CLAIMS

What is claimed is:

1. A zinc finger protein comprising 4, 5 or 6 zinc finger domains comprising a recognition helix region, wherein the zinc finger proteins comprise the recognition helix regions in the order shown in a single row of Table 1.

2. A fusion protein comprising a zinc finger protein of claim 1 and a wild-type or engineered cleavage domain or wild-type or engineered cleavage half-domain.

3. A polynucleotide encoding one or more proteins of claim 1 or claim 2.

4. An isolated cell comprising one or more fusion proteins according to claim 2 or one or more polynucleotides according to claim 3.

5. The cell of claim 4, wherein the cell is selected from the group consisting of a red blood cell (RBC) or precursor cell.

6. The cell of claim 5, wherein the precursor cell is a CD34+ hematopoietic stem cell.

7. A kit comprising a protein according to claim 1 or claim 2 or a polynucleotide according to claim 3.

8. A method of altering globin gene expression in a cell, the method comprising:

introducing, into the cell, one or more proteins according to claim 1 or claim 2 or one or more polynucleotides according to claim 3, under conditions such that the one or more proteins are expressed and expression of the globin gene is altered.

9. The method of claim 8, wherein the proteins increase expression of a globin gene.

10. The method of claim 9, wherein the globin gene is a gamma globin or beta globin gene.

11. The method of any of claims 8 to 10, further comprising integrating a donor sequence into the genome of the cell.

12. The method of claim 11, wherein the donor sequence is introduced to the cell using a viral vector, an oligonucleotide or a plasmid.

13. The method of any of claims 8 to 12, wherein the cell is a red blood cell (RBC) precursor cell.

14. The cell of claim 13, wherein the RBC precursor cell is a CD34+ hematopoietic stem cell.

15. The method of any of claims 8 to 14, wherein the donor sequence comprises a transgene under the control of an endogenous promoter.

16. The method of any of claims 8 to 14, wherein the donor sequence comprises a transgene under the control of an exogenous promoter.

CLAIMS

What is claimed is:

1. An isolated, non-naturally occurring fusion protein comprising a transcription activator like effector (TALE) DNA binding domain that binds to a target site in an endogenous BCL11A gene comprising a nucleotide sequence selected from the group consisting of SEQ ID NO: 236,238, 240 and 242, and a nuclease cleavage domain, wherein the fusion protein cleaves the endogenous BCL11A gene, wherein the TALE domain comprises a repeat variable diresidue (RVD) sequence in order presented and selected from a single row of table 1C.

2. An isolated polynucleotide encoding the non-naturally occurring fusion protein of claim 1.

3. An isolated cell comprising the non-naturally occurring fusion protein of claim 1.

4. An isolated cell comprising the polynucleotide of claim 2.

5. The cell of claim 4, wherein the cell is a red blood cell (RBC) precursor cell.

6. The cell of claim 3, wherein the cell is a red blood cell (RBC).

7. The cell of claim 5, wherein the RBC precursor cell is a CD34+ hematopoietic stem cell.

8. A kit comprising the non-naturally occurring fusion protein of claim 1.

9. A kit comprising the polynucleotide of claim 2.

10. A method of increasing gamma-globin gene expression in an isolated cell, the method comprising:

transfecting the isolated cell with the polynucleotides of claim 5,wherein the isolated cell is a red blood cell (RBC) precursor cell or a hematopoietic stem cell, and

culturing said transfected cells under conditions such that said fusion protein is expressed and the endogenous BCL11A gene is cleaved, thereby increasing expression of the gamma-globin gene.

11. The method of claim 10, wherein the hematopoietic stem cell is a CD34+ stem cell.