CLAIMS

1. Use of a recombinant negative-strand RNA virus vector in the manufacture of a medicament for *ex vivo* and *in vivo* gene therapy, for reprogramming cells to a cell of a less differentiated state, for regeneration therapies, or for programming cells to cells of a specifically differentiated cellular state,

wherein the recombinant negative-strand RNA virus vector comprises at least one heterologous nucleic acid sequence,

wherein the recombinant negative-strand RNA virus vector includes a viral genome coding for a mutated P protein, which mutation provides a loss of the viral genome replication ability without a loss of the viral transcription ability, and

wherein said at least one heterologous nucleic acid sequence encodes a cellular reprogramming or programming factor or a therapeutic protein.

2. Use of a cell or population of cells infected with a recombinant negative-strand RNA virus vector in the manufacture of a medicament, for *ex vivo* and *in vivo* gene therapy, for reprogramming cells to a cell of a less differentiated state, for regeneration therapies, or for programming cells to cells of a specifically differentiated cellular state,

wherein the recombinant negative-strand RNA virus vector comprises at least one heterologous nucleic acid sequence,

wherein the recombinant negative-strand RNA virus vector includes a viral genome coding for a mutated P protein, which mutation provides a loss of the viral genome replication ability without a loss of the viral transcription ability, and

wherein said at least one heterologous nucleic acid sequence encodes a cellular reprogramming or programming factor or a therapeutic protein.

3. Use of a pharmaceutical composition comprising a cell or population of cells infected with a recombinant negative-strand RNA virus vector, in the manufacture of a medicament for *ex vivo* and *in vivo* gene therapy, or for reprogramming cells to a cell of a less differentiated state, for use in regeneration therapies, or for programming cells to cells of a specifically differentiated cellular state,

wherein the recombinant negative-strand RNA virus vector comprises at least one heterologous nucleic acid sequence,

wherein the recombinant negative-strand RNA virus vector includes a viral genome coding for a mutated P protein, which mutation provides a loss of the viral genome replication ability without a loss of the viral transcription ability, and

wherein said at least one heterologous nucleic acid sequence encodes a cellular reprogramming or programming factor or a therapeutic protein.

4. Use according to any of claims 1 to 3, wherein said recombinant negative-strand RNA virus vector is a paramyxovirus including Sendai virus, parainfluenzavirus, Newcastle disease virus, mumps virus, measles virus, rinderpest virus and human respiratory syncytial virus, or a rhabdovirus vector including vesicular stomatitis virus or rabies virus.

5. Use according to any of claims 1 to 4, wherein the mutation of the P protein is a deletion, insertion or replacement of one or more amino acids of or into the amino acid sequence 2-77 of the P protein of Sendai virus or, in case of a virus other than Sendai, of or into an amino acid sequence homologous to the amino acid sequence 2-77 of the P protein of Sendai virus.

6. Use according to claim 5, wherein the mutation is a deletion of

(a) amino acids 2 to 77 of the P protein of Sendai virus or, in case of a virus other than Sendai, a deletion of the amino acids homologous to amino acids 2-77 of the P protein of Sendai virus or

(b) amino acids 33-41 of the P protein of Sendai virus or, in case of a virus other than Sendai, a deletion of the amino acids homologous to amino acids 33-41 of the P protein of Sendai virus.

7. Use according to any of claims 1 to 6, wherein the cellular reprogramming factor is selected from the group consisting of Nanog, Oct-3/4, Sox2, c-Myc, Klf4, Lin28, ASCL1, MYT1L, TBX3b, SV40 large T, hTERT, miR-291, miR-294, miR-295, and combinations thereof, and/or wherein the programming factor is selected from the group consisting of nerve growth factor (NGF), fibroblast growth factor (FGF), interleukin-6 (IL-6), bone morphogenic protein (BMP), neurogenin3 (Ngn3), pancreatic and duodenal homeobox 1 (Pdx1), Mafa, and combinations thereof.

