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(54) **VIRAL VECTORS FOR TREATING PARKINSON'S DISEASE**

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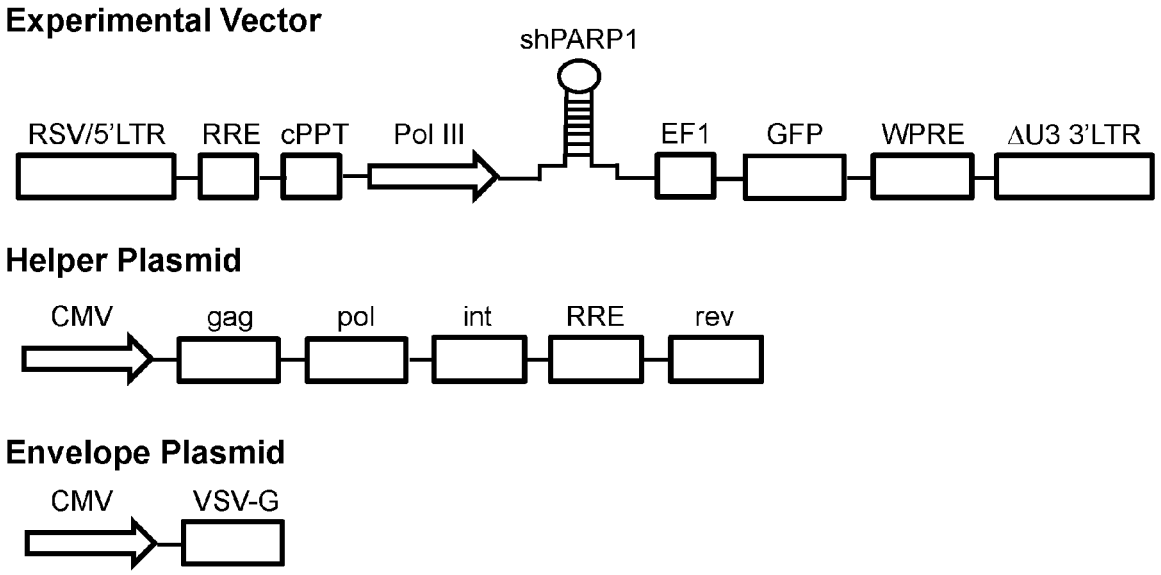
(57) **ABSTRACT**

A lentiviral vector system for expressing a lentiviral particle is disclosed. The lentiviral vector system includes a therapeutic vector, an envelope plasmid, and at least one helper plasmid. The lentiviral vector system can produce a lentiviral particle for inhibiting PARP expression in neuron cells of a subject afflicted with Parkinson's disease.

Specification includes a Sequence Listing.



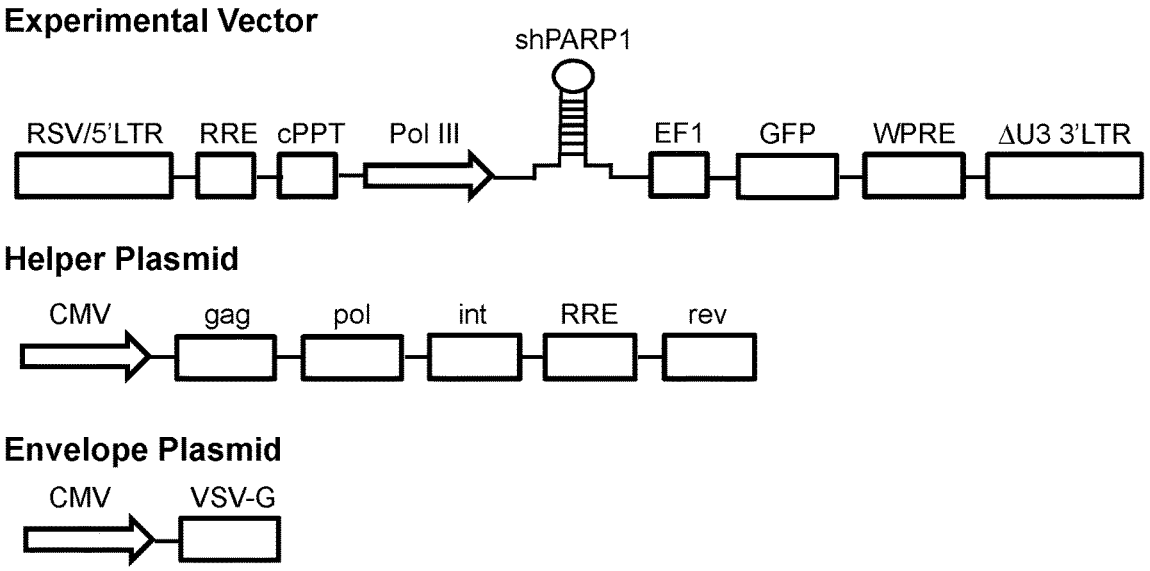

Experimental Vector
shPARP1
RSV/5'LTR
RRE
cPPT
Pol III
EF1
GFP
WPRE
ΔU3 3'LTR
Helper Plasmid
CMV
gag
pol
int
RRE
rev
Envelope Plasmid
CMV
VSV-G

FIG. 1A

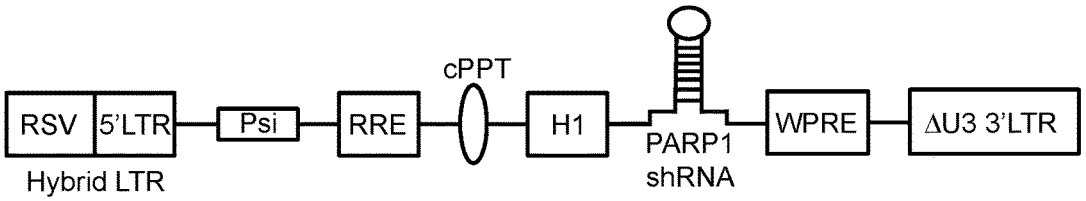
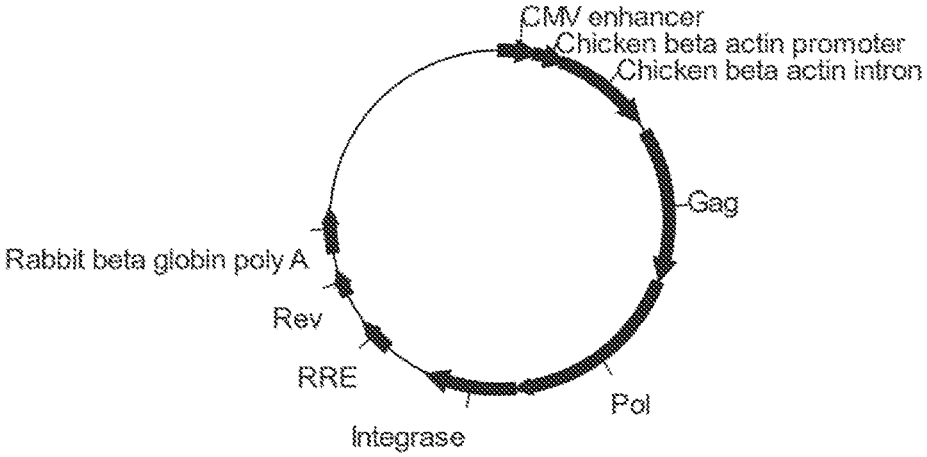
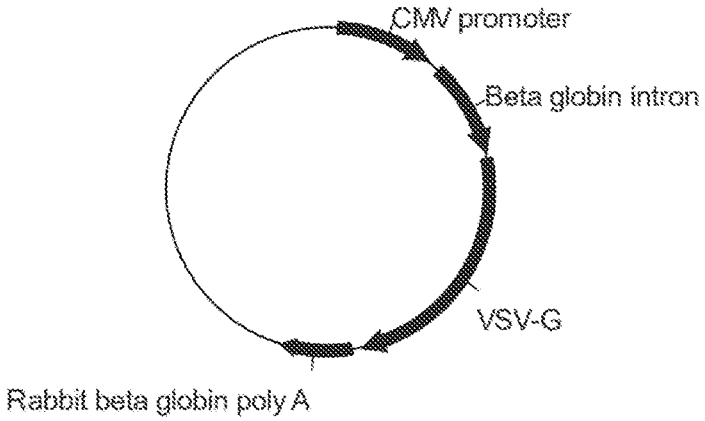

cPPT
RSV
5'LTR
Psi
RRE
H1
PARP1
shRNA
WPRE
ΔU3 3'LTR
Hybrid LTR

FIG. 1B

AGT Helper plus Rev plasmid



AGT Envelope plasmid



Lentiviral vector expressing PARP1 shRNA and GFP

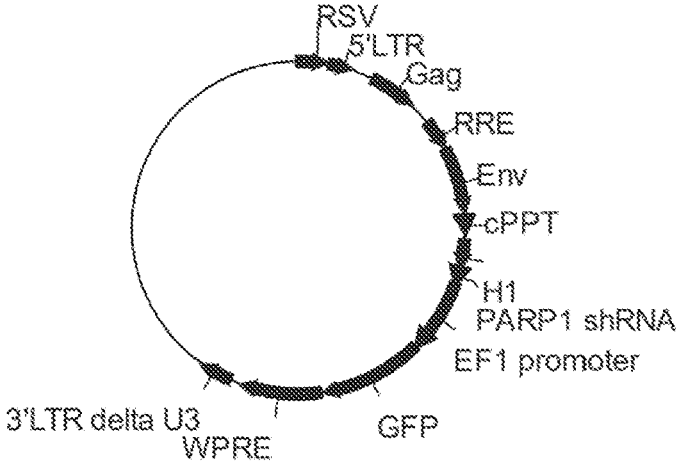
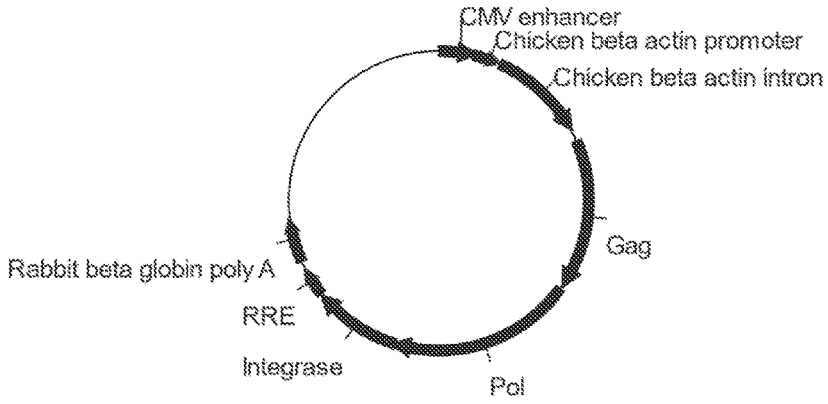
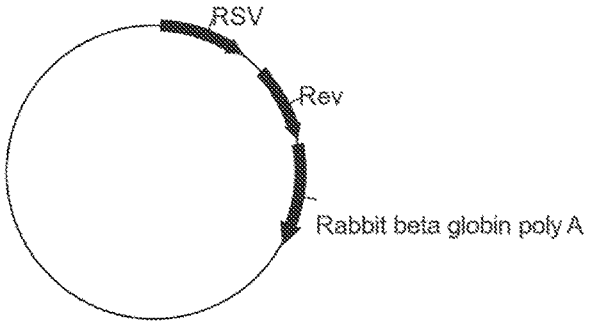


FIG. 1C

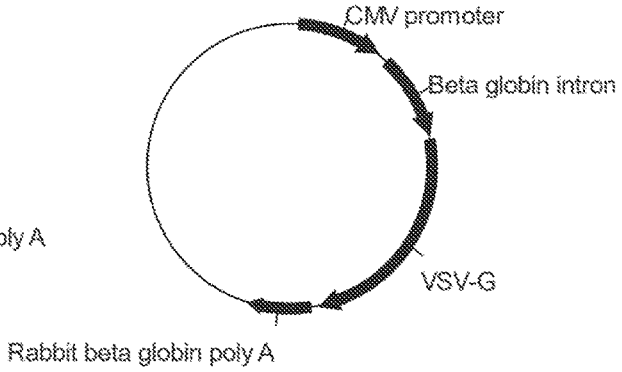
AGT Helper plasmid



AGT Rev plasmid



AGT Envelope plasmid



Lentiviral vector expressing PARP1 shRNA and GFP

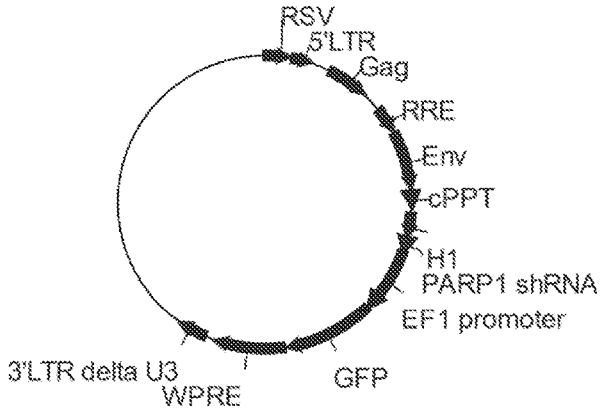
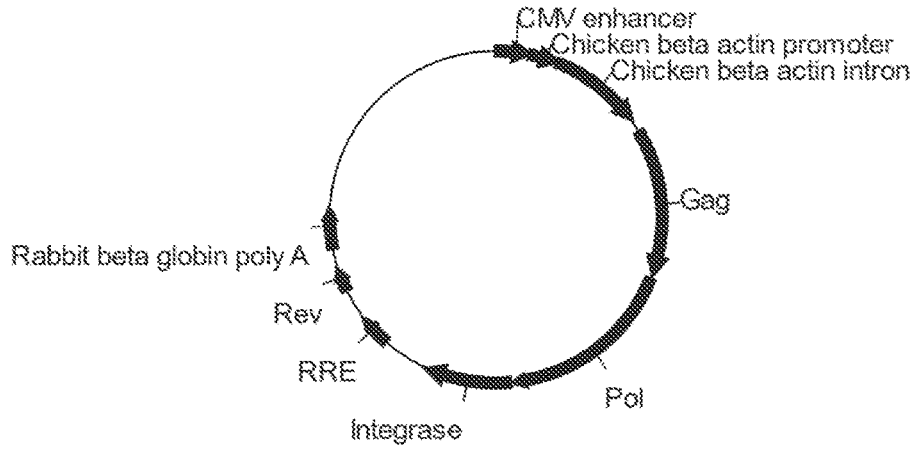
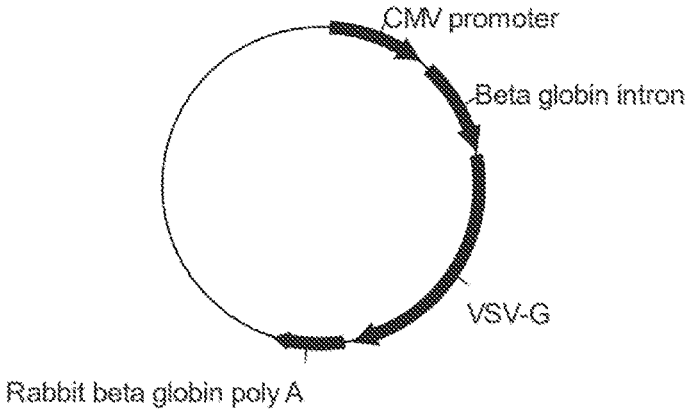


FIG. 1D

AGT Helper plus Rev plasmid



AGT Envelope plasmid



Lentiviral vector expressing PARP1 shRNA

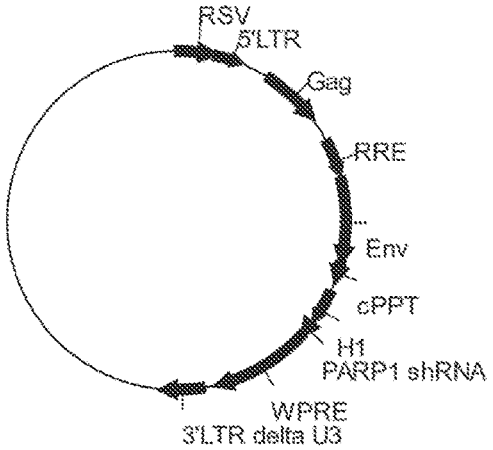
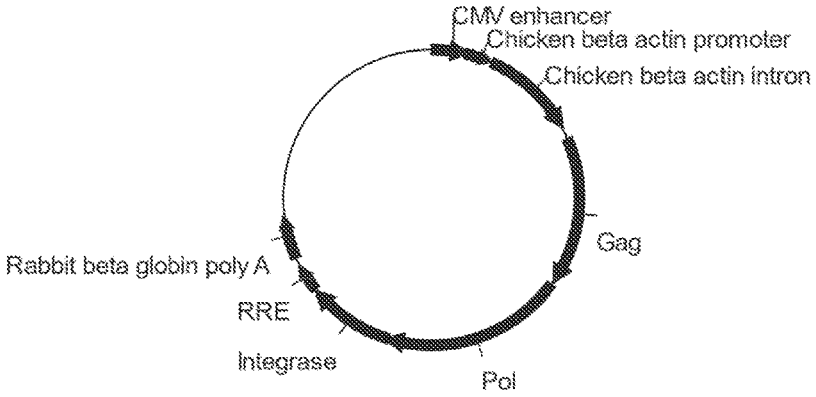
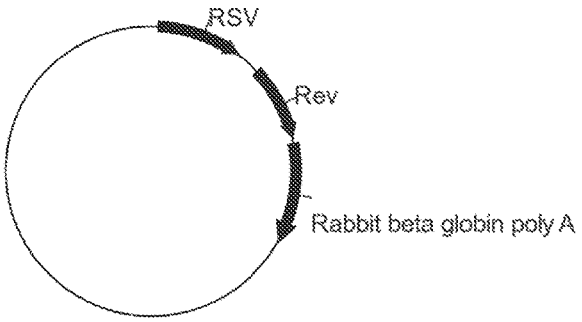


FIG. 1E

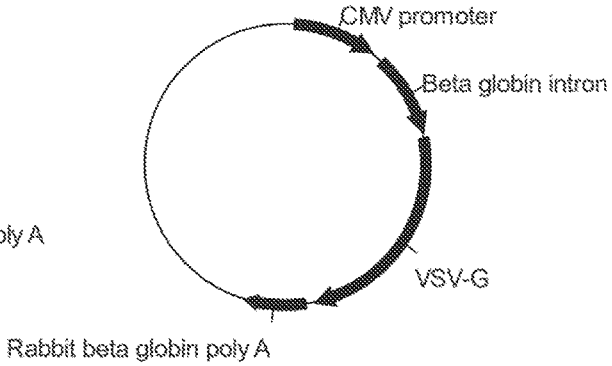
AGT Helper plasmid



AGT Rev plasmid



AGT Envelope plasmid



Lentiviral vector expressing PARP1 shRNA

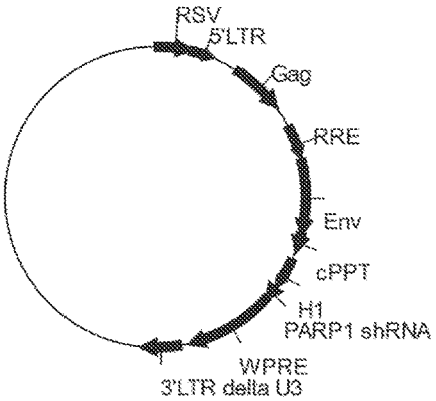


FIG. 1F

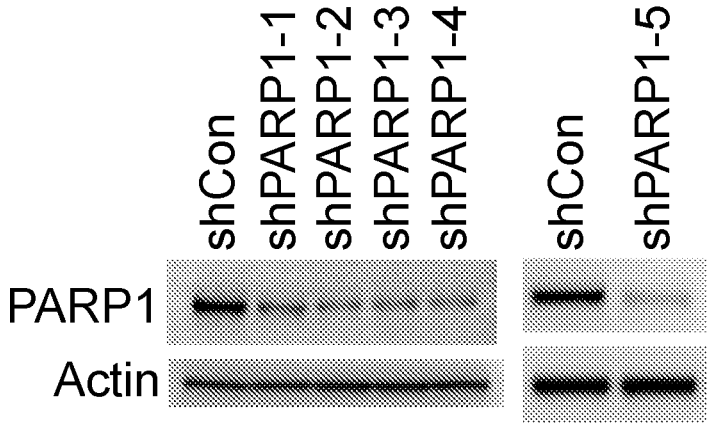

shCon
shPARP1-1
shPARP1-2
shPARP1-3
shPARP1-4
shCon
shPARP1-5
PARP1
Actin

FIG. 2

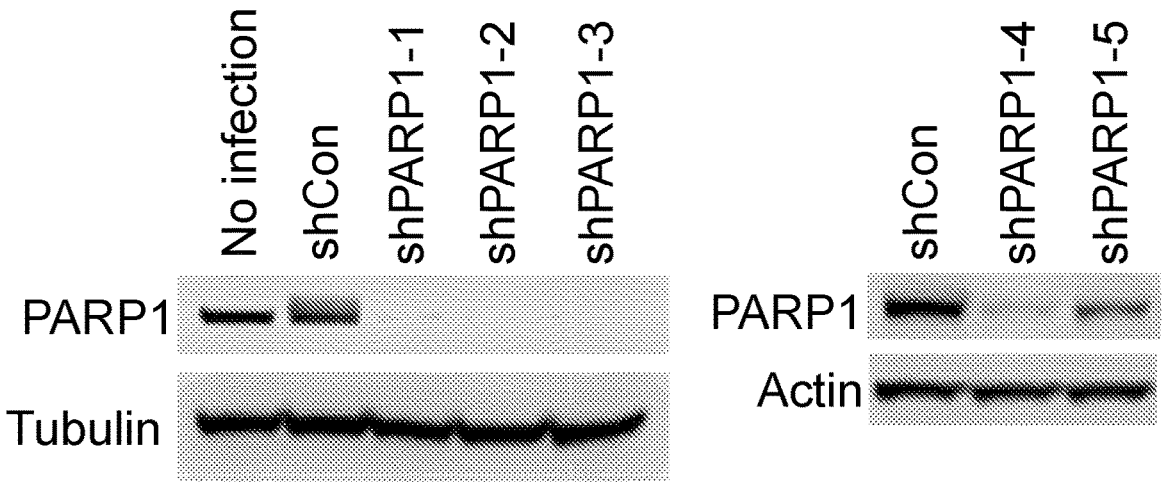

No infection
shCon
shPARP1-1
shPARP1-2
shPARP1-3
PARP1
Tubulin
shCon
shPARP1-4
shPARP1-5
PARP1
Actin

FIG. 3

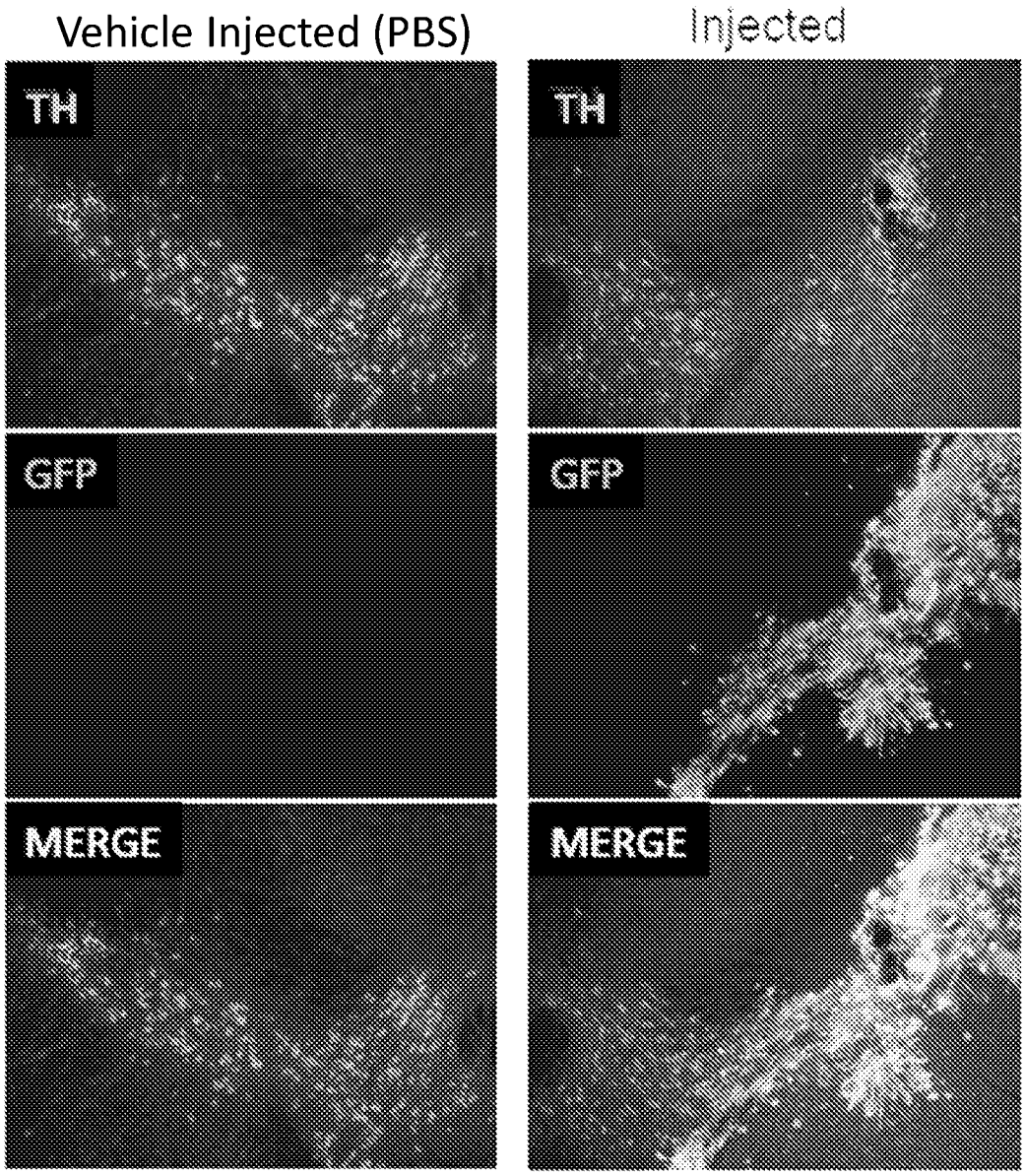


FIG. 4

VIRAL VECTORS FOR TREATING PARKINSON'S DISEASE

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority to: U.S. Provisional Patent Application No. 62/365,316 filed on Jul. 21, 2016 entitled "VIRAL VECTORS FOR TREATING PARKINSON'S DISEASE", the disclosure of which is incorporated herein by reference.

FIELD

[0002] Aspects of the invention relate to using vectors to treat Parkinson's disease. More specifically, aspects of the invention relate to using lentiviral vectors, including PARP-containing lentiviral vectors, to treat Parkinson's disease.

BACKGROUND

[0003] Parkinson's disease ("PD") is the second most common neurodegenerative disorder in the United States. Approximately 1 million Americans are afflicted with PD, with more than 60,000 new cases diagnosed each year. See, e.g., Fahn, S., 991 *Ann. N.Y. Acad. Sci.* 1-14 (2003). The incidence is expected to double by 2030. See, e.g., Dorsey, E. R., et al., 68(5) *Neurology,* 384-6 (2007). PD is a chronic progressive condition that generally appears late in life. PD is caused by the degeneration and death of dopamine producing neurons in the substantia nigra region of the basal ganglia. The deteriorated neurons and reduced dopamine result in abnormal neural activity and a chronic, progressive deterioration of motor function control. Patients with PD suffer from significant quality-of-life issues due to symptoms that include bradykinesia, rigidity, tremor, and postural instability. Additional complications due to PD include non-motor symptoms, such as dysphagia, and neuropsychiatric effects. See, e.g., Weintraub, D. et al., 14(2 Suppl) *Am. J Manag. Care*, S40-8 (2008).

[0004] PD can be treated with L-DOPA or dopamine agonists, but there are significant side effects and the continuous neuronal death results in an increasing requirement for L-DOPA or dopamine agonists. Gene therapy has the potential to modify the behavior of neurons in the substantia nigra. Consequently, gene therapy has been considered as a possibility for effectively treating PD.

[0005] Initial clinical studies on PD gene therapy attempted to increase dopamine production in the substantia nigra by elevating the level of dopamine-synthesizing enzymes, particularly aromatic L-amino acid decarboxylase (AADC). Adeno-associated viral vectors (AAV) carrying the complementary DNA sequence for AADC were injected into the substantia nigra of patients afflicted with PD. In one study, delivery of AADC using adeno-associated virus (AAV) was well tolerated, but the clinical outcomes trended to only modest improvement. See, e.g., Eberling et al., 70(21) *Neurology,* 1989-93 (2008). After longer (e.g., 4-year) follow-up, the clinical impact was largely lost, and it was concluded that the dosing was insufficient for sustained clinical improvement.

[0006] An alternate approach sought to treat PD using gene therapy to increase expression of neurturin, a neurotrophic growth factor, in the substantia nigra. Results from AAV delivery of the neurturin gene to the brains of patients afflicted with PD showed no improvement over sham controls. See, e.g., Marks Jr. et al., 9(12) *Lancet Neurol.,* 1164-72 (2010).

[0007] Gene therapy trials designed to increase dopamine production or provide neurotrophic growth factors have not provided a significant, durable objective clinical response in patients with PD. See, e.g., Eberling et al., supra. Part of the reason why treatment for PD is complex and challenging is that disease progression is due to the accelerated death of dopaminergic neurons that eventually reduces dopamine below survivable levels.

[0008] Accordingly, current treatments for PD symptoms include drugs, ablative surgical intervention, and neural stimulation.

SUMMARY

[0009] In an aspect of the present disclosure, a lentiviral vector system is provided for expressing a lentiviral particle. The system includes a therapeutic vector which encodes a short hairpin RNA ("shRNA") for inhibiting Poly(ADP-ribose) polymerase ("PARP") expression. The system also includes an envelope plasmid comprising a neuron-specific sequence for targeting the shRNA to a neuron; and at least one helper plasmid comprising gag, pol, and rev genes. When the therapeutic vector, the envelope plasmid, and the at least one helper plasmid are transfected into a packaging cell line, a neuron-specific lentiviral particle optimized for inhibiting PARP expression is produced by the packaging cell line.

[0010] In embodiments, the shRNA comprises a PARP-specific shRNA. In embodiments, the shRNA comprises a PARP1-specific shRNA. In embodiments, the shRNA comprises at least 80% sequence identity with any one of SEQ ID NOs: 6-10. In embodiments, the shRNA comprises a shRNA having at least 85% sequence identity with any one of SEQ ID NOs: 6-10. In embodiments, the shRNA comprises a shRNA having at least 90% sequence identity with any one of SEQ ID NOs: 6-10. In embodiments, the shRNA comprises a shRNA having at least 95% sequence identity with any one of SEQ ID NOs: 6-10. In embodiments, the shRNA comprises any one of SEQ ID NOs: 6-10.

[0011] In embodiments, the shRNA comprises a shRNA having at least 80% sequence identity with any one of SEQ ID NOs: 16-20. In embodiments, the shRNA comprises a shRNA having at least 85% sequence identity with any one of SEQ ID NOs: 16-20. In embodiments, the shRNA comprises a shRNA having at least 90% sequence identity with any one of SEQ ID NOs: 16-20. In embodiments, the shRNA comprises a shRNA having at least 95% sequence identity with any one of SEQ ID NOs: 16-20. In embodiments, the shRNA comprises any one of SEQ ID NOs: 16-20. In embodiments, the neuron-specific sequence encodes VSV-G, FUG-C, or gp64, or a variant thereof. Optionally, the neuron-specific sequence encodes only VSV-G, or a variant thereof. The neuron-specific sequence may encode a protein that improves transduction into a neuron. The neuron-specific sequence may encode a protein that improves transduction into a neuron expressing tyrosine hydroxylase (TH+).

[0012] In another aspect, a method of treating a subject suffering from Parkinson's disease is disclosed. The method involves administering to the subject a therapeutic vector comprising a shRNA for inhibiting PARP expression; an envelope plasmid comprising a neuron-specific sequence for

targeting the shRNA to a neuron; and at least one helper plasmid comprising gag, pol, and rev genes. When the therapeutic vector, the envelope plasmid, and the at least one helper plasmid are transfected into at least one packaging cell, a neuron-specific lentiviral particle optimized for inhibiting PARP expression is produced by the packaging cell, and lentiviral particle is administered to the subject in need thereof. In embodiments, the lentiviral particle transduces a host cell to deliver the PARP shRNA. In embodiments, the shRNA comprises a PARP-specific shRNA. In embodiments, the shRNA comprises a PARP1-specific shRNA. In embodiments, the shRNA comprises a shRNA having at least 80% sequence identity with any one of SEQ ID NOs: 6-10. In embodiments, the shRNA comprises a shRNA having at least 85% sequence identity with any one of SEQ ID NOs: 6-10. In embodiments, the shRNA comprises a shRNA having at least 90% sequence identity with any one of SEQ ID NOs: 6-10. In embodiments, the shRNA comprises a shRNA having at least 95% sequence identity with any one of SEQ ID NOs: 6-10. In embodiments, the shRNA comprises any one of SEQ ID NOs: 6-10. In embodiments, the shRNA comprises a shRNA having at least 80% sequence identity with any one of SEQ ID NOs: 16-20. In embodiments, the shRNA comprises a shRNA having at least 85% sequence identity with any one of SEQ ID NOs: 16-20. In embodiments, the shRNA comprises a shRNA having at least 90% sequence identity with any one of SEQ ID NOs: 16-20. In embodiments, the shRNA comprises a shRNA having at least 95% sequence identity with any one of SEQ ID NOs: 16-20. In embodiments, the shRNA comprises any one of SEQ ID NOs: 16-20. The neuron-specific sequence may encode VSV-G, FUG-C, or gp64, or variants thereof. The neuron-specific sequence may encode only VSV-G, or variants thereof. The neuron-specific sequence may encode a protein that improves transduction into a neuron of the subject. The neuron-specific sequence may encode a protein that improves transduction into a neuron expressing tyrosing hydroxylase (TH+) of the subject.

[0013] In another aspect, a method of treating a subject suffering from Parkinson's disease is disclosed. The method involves administering to the subject a therapeutically effective amount of a lentiviral particle expressed by the lentiviral vector system as described herein. The method may also include a second therapeutic regimen. The second therapeutic regimen may include ablative surgical intervention, neural stimulation, L-DOPA administration, or dopamine agonist administration.

[0014] In another aspect, use of a therapeutic vector, an envelope plasmid, and at least one helper plasmid is disclosed for treating a subject suffering from Parkinson's disease. The therapeutic vector includes a shRNA to inhibit PARP expression. The envelope plasmid includes a neuron-specific sequence to target the shRNA to a neuron. One or more helper plasmids include at least one or more of a gag, pol, or rev gene.

[0015] By suppressing PARP levels, the lentiviral vector system disclosed herein reduces rates for neuronal death, preserves the capacity for normal dopamine production and delay or prevent the onset of Parkinson's disease. The lentiviral vector system disclosed herein, unlike AAVs, has a higher capacity for transducing resting cells, can be optimized to efficiently transduce neurons, and can generate a permanent modification by inserting a transgene into cellular DNA. Additionally, the lentiviral vector system disclosed herein is less inflammatory than AAVs, which allows for greater dose escalation, and allows for greater flexibility in vector design when testing for alternate envelope glycoproteins, vector composition, doses, and associated delivery methods.

[0016] Other aspects and advantages of the inventions described herein will become apparent from the following detailed description, taken in conjunction with the accompanying drawings, which illustrate by way of example the aspects of the inventions.

BRIEF DESCRIPTION OF THE DRAWINGS

[0017] The patent application or application file contains at least one drawing executed in color. If applicable, copies of this patent or patent application publication with color drawing(s) will be provided by the Office upon request and payment of the necessary fee.

[0018] FIG. **1**A depicts an exemplary lentiviral vector system comprised of an experimental therapeutic vector, an envelope plasmid, and a helper plasmid. The experimental therapeutic vector detailed in FIG. **1**A contains GFP. FIG. **1**B depicts an exemplary therapeutic vector designed to reduce expression of PARP1 in substantia nigra neurons in patients afflicted with PD. The therapeutic vector detailed in FIG. **1**B does not contain GFP. FIG. **1**C depicts an exemplary 3-vector lentiviral vector system in a circularized form that includes the experimental therapeutic vector detailed in FIG. **1**A. FIG. **1**D depicts an exemplary 4-vector lentiviral vector system in a circularized form that includes the experimental therapeutic vector detailed in FIG. **1**A. FIG. **1**E depicts an exemplary 3-vector lentiviral vector system in a circularized form that includes the therapeutic vector detailed in FIG. **1**B. FIG. **1**F depicts an exemplary 4-vector lentiviral vector system in a circularized form that includes the therapeutic vector detailed in FIG. **1**B.

[0019] FIG. **2** depicts results from a knockdown experiment involving PARP1 in human cells.

[0020] FIG. **3** depicts results from a knockdown experiment involving PARP1 in mouse cells.

[0021] FIG. **4** depicts neurons transduced with an exemplary lentiviral vector.

DETAILED DESCRIPTION

Overview of the Disclosure

[0022] Aspects of the present invention describe the development of a lentiviral vector system for treating PD. The lentiviral vector system includes a therapeutic vector that includes an inhibitory RNA construct for reducing the expression of PARP. The PARP1 protein has been implicated for its role in PD.

Definitions and Interpretation

[0023] Unless otherwise defined herein, scientific and technical terms used in connection with the present disclosure shall have the meanings that are commonly understood by those of ordinary skill in the art. Further, unless otherwise required by context, singular terms shall include pluralities and plural terms shall include the singular. Generally, nomenclature used in connection with, and techniques of, cell and tissue culture, molecular biology, immunology, microbiology, genetics and protein and nucleic acid chemistry and hybridization described herein are those well-

known and commonly used in the art. The methods and techniques of the present disclosure are generally performed according to conventional methods well-known in the art and as described in various general and more specific references that are cited and discussed throughout the present specification unless otherwise indicated. See, e.g.: Sambrook J. & Russell D. Molecular Cloning: A Laboratory Manual, 3rd ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y. (2000); Ausubel et al., Short Protocols in Molecular Biology: A Compendium of Methods from Current Protocols in Molecular Biology, Wiley, John & Sons, Inc. (2002); Harlow and Lane Using Antibodies: A Laboratory Manual; Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y. (1998); and Coligan et al., Short Protocols in Protein Science, Wiley, John & Sons, Inc. (2003). Any enzymatic reactions or purification techniques are performed according to manufacturer's specifications, as commonly accomplished in the art or as described herein. The nomenclature used in connection with, and the laboratory procedures and techniques of, analytical chemistry, synthetic organic chemistry, and medicinal and pharmaceutical chemistry described herein are those well-known and commonly used in the art.

[0024] As used herein, the term "includes" means includes without limitation.

[0025] As used herein, the term "lentiviral vector" is synonymous with the term "therapeutic vector." The term "experimental therapeutic vector" means a therapeutic vector that includes an experimental feature such as GFP.

[0026] As used herein, the term "miRNA" means a microRNA.

[0027] As used herein, the term "packaging cell line" refers to any cell line that can be used to express a lentiviral particle.

[0028] As used herein, the term "Parkinson's disease," which is also referred to herein as "PD," refers to the known neurodegenerative disease, as well as all symptoms related thereto. Treatment of "Parkinson's disease," therefore, may relate to treatment of all or some of the symptoms associated with Parkinson's disease.

[0029] As used herein, the term "PARP" stands for poly ADP ribose polymerase and includes all PARP-family members, and includes the specific PARP-family member, PARP1 (accession number NM_001618.3) and variants thereof.

[0030] The term "percent identity," which is also referred to herein as "sequence identity," in the context of two or more nucleic acid or polypeptide sequences, refer to two or more sequences or subsequences that have a specified percentage of nucleotides or amino acid residues that are the same, when compared and aligned for maximum correspondence, as measured using one of the sequence comparison algorithms described below (e.g., BLASTP and BLASTN or other algorithms available to persons of skill) or by visual inspection. Depending on the application, the "percent identity" can exist over a region of the sequence being compared, e.g., over a functional domain, or, alternatively, exist over the full length of the two sequences to be compared. For sequence comparison, typically one sequence acts as a reference sequence to which test sequences are compared. When using a sequence comparison algorithm, test and reference sequences are input into a computer, subsequence coordinates are designated, if necessary, and sequence algorithm program parameters are designated. The sequence comparison algorithm then calculates the percent sequence identity for the test sequence(s) relative to the reference sequence, based on the designated program parameters.

[0031] Optimal alignment of sequences for comparison can be conducted, e.g., by the local homology algorithm of Smith & Waterman, *Adv. Appl. Math.* 2:482 (1981), by the homology alignment algorithm of Needleman & Wunsch, *J. Mol. Biol.* 48:443 (1970), by the search for similarity method of Pearson & Lipman, *Proc. Natl. Acad. Sci. U.S.A.* 85:2444 (1988), by computerized implementations of these algorithms (GAP, BESTFIT, FASTA, and TFASTA in the Wisconsin Genetics Software Package, Genetics Computer Group, 575 Science Dr., Madison, Wis.), or by visual inspection (see generally Ausubel et al., infra).

[0032] One example of an algorithm that is suitable for determining percent sequence identity and sequence similarity is the BLAST algorithm, which is described in Altschul et al., *J. Mol. Biol.* 215:403-410 (1990). Software for performing BLAST analyses is publicly available through the National Center for Biotechnology Information website.

[0033] The percent identity between two nucleotide sequences can be determined using the GAP program in the GCG software package (available at http://www.gcg.com), using a NWSgapdna.CMP matrix and a gap weight of 40, 50, 60, 70, or 80 and a length weight of 1, 2, 3, 4, 5, or 6. The percent identity between two nucleotide or amino acid sequences can also be determined using the algorithm of E. Meyers and W. Miller (*CABIOS,* 4:11-17 (1989)) which has been incorporated into the ALIGN program (Version 2.0), using a PAM120 weight residue table, a gap length penalty of 12 and a gap penalty of 4. In addition, the percent identity between two amino acid sequences can be determined using the Needleman and Wunsch (*J. Mol. Biol.* (48):444-453 (1970)) algorithm which has been incorporated into the GAP program in the GCG software package (available at http://www.gcg.com), using either a Blossum 62 matrix or a PAM250 matrix, and a gap weight of 16, 14, 12, 10, 8, 6, or 4 and a length weight of 1, 2, 3, 4, 5, or 6.

[0034] The nucleic acid and/or protein sequences of the present disclosure can further be used as a "query sequence" to perform a search against public databases to, for example, identify related sequences. Such searches can be performed using the NBLAST and XBLAST programs (version 2.0) of Altschul et al. (1990) *J. Mol. Biol.* 215:403-10. BLAST nucleotide searches can be performed with the NBLAST program, score=100, word length=12 to obtain nucleotide sequences homologous to the nucleic acid molecules provided in the disclosure. BLAST protein searches can be performed with the XBLAST program, score=50, wordlength=3 to obtain amino acid sequences homologous to the protein molecules of the disclosure. To obtain gapped alignments for comparison purposes, Gapped BLAST can be utilized as described in Altschul et al., (1997) *Nucleic Acids Res.* 25(17):3389-3402. When utilizing BLAST and Gapped BLAST programs, the default parameters of the respective programs (e.g., XBLAST and NBLAST) can be used. See http://www.ncbi.nlm.nih.gov.

[0035] As used herein, the term "plasmid" is synonymous with the term "vector."

[0036] As used herein, the term "SEQ ID NO" is synonymous with the term "Sequence ID No."

[0037] As used herein, the term "shRNA" refers to a short hairpin RNA.

[0038] As used herein, the term "subject" includes a human patient but also includes other mammals.

[0039] As used herein, the term "TH" refers to tyrosine hydroxylase.

Description of Aspects of the Disclosure

[0040] In an aspect of the disclosure, the present disclosure provides a lentiviral vector system for expressing a lentiviral particle. The system includes a therapeutic vector which includes a shRNA for inhibiting PARP-family member expression. There are numerous PARP family members and this disclosure is not limited to any one particular PARP-family member. However, in embodiments, the lentiviral vector system specifically inhibits PARP1.

[0041] The system includes at least one helper plasmid comprising at least one of a gag, pol, or rev gene. Each of the gag, pol and rev genes may be provided on individual plasmids, or one or more genes may be provided together on the same plasmid. In embodiments, the gag, pol, and rev genes are provided on the same plasmid (e.g., FIG. **1**C). In embodiments, the gag and pol genes are provided on a first plasmid and the rev gene is provided on a second plasmid (e.g., FIG. **1**D). In further embodiments, 3-vector and 4-vector systems are provided herein.

[0042] As detailed herein, the therapeutic vector, the envelope plasmid and at least one helper plasmid are transfected into a packaging cell line. A non-limiting example of a packaging cell line is the 293T/17 HEK cell line. When the therapeutic vector, the envelope plasmid, and at least one helper plasmid are transfected into the packaging cell line, a lentiviral particle is produced. Under the experimental conditions described herein, the lentiviral particle produced by the lentiviral vector system can be a neuron-specific lentiviral particle which is optimized for inhibiting PARP expression.

[0043] In embodiments, the shRNA comprises a PARP-specific shRNA. In embodiments, the shRNA comprises a PARP1-specific shRNA. In embodiments, the shRNA comprises a shRNA having at least 80%, or at least 81%, or at least 82%, or at least 83%, or at least 84% sequence identity with any one of SEQ ID NOs: 6-10. In embodiments, the shRNA comprises a shRNA having at least 85%, or at least 86%, or at least 87%, or at least 88%, or at least 89% sequence identity with any one of SEQ ID NOs: 6-10. In embodiments, the shRNA comprises a shRNA having at least 90%, or at least 91%, or at least 92%, or at least 93%, or at least 94% sequence identity with any one of SEQ ID NOs: 6-10. In embodiments, the shRNA comprises a shRNA having at least 95%, or at least 96%, or at least 97%, or at least 98%, or at least 99% with any one of SEQ ID NOs: 6-10. In embodiments, the shRNA comprises any one of SEQ ID NOs: 6-10.

[0044] In embodiments, the shRNA comprises a shRNA having at least 80%, or at least 81%, or at least 82%, or at least 83%, or at least 84% sequence identity with any one of SEQ ID NOs: 16-20. In embodiments, the shRNA comprises a shRNA having at least 85%, or at least 86%, or at least 87%, or at least 88%, or at least 89% sequence identity with any one of SEQ ID NOs: 16-20. In embodiments, the shRNA comprises a shRNA having at least 90%, or at least 91%, or at least 92%, or at least 93%, or at least 94% sequence identity with any one of SEQ ID NOs: 16-20. In embodiments, the shRNA comprises a shRNA having at least 95%, or at least 96%, or at least 97%, or at least 98%, or at least 99% sequence identity with any one of SEQ ID NOs: 16-20. In embodiments, the shRNA comprises any one of SEQ ID NOs: 16-20. In embodiments, any of the foregoing shRNAs can be replaced with a suitable miRNA. In embodiments, the neuron-specific sequence encodes VSV-G, FUG-C, or gp64 or any other sequence that confers tropic specificity to neuron cells. Optionally, the neuron-specific sequence encodes only VSV-G. In embodiments, the neuron-specific sequence encodes a protein that improves transduction into a neuron. In embodiments, the neuron-specific sequence encodes a protein that improves transduction into a TH+ neuron.

[0045] In another aspect of the disclosure, a method of treating a subject suffering from PD is disclosed. In embodiments, the subject is a human being afflicted with mild, moderate, or severe PD. In embodiments, the subject is a human being afflicted with any symptom commonly or uncommonly associated with PD.

[0046] The method involves administering to the subject a lentiviral therapeutic vector comprising a shRNA for inhibiting PARP expression. In embodiments, the lentiviral vector is packaged as a lentiviral particle that transduces a host cell to deliver the PARP shRNA.

[0047] In embodiments, the shRNA comprises a PARP-specific shRNA. In embodiments, the shRNA comprises a PARP1-specific shRNA. In embodiments, the shRNA comprises a shRNA having at least 80%, or at least 81%, or at least 82%, or at least 83%, or at least 84% sequence identity with any one of SEQ ID NOs: 6-10. In embodiments, the shRNA comprises a shRNA having at least 85%, or at least 86%, or at least 87%, or at least 88%, or at least 89% sequence identity with any one of SEQ ID NOs: 6-10. In embodiments, the shRNA comprises a shRNA having at least 90%, or at least 91%, or at least 92%, or at least 93%, or at least 94% sequence identity with any one of SEQ ID NOs: 6-10. In embodiments, the shRNA comprises a shRNA having at least 95%, or at least 96%, or at least 97%, or at least 98%, or at least 99% sequence identity with any one of SEQ ID NOs: 6-10. In embodiments, the shRNA comprises any one of SEQ ID NOs: 6-10.

[0048] In embodiments, the shRNA comprises a shRNA having at least 80%, or at least 81%, or at least 82%, or at least 83%, or at least 84% sequence identity with any one of SEQ ID NOs: 16-20. In embodiments, the shRNA comprises a shRNA having at least 85%, or at least 86%, or at least 87%, or at least 88%, or at least 89% sequence identity with any one of SEQ ID NOs: 16-20. In embodiments, the shRNA comprises a shRNA having at least 90%, or at least 91%, or at least 92%, or at least 93%, or at least 94% sequence identity with any one of

[0049] SEQ ID NOs: 16-20. In embodiments, the shRNA comprises a shRNA having at least 95%, or at least 96%, or at least 97%, or at least 98%, or at least 99% sequence identity with any one of SEQ ID NOs: 16-20. In embodiments, the shRNA comprises any one of SEQ ID NOs: 16-20. In embodiments, any of the foregoing shRNAs can be replaced with a suitable miRNA. In embodiments, the neuron-specific sequence encodes VSV-G, FUG-C, or gp64 or any other sequence that confers tropic specificity to neuron cells. Optionally, the neuron-specific sequence encodes only VSV-G. In embodiments, the neuron-specific sequence encodes a protein that improves transduction into

a neuron of the subject. In embodiments, the neuron-specific sequence encodes a protein that improves transduction into a TH+ neuron of the subject.

[0050] In another aspect, a method of treating a subject suffering from PD is disclosed. The method involves administering to the subject a therapeutically effective amount of a lentiviral particle expressed by the lentiviral vector system as described herein. In embodiments, the method includes a second therapeutic regimen. In embodiments, the second therapeutic regimen includes, but is not limited to: ablative surgical intervention, neural stimulation, L-DOPA administration, dopamine agonist administration, or any other known Parkinson's disease treatment. In embodiments, the system disclosed herein can be used to treat PD while eliminating the need for increasing doses of L-DOPA.

Lentiviral Vector System

[0051] A lentiviral virion (particle) is expressed by a vector system encoding the necessary viral proteins to produce a virion (viral particle). There is at least one vector containing a nucleic acid sequence encoding the lentiviral poi proteins necessary for reverse transcription and integration, operably linked to a promoter. In another embodiment, the pol proteins are expressed by multiple vectors.

[0052] In another aspect, use of a therapeutic vector, an envelope plasmid, and at least one helper plasmid is disclosed for treating a subject suffering from PD. The therapeutic vector includes a shRNA to inhibit PARP expression. In embodiments, the envelope plasmid includes a neuron-specific sequence to target the shRNA to a neuron and at least one helper plasmid that includes gag, pol, and rev genes.

[0053] By suppressing PARP levels, the lentiviral vector system disclosed herein will reduce rates for neuronal death, preserve the capacity for normal dopamine production and delay and/or prevent the onset of PD. The lentiviral vector system disclosed herein, unlike AAV systems known in the art, has a higher capacity for transducing resting cells, can be optimized to efficiently transduce neurons, and can generate a permanent modification by inserting a transgene into cellular DNA. Additionally, the lentiviral vector system disclosed herein is less inflammatory than AAV systems, which allows for greater dose escalation, and allows for greater flexibility in vector design when testing for alternate envelope glycoproteins, vector composition, doses and associated delivery methods.

[0054] The disclosed lentiviral vector system can be optimized for short, medium, or long-term suppression of PARP expression in subjects afflicted with PD. Accordingly, dosing regimens may vary based upon the severity of the PD, or the associated PD symptoms. The lentiviral particles disclosed herein may be administered to a subject in need thereof in varying doses. A subject may be administered $\geq 10^6$ transducing units of lentiviral particle suspension (where 1 dose is needed on average to transduce 1 target cell). A subject may be administered $\geq 10^6$, $\geq 10^7$, $\geq 10^8$, $\geq 10^9$, or $\geq 10^{10}$ transducing units. Upper dosing limits will be determined by a variety of factors understood by those persons skilled in the art.

[0055] The vector(s) forming the lentiviral particle preferably do not contain a nucleic acid sequence from the lentiviral genome that expresses an envelope protein. Preferably, a separate vector that contains a nucleic acid sequence encoding an envelope protein operably linked to a promoter is used. This env vector also does not contain a lentiviral packaging sequence. In one embodiment, the env nucleic acid sequence encodes a lentiviral envelope protein.

[0056] In another embodiment, the envelope protein is not from the lentivirus, but from a different virus. The resultant particle is referred to as a pseudotyped particle. By appropriate selection of envelopes one can "infect" virtually any cell. For example, one can use an env gene that encodes an envelope protein that targets an endocytic compartment such as that of the influenza virus, VSV-G, alpha viruses (Semliki forest virus, Sindbis virus), arenaviruses (lymphocytic choriomeningitis virus). flaviviruses (tick-home encephalitis virus, Dengue virus, hepatitis C virus, GB virus), rhabdoviruses (vesicular stomatitis virus, rabies virus), paramyxoviruses (mumps or measles). picornaviruses (Mengo, Polio, and Coxsackie), and orthomyxoviruses (influenza virus). Other envelopes that can preferably be used include those from Moloney Leukemia Virus such as MLV-E, MLV-A and GALV. These latter envelopes are particularly preferred where the host cell is a primary cell. Other envelope proteins can be selected depending upon the desired host cell. For example, targeting specific receptors such as a dopamine receptor can be used for brain delivery. Another target can be vascular endothelium. These cells can be targeted using a filovirus envelope. For example, the GP of Ebola., which by post-transcriptional modification become the GP, and GP_2 glycoproteins. In another embodiment, one can use different lentiviral capsids with a pseudotyped envelope (for example, Hy or SHIV [U.S. Pat. No. 5,654,195]). A SHIV pseudotyped vector can readily be used in animal models such as monkeys.

[0057] As detailed herein, a lentiviral vector system typically includes at least one helper plasmid comprising at least one of a gag, pol, or rev gene. Each of the gag, pol and rev genes may be provided on individual plasmids, or one or more genes may be provided together on the same plasmid. In one embodiment, the gag, pol, and rev genes are provided on the same plasmid (e.g., FIG. **1**C). In another embodiment, the gag and pol genes are provided on a first plasmid and the rev gene is provided on a second plasmid (e.g., FIG. **1**D). Accordingly, both 3-vector and 4-vector systems can be used to produce a lentivirus as described in the Examples section and elsewhere herein. The therapeutic vector, the envelope plasmid and at least one helper plasmid are transfected into a packaging cell line. A non-limiting example of a packaging cell line is the 293T/17 HEK cell line. When the therapeutic vector, the envelope plasmid, and at least one helper plasmid are transfected into the packaging cell line, a lentiviral particle is produced.

[0058] In another aspect, a lentiviral vector system for expressing a lentiviral particle is disclosed. The system includes a lentiviral vector as described herein; an envelope plasmid for expressing an envelope protein optimized for infecting a cell; and at least one helper plasmid for expressing gag, pol, and rev genes, wherein when the lentiviral vector, the envelope plasmid, and the at least one helper plasmid are transfected into a packaging cell line, a lentiviral particle is produced by the packaging cell line, wherein the lentiviral particle is capable of inhibiting production of PARP1.

[0059] In another aspect, and as detailed in FIG. **1**C, the lentiviral vector, which is also referred to herein as a therapeutic vector, includes the following elements: a hybrid 5' long terminal repeat (RSV/5' LTR) (SEQ ID NOS: 21-22),

a HIV gag (SEQ ID NO: 23), a RRE (Rev-response element) (SEQ ID NO: 24), a Env element (SEQ ID NO: 25), a cPPT (SEQ ID NO: 26), a H1 promoter (SEQ ID NO: 27), a shRNA targeting PARP1 (shPARP1) (SEQ ID NOS: 6-10), a EF1 promoter (SEQ ID NO: 28), a GFP element (SEQ ID NO:29), a Woodchuck Post-Transcriptional Regulatory Element (WPRE) (SEQ ID NO: 30), and a 3' LTR delta U3 (SEQ ID NO: 31). In another aspect, sequence variation, by way of substitution, deletion, addition, or mutation can be used to modify the sequences references herein.

[0060] In another aspect, and as detailed herein for example in FIG. **1**C, a helper plasmid has been designed to include the following elements: CMV enhancer (SEQ ID NO: 32); a chicken beta actin promoter (SEQ ID NO: 33); a chicken beta actin intron (SEQ ID NO: 34); a HIV gag (SEQ ID NO: 23); a HIV Pol (SEQ ID NO: 35); a HIV Int (SEQ ID NO: 36); a HIV RRE (SEQ ID NO: 24); a HIV Rev (SEQ ID NO: 37); and a rabbit beta globin poly A (SEQ ID NO: 38). In another aspect, the helper plasmid may be modified to include a first helper plasmid for expressing the gag and pol genes, and a second and separate plasmid for expressing the rev gene. In another aspect, sequence variation, by way of substitution, deletion, addition, or mutation can be used to modify the sequences references herein.

[0061] In another aspect, and as detailed herein for example in FIG. **1**C, an envelope plasmid has been designed to include the following elements being from left to right: a CMV promoter (SEQ ID NO: 39); a beta globin intron (SEQ ID NO: 40); a VSV-G (SEQ ID NO:

[0062] 25); and a rabbit beta globin poly A (SEQ ID NO: 38). In another aspect, sequence variation, by way of substitution, deletion, addition, or mutation can be used to modify the sequences references herein.

[0063] In another aspect, the plasmids used for lentiviral packaging can be modified with similar elements and the intron sequences can potentially be removed without loss of vector function. For example, the following elements can replace similar elements in the plasmids that comprise the packaging system: Elongation Factor-1 (EF-1), phosphoglycerate kinase (PGK), and ubiquitin C (UbC) promoters can replace the CMV or CAG promoter. SV40 poly A and bGH poly A can replace the rabbit beta globin poly A. The HIV sequences in the helper plasmid can be constructed from different HIV strains or clades. The VSV-G glycoprotein can be substituted with membrane glycoproteins from feline endogenous virus (RD114), gibbon ape leukemia virus (GALV), Rabies (FUG), lymphocytic choriomeningitis virus (LCMV), influenza A fowl plague virus (FPV), Ross River alphavirus (RRV), murine leukemia virus 10A1 (MLV), or Ebola virus (EboV).

[0064] Of note, lentiviral packaging systems can be acquired commercially (e.g., Lenti-vpak packaging kit from OriGene Technologies, Inc., Rockville, Md.), and can also be designed as described herein. Moreover, it is within the skill of a person skilled in the art to substitute or modify aspects of a lentiviral packaging system to improve any number of relevant factors, including the production efficiency of a lentiviral particle.

Doses and Dosage Forms

[0065] Dosing may occur once per day or several times per day. Dosing may occur with intervals in between dosing. For example, a subject may be treated on a first day, and then treated every other day, or every second day, or every third day, or every fourth day, or every fifth day, or every sixth day, or every seventh day, or every second week, or every month, etc. However, dosing can also occur once, twice, or several times per year, and such a dosing schedule can be repeated on a yearly basis. A lentiviral particle can be delivered by any method suitable for treating symptoms associated with PD. For example, dosing can be made via direct injection into the brain stem using a guided needle. This will likely occur in conjunction with deep brain stimulation.

[0066] In another aspect, a pharmaceutical composition comprising a lentiviral particle as described herein can be formulated in a solid dosage form. The solid dosage form can include excipients known to those skilled in the art. The lentiviral particle as described herein can be formulated in a gel form, a foam form, a biodegradable capsule form, a nanoparticle form, or can be formulated with liposomes or other structures known to those skilled in the art. The solid dosage form can be formulated for immediate release or a modified release. Modified release dosage forms include controlled or extended release forms.

[0067] The following examples are given for the purpose of illustrating various embodiments of the invention and are not meant to limit the invention in any fashion. The present examples, along with the methods described herein are presently representative of preferred embodiments, are exemplary, and are not intended as limitations on the scope of the invention. Changes therein, and other uses which are encompassed within the spirit of the invention as defined by the scope of the claims, will occur to those persons skilled in the art.

EXAMPLES

Example 1

Development of a Lentiviral Vector System

[0068] A lentiviral vector system was developed as summarized generally in FIG. **1**. Lentiviral particles were produced in 293T/17 HEK cells (purchased from American Type Culture Collection, Manassas, Va.) following transfection with the therapeutic vector, the envelope plasmid, and the helper plasmid. The transfection of 293T/17 HEK cells, which produced functional viral particles, employed the reagent Poly(ethylenimine) (PEI) to increase the efficiency of plasmid DNA uptake. The plasmids and DNA were initially added separately in culture medium without serum in a ratio of 3:1 (mass ratio of PEI to DNA). After 2-3 days, cell medium was collected and lentiviral particles were purified by high-speed centrifugation and/or filtration followed by anion-exchange chromatography. The concentration of lentiviral particles can be expressed in terms of transducing units/ml (TU/ml). The determination of TU was accomplished by measuring HIV p24 levels in culture fluids (p24 protein is incorporated into lentiviral particles), measuring the number of viral DNA copies per cell by quantitative PCR, or by infecting cells and using light (if the vectors encode luciferase or fluorescent protein markers).

[0069] A 3-vector system (i.e., a 2-vector lentiviral packaging system) was designed for the production of lentiviral particles. A schematic of the 3-vector system is shown in FIGS. **1**A, **1**C, and **1**E. Briefly, and with reference to FIGS. **1**C and **1**E, the top-most vector is a helper plasmid, which, in this case, includes Rev. The vector appearing in the

middle of FIGS. **1**C and **1**E is the envelope plasmid. The bottom-most vector is the therapeutic vector, as described herein.

[0070] Referring to FIGS. **1**C and **1**E, the Helper plus Rev plasmid includes a CMV enhancer (SEQ ID NO: 32); a chicken beta actin promoter (SEQ ID NO: 33); a chicken beta actin intron (SEQ ID NO: 34); a HIV gag (SEQ ID NO: 23); a HIV Pol (SEQ ID NO: 35); a HIV Int (SEQ ID NO: 36); a HIV RRE (SEQ ID NO: 24); a HIV Rev (SEQ ID NO: 37); and a rabbit beta globin poly A (SEQ ID NO: 38). The Helper plus Rev plasmid is also shown in a linear form in FIG. **1**A.

[0071] Referring to FIGS. **1**C and **1**E, the Envelope plasmid includes a CMV promoter (SEQ ID NO: 39); a beta globin intron (SEQ ID NO: 40); a VSV-G (SEQ ID NO: 25); and a rabbit beta globin poly A (SEQ ID NO: 38). The Envelope plasmid is also shown in a linear form in FIG. **1**A.

[0072] Synthesis of a 2-Vector Lentiviral Packaging System including Helper (plus Rev) and Envelope Plasmids.

[0073] Materials and Methods:

[0074] Construction of the helper plasmid: The helper plasmid was constructed by initial PCR amplification of a DNA fragment from the pNL4-3 HIV plasmid (NIH Aids Reagent Program) containing Gag, Pol, and Integrase genes. Primers were designed to amplify the fragment with EcoRI and NotI restriction sites which could be used to insert at the same sites in the pCDNA3 plasmid (Invitrogen). The forward primer was (5'-TAAGCAGAATTC ATGAATTTGCCAGGAAGAT-3') (SEQ ID NO: 41) and reverse primer was (5'-CCATACAATGAATGGACACTAGGCGGCCGCACGAAT-3') (SEQ ID NO: 42).

[0075] The sequence for the Gag, Pol, Integrase fragment was as follows:

(SEQ ID NO: 43)

GAATTCATGAATTTGCCAGGAAGATGGAAACCAAAAATGATAGGGGGAATTGGA

GGTTTTATCAAAGTAAGACAGTATGATCAGATACTCATAGAAATCTGCGGACATA

AAGCTATAGGTACAGTATTAGTAGGACCTACACCTGTCAACATAATTGGAAGAA

ATCTGTTGACTCAGATTGGCTGCACTTTAAATTTTCCCATTAGTCCTATTGAGACT

GTACCAGTAAAATTAAAGCCAGGAATGGATGGCCCAAAAGTTAAACAATGGCCA

TTGACAGAAGAAAAAATAAAAGCATTAGTAGAAATTTGTACAGAAATGGAAAAG

GAAGGAAAAATTTCAAAAATTGGGCCTGAAAATCCATACAATACTCCAGTATTT

GCCATAAAGAAAAAAGACAGTACTAAATGGAGAAAATTAGTAGATTTCAGAGAA

CTTAATAAGAGAACTCAAGATTTCTGGGAAGTTCAATTAGGAATACCACATCCTG

CAGGGTTAAAACAGAAAAAATCAGTAACAGTACTGGATGTGGGCGATGCATATT

TTTCAGTTCCCTTAGATAAAGACTTCAGGAAGTATACTGCATTTACCATACCTAG

TATAAACAATGAGACACCAGGGATTAGATATCAGTACAATGTGCTTCCACAGGG

-continued

ATGGAAAGGATCACCAGCAATATTCCAGTGTAGCATGACAAAAATCTTAGAGCC

TTTTAGAAAACAAAATCCAGACATAGTCATCTATCAATACATGGATGATTTGTAT

GTAGGATCTGACTTAGAAATAGGGCAGCATAGAACAAAAATAGAGGAACTGAG

ACAACATCTGTTGAGGTGGGGATTTACCACACCAGACAAAAAACATCAGAAAGA

ACCTCCATTCCTTTGGATGGGTTATGAACTCCATCCTGATAAATGGACAGTACAG

CCTATAGTGCTGCCAGAAAAGGACAGCTGGACTGTCAATGACATACAGAAATTA

GTGGGAAAATTGAATTGGGCAAGTCAGATTTATGCAGGGATTAAAGTAAGGCAA

TTATGTAAACTTCTTAGGGGAACCAAAGCACTAACAGAAGTAGTACCACTAACA

GAAGAAGCAGAGCTAGAACTGGCAGAAAACAGGGAGATTCTAAAAGAACCGGT

ACATGGAGTGTATTATGACCCATCAAAAGACTTAATAGCAGAAATACAGAAGCA

GGGGCAAGGCCAATGGACATATCAAATTTATCAAGAGCCATTTAAAAATCTGAA

AACAGGAAAGTATGCAAGAATGAAGGGTGCCCACACTAATGATGTGAAACAATT

AACAGAGGCAGTACAAAAAATAGCCACAGAAAGCATAGTAATATGGGGAAAGA

CTCCTAAATTTAAATTACCCATACAAAAGGAAACATGGGAAGCATGGTGGACAG

AGTATTGGCAAGCCACCTGGATTCCTGAGTGGGAGTTTGTCAATACCCCTCCCTT

AGTGAAGTTATGGTACCAGTTAGAGAAAGAACCCATAATAGGAGCAGAAACTTT

CTATGTAGATGGGGCAGCCAATAGGGAAACTAAATTAGGAAAAGCAGGATATGT

AACTGACAGAGGAAGACAAAAAGTTGTCCCCCTAACGGACACAACAAATCAGAA

GACTGAGTTACAAGCAATTCATCTAGCTTTGCAGGATTCGGGATTAGAAGTAAAC

ATAGTGACAGACTCACAATATGCATTGGGAATCATTCAAGCACAACCAGATAAG

AGTGAATCAGAGTTAGTCAGTCAAATAATAGAGCAGTTAATAAAAAAGGAAAAA

GTCTACCTGGCATGGGTACCAGCACACAAAGGAATTGGAGGAAATGAACAAGTA

GATAAATTGGTCAGTGCTGGAATCAGGAAAGTACTATTTTTAGATGGAATAGATA

AGGCCCAAGAAGAACATGAGAAATATCACAGTAATTGGAGAGCAATGGCTAGTG

ATTTTAACCTACCACCTGTAGTAGCAAAAGAAATAGTAGCCAGCTGTGATAAATG

TCAGCTAAAAGGGGAAGCCATGCATGGACAAGTAGACTGTAGCCCAGGAATATG

GCAGCTAGATTGTACACATTTAGAAGGAAAAGTTATCTTGGTAGCAGTTCATGTA

-continued

GCCAGTGGATATATAGAAGCAGAAGTAATTCCAGCAGAGACA-
GGGCAAGAAAC

AGCATACTTCCTCTTAAAATTAGCAGGAAGATGGCCAGTAAAAACAGTA-
CATAC

AGACAATGGCAGCAATTTCACCAGTACTACAGTTAAGGCCGCCTGTTG-
GTGGGC

GGGGATCAAGCAGGAATTTGGCATTCCCTACAATCCCCAAAGTCAAGGAG-
TAAT

AGAATCTATGAATAAAGAATTAAAGAAAATTATAGGACAGGTAAGA-
GATCAGGC

TGAACATCTTAAGACAGCAGTACAAATGGCAGTATTCATCCACAATTT-
TAAAAGA

AAAGGGGGGATTGGGGGGTACAGTGCAGGGGAAAGAATAGTAGA-
CATAATAGC

AACAGACATACAAACTAAAGAATTACAAAAACAAATTACAAAAAT-
TCAAAATTT

TCGGGTTTATTACAGGGACAGCAGAGATCCAGTTTGGAAAGGACCAG-
CAAAGCT

CCTCTGGAAAGGTGAAGGGGCAGTAGTAATACAAGATAATAGT-
GACATAAAAGT

AGTGCCAAGAAGAAAAGCAAAGATCATCAGGGATTATGGAAAACAGATG-
GCAG

GTGATGATTGTGTGGCAAGTAGACAGGATGAGGATTAA

[0076] Next, a DNA fragment containing the Rev, RRE, and rabbit beta globin poly A sequence with XbaI and XmaI flanking restriction sites was synthesized by MWG Operon. The DNA fragment was then inserted into the plasmid at the XbaI and XmaI restriction sites The DNA sequence was as follows:

(SEQ ID NO: 44)

TCTAGAATGGCAGGAAGAAGCGGAGACAGCGACGAAGAGCTCATCAGAA

CAGTCAGACTCATCAAGCTTCTCTATCAAAGCAACCCACCTCCCAATCC

CGAGGGGACCCGACAGGCCCGAAGGAATAGAAGAAGAAGGTGGAGAGAG

AGACAGAGACAGATCCATTCGATTAGTGAACGGATCCTTGGCACTTATC

TGGGACGATCTGCGGAGCCTGTGCCTCTTCAGCTACCACCGCTTGAGAG

ACTTACTCTTGATTGTAACGAGGATTGTGGAACTTCTGGGACGCAGGGG

GTGGGAAGCCCTCAAATATTGGTGGAATCTCCTACAATATTGGAGTCAG

GAGCTAAAGAATAGAGGAGCTTTGTTCCTTGGGTTCTTGGGAGCAGCAG

GAAGCACTATGGGCGCAGCGTCAATGACGCTGACGGTACAGGCCAGACA

ATTATTGTCTGGTATAGTGCAGCAGCAGAACAATTTGCTGAGGGCTATT

GAGGCGCAACAGCATCTGTTGCAACTCACAGTCTGGGGCATCAAGCAGC

TCCAGGCAAGAATCCTGGCTGTGGAAAGATACCTAAAGGATCAACAGCT

CCTAGATCTTTTTCCCTCTGCCAAAAATTATGGGGACATCATGAAGCCC

CTTGAGCATCTGACTTCTGGCTAATAAAGGAAATTTATTTTCATTGCAA

TAGTGTGTTGGAATTTTTTGTGTCTCTCACTCGGAAGGACATATGGGAG

GGCAAATCATTTAAAACATCAGAATGAGTATTTGGTTTAGAGTTTGGCA

ACATATGCCATATGCTGGCTGCCATGAACAAAGGTGGCTATAAAGAGGT

-continued

CATCAGTATATGAAACAGCCCCCTGCTGTCCATTCCTTATTCCATAGAA

AAGCCTTGACTTGAGGTTAGATTTTTTTTATATTTTGTTTTGTGTTATT

TTTTTCTTTAACATCCCTAAAATTTTCCTTACATGTTTTACTAGCCAGA

TTTTTCCTCCTCTCCTGACTACTCCCAGTCATAGCTGTCCCTCTTCTCT

TATGAAGATCCCTCGACCTGCAGCCCAAGCTTGGCGTAATCATGGTCAT

AGCTGTTTCCTGTGTGAAATTGTTATCCGCTCACAATTCCACACAACAT

ACGAGCCGGAAGCATAAAGTGTAAAGCCTGGGGTGCCTAATGAGTGAGC

TAACTCACATTAATTGCGTTGCGCTCACTGCCCGCTTTCCAGTCGGGAA

ACCTGTCGTGCCAGCGGATCCGCATCTCAATTAGTCAGCAACCATAGTC

CCGCCCCTAACTCCGCCCATCCCGCCCCTAACTCCGCCCAGTTCCGCCC

ATTCTCCGCCCCATGGCTGACTAATTTTTTTTATTTATGCAGAGGCCGA

GGCCGCCTCGGCCTCTGAGCTATTCCAGAAGTAGTGAGGAGGCTTTTTT

GGAGGCCTAGGCTTTTGCAAAAAGCTAACTTGTTTATTGCAGCTTATAA

TGGTTACAAATAAAGCAATAGCATCACAAATTTCACAAATAAAGCATTT

TTTTCACTGCATTCTAGTTGTGGTTTGTCCAAACTCATCAATGTATCTT

ATCAGCGGCCGCCCCGGG

[0077] Finally, the CMV promoter of pCDNA3.1 was replaced with the CAG enhancer/promoter plus a chicken beta actin intron sequence. A DNA fragment containing the CAG enhancer/promoter/intron sequence with MluI and EcoRI flanking restriction sites was synthesized by MWG Operon. The DNA fragment was then inserted into the plasmid at the MluI and EcoRI restriction sites. The DNA sequence was as follows:

(SEQ ID NO: 45)

ACGCGTTAGTTATTAATAGTAATCAATTACGGGGTCATTAGTTCATAGC

CCATATATGGAGTTCCGCGTTACATAACTTACGGTAAATGGCCCGCCTG

GCTGACCGCCCAACGACCCCCGCCCATTGACGTCAATAATGACGTATGT

TCCCATAGTAACGCCAATAGGGACTTTCCATTGACGTCAATGGGTGGAC

TATTTACGGTAAACTGCCCACTTGGCAGTACATCAAGTGTATCATATGC

CAAGTACGCCCCCTATTGACGTCAATGACGGTAAATGGCCCGCCTGGCA

TTATGCCCAGTACATGACCTTATGGGACTTTCCTACTTGGCAGTACATC

TACGTATTAGTCATCGCTATTACCATGGGTCGAGGTGAGCCCCACGTTC

TGCTTCACTCTCCCCATCTCCCCCCCCTCCCCACCCCCAATTTTGTATT

TATTTATTTTTTAATTATTTTGTGCAGCGATGGGGGCGGGGGGGGGGGG

GGCGCGCGCCAGGCGGGGCGGGGCGGGGCGAGGGGCGGGGCGGGGCGAG

GCGGAGAGGTGCGGCGGCAGCCAATCAGAGCGGCGCGCTCCGAAAGTTT

CCTTTTATGGCGAGGCGGCGGCGGCGGCGGCCCTATAAAAAGCGAAGCG

CGCGGCGGGCGGGAGTCGCTGCGTTGCCTTCGCCCCGTGCCCCGCTCCG

CGCCGCCTCGCGCCGCCCGCCCCGGCTCTGACTGACCGCGTTACTCCCA

CAGGTGAGCGGGCGGGACGGCCCTTCTCCTCCGGGCTGTAATTAGCGCT

-continued

TGGTTTAATGACGGCTCGTTTCTTTTCTGTGGCTGCGTGAAAGCCTTAA

AGGGCTCCGGGAGGGCCCTTTGTGCGGGGGGGAGCGGCTCGGGGGGTGC

GTGCGTGTGTGTGTGCGTGGGGAGCGCCGCGTGCGGCCCGCGCTGCCCG

GCGGCTGTGAGCGCTGCGGGCGCGGCGCGGGGCTTTGTGCGCTCCGCGT

GTGCGCGAGGGGAGCGCGGCCGGGGGCGGTGCCCCGCGGTGCGGGGGGG

CTGCGAGGGGAACAAAGGCTGCGTGCGGGGTGTGTGCGTGGGGGGGTGA

GCAGGGGGTGTGGGCGCGGCGGTCGGGCTGTAACCCCCCCCTGCACCCC

CCTCCCCGAGTTGCTGAGCACGGCCCGGCTTCGGGTGCGGGGCTCCGTG

CGGGGCGTGGCGCGGGGCTCGCCGTGCCGGGCGGGGGGTGGCGGCAGGT

GGGGGTGCCGGGCGGGGCGGGGCCGCCTCGGGCCGGGGAGGGCTCGGGG

GAGGGGCGCGGCGGCCCCGGAGCGCCGGCGGCTGTCGAGGCGCGGCGAG

CCGCAGCCATTGCCTTTTATGGTAATCGTGCGAGAGGGCGCAGGGACTT

CCTTTGTCCCAAATCTGGCGGAGCCGAAATCTGGGAGGCGCCGCCGCAC

CCCCTCTAGCGGGCGCGGGCGAAGCGGTGCGGCGCCGGCAGGAAGGAAA

TGGGCGGGGAGGGCCTTCGTGCGTCGCCGCGCCGCCGTCCCCTTCTCCA

TCTCCAGCCTCGGGGCTGCCGCAGGGGGACGGCTGCCTTCGGGGGGGAC

GGGGCAGGGCGGGGTTCGGCTTCTGGCGTGTGACCGGCGGGAATTC

[0078] Construction of the VSV-G Envelope Plasmid:

[0079] The vesicular stomatitis Indiana virus glycoprotein (VSV-G) sequence was synthesized by MWG Operon with flanking EcoRl restriction sites. The DNA fragment was then inserted into the pCDNA3.1 plasmid (Invitrogen) at the EcoRI restriction site and the correct orientation was determined by sequencing using a CMV specific primer. The DNA sequence was as follows:

(SEQ ID NO: 46)

GAATTCATGAAGTGCCTTTTGTACTTAGCCTTTTTATTCATTGGGGTGA

ATTGCAAGTTCACCATAGTTTTTCCACACAACCAAAAAGGAAACTGGAA

AAATGTTCCTTCTAATTACCATTATTGCCCGTCAAGCTCAGATTTAAAT

TGGCATAATGACTTAATAGGCACAGCCTTACAAGTCAAAATGCCCAAGA

GTCACAAGGCTATTCAAGCAGACGGTTGGATGTGTCATGCTTCCAAATG

GGTCACTACTTGTGATTTCCGCTGGTATGGACCGAAGTATATAACACAT

TCCATCCGATCCTTCACTCCATCTGTAGAACAATGCAAGGAAAGCATTG

AACAAACGAAACAAGGAACTTGGCTGAATCCAGGCTTCCCTCCTCAAAG

TTGTGGATATGCAACTGTGACGGATGCCGAAGCAGTGATTGTCCAGGTG

ACTCCTCACCATGTGCTGGTTGATGAATACACAGGAGAATGGGTTGATT

CACAGTTCATCAACGGAAAATGCAGCAATTACATATGCCCCACTGTCCA

TAACTCTACAACCTGGCATTCTGACTATAAGGTCAAAGGGCTATGTGAT

TCTAACCTCATTTCCATGGACATCACCTTCTTCTCAGAGGACGGAGAGC

TATCATCCCTGGGAAAGGAGGGCACAGGGTTCAGAAGTAACTACTTTGC

TTATGAAACTGGAGGCAAGGCCTGCAAAATGCAATACTGCAAGCATTGG

-continued

GGAGTCAGACTCCCATCAGGTGTCTGGTTCGAGATGGCTGATAAGGATC

TCTTTGCTGCAGCCAGATTCCCTGAATGCCCAGAAGGGTCAAGTATCTC

TGCTCCATCTCAGACCTCAGTGGATGTAAGTCTAATTCAGGACGTTGAG

AGGATCTTGGATTATTCCCTCTGCCAAGAAACCTGGAGCAAAATCAGAG

CGGGTCTTCCAATCTCTCCAGTGGATCTCAGCTATCTTGCTCCTAAAAA

CCCAGGAACCGGTCCTGCTTTCACCATAATCAATGGTACCCTAAAATAC

TTTGAGACCAGATACATCAGAGTCGATATTGCTGCTCCAATCCTCTCAA

GAATGGTCGGAATGATCAGTGGAACTACCACAGAAAGGGAACTGTGGGA

TGACTGGGCACCATATGAAGACGTGGAAATTGGACCCAATGGAGTTCTG

AGGACCAGTTCAGGATATAAGTTTCCTTTATACATGATTGGACATGGTA

TGTTGGACTCCGATCTTCATCTTAGCTCAAAGGCTCAGGTGTTCGAACA

TCCTCACATTCAAGACGCTGCTTCGCAACTTCCTGATGATGAGAGTTTA

TTTTTTGGTGATACTGGGCTATCCAAAAATCCAATCGAGCTTGTAGAAG

GTTGGTTCAGTAGTTGGAAAAGCTCTATTGCCTCTTTTTTCTTTATCAT

AGGGTTAATCATTGGACTATTCTTGGTTCTCCGAGTTGGTATCCATCTT

TGCATTAAATTAAAGCACACCAAGAAAAGACAGATTTATACAGACATAG

AGATGAGAATTC

[0080] A 4-vector system (i.e., a 3-vector lentiviral packaging system) has also been designed and produced using the methods and materials described herein. A schematic of the 4-vector system is shown in FIGS. **1**D and **1**F. Briefly, and with reference to FIGS. **1**D and **1**F, the top-most vector is a helper plasmid, which, in this case, does not include Rev. The vector second from the top, oriented at the left aspect of the page, is a separate Rev plasmid. The vector second from the bottom, oriented at the right aspect of the page, is the envelope plasmid. The bottom-most vector is an experimental therapeutic vector.

[0081] Referring to FIGS. **1**D and **1**F, the Helper plasmid includes a CMV enhancer (SEQ ID NO: 32); a chicken beta actin promoter (SEQ ID NO: 33); a chicken beta actin intron (SEQ ID NO: 34); a HIV gag (SEQ ID NO: 23); a HIV Pol (SEQ ID NO: 35); a HIV Int (SEQ ID NO: 36); a HIV RRE (SEQ ID NO: 24); and a rabbit beta globin poly A (SEQ ID NO: 38).

[0082] Referring to FIGS. **1**D and IF, the Rev plasmid includes a RSV promoter (SEQ ID NO: 47); a HIV Rev (SEQ ID NO: 37); and a rabbit beta globin poly A (SEQ ID NO: 38).

[0083] Referring to FIGS. **1**D and IF, the Envelope plasmid includes a CMV promoter (SEQ ID NO: 39); a beta globin intron (SEQ ID NO: 40); a VSV-G (SEQ ID NO: 25); and a rabbit beta globin poly A (SEQ ID NO: 38). The Envelope plasmid is also shown in a linear form in FIG. **1**A.

[0084] Synthesis of a 3-Vector Lentiviral Packaging System including Helper, Rev, and Envelope Plasmids.

[0085] Materials and Methods:

[0086] Construction of the Helper Plasmid without Rev:

[0087] The Helper plasmid without Rev was constructed by inserting a DNA fragment containing the RRE and rabbit beta globin poly A sequence. This sequence was synthesized by MWG Operon with flanking XbaI and XmaI restriction sites. The RRE/rabbit poly A beta globin sequence was then

inserted into the Helper plasmid at the XbaI and XmaI restriction sites. The DNA sequence is as follows:

(SEQ ID NO: 44)

TCTAGAAGGAGCTTTGTTCCTTGGGTTCTTGGGAGCAGCAGGAAGCACT

ATGGGCGCAGCGTCAATGACGCTGACGGTACAGGCCAGACAATTATTGT

CTGGTATAGTGCAGCAGCAGAACAATTTGCTGAGGGCTATTGAGGCGCA

ACAGCATCTGTTGCAACTCACAGTCTGGGGCATCAAGCAGCTCCAGGCA

AGAATCCTGGCTGTGGAAAGATACCTAAAGGATCAACAGCTCCTAGATC

TTTTTCCCTCTGCCAAAAATTATGGGGACATCATGAAGCCCCTTGAGCA

TCTGACTTCTGGCTAATAAAGGAAATTTATTTTCATTGCAATAGTGTGT

TGGAATTTTTTGTGTCTCTCACTCGGAAGGACATATGGGAGGGCAAATC

ATTTAAAACATCAGAATGAGTATTTGGTTTAGAGTTTGGCAACATATGC

CATATGCTGGCTGCCATGAACAAAGGTGGCTATAAAGAGGTCATCAGTA

TATGAAACAGCCCCCTGCTGTCCATTCCTTATTCCATAGAAAAGCCTTG

ACTTGAGGTTAGATTTTTTTTATATTTTGTTTTGTGTTATTTTTTTCTT

TAACATCCCTAAAATTTTCCTTACATGTTTTACTAGCCAGATTTTTCCT

CCTCTCCTGACTACTCCCAGTCATAGCTGTCCCTCTTCTCTTATGAAGA

TCCCTCGACCTGCAGCCCAAGCTTGGCGTAATCATGGTCATAGCTGTTT

CCTGTGTGAAATTGTTATCCGCTCACAATTCCACACAACATACGAGCCG

GAAGCATAAAGTGTAAAGCCTGGGGTGCCTAATGAGTGAGCTAACTCAC

ATTAATTGCGTTGCGCTCACTGCCCGCTTTCCAGTCGGGAAACCTGTCG

TGCCAGCGGATCCGCATCTCAATTAGTCAGCAACCATAGTCCCGCCCCT

AACTCCGCCCATCCCGCCCCTAACTCCGCCCAGTTCCGCCCATTCTCCG

CCCCATGGCTGACTAATTTTTTTTATTTATGCAGAGGCCGAGGCCGCCT

CGGCCTCTGAGCTATTCCAGAAGTAGTGAGGAGGCTTTTTTGGAGGCCT

AGGCTTTTGCAAAAAGCTAACTTGTTTATTGCAGCTTATAATGGTTACA

AATAAAGCAATAGCATCACAAATTTCACAAATAAAGCATTTTTTTCACT

GCATTCTAGTTGTGGTTTGTCCAAACTCATCAATGTATCTTATCACCCG

GG

[0088] Construction of the Rev Plasmid:

[0089] The RSV promoter and HIV Rev sequence was synthesized as a single DNA fragment by MWG Operon with flanking MfeI and XbaI restriction sites. The DNA fragment was then inserted into the pCDNA3.1 plasmid (Invitrogen) at the MfeI and XbaI restriction sites in which the CMV promoter is replaced with the RSV promoter. The DNA sequence was as follows:

(SEQ ID NO: 48)

CAATTGCGATGTACGGGCCAGATATACGCGTATCTGAGGGGACTAGGGT

GTGTTTAGGCGAAAAGCGGGGCTTCGGTTGTACGCGGTTAGGAGTCCCC

TCAGGATATAGTAGTTTCGCTTTTGCATAGGGAGGGGGAAATGTAGTCT

TATGCAATACACTTGTAGTCTTGCAACATGGTAACGATGAGTTAGCAAC

ATGCCTTACAAGGAGAGAAAAAGCACCGTGCATGCCGATTGGTGGAAGT

-continued

AAGGTGGTACGATCGTGCCTTATTAGGAAGGCAACAGACAGGTCTGACA

TGGATTGGACGAACCACTGAATTCCGCATTGCAGAGATAATTGTATTTA

AGTGCCTAGCTCGATACAATAAACGCCATTTGACCATTCACCACATTGG

TGTGCACCTCCAAGCTCGAGCTCGTTTAGTGAACCGTCAGATCGCCTGG

AGACGCCATCCACGCTGTTTTGACCTCCATAGAAGACACCGGGACCGAT

CCAGCCTCCCCTCGAAGCTAGCGATTAGGCATCTCCTATGGCAGGAAGA

AGCGGAGACAGCGACGAAGAACTCCTCAAGGCAGTCAGACTCATCAAGT

TTCTCTATCAAAGCAACCCACCTCCCAATCCCGAGGGGACCCGACAGGC

CCGAAGGAATAGAAGAAGAAGGTGGAGAGAGAGACAGAGACAGATCCAT

TCGATTAGTGAACGGATCCTTAGCACTTATCTGGGACGATCTGCGGAGC

CTGTGCCTCTTCAGCTACCACCGCTTGAGAGACTTACTCTTGATTGTAA

CGAGGATTGTGGAACTTCTGGGACGCAGGGGGTGGGAAGCCCTCAAATA

TTGGTGGAATCTCCTACAATATTGGAGTCAGGAGCTAAAGAATAGTCTA

GA

[0090] The plasmids for the 3-vector and 4-vector packaging systems can be modified with similar elements and the intron sequences could potentially be removed without loss of vector function. For example, the following elements could replace similar elements in the 3-vector and 4-vector packaging system:

[0091] Promoters: Elongation Factor-1 (EF-1) (SEQ ID NO: 28), phosphoglycerate kinase

[0092] (PGK) (SEQ ID NO: 49), and ubiquitin C (UbC) (SEQ ID NO: 50) can replace the CMV or CAG promoter (SEQ ID NO: 39). These sequences can also be further varied by addition, substitution, deletion or mutation.

[0093] Poly A sequences: SV40 poly A (SEQ ID NO: 51) and bGH poly A (SEQ ID NO: 52) can replace the rabbit beta globin poly A (SEQ ID NO: 38). These sequences can also be further varied by addition, substitution, deletion or mutation.

[0094] HIV Gag, Pol, and Integrase sequences: the HIV sequences in the Helper plasmid can be constructed from different HIV strains or clades. For example, HIV Gag (SEQ ID NO: 23); HIV Pol (SEQ ID NO: 35); and HIV Int (SEQ ID NO: 36) from the Bal strain can be interchanged with the gag, pol, and int sequences contained in the helper/helper plus Rev plasmids as outlined herein. These sequences can also be further varied by addition, substitution, deletion or mutation.

[0095] Envelope: The VSV-G glycoprotein can be substituted with membrane glycoproteins from feline endogenous virus (RD114) (SEQ ID NO: 53), gibbon ape leukemia virus (GALV) (SEQ ID NO: 54), Rabies (FUG) (SEQ ID NO: 55), lymphocytic choriomeningitis virus (LCMV) (SEQ ID NO: 56), influenza A fowl plague virus (FPV) (SEQ ID NO: 57), Ross River alphavirus (RRV) (SEQ ID NO: 58), murine leukemia virus 10A1 (MLV) (SEQ ID NO: 59), or Ebola virus (EboV) (SEQ ID NO: 60). Sequences for these envelopes are identified in the sequence portion herein. Further, these sequences can also be further varied by addition, substitution, deletion or mutation.

[0096] In summary, the 3-vector versus 4-vector systems can be compared and contrasted, in part, as follows. The

3-vector lentiviral vector system contains: 1. Helper plasmid: HIV Gag, Pol, Integrase, and Rev/Tat; 2. Envelope plasmid: VSV-G envelope; and 3. Therapeutic vector: RSV/5' LTR, HIV Gag, RRE, Env, cPPT, H1, shPARP1, EF1, GFP, WPRE, and a 3'LTR Δ U3. The 4-vector lentiviral vector system contains: 1. Helper plasmid: HIV Gag, Pol, and Integrase; 2. Rev plasmid: Rev; 3. Envelope plasmid: VSV-G envelope; and 4. Therapeutic vector: RSV/5' LTR, HIV Gag, RRE, Env, a cPPT, a H1 element, shPARP1, EF1, GFP, WPRE, and a 3'Δ LTR. Sequences corresponding with the above elements are identified in the sequence listings portion herein.

Example 2

Development of PARP1 Inhibitory RNA for use in a Lentiviral Vector in the Lentiviral Vector System

[0097] The purpose of this Example was to develop a PARP1 inhibitor RNA lentivirus vector.

[0098] Inhibitory RNA Design. The sequence of *Homo sapiens* poly ADP-ribose polymerase (PARP1) mRNA (NM_001618) or *Mus musculus* Parp1 mRNA (NM_007415) was used to search for potential siRNA or shRNA candidates to knock-down PARP1 levels in human or mouse cells. Potential RNA interference sequences were chosen from candidates selected by siRNA or shRNA design programs such as those from the Broad Institute (MIT) Genetic Perturbation Platform (GPP) Web Portal or the BLOCK-iT™ RNAi Designer from ThermoFisher Scientific. Potential RNA interference sequences were chosen from candidates selected by siRNA or shRNA design programs such as from GPP Web Portal hosted by the Broad Institute (http://portals.broadinstitute.org/gpp/public/) or the BLOCK-iT RNAi Designer from Thermo Scientific (https://rnaidesigner.thermofisher.com/rnaiexpress/).

[0099] Vector Construction. For PARP1 shRNAs, oligonucleotide sequences containing BamHI and EcoRI restriction sites were synthesized by MWG operon. Oligonucleotide sequences were annealed by incubation at 70 degrees Celsius and cooling to room temperature. Annealed oligonucleotides were digested with the restriction enzymes BamHI and EcoRI for one hour at 37 degrees Celsius and then the enzymes were heat-inactivated at 70 degrees Celsius for 20 minutes. In parallel, a lentiviral vector was digested with the restriction enzymes BamHI and EcoRI for one hour at 37 degrees Celsius. The digested lentiviral vector was purified by agarose gel electrophoresis and extracted from the gel using a DNA gel extraction kit from Invitrogen. The DNA concentration was determined by spectrophotometry at the absorbance wavelength of 260 nm. The vector and oligonucleotide sequences were ligated in the ratio 3:1 (insert to vector). The ligation reaction was carried out with T4 DNA ligase for 30 minutes at room temperature. 2.5 microliters of the ligation mixture was added to 25 microliters of STBL3 competent bacterial cells. Transformation was carried out by heat-shock at 42 degrees Celsius. Bacterial cells were streaked onto agar plates containing ampicillin and then colonies were expanded in LB broth. To check for insertion of the oligo sequences, plasmid DNA was extracted from harvested bacteria cultures with the Invitrogen DNA mini prep kit. Insertion of the shRNA sequence in the lentiviral vector was verified by DNA sequencing using a specific primer for which ever promoter is used to regulate shRNA expression. The lentiviral vectors containing a correct PARP1 sequence were then used to package lentiviral particles to test for their ability to knock-down PARP1. Mammalian cells were transduced with lentiviral particles either in the presence or absence of polybrene. Cells were collected after 2-4 days and protein was analyzed by western blot for PARP1 expression.

[0100] The *Homo sapiens* PARP1 target sequences summarized in Table 1 were identified in respect of these experiments and in relation to the shRNA oligonucleotide sequences outlined in Table 2 herein.

TABLE 1

Homo sapiens PARP1 Target Sequences

SEQ ID NO.:	Sequence
1	CTTCGTTAGAATGTCTGCCTT
2	GCAGCTTCATAACCGAAGATT
3	CCGAGAAATCