Claims

1. A gene vector for use in gene therapy comprising a miRNA ~~sequence~~ target sequence and a transgene operably linked to said miRNA target sequence, wherein the miRNA target sequence is for preventing or reducing expression of the transgene in a cell which comprises a corresponding endogenous miRNA.

2. A gene vector for use in therapy comprising a miRNA ~~sequence~~ target sequence, wherein the miRNA target sequence is for preventing or reducing expression of a gene in a cell which comprises a corresponding endogenous miRNA.

3. ~~A~~ The gene vector for use according to claim 1 or 2 in the form of a non-viral gene vector.

4. ~~A~~ The gene vector for use according to claim 3, wherein the non-viral gene vector comprises an expression vector or plasmid which comprises the miRNA ~~sequence~~ target sequence and optionally at least one transgene.

5. ~~A~~ The gene vector for use according to claim 1 or 2 in the form of a viral vector ~~comprising a miRNA sequence target~~.

6. ~~A~~ The gene vector for use according to claim 5 comprising the genome (RNA or DNA) of the viral vector, which genome comprises the miRNA ~~sequence~~ target sequence.

7. ~~A~~ The gene vector for use according to claim 6 comprising the genome of the viral vector, which genome comprises at least one transgene which is operably linked to the miRNA ~~sequence~~ target sequence.

8. ~~A~~ The gene vector for use according to any one of claims 5 to 7, wherein the viral vector is selected from the group of retroviruses, lentiviruses, adenoviruses, adeno-associated viruses, ~~herpex~~ herpes simplex viruses, picornaviruses, and alphaviruses.

9. ~~A~~ The gene vector for use according to any one of claims 5 to 7, wherein the viral vector is derivable from a lentivirus.

10. ~~A~~ The gene vector for use according to any one of claims 5 to 8, wherein the viral vector is in the form of a viral vector particle.

11. ~~A~~ The gene vector for use according to any ~~preceding claim~~one of claims 5 to 10, wherein the miRNA ~~sequence~~ target sequence controls expression of the viral vector in a target cell.

12. ~~A~~ The gene vector for use according to any preceding claim which comprises more than one miRNA target sequence ~~targets~~, which may be the same or different, in tandem and/or in different orientations.

13. ~~A~~ The gene vector for use according to any preceding claim wherein the miRNA ~~sequence~~ target sequence is one targeted by has-mir-142as (also called has-mir-142-3p) miRNA, let-7a, mir-15a, mir-16, mir-17-5p, mir-19, mir-142-5p, mir-145 and/or mir-218 miRNA.

14. ~~A~~ The gene vector for use according to any ~~preceding claim~~one of claims 1 or 3 to 13, wherein the transgene codes for suitable therapeutic genes include those coding for tumour suppressor proteins, enzymes, pro-drug activating enzymes, immunomodulatory molecules, antibodies, engineered immunoglobulin-like molecules, fusion proteins, hormones, membrane proteins, vasoactive proteins or peptides, cytokines, chemokines, anti-viral proteins, antisense RNAs and ribozymes.

15. ~~A~~ The gene vector for use according to any preceding claim, wherein the vector comprises a tissue specific promoter.

16. A set of DNA constructs for producing a viral vector particle comprising a DNA construct encoding a packageable viral vector genome comprising a miRNA ~~sequence~~ target sequence~~,~~ and a transgene operably linked to said miRNA target sequence, wherein the miRNA target sequence is for preventing or reducing

expression of the transgene in a cell which comprises a corresponding endogenous miRNA.

17. A process for preparing a viral vector particle comprising introducing the set of DNA constructs of claim 16 into a host cell, and obtaining the viral vector particle.

18. ~~A~~ The process according to claim 17, wherein the host cell comprises a corresponding miRNA.

19. A viral vector particle for use in gene therapy, wherein the particle is produced by the process of claim 17 ~~to~~ or 18.

