

## WHAT IS CLAIMED IS:

1. A SIRP $\alpha$ -41BBL fusion protein comprising a single amino acid linker between said SIRP $\alpha$  and said 41BBL.
2. A SIRP $\alpha$ -41BBL fusion protein in a form of at least a homo-trimer.
3. The SIRP $\alpha$ -41BBL fusion protein of claim 2, wherein said at least homo-trimer is at least 140 kD in molecular weight as determined by SDS-PAGE.
4. The SIRP $\alpha$ -41BBL fusion protein of any one of claims 2-3, wherein the SIRP $\alpha$ -41BBL fusion protein comprises a linker between said SIRP $\alpha$  and said 41BBL.
5. The SIRP $\alpha$ -41BBL fusion protein of claim 4, wherein the linker has a length of one to six amino acids.
6. The SIRP $\alpha$ -41BBL fusion protein of claim 4, wherein the linker is a single amino acid linker.
7. The SIRP $\alpha$ -41BBL fusion protein of claim 4, wherein the linker is not an Fc domain of an antibody or a fragment thereof.
8. The SIRP $\alpha$ -41BBL fusion protein of any one of claims 1, 4 and 6, wherein the linker is glycine.
9. The SIRP $\alpha$ -41BBL fusion protein of any one of claims 1-8, being soluble.
10. The SIRP $\alpha$ -41BBL fusion protein of any one of claims 1-9, wherein said SIRP $\alpha$  comprises an extracellular domain of said SIRP $\alpha$  or a functional fragment thereof.
11. The SIRP $\alpha$ -41BBL fusion protein of any one of claims 1-10, wherein said 41BBL comprises an extracellular domain of said 41BBL or a functional fragment thereof.

12. The SIRP $\alpha$ -41BBL fusion protein of any one of claims 1-11, wherein said fusion protein is capable of at least one of:

- (i) binding CD47 and 41BB;
- (ii) activating said 41BB signaling pathway in a cell expressing said 41BB;
- (iii) co-stimulating immune cells expressing said 41BB; and/or
- (iv) enhancing phagocytosis of pathologic cells expressing said CD47 by phagocytes compared to same in the absence of said SIRP $\alpha$ -41BBL fusion protein.

13. The SIRP $\alpha$ -41BBL fusion protein of any one of claims 1-12, wherein said SIRP $\alpha$ -41BBL fusion protein amino acid sequence comprises SEQ ID NO: 1.

14. The SIRP $\alpha$ -41BBL fusion protein of any one of claims 1-12, wherein said SIRP $\alpha$ -41BBL fusion protein amino acid sequence consists of SEQ ID NO: 1.

15. A polynucleotide encoding the SIRP $\alpha$ -41BBL fusion protein of any one of claims 1-14.

16. A nucleic acid construct comprising the polynucleotide of claim 15, and a regulatory element for directing expression of said polynucleotide in a host cell.

17. The polynucleotide of claim 15 or the nucleic acid construct of claim 16, wherein said polynucleotide comprises SEQ ID NO: 8.

18. A host cell comprising the SIRP $\alpha$ -41BBL fusion protein of any one of claims 1-14 or the polynucleotide or the nucleic acid construct of any one of claims 15-17.

19. A method of producing a SIRP $\alpha$ -41BBL fusion protein, the method comprising expressing in a host cell the polynucleotide or the nucleic acid construct of any one of claims 15-17.

20. The method of claim 19, comprising isolating the fusion protein.

21. The host cell of claim 18 or the method of any one of claims 19-20, wherein said cell is selected from the group consisting of CHO, PERC.6 and 293.

22. A method of treating cancer comprising administering the SIRP $\alpha$ -41BBL fusion protein of any one of claims 1-14 to a subject in need thereof.

23. A method of treating a disease that can benefit from activating immune cells comprising administering to a subject in need thereof the SIRP $\alpha$ -41BBL fusion protein of any one of claims 1-14, the polynucleotide or the nucleic acid construct of any one of claims 15-17 or the host cell of any one of claims 18 and 21.

24. An article of manufacture identified for the treatment of a disease that can benefit from activating immune cells comprising a packaging material packaging a therapeutic agent for treating said disease; and a SIRP $\alpha$ -41BBL fusion protein, a polynucleotide encoding same, a nucleic acid construct encoding same or a host cell expressing same.

25. The method of claim 23 or the article of manufacture of claim 24, wherein said disease comprises a hyper-proliferative disease.

26. The method or the article of manufacture of claim 25, wherein said hyper-proliferative disease comprises sclerosis or fibrosis, Idiopathic pulmonary fibrosis, psoriasis, systemic sclerosis/scleroderma, primary biliary cholangitis, primary sclerosing cholangitis, liver fibrosis, prevention of radiation-induced pulmonary fibrosis, myelofibrosis or retroperitoneal fibrosis.

27. The method or the article of manufacture of claim 25, wherein said hyper-proliferative disease comprises cancer.

28. A method of treating cancer comprising administering to a subject in need thereof an anti-cancer agent; and a SIRP $\alpha$ -41BBL fusion protein, a polynucleotide encoding same, a nucleic acid construct encoding same or a host cell expressing same.

29. The method or the article of manufacture of any one of claims 22 and 27-28, wherein said cancer is selected from the group consisting of lymphoma, leukemia, colon cancer, pancreatic cancer, ovarian cancer, lung cancer and squamous cell carcinoma.

30. The method or the article of manufacture of any one of claims 22 and 27-29, wherein cells of said cancer express CD47.

31. The method of claim 23 or the article of manufacture of claim 24, wherein said disease comprises a disease associated with immune suppression or medication induced immunosuppression.

32. The method or the article of manufacture of claim 31, wherein said disease comprises HIV, Measles, influenza, LCCM, RSV, Human Rhinoviruses, EBV, CMV or Parvo viruses.

33. The method of claim 23 or the article of manufacture of claim 24, wherein said disease comprises an infection.

34. The method or the article of manufacture of any one of claims 23-29 and 31-33, wherein diseased cells of said subject express CD47.

35. A method of activating T cells, the method comprising in-vitro activating T cells in the presence of a SIRP $\alpha$ -41BBL fusion protein and cells expressing CD47.

36. A method of activating phagocytes, the method comprising in-vitro activating phagocytes in the presence of a SIRP $\alpha$ -41BBL fusion protein and cells expressing CD47.

37. A method of activating immune cells, the method comprising in-vitro activating immune cells in the presence of a SIRP $\alpha$ -41BBL fusion protein, a polynucleotide encoding same, a nucleic acid construct encoding same or a host cell expressing same.

38. The method of any one of claims 36-37, wherein said activating is in the presence of cells expressing CD47 or exogenous CD47.

39. The method of any one of claims 35-36 and 38, wherein said cells expressing said CD47 comprise pathologic cells.

40. The SIRP $\alpha$ -41BBL fusion protein of claim 12 or the method of claim 39, wherein said pathologic cells comprise cancer cells.

41. The method of claim 40, wherein said cancer is selected from the group consisting of lymphoma, carcinoma and leukemia.

42. The method of any one of claims 36-41, wherein said activating is in the presence of an anti-cancer agent.

43. The article of manufacture of any one of claims 24 and 27 or the method of any one of claims 28 and 42, wherein said anti-cancer agent comprises an antibody.

44. The article of manufacture or the method of claim 43, wherein said antibody is selected from the group consisting rituximab, cetuximab, trastuzumab, edrecolomab, almetuzumab, gemtuzumab, ibritumomab, panitumumab, Belimumab, Bevacizumab, Bivatuzumab mertansine, Blinatumomab, Blontuvetmab, Brentuximab vedotin, Catumaxomab, Cixutumumab, Daclizumab, Adalimumab, Bezlotoxumab, Certolizumab pegol, Citatuzumab bogatox, Daratumumab, Dinutuximab, Elotuzumab, Ertumaxomab, Etaracizumab, Gemtuzumab ozogamicin, Girentuximab, Necitumumab, Obinutuzumab, Ofatumumab, Pertuzumab, Ramucirumab, Siltuximab, Tositumomab, Trastuzumab and ipilimumab.

45. The article of manufacture or the method of claim 43, wherein said antibody is selected from the group consisting of rituximab, cetuximab and almetuzumab.

46. The method of any one of claims 37-45, comprising adoptively transferring said immune cells following said activating to a subject in need thereof.

47. The method of claim 46, wherein said subject is afflicted with a disease associated with said cells expressing said CD47.

48. The method or the article of manufacture of any one of claims 23-47, wherein said SIRP $\alpha$ -41BBL fusion protein comprises the SIRP $\alpha$ -41BBL fusion protein of any one of claims 1-14, the polynucleotide or the nucleic acid construct comprises the polynucleotide or the nucleic acid construct of any one of claims 15-17, and the host cell comprises the host cell of any one of claims 18 and 21.

49. The method of any one of claims 37-48, wherein said immune cells comprise T cells.

50. The method of any one of claim 37-48, wherein said immune cells comprise phagocytes.