blood cells from a defined, well-characterized, source. Additionally, RBCs produced by the novel methods of the present disclosure may also contain and/or express one or more recombinant protein of interest that can be used to treat a subject in need thereof.

[0013] Accordingly, certain examples of the present disclosure relate to a method for producing a population of mature red blood cells from hematopoietic stem cells, by: culturing the hematopoietic stem cells in the presence of EPO and one or more first recombinant protein, or biologically active fragment thereof, that promotes cell survival and/or proliferation; under conditions that induce differentiation of the hematopoietic stem cells to mature red bloods cells, thereby producing a population of mature red blood cells. In one aspect, the present disclosure refers to a method for producing a population of mature red blood cells from hematopoietic stem cells, comprising: culturing hematopoietic stem cells in a culture media comprising erythropoietin (EPO) and one or more first recombinant protein that promotes cell survival and proliferation under conditions that induce differentiation of the hematopoietic stem cells to mature red bloods cells, thereby producing a population of mature red blood cells, wherein the first recombinant protein comprises a MYC polypeptide or a biologically active fragment thereof. In some examples, the hematopoietic stem cells are conditionally immortalized hematopoietic stem cells. In some examples that may be combined with any of the preceding examples, the hematopoietic stem cells are protein transduced hematopoietic stem cells, and the one or more first recombinant protein, or biologically active fragment thereof, is an exogenous protein. In some examples that may be combined with any of the preceding examples, the hematopoietic stem cells are transgenic hematopoietic stem cells. In some examples that may be combined with any of the preceding examples, the one or more first recombinant protein, or biologically active fragment thereof, is one or more polypeptide selected from a MYC polypeptide, an ICN-1 polypeptide, homologues thereof, and biologically active fragments thereof. In some examples that may be combined with any of the preceding examples, the MYC polypeptide is one or more MYC polypeptide selected from n-Myc, c-Myc, l-Myc, v-Myc, and s-Myc. In some examples that may be combined with any of the preceding examples, one or more of the one or more first recombinant protein, or biologically active fragment thereof, contains a protein transduction domain. In some examples that may be combined with any of the preceding examples, the protein transduction domain is one or more protein transduction domain selected from TAT, VPR, and EPTD. In some examples that may be combined with any of the preceding examples, the one or more first recombinant protein, or biologically active fragment thereof, is TAT-MYC. In some examples that may be combined with any of the preceding examples, the one or more first recombinant protein, or biologically active fragment thereof, is provided as a bolus. In some examples that may be combined with any of the preceding examples, the one or more first recombinant protein is provided as a bolus about every 24 hours, about every 48 hours, or about every 72 hours. In some examples that may be combined with any of the preceding examples, the method

What is claimed is:

1. A method for producing a population of mature red blood cells from hematopoietic stem cells, comprising:

culturing hematopoietic stem cells in a culture media comprising erythropoietin (EPO) and one or more first recombinant protein that promotes cell survival and proliferation under conditions that induce differentiation of the hematopoietic stem cells to mature red bloods cells, thereby producing a population of mature red blood cells,

wherein the first recombinant protein comprises a MYC polypeptide or a biologically active fragment thereof.

2. The method of claim 1, wherein the MYC polypeptide or biologically active fragment thereof, is TAT-MYC.

3. The method of any one of claims 1 or 2, further comprising culturing the population of mature red blood cells in the presence of one or more second recombinant protein, or biologically active fragment thereof, that inhibits apoptosis.

4. The method of claim 3, wherein the one or more second recombinant protein, or biol\ogically active fragment thereof, comprises one or more Bcl2 homology domains selected from the group consisting of BH1, BH2, BH3, and BH4.

5. The method of any one of claims 1 to 4, wherein the hematopoietic stem cells further comprise one or more recombinant proteins of interest, or biologically active fragment thereof.

6. The method of any one of claims 1 to 5, wherein the hematopoietic stem cells comprise one or more transgenes that encode one or more recombinant proteins of interest, or biologically active fragment thereof.

7. The method of either one of claims 5 or 6, wherein the expression or function of one or more recombinant proteins of interest, or biologically active fragment thereof is controllable or inducible.

8. The method of any one of claims 1 to 7, wherein the population of mature red blood cells is produced in 7 to 14 days.

9. The method of any one of claims 1 to 8, wherein the population of mature red blood cells exhibits one or more characteristics selected from the group consisting of a population of mature red blood cells, wherein 40% to 100% of the cells are anucleated; a population of mature red blood cells, wherein 40% to 100% of the cells express GPA; a population of mature red blood cells, wherein 40% to 100% of the cells express adult hemoglobin; a population of mature red blood cells, wherein 40% to 100% of the cells exhibit decreased levels of CD71 expression; a population of mature red blood cells, wherein 40% to 100% of the cells exhibit decreased levels of fetal hemoglobin expression.