CLAIMS

1. A self-inactivating (SIN) lentiviral vector comprising:

(a) a modified HIV-1 strain NL4-3 5´ long terminal repeat (LTR) comprising a CMV promoter;

(b) a Psi (Ψ) packaging signal;

(c) an HIV-1 strain NL4-3 central polypurine tract (cPPT)/FLAP element;

(d) an HIV-1 strain HXB3 RRE RNA export element;

(e) an HIV-1 strain NL4-3 env splice acceptor sequence;

(f) a human β-globin promotor operably linked to a polynucleotide encoding a shmiR that comprises an antisense sequence that hybridizes to a human BCL11A mRNA, wherein the shmiR comprises the sequence set forth in SEQ ID NO: 1;

(g) a human β-globin LCR comprising a HS2 DNAse I hypersensitive site comprising about 638 nucleotides, and a HS3 DNAse I hypersensitive site comprising about 847 nucleotides; and

(h) an HIV-1 strain NL4-3 3´ SIN LTR.

2. The lentiviral vector of claim 1, wherein the lentiviral vector does not comprise an HS4 DNAse I hypersensitivity site.

3. The lentiviral vector of claim 1, further comprising:

(a) a polynucleotide of about 459 nucleotides that encodes a gag protein; comprising one or more mutated ATG start codons and/or

(b) a synthetic poly(A) sequence disposed between an HIV-1 env splice acceptor sequence and the shmiR.

4. The lentiviral vector of claim 1, wherein:

(a) the HIV-1 env splice acceptor sequence comprises about 176 nucleotides; and/or

(b) the cPPT/FLAP element comprises about 381 nucleotides.

5. The lentiviral vector of claim 1, wherein the vector comprises an expression cassette comprising the erythroid specific promoter and the polynucleotide encoding the shmiR are in the reverse orientation compared to the transcription of the lentiviral genomic RNA.

6. A lentiviral transfer vector comprising the polynucleotide sequence set forth in SEQ ID NO: 4.

7. A cell comprising the lentiviral transfer vector of claim 6.

8. A lentiviral vector particle produced from the cell of claim 7.

9. A cell transduced with the lentiviral vector particle of claim 8.

10. The cell of claim 9, wherein the cell is a hematopoietic stem cell or hematopoietic progenitor cell.

11. A composition comprising a population of cells comprising a plurality of the cells according to claim 9.

12. A method of transducing a population of hematopoietic cells comprising culturing the cells in a culture medium, in the presence of a lentiviral vector according to claim 1.

13. Use of a composition according to claim 11 in the manufacture of a medicament for the treatment of hemoglobinopathy in a subject.