8. Use according to any of claims 1 to 6, wherein the therapeutic protein is selected from the group consisting of adenosine deaminase (ADA), p91-PHOX, factor IX, factor VIII,

cystic fibrosis transmembrane conductance regulator (CFTR), β-globin (HBB), dystrophin, hypoxanthine-guanine phosphoribosyltransferase (HGPRT), phenylalanine hydroxylase (PAH), glucosylceramidase (GBA and GBA2), fibrillin-1 (FBN1), huntingtin (HTT), apolipoprotein B (apoB), low density lipoprotein receptor (LDLR), low density lipoprotein receptor adaptor protein 1 (LDLRAP1), proprotein convertase subtilisin/kexin type 9 (PCSK9), synuclein alpha (SNCA), parkin (PRKN), leucine-rich repeat kinase 2 (LRRK2), PTEN induced putative kinase 1 (PINK1), parkinson protein 7 (DJ-1), ATPase type 13A2 (ATP13A2), cancer suicide gene products, anti-angiogenic factors, cancer self antigens including tyrosinase-related protein 2 (TRP-2) and carcinoembryonic antigen (CEA), immune stimulating factors, growth factors including granulocyte-macrophage colony-stimulating-factor (GM-CSF) and epithelial growth factor (EGF), cytokines including interleukins IL-2, IL-4, IL-5, IL-12, and IL-17, immunosuppressants, and combinations thereof.

9. Use according to any of claims 1 to 7, wherein the cell to be programmed is a terminally differentiated somatic cell.

10. Use according to any of claims 1 to 6 or 8, for treating a genetic disorder,

wherein said at least one heterologous nucleic acid sequence encodes a therapeutic protein capable of treating said genetic disorder.

CLAIMS

1. A method of expressing at least one heterologous nucleic acid sequence in a cell, the method comprising

introducing at least one heterologous nucleic acid sequence into a cell by infecting said cell with a recombinant negative-strand RNA virus vector comprising said at least one heterologous nucleic acid sequence,

wherein the recombinant negative-strand RNA virus vector includes a viral genome coding for a mutated P protein, which leads to a loss of the viral genome replication ability without a loss of the viral transcription ability, and

wherein said at least one heterologous nucleic acid sequence encodes a cellular reprogramming or programming factor or a therapeutic protein.

2. The method of claim 1, wherein said recombinant negative-strand RNA virus vector is a paramyxovirus including Sendai virus, parainfluenzavirus, Newcastle disease virus, mumps virus, measles virus, rinderpest virus and human respiratory syncytial virus, or a rhabdovirus vector including vesicular stomatitis virus or rabies virus.

3. The method of claim 1 or 2, wherein the mutation of the P protein is a deletion, insertion or replacement of one or more amino acids of or into the amino acid sequence 2-77 of the P protein of Sendai virus or, in case of a virus other than Sendai, of or into an amino acid sequence homologous to the amino acid sequence 2-77 of the P protein of Sendai virus.

4. The method of claim 3, wherein the mutation is a deletion of

(a) amino acids 2 to 77 of the P protein of Sendai virus or, in case of a virus other than Sendai, a deletion of the amino acids homologous to amino acids 2-77 of the P protein of Sendai virus or

(b) amino acids 33-41 of the P protein of Sendai virus or, in case of a virus other than Sendai, a deletion of the amino acids homologous to amino acids 33-41 of the P protein of Sendai virus.

5. The method of any one of claims 1 to 4, wherein the cellular reprogramming factor is selected from the group consisting of Nanog, Oct-3/4, Sox2, c-Myc, Klf4, Lin28, ASCL1, MYT1L, TBX3b, SV40 large T, hTERT, miR-291, miR-294, miR-295, and combinations thereof, and/or wherein the programming factor is selected from the group consisting of nerve growth factor (NGF), fibroblast growth factor (FGF), interleukin-6 (IL-6), bone morphogenic protein (BMP), neurogenin3 (Ngn3), pancreatic and duodenal homeobox 1 (Pdx1), Mafa, and combinations thereof.

