successfully transfect or transduce a myeloid cell, or otherwise induce a genetic modification in a myeloid cell, with the purpose of augmenting a functional aspect of a myeloid cell, additionally, without compromising the cell's differentiation capability, maturation potential, and/or its plasticity.

[0011a] In one aspect, provided herein is a pharmaceutical composition comprising: (A) a population of myeloid cells comprising CD14+ cells comprising a recombinant polynucleic acid encoding a chimeric fusion protein (CFP), wherein the CFP comprises : (i) an extracellular domain comprising an antigen binding domain that binds to a CD5 antigen, (ii) a transmembrane domain operatively linked to the extracellular domain; and (iii) an intracellular domain with at least one intracellular signaling domain; and (B) a pharmaceutically acceptable excipient.

[0011b] In one aspect, provided herein is a use of the pharmaceutical composition as described herein in the manufacture of a medicament for treating a cancer in a human subject in need thereof, wherein the cancer is a lymphoma.

[0011c] In one aspect, provided herein is a method of making a population of cells comprising CD14+ cells comprising a recombinant polynucleic acid encoding a chimeric fusion protein (CFP), the method comprising: (a) selecting CD14+ cells from a biological sample from a human subject, wherein the biological sample from a human subject is a peripheral blood sample or an apheresis sample, thereby obtaining a population of CD14+ cells isolated from the biological sample from a human subject, and (b) contacting a recombinant polynucleic acid comprising a sequence encoding a CFP to the population of CD14+ cells isolated from the biological sample of (a), thereby introducing the recombinant polynucleic acid into the population of CD14+ cells isolated from the biological sample of (a) and obtaining the population of cells with CD14+ cells comprising a recombinant polynucleic acid encoding a CFP, wherein the CFP comprises (i) an extracellular domain, (ii) a transmembrane domain operatively linked to the extracellular domain; and (iii) an intracellular domain with at least one intracellular signaling domain; wherein the CFP is capable of binding CD5.

[0011d] In one aspect, provided herein is the pharmaceutical composition as described herein for use in therapy.

INCORPORATION BY REFERENCE

[0012] All publications, patents, and patent applications mentioned in this specification are herein incorporated by reference to the same extent as if each individual publication, patent, or patent application was specifically and individually indicated to be incorporated by reference.

BRIEF DESCRIPTION OF THE DRAWINGS

[0013] The novel features of the invention are set forth with particularity in the appended claims. A better understanding of the features and advantages of the present invention will be obtained by

reference to the following detailed description that sets forth illustrative embodiments, in which the principles of the invention are utilized, and the accompanying drawings.

[0014] **FIG. 1A** depicts a diagram showing some of the potentially engineerable functions of myeloid cells.

[0015] **FIG. 1B** depicts a diagram, indicating the presence of various cell types in different types of cancer. Macrophages are the most abundant cells in the depicted cancer types.

[0016] **FIG. 2A** depicts a schematic showing an exemplary chimeric receptor fusion protein (CFP) containing an extracellular binding domain, a transmembrane domain, a first intracellular signaling domain and a second intracellular signaling domain. The signaling domains can be derived from other receptors and be designed to elicit any number of cell functions.

[0017] **FIG. 2B** depicts a schematic showing an exemplary CFP containing an extracellular binding domain, a transmembrane domain, and an intracellular signaling domain (left), and a CFP containing an extracellular binding domain, a transmembrane domain, a first intracellular signaling domain, a second intracellular signaling domain, a third intracellular signaling domain, and one or more additional intracellular signaling domains. The signaling domains can be derived from other receptors and be designed to elicit any number of cell functions.

[0018] **FIG. 2C** depicts a schematic showing an exemplary CFP dimer containing an anti-CD5 extracellular binding domain, a transmembrane domain, and an intracellular signaling domain containing an intracellular domain derived from FcRγ fused to a PI3K recruitment domain.

[0019] **FIG. 2D** depicts a schematic showing an exemplary CFP dimer containing an extracellular antigen binding domain, a transmembrane domain, and an intracellular signaling domain containing a phagocytosis domain a PI3K recruitment domain and a pro-inflammation domain.

CLAIMS

What is claimed is:

1. A pharmaceutical composition comprising:

(A) a population of myeloid cells comprising CD14+ cells comprising a recombinant polynucleic acid encoding a chimeric fusion protein (CFP), wherein the CFP comprises :

(i) an extracellular domain comprising an antigen binding domain that binds to a CD5 antigen, (ii) a transmembrane domain operatively linked to the extracellular domain; and

(iii) an intracellular domain with at least one intracellular signaling domain; and

(B) a pharmaceutically acceptable excipient.

2. The pharmaceutical composition of claim 1, wherein the CD5 antigen binding domain is an antibody domain or a fragment thereof, a single chain variable fragment (ScFv), an Fab, a single domain antibody, a nanobody, a V_H domain, a V_L domain, a V_{HH} domain, a VNAR domain, a bispecific antibody, a diabody or a combination thereof, wherein the antigen binding domain of the CFP binds to CD5 antigen with an affinity of 250 nM or less.

3. The pharmaceutical composition of claim 1, wherein the intracellular domain further comprises one or more additional intracellular signaling domains.

4. The pharmaceutical composition of claim 3, wherein the one or more additional intracellular signaling domains comprises an intracellular signaling domain from a receptor other than Megf10, MerTk, Fc α R, and Bai1.

5. The pharmaceutical composition of claim 1, wherein the intracellular domain of the CFP comprises an intracellular signaling domain of an FcR gamma.

