CLAIMS

1. A genetically modified red blood precursor cell characterized by a genomic modification within exon 2 or exon 4 of BCL11A or within BCL11A-XL made following cleavage within the BCL11A gene by a zinc finger nuclease (ZFN), a TALE nuclease (TALEN) or a CRISPR/Cas system that binds to a target site within any one of SEQ ID NOs: 56, 63, 66, 71, 160, 170, 179, 183, 189, 193, 197, 200, 203, 207, 211 and 213 such that the BCL11A gene is inactivated and gamma globin expression is increased.

2. The genetically modified red blood precursor cell of claim 1, wherein the cell is a hematopoietic stem cell.

3. The genetically modified red blood precursor cell of claim 1, wherein:

(a) the BCL11A gene is cleaved by a zinc finger nuclease;

(b) the nuclease is introduced into the cell as a polynucleotide; or

(c) the genomic modification comprises integration of a donor polynucleotide encoding a transgene.

4. The genetically modified red blood precursor cell of claim 1, wherein the zinc finger nuclease comprises a zinc finger protein comprising 5 or 6 zinc finger domains comprising a recognition helix and further wherein the zinc finger protein comprises the recognition helix regions in the order shown in a single row of Table 1A of the proteins designated SBS#39172, SBS#43490, SBS#44642, SBS#45148, SBS#45147, SBS#39145, SBS#44490, SBS#44489, SBS#45081, SBS#44493, SBS#29527, SBS#29528, SBS#29525, SBS#29526, SBS#34678, SBS#34642, SBS#44889, SBS#44888, SBS#44905, SBS#44904, SBS#44911, SBS#44910, SBS#44945, SBS#44944, SBS#44947 or SBS#44946.

5. A zinc finger protein comprising 5 or 6 zinc finger domains comprising a recognition helix region, wherein the zinc finger protein comprises the recognition helix regions in the order shown in a single row of Table 1A of the proteins designated SBS#39172, SBS#43490, SBS#44642, SBS#45148, SBS#45147, SBS#39145, SBS#44490, SBS#44489, SBS#45081, SBS#44493, SBS#29527, SBS#29528, SBS#29525, SBS#29526, SBS#34678, SBS#34642, SBS#44889, SBS#44888, SBS#44905, SBS#44904, SBS#44911, SBS#44910, SBS#44945, SBS#44944, SBS#44947 or SBS#44946.

6. A fusion protein comprising the zinc finger protein of claim 5 and a wild-type or engineered cleavage domain or wild-type or engineered cleavage half-domain.

7. A polynucleotide encoding one or more proteins of claim 5 or claim 6.

8. An isolated cell comprising one or more fusion proteins of claim 6 or one or more polynucleotides of claim 7.

9. The cell of claim 8, wherein the cell is selected from the group consisting of a red blood cell (RBC) or a precursor cell, such as a CD34+ hematopoietic stem cell.

10. A kit comprising the protein of claim 5, the fusion protein of claim 6 or the polynucleotide of claim 7.

11. An in vitro method of altering globin gene expression in a cell, the method comprising: introducing, into the cell, one or more proteins of claim 5 or claim 6 or one or more polynucleotides of claim 7, under conditions such that the one or more proteins are expressed and expression of the globin gene is altered.

12. Use of one or more proteins of claim 5 or claim 6 or one or more polynucleotides of claim 7 in the manufacture of a medicament for treating a hemoglobinopathy, wherein the one of more proteins of claim 5 or claim 6 or one or more polynucleotides of claim 7 is to be introduced into the cell, under conditions such that one of more proteins are expressed and expression of the globin gene is altered.

13. The method of claim 11, wherein:

(a) the proteins increase expression of the globin gene, such as a gamma globin or beta globin gene;

(b) the method further comprises integrating a donor sequence into the genome of the cell, for example, by introducing the donor sequence to the cell using a viral vector, an oligonucleotide or a plasmid;

(c) the cell is a red blood cell (RBC) precursor cell, such as a CD34+ hematopoietic stem cell; and/or

(d) the donor sequence comprises a transgene under the control of an endogenous promoter or an exogenous promoter.

14. The use of claim 12, wherein the hemoglobinopathy is a thalassemia.

15. Use of one or more proteins of claim 5 or claim 6 or one or more polynucleotides of claim 7 in the manufacture of a medicament for treating sickle cell disease, wherein the one of more proteins of claim 5 or claim 6 or one or more polynucleotides of claim 7 is to be introduced into the cell, under conditions such that one of more proteins are expressed and expression of the globin gene is altered.