6. The method of any one of claims 1 to 5, wherein the therapeutic protein is selected from the group consisting of adenosine deaminase (ADA), p91-PHOX, factor IX, factor VIII, cystic fibrosis transmembrane conductance regulator (CFTR), β-globin (HBB), dystrophin, hypoxanthine-guanine phosphoribosyltransferase (HGPRT), phenylalanine hydroxylase (PAH), glucosylceramidase (GBA and GBA2), fibrillin-1 (FBN1), huntingtin (HTT), apolipoprotein B (apoB), low density lipoprotein receptor (LDLR), low density lipoprotein receptor adaptor protein 1 (LDLRAP1), proprotein convertase subtilisin/kexin type 9 (PCSK9), synuclein alpha (SNCA), parkin (PRKN), leucine-rich repeat kinase 2 (LRRK2), PTEN induced putative kinase 1 (PINK1), parkinson protein 7 (DJ-1), ATPase type 13A2 (ATP13A2), cancer suicide gene products, anti-angiogenic factors, cancer self antigens including tyrosinase-related protein 2 (TRP-2) and carcinoembryonic antigen (CEA), immune stimulating factors, growth factors including granulocyte-macrophage colony-stimulating-factor (GM-CSF) and epithelial growth factor (EGF), cytokines including interleukins IL-2, IL-4, IL-5, IL-12, and IL-17, immunosuppressants, and combinations thereof.

7. The method of any one of claims 1 to 6 which is an *in vitro* method of reprogramming an at least partially differentiated cell to a less differentiated cell or programming a cell to be programmed to a desired differentiated state, the method comprising:

(a) providing an at least partially differentiated cell or a cell to be programmed from a donor,

(b) introducing at least one heterologous nucleic acid sequence into the cell provided in step (a) by infecting the cell with the recombinant negative-strand RNA virus vector comprising said at least one heterologous nucleic acid sequence, and

(c) culturing the infected cell under conditions effective to express said at least one heterologous nucleic acid sequence,

wherein said at least one heterologous nucleic acid sequence encodes a cellular reprogramming or programming factor.

8. The method of claim 7, wherein the at least partially differentiated cell is a mammalian cell selected from the group consisting of a terminally differentiated somatic cell, a precursor cell, a lineage-restricted stem cell, a somatic stem cell and a progenitor cell.

9. The method of claim 7 or 8, wherein the at least partially differentiated cell is reprogrammed to an oligopotent, multipotent or pluripotent cell.

10. The method of claim 7, wherein the cell to be programmed is a terminally differentiated somatic cell.

11. The method of any one of claims 1 to 6 which is an *in vivo* method of treating a genetic disorder, the method comprising

administering to a patient a recombinant negative-strand RNA virus vector comprising at least one heterologous nucleic acid sequence to introduce said at least one heterologous nucleic acid sequence into a cell of the patient,

wherein said at least one heterologous nucleic acid sequence encodes a therapeutic protein capable of treating said genetic disorder.

12. The method of any one of claims 1 to 6 which is an *in vitro* method of treating a genetic disorder, the method comprising:

(a) providing a cell from a donor,

(b) introducing at least one heterologous nucleic acid sequence into the cell provided in step (a) by infecting the cell with the recombinant negative-strand RNA virus vector comprising said at least one heterologous nucleic acid sequence, and

(c) culturing the infected cell under conditions effective to express said at least one heterologous nucleic acid sequence and/or to allow the cell to expand,

wherein said at least one heterologous nucleic acid sequence encodes a therapeutic protein capable of treating said genetic disorder.

13. A cell or a population of cells prepared *in vitro* by the methods of any one of claims 1 to 10 and 12.

14. The cell or a population of cells of claim 13 for use as a medicament.

15. A pharmaceutical composition comprising a cell or a population of cells according to claim 13, or a redifferentiated cell or a population of redifferentiated cells derived from a cell or a population of cells prepared by the *in vitro* method of reprogramming according to any one of claims 7 to 9.