CLAIMS

~~1. A gene vector for use in gene therapy comprising at least one miRNA sequence target operably linked to a nucleotide sequence having a corresponding miRNA in a hematopoietic progenitor cell (HSPC) which prevents or reduces expression of the nucleotide sequence in a HSPC but not in a differentiated cell.~~

~~2. A gene vector for use in gene therapy comprising at least one miRNA sequence target operably linked to a nucleotide sequence having a corresponding miRNA in a hematopoietic stem cell (HSC) which prevents or reduces expression of the nucleotide sequence in a HSC but not in a differentiated cell.~~

~~3.~~1. A gene vector for use in gene therapy comprising at least one miRNA ~~sequence target~~target sequence corresponding to a miRNA selected from the group comprising mir-130a~~,~~ and mir-126~~, mir-223, 126/130aT (2/2 combination) and 126T (2 targets)~~ operably linked to a nucleotide sequence.

2. A gene vector according to claim ~~3~~1 comprising ~~the~~ at least one miRNA ~~sequence targets~~target sequence corresponding to mir-130a and at least one miRNA target sequence corresponding to mir-126.

~~4.~~3. A gene vector according to 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.

~~5. A gene vector according to any preceding claim wherein the nucleotide sequence controls the expression of the vector.~~

~~6.~~4. A gene vector according to claims ~~1-5~~1-3 wherein the nucleotide sequence is a transgene.

~~7.~~5. A gene vector according to any preceding claim wherein the vector is a viral vector.

~~8.~~6. A gene vector according to any preceding claim wherein the vector is derivable from a lentivirus.

~~9.~~7. A gene vector according to any preceding claim wherein the vector comprises a tissue specific promoter.

8. A gene vector according to ~~any preceding~~ claim 7 wherein the tissue specific promoter is selected from the group comprising CD11b, c-Fes and CYBB and TEK.

~~10.~~9. A gene vector according to claim 7 wherein the tissue specific promoter is a myeloid specific promoter.

~~11.~~10. A gene vector according to any preceding claim wherein the ~~transgene~~ nucleotide sequence codes for an enzyme.

~~12.~~11. A gene vector according to claim ~~11~~ 10 wherein the enzyme is selected from the group lysosomal enzyme galactocerebrosidase, gp91 phox and interferon-alpha.

~~13.~~12. A set of DNA constructs for producing a viral vector particle comprising a DNA construct encoding a packagable viral vector genome comprising at least one miRNA ~~sequence target~~target sequence as defined in any one of claims 1 to ~~5~~3, and optionally a transgene.

~~14.~~13. A process for preparing a viral vector particle comprising introducing the set of DNA constructs of claim ~~13~~ 12 into a host cell, and obtaining the viral vector particle.

~~15.~~14. A process according to claim ~~14~~ 13 wherein the host cell comprises the corresponding miRNA.

~~16. A viral vector particle produced by the process of claim 14 or 15.~~

~~17.~~15. A pharmaceutical composition comprising the gene vector ~~or particle according to~~as defined in any one of claims ~~1-12~~1-11 ~~or 16~~.

~~18.~~16. A cell infected or transduced with the gene vector ~~or particle of~~as defined in any one of claims ~~1-12~~1-11 ~~or 16~~.

~~19.~~17. A cell according to claim ~~18~~ 16 which is a hematopoietic stem cell or a hematopoietic progenitor cell.

~~20.~~18. Combination of at least two different miRNA~~s~~ ~~sequence target~~target sequences corresponding to miRNAs selected from the group comprising mir-130a~~,~~ and mir-126~~, mir-223 and126/130aT (2/2 combination) and 126T (2 targets)~~.

~~21.~~19. Combination according to claim ~~20~~ 18 wherein the miRNA ~~sequence target~~target sequences are for simultaneous, separate or sequential use.

~~22.~~20. Use of the vector of any one of claims ~~1-12~~1-11, ~~a particle of claim 16,~~ a pharmaceutical composition according to claim ~~17~~15, a cell according to claims ~~18-19~~16-17 or a combination according to claims ~~20-21~~18-19 for the manufacture of a medicament for preventing or reducing expression of a transgene in a hematopoietic stem cell or a hematopoietic progenitor cell.

~~23.~~21. Use of the gene vector of any one of claims ~~1-12~~1-11, ~~a particle of claim 16,~~ a pharmaceutical composition according to claim ~~17~~15, a cell according to claims ~~18-19~~16-17 or a combination according to claims ~~20-21~~18-19 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.

~~24.~~22. Use of the gene vector of any one of claims ~~1-12~~1-11, ~~a particle of claim 16,~~ a pharmaceutical composition according to claim ~~17~~15, a cell according to claims ~~18-19~~16-17 or a combination according to claims ~~20-21~~18-19 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.

