in the vector. However, promoters are often spread over a long range of DNA and poorly characterized, and can thus not be easily reconstituted in their entirety in a vector construct. Furthermore, expression levels from tissue-specific promoters reconstituted in gene-transfer vectors are often not sufficient to achieve phenotypic correction, most likely because of imperfect reconstitution and/or detrimental influence of the chromatin at the semi-random vector integration site. Thus, additional strategies to regulate a transgene are direly needed.

Summary

In one aspect, the present disclosure refers to a use of a gene vector comprising at least one miRNA target sequence corresponding to a miRNA selected from the group consisting of mir-130a and mir-126 operably linked to a nucleotide sequence for the manufacture of a medicament for preventing or reducing expression of the nucleotide sequence in a hematopoietic stem cell or a hematopoietic progenitor cell, wherein the nucleotide sequence is a transgene encoding an enzyme selected from the group lysosomal enzyme galactocerebrosidase, and gp91 phox; or wherein the nucleotide sequence is a transgene encoding interferon-alpha.

In another aspect, the present disclosure refers to a use of a cell for the manufacture of a medicament for preventing or reducing expression of the nucleotide sequence in a hematopoietic stem cell or a hematopoietic progenitor cell, wherein the cell is infected or transduced with the gene vector as disclosed herein.

In another aspect, the present disclosure refers to a use of the gene vector as disclosed herein, or the cell as disclosed herien for the manufacture of a medicament for treating a disease selected from Globoid Cell Leukodystrophy, Chronic Granulomatous Disease Severe Combined Immunodeficiency (SCID) and solid tumours.

In another aspect, the present disclosure refers to a use of the gene vector as disclosed herein, or the cell as disclosed herein for the manufacture of a medicament for increasing the chances of survival of a hematopoietic stem cell or a hematopoietic progenitor cell in relation to gene therapy.

In another aspect, the present disclosure refers to a use of the gene vector as disclosed herein, or the cell as disclosed herein for the manufacture of a medicament for preventing apoptosis of a hematopoietic stem cell or a hematopoietic progenitor cell, whereby the apoptosis is caused by expression of the nucleotide sequence.

In another aspect, the present disclosure refers to a use of the gene vector as disclosed herein, or the cell as disclosed herein for the manufacture of a medicament for monitoring a stage of differentiation of a hematopoietic stem cell or a hematopoietic progenitor cell.

In another aspect, the present disclosure refers to a method of determining the differentiation stage of a hematopoietic stem cell or a hematopoietic progenitor cell, comprising determining the expression level of a transgene in said hematopoietic stem cell or said hematopoietic progenitor cell, wherein the transgene is operably linked to a miRNA target sequence, whereby the corresponding miRNA prevents or reduces expression of the transgene in a hematopoietic progenitor cell (HSPC) or a hematopoietic stem cell (HSC) but not in a differentiated cell, wherein the miRNA is selected from the group comprising mir-130a and mir-126.

CLAIMS

1. Use of a gene vector comprising at least one miRNA target sequence corresponding to a miRNA selected from the group consisting of mir-130a and mir-126 operably linked to a nucleotide sequence for the manufacture of a medicament for preventing or reducing expression of the nucleotide sequence in a hematopoietic stem cell or a hematopoietic progenitor cell, wherein the nucleotide sequence is a transgene encoding an enzyme selected from the group lysosomal enzyme galactocerebrosidase, and gp91 phox; or wherein the nucleotide sequence is a transgene encoding interferon-alpha.

2. The use of claim 1, wherein the gene vector comprises at least one miRNA target sequence corresponding to mir-130a and at least one miRNA target sequence corresponding to mir-126.

3. The use of claim 2, wherein the number of copies of the miRNA target sequence corresponding to mir-130a is twice the number of copies of the miRNA target sequence corresponding to mir-126.

4. The use of any one of claims 1 to 3, wherein the nucleotide sequence controls the expression of the vector.

5. The use of any one of claims 1 to 4, wherein the vector is a viral vector.

6. The use of any one of claims 1 to 5, wherein the vector is derivable from a lentivirus.

7. The use of any one of claims 1 to 6, wherein the vector comprises a tissue specific promoter.

8. The use of claim 7, wherein the tissue specific promoter is selected from the group consisting of CD11b, c-Fes and CYBB and TEK.

9. The use of claim 7, wherein the tissue specific promoter is a myeloid specific promoter.

10. The use of any one of claims 1 to 9, wherein the nucleotide sequence is a transgene encoding interferon-alpha.

11. The use of any one of claims 1 to 10, wherein the gene vector is in the form of a viral vector particle.

12. Use of a cell for the manufacture of a medicament for preventing or reducing expression of the nucleotide sequence in a hematopoietic stem cell or a hematopoietic progenitor cell, wherein the cell is infected or transduced with the gene vector as defined in any one of claims 1 to 11.

13. The use of claim 12, wherein the cell is a hematopoietic stem cell or a hematopoietic progenitor cell.

14. Use of the gene vector as defined in any one of claims 1 to 11, or the cell as defined in claim 12 or 13 for the manufacture of a medicament for treating a disease selected from Globoid Cell Leukodystrophy, Chronic Granulomatous Disease Severe Combined Immunodeficiency (SCID) and solid tumours.

15. Use of the gene vector as defined in any one of claims 1 to 11, or the cell as defined in claim 12 or 13 for the manufacture of a medicament for increasing the chances of survival of a hematopoietic stem cell or a hematopoietic progenitor cell in relation to gene therapy.

16. Use of the gene vector as defined in any one of claims 1 to 11, or the cell as defined in claim 12 or 13 for the manufacture of a medicament for preventing apoptosis of a hematopoietic stem cell or a hematopoietic progenitor cell, whereby the

apoptosis is caused by expression of the nucleotide sequence.

17. Use of the gene vector as defined in any one of claims 1 to 11, or the cell as defined in claim 12 or 13 for the manufacture of a medicament for monitoring a stage of differentiation of a hematopoietic stem cell or a hematopoietic progenitor cell.

18. The use of any one of claims 1 to 17, wherein the medicament is for hematopoietic cell therapy.

19. A method of determining the differentiation stage of a hematopoietic stem cell or a hematopoietic progenitor cell, comprising determining the expression level of a transgene in said hematopoietic stem cell or said hematopoietic progenitor cell, wherein the transgene is operably linked to a miRNA target sequence, whereby the corresponding miRNA prevents or reduces expression of the transgene in a hematopoietic progenitor cell (HSPC) or a hematopoietic stem cell (HSC) but not in a differentiated cell, wherein the miRNA is selected from the group comprising mir-130a and mir-126.