.g., a phagocytic cell), and facilitate the phagocytosis of the CD47-expressing cell. Also disclosed are antibodies that are bispecific for SIRPα and a second antigen (e.g., a tumor antigen). These bi-specific macrophage enhancing (BiME) antibodies exhibit enhanced properties.

SUMMARY

[0005] Compositions and methods are provided relating to anti-SIRPα antibodies.

[0005a] In one aspect of the present disclosure, there is provided an antibody that specifically binds to human SIRPα but does not stimulate SIRPα signaling in a cell expressing the SIRPα, wherein the antibody comprises a heavy chain variable region comprising each of the CDR sequences set forth in SEQ ID NOs: 2-4, and a light chain variable region comprising each of the CDR sequences set forth in SEQ ID NOs: 6-8.

[0005b] In another aspect of the present disclosure, there is provided a polynucleotide encoding an antibody disclosed herein.

[0005c] In a further aspect of the present disclosure, there is provided a cell that produces an antibody disclosed herein.

[0005d] In another aspect of the present disclosure, there is provided a pharmaceutical composition comprising an antibody disclosed herein.

[0005e] In a further aspect of the present disclosure, there is provided a use of a composition comprising an antibody disclosed herein in the manufacture of a medicament treating cancer in combination with a second antibody that specifically binds to a marker of a CD47-expressing cancer cell.

[0005f] In another aspect of the present disclosure, there is provided a method of detecting the presence of SIRPα in a biological sample or tissue, the method comprising: contacting the biological sample or tissue with the antibody disclosed herein, and determining the presence or absence of antibody bound to the biological sample or tissue.

THAT WHICH IS CLAIMED IS:

1. An antibody that specifically binds to human SIRPα but does not stimulate SIRPα signaling in a cell expressing the SIRPα, wherein the antibody comprises a heavy chain variable region comprising each of the CDR sequences set forth in SEQ ID NOs: 2-4, and a light chain variable region comprising each of the CDR sequences set forth in SEQ ID NOs: 6-8.

2. The antibody of claim 1, comprising an amino acid sequence as set forth in any one of SEQ ID NOs: 9-10.

3. The antibody of claim 1, wherein the heavy chain comprises an amino acid sequence as set forth in any one of SEQ ID NOs: 1, 11, 13, 15, and 17.

4. The antibody of claim 1, wherein the light chain comprises an amino acid sequence as set forth in any one of SEQ ID NOs: 5, 12, 14, 16, and 18.

5. The antibody of claim 1, wherein:

(a) the heavy chain comprises an amino acid sequence as set forth in any one of SEQ ID NOs: 1, 11, 13, 15, and 17; and

(b) the light chain comprises an amino acid sequence as set forth in any one of SEQ ID NOs: 5, 12, 14, 16, and 18.

6. The antibody of claim 1, wherein:

(a) the heavy chain comprises the amino acid sequence of SEQ ID NO: 1, and the light chain comprises the amino acid sequence of SEQ ID NO: 5;

(b) the heavy chain comprises the amino acid sequence of SEQ ID NO: 11, and the light chain comprises the amino acid sequence of SEQ ID NO: 12;

(c) the heavy chain comprises the amino acid sequence of SEQ ID NO: 13, and the light chain comprises the amino acid sequence of SEQ ID NO: 14;

(d) the heavy chain comprises the amino acid sequence of SEQ ID NO: 15, and the light chain comprises the amino acid sequence of SEQ ID NO: 16; or

(e) the heavy chain comprises the amino acid sequence of SEQ ID NO: 17, and the light chain comprises the amino acid sequence of SEQ ID NO: 18.

7. The antibody of any of claims 1-6, wherein the antibody does not activate SIRPα upon binding.

8. The antibody of any of claims 1-7, wherein the antibody is a chimeric or humanized antibody.

9. The antibody of claim 8, wherein the antibody is a humanized monoclonal antibody.

10. The antibody of any of claims 1-9, wherein the antibody is a multispecific antibody that specifically binds to SIRPα and at least a second antigen.

11. The antibody of claim 10, wherein the second antigen is a marker of a CD47-expressing cell.

12. The antibody of claim 11, wherein the second antigen is selected from: CD19, CD20, CD22, CD24, CD25, CD30, CD33, CD38, CD44, CD52, CD56, CD70, CD96, CD97, CD99, CD123, CD279 (PD-1), EGFR, HER2, CD117, C-Met, PTHR2, and HAVCR2 (TIM3).

13. A polynucleotide encoding an antibody set forth in any of claims 1-12.

14. A cell that produces an antibody set forth in any of claims 1-12.

15. A pharmaceutical composition comprising an antibody set forth in any of claims 1-12.

16. The pharmaceutical composition of claim 15, further comprising a second antibody that specifically binds to a marker of a CD47-expressing cancer cell.

17. The pharmaceutical composition of claim 16, wherein the second antibody specifically binds to one or more markers selected from the group consisting of: CD19, CD20, CD22, CD24, CD25, CD30, CD33, CD38, CD44, CD52, CD56, CD70, CD96, CD97, CD99, CD123, CD279 (PD-1), EGFR, HER2, CD117, C-Met, PTHR2, and HAVCR2 (TIM3).

18. The pharmaceutical composition of claim 15, comprising a pharmaceutically acceptable excipient.

19. Use of a composition comprising an antibody set forth in any of claims 1-12 in the manufacture of a medicament for treating cancer in combination with a second antibody that specifically binds to a marker of a CD47-expressing cancer cell.

20. The use according to claim 19, wherein the individual is human.

21. The use according to claim 19, wherein the cancer cell marker is selected from: CD19, CD20, CD22, CD24, CD25, CD30, CD33, CD38, CD44, CD52, CD56, CD70, CD96, CD97, CD99, CD123, CD279 (PD-1), EGFR, HER2, CD117, C-Met, PTHR2, and HAVCR2 (TIM3).

22. A method of detecting the presence of SIRPα in a biological sample or tissue, the method comprising: contacting the biological sample or tissue with the antibody set forth in any of claims 1-12, and determining the presence or absence of antibody bound to the biological sample or tissue.

23. Use of an anti-SIRPα antibody set forth in any of claims 1-12 in the manufacture of a detecting agent for a method of detecting SIRPα expressing cells in an individual, wherein the antibody is detectably labeled; and wherein said agent is to be administered to the individual; and thereafter detecting the presence or absence of the label in the individual.

24. The use according to claim 23, wherein the detectable label is a radioisotope label.

25. The use according to claim 23, wherein the detecting step comprises detecting the presence or absence of the label with positron emission tomography (PET).

26. The use according to any of claims 23 to 25, wherein the individual has or is suspected of having cancer, inflammation, an inflammatory disease, and/or a chronic infection.