20. A pharmaceutical composition for use in gene therapy, wherein the composition ~~comprising~~ comprises the gene vector as defined in any one of claims 1 to 15 or particle ~~according to any one of claims 1-15 or~~as defined in claim 19.

21. A cell for use in gene therapy, wherein the cell is infected or transduced with the gene vector ~~or particle of~~as defined in any one of claims 1- to 15 or particle as defined in claim 19.

22. ~~A~~ The cell for use according to claim 21 which is a hematopoietic, kidney, neuronal, lung, liver, spleen, heart, tumour or embryonic stem cell.

23. Use of the gene vector ~~of any one of claims 1-15, the particle of claim 19 or a pharmaceutical composition according to claim 20~~as defined in any one of claims 1 to 15 or pharmaceutical composition as defined in claim 20 comprising a transgene operably linked to the miRNA target sequence for the manufacture of a medicament for preventing or reducing expression of the transgene in a cell which comprises a corresponding miRNA.

~~24. A gene vector of any one of claims 1-15, the particle of claim 19 or a pharmaceutical composition according to claim 20 comprising a transgene operably linked to the miRNA target sequence for preventing or reducing expression of the transgene in a cell which comprises a corresponding miRNA for use in gene therapy.~~

~~25~~24. Use of the gene vector ~~of any one of claims 1-15, the particle of claim 19 or a pharmaceutical composition according to claim 20~~ as defined in any one of claims 1 to 15 or pharmaceutical composition as defined in claim 20 comprising a transgene operably linked to the miRNA target sequence for the manufacture of a medicament for treating cancer.

~~26~~25. Use of the gene vector ~~of any one of claims 1-15, the particle of claim 19 or a pharmaceutical composition according to claim 20~~as defined in any one of claims 1 to 15 or pharmaceutical composition as defined in claim 20 comprising a transgene operably linked to the miRNA target sequence for the manufacture of a medicament for treating haemophilia.

~~27~~26. Use of the gene vector ~~of any one of claims 1-15, the particle of claim 19 or a pharmaceutical composition according to claim 20~~as defined in any one of claims 1 to 15 or pharmaceutical composition as defined in claim 20 comprising a transgene operably linked to the miRNA target sequence for the manufacture of a medicament for preventing immune-mediated rejection of a transferred gene.

~~28~~27. Use of the gene vector ~~according to any one of claims 1 to 15, the particle of claim 19 or a pharmaceutical composition according to claim 20~~ as defined in any one of claims 1 to 15 or pharmaceutical composition as defined in claim 20 for the manufacture of a medicament for preventing immune mediated rejection of a transferred gene.

~~29~~28. Use of the gene vector ~~according to any one of claims 1 to 15, the particle of claim 19 or a pharmaceutical composition according to claim 20~~ as defined in any one of claims 1 to 15 or pharmaceutical composition as defined in claim 20 for the manufacture of a medicament for preventing immune response to a circulating antigen.

~~30~~29. Use of the gene vector ~~according to any one of claims 1 to 15, the particle of claim 19 or a pharmaceutical composition according to claim 20~~ as defined in any one of claims 1 to 15 or pharmaceutical composition as defined in claim 20 for the

manufacture of a medicament for treating a disease selected from cancer, neurological diseases, inherited diseases, heart diseases, stroke, arthritis, viral infections and diseases of the immune system.

~~31~~30. Use of the gene vector ~~according to any one of claims 1 to 15, the particle of claim 19 or a pharmaceutical composition according to claim 20~~ as defined in any one of claims 1 to 15 or pharmaceutical composition as defined in claim 20 for the manufacture of a medicament for gene therapy.

~~32~~31. Use of a miRNA ~~sequence~~ target sequence for use in a therapeutic application.

~~33~~32. ~~Use~~ The use according to claim 32, wherein the therapeutic application involves regulating a gene using the corresponding endogenous miRNA.