Claims

1. An expression cassette comprising a polynucleotide sequence comprising in the following 5' to 3' order:

a) a promoter sequence;

b) a sequence encoding a gene product; and

c) an ribonucleic acid (RNA) export signal,

wherein the promoter sequence is operably linked to the sequence encoding the pyruvate kinase polypeptide.

2. The expression cassette of claim 1, wherein the promoter is a phosphoglycerate kinase (PGK) promoter.

3. The expression cassette of claim 1 or claim 2, wherein the gene product is a therapeutic gene product.

4. The expression cassette of claim 3, wherein the therapeutic gene product is a pyruvate kinase (PK) polypeptide, optionally a pyruvate kinase, liver and red blood cell (PKLR) polypeptide.

5. The expression cassette of any of claims 1-4, wherein the sequence encoding the gene product is codon-optimized.

6. The expression cassette of any of claims 1-5, wherein the RNA export signal is a mutated post-transcriptional regulatory element of the woodchuck hepatitis virus (Wpre).

7. The expression cassette of claim 6, wherein the mutated Wpre is a chimeric Wpre comprising a sequence having at least 80% identity to SEQ ID NO:1.

8. The expression cassette of any of claims 1-7, further comprising one or more enhancer sequences.

9. The expression cassette of any of claims 1-8, further comprising a polypurine tract (PPT) or polyadenylation (polyA) signal sequence.

10. The expression cassette of any of claims 1-9, further comprising one or more of the following sequences:

i) a packing signal sequence;

ii) a truncated Gag sequence;

iii) a Rev responsive element (RRE);

iv) a central polypurine tract (cPPT);

v) a central terminal sequence (CTS); and

vi) an upstream sequence element (USE), optionally from simian virus 40 (SV40-USE).

11. The expression cassette of any one of claims 1-10, further comprising 5' and 3' long terminal repeat sequences.

12. A recombinant gene delivery vector comprising the expression cassette of any one of claims 1-11.

13. The recombinant gene delivery vector of claim 12, wherein the recombinant gene delivery vector is a virus or viral vector.

14. The recombinant gene delivery vector of claim 13, wherein the virus or viral vector is a lentivirus (LV).

15. A cell comprising the expression cassette of any of claims 1-11 or the gene delivery vector of any of claims 12-14.

16. The cell of claim 15, wherein the cell is a hematopoietic stem cell.

17. The cell of claim 15, wherein the cell is a committed hematopoietic erythroid progenitor cell.

18. A pharmaceutical composition comprising a pharmaceutically acceptable

excipient and the recombinant gene delivery vector of any of claims 12-14 or the cell of any of claims 15-17.

19. A method of treating or preventing a disease or disorder in a subject in need thereof, comprising providing to the subject the pharmaceutical composition of claim 18.

20. The method of claim 19, wherein the disease or disorder is a Pyruvate Kinase Deficiency (PKD) and the gene product is a pyruvate kinase (PK) polypeptide, optionally a pyruvate kinase, liver and red blood cell (PKLR) polypeptide.

21. The method of claim 19 or claim 20, wherein the pharmaceutical composition comprises the recombinant gene delivery vector.

22. The method of claim 19 or claim 20, wherein the pharmaceutical composition comprises the cell.

23. The method of claim 22, wherein the cell is autologous to the subject.

24. The method of claim 22, wherein the cell is allogeneic to the subject.

25. A method for expressing a transgene in erythroid cells, comprising contacting one or more erythroid cells with an effective amount of a recombinant viral vector, wherein the vector comprises a human phosphoglycerate kinase promoter, a codon optimized version of a human pyruvate kinase, liver and red blood cell (PKLR) cDNA transgene, and a mutated post-transcriptional regulatory element of the woodchuck hepatitis virus, wherein following said contacting, PKLR is expressed at detectable levels in the one or more erythroid cells.