~~25.~~23. Use of the gene vector of any one of claims ~~1-12~~1-11, ~~a particle of claim 16,~~ a pharmaceutical composition according to claim ~~17~~15, a cell according to claims ~~18-~~

~~19~~16-17 or a combination according to claims ~~20-21~~18-19 for the manufacture of a medicament for increasing the safety and/or efficacy of gene therapy.

~~26.~~24. Use of the gene vector of any one of claims ~~1-12~~1-11, ~~a particle of claim 16,~~ a pharmaceutical composition according to claim ~~17~~15, a cell according to claims ~~18-19~~16-17 or a combination according to claims ~~20-21~~18-19 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 transgene.

~~27.~~25. Use of the gene vector of any one of claims ~~1-12~~1-11, ~~a particle of claim 16,~~ a pharmaceutical composition according to claim ~~17~~15, a cell according to claims ~~18-19~~16-17 or a combination according to claims ~~20-21~~18-19 for the manufacture of a medicament for monitoring a stage of differentiation of a hematopoietic stem cell or a hematopoietic progenitor cell.

~~28.~~26. Use according to any one of claims ~~22-27~~20-25 wherein the medicament is for hematopoietic cell therapy.

~~29. A gene vector of any one of claims 1-12, a particle of claim 16, a pharmaceutical composition according to claim 17, a cell according to claims 18-19 or a combination according to claims 20-21 for preventing or reducing expression of a transgene in a hematopoietic stem cell or a hematopoietic progenitor cell.~~

~~30. A gene vector of any one of claims 1-12, a particle of claim 16, a pharmaceutical composition according to claim 17, a cell according to claims 18-19 or a combination according to claims 20-21 for treating a disease selected from Globoid Cell Leukodystrophy, Chronic Granulomatous Disease Severe Combined Immunodeficiency (SCID) and solid tumours.~~

~~31. A gene vector of any one of claims 1-12, a particle of claim 16, a pharmaceutical composition according to claim 17, a cell according to claims 18-19 or a combination according to claims 20-21 for increasing the chances of survival of a hematopoietic stem cell or a hematopoietic progenitor cell in relation to gene therapy.~~

~~32. A gene vector of any one of claims 1-12, a particle of claim 16, a pharmaceutical composition according to claim 17, a cell according to claims 18-19 or a combination according to claims 20-21 for increasing the safety and/or efficacy of gene therapy.~~

~~33. A gene vector of any one of claims 1-12, a particle of claim 16, a pharmaceutical composition according to claim 17, a cell according to claims 18-19 or a combination according to claims 20-21 for preventing apoptosis of a hematopoietic stem cell or a hematopoietic progenitor cell, whereby the apoptosis is caused by expression of the transgene.~~

~~34. A gene vector of any one of claims 1-12, a particle of claim 16, a pharmaceutical composition according to claim 17, a cell according to claims 18-19 or a combination according to claims 20-21 for monitoring a stage of differentiation of a hematopoietic stem cell or a hematopoietic progenitor cell.~~

~~35. A gene vector according to any one of claims 29-34 for use in hematopoietic stem therapy.~~

~~36.~~27. Use of a miRNA ~~sequence target~~target sequence corresponding to a miRNA selected from the group of mir-130a~~,~~ and mir-126~~, mir-223, 126/130aT (2/2 combination) and 126T (2 targets)~~ for the manufacture of a medicament for use in gene therapy.

~~37. The miRNA sequence target corresponding to a miRNA selected from the group of mir-130a, mir-126 and mir-223 for use in gene therapy.~~

~~38.~~28. A ~~M~~method of determining the differentiation stage of a hematopoietic stem cell or a hematopoietic progenitor cell, comprising determining the level of expression of a miRNA in the cell, ~~wherein the miRNA corresponds to a miRNA target sequence operably linked to a nucleotides sequences, wherein the miRNA prevents or reduces expression of the nucleotide sequence 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.

~~39.~~29. A ~~M~~method of determining the differentiation stage of a hematopoietic stem cell or a hematopoietic progenitor cell, comprising determining the level of expression of at least two different miRNAs in the cell, ~~wherein the miRNAs correspond to miRNA target sequences operably linked to nucleotide sequences, wherein the miRNAs prevent or reduce expression of the nucleotide sequences in a hematopoietic progenitor cell (HSPC) or a hematopoietic stem cell (HSC) but not in a differentiated cell~~ and comparing the expression level of the different miRNAs, wherein the miRNAs are selected from the group comprising mir-130a and mir-126**.**

~~40.~~30. ~~Method~~ 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 ~~sequence target~~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.

~~41. Method according to claims 38-40 wherein the miRNA is selected from the group comprising mir-130a, mir-126, mir-223, 126/130aT (2/2 combination) and 126T (2 targets).~~