6. The pharmaceutical composition of claim 5, wherein the intracellular domain comprises an intracellular signaling domain with at least 90% sequence identity to SEQ ID NO: 3.

7. The pharmaceutical composition of claim 3, wherein the one or more additional intracellular signaling domains comprises a proinflammatory signaling domain, wherein the proinflammatory signaling domain is a PI3K recruitment domain.

8. The pharmaceutical composition of claim 7, wherein the PI3K recruitment domain comprises a sequence with at least 90% sequence identity to SEQ ID NO: 4.

9. The pharmaceutical composition of claim 3, wherein the one or more additional intracellular signaling domains comprise an intracellular signaling domain from an intracellular signaling domain of CD40.

10. The pharmaceutical composition of claim 9, wherein the intracellular signaling domain from an intracellular signaling domain of CD40 comprises a sequence with at least 90% sequence identity to SEQ ID NO: 5

11. The pharmaceutical composition of claim 1, wherein the transmembrane domain comprises a CD8 transmembrane domain, comprising an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 6 or SEQ ID NO: 7 or SEQ ID NO: 29; or

wherein the transmembrane domain comprises a transmembrane domain from CD2, CD28 or CD68, comprising an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 34, SEQ ID NO: 18 or SEQ ID NO: 19.

12. The pharmaceutical composition of claim 1 or 11, wherein the extracellular domain further comprises a hinge domain from CD8, wherein the hinge domain is operatively linked to the transmembrane domain and the CD5 binding domain.

13. The pharmaceutical composition of claim 1, wherein the recombinant polynucleic acid is an mRNA.

14. The pharmaceutical composition of claim 1, wherein the CFP comprises a sequence having at least 90% sequence identity to SEQ ID NO: 14.

15. The pharmaceutical composition of claim 1, wherein the pharmaceutical composition comprises at least 6x10^6 myeloid cells.

16. Use of the pharmaceutical composition of any one of claims 1-15 in the manufacture of a medicament for treating a cancer in a human subject in need thereof, wherein the cancer is a lymphoma.

17. The use of claim 16, wherein the cancer is T cell lymphoma.

18. A method of making a population of cells comprising CD14+ cells comprising a recombinant polynucleic acid encoding a chimeric fusion protein (CFP), the method comprising:

(a) selecting CD14+ cells from a biological sample from a human subject, wherein the biological sample from a human subject is a peripheral blood sample or an apheresis sample, thereby obtaining a population of CD14+ cells isolated from the biological sample from a human subject, and

(b) contacting a recombinant polynucleic acid comprising a sequence encoding a CFP to the population of CD14+ cells isolated from the biological sample of (a), thereby introducing the recombinant polynucleic acid into the population of CD14+ cells isolated from the biological sample of (a) and obtaining the population of cells with CD14+ cells comprising

a recombinant polynucleic acid encoding a CFP, wherein the CFP comprises (i) an extracellular domain, (ii) a transmembrane domain operatively linked to the extracellular domain; and (iii) an intracellular domain with at least one intracellular signaling domain; wherein the CFP is capable of binding CD5.

19. The method of claim 18, wherein selecting CD14+ cells comprises negative selection.

20. The method of claim 19, wherein negative selection comprises contacting the biological sample with an antibody targeting a cell surface molecule selected from the group consisting of CD16, CD3, CD8, CD11c, CD40, CD206 and any combination thereof; and

wherein selecting CD14+ cells comprises selecting CD14+ cells without contacting the biological sample with an antibody targeting CD14.

21. The method of claim 18, wherein selecting CD14+ cells comprises selecting CD14+ cells by density centrifugation.

22. The method of claim 18, wherein selecting CD14+ cells comprises selecting CD14+ cells by elutriation.

23. The method of claim 18, wherein the population of cells with CD14+ cells comprising a recombinant polynucleic acid encoding a CFP is a population of cells with at least $1x10^6$ CD14+/CD16- cells containing a recombinant polynucleic acid encoding a CFP.

24. The method of claim 18, wherein selecting CD14+ cells comprises fluorescence activated cell sorting (FACS) or magnetic activated cell sorting (MACS).

25. The method of claim 18, wherein the recombinant polynucleic acid is RNA.

26. The method of claim 25, wherein the RNA is mRNA.

27. The method of claim 18, wherein contacting a recombinant polynucleic acid comprising a sequence encoding a CFP into the population of CD14+ cells isolated from the biological sample of (a) comprises electroporating the population of CD14+ cells isolated from the biological sample of (a) in the presence of the recombinant polynucleic acid.

28. The method of claim 18, further comprising expressing the CFP in the CD14+ cells of (b) containing a recombinant polynucleic acid encoding a CFP.

29. The method of claim 18, wherein the population of cells with CD14+ cells containing a recombinant polynucleic acid encoding a CFP comprises at least $1x10^6$ cells.

30. The method of claim 18, wherein the intracellular domain comprises at least two intracellular signaling domains.

31. The method of claim 18, wherein the intracellular signaling domain comprises an intracellular signaling domain derived from FcγR or FcεR.
32. The method of claim 31, wherein the intracellular domain comprises a PI3K recruitment domain.
33. The method of claim 18, wherein the transmembrane domain comprise a CD8 transmembrane domain, a CD28 transmembrane domain, a CD2 transmembrane domain, or a CD68 transmembrane domain.
34. The method of claim 18, wherein at least 50% of the population of CD14+ cells isolated from the biological sample of (a) express the CFP 24 hours after (b).
35. The pharmaceutical composition of any one of claims 1-15 for use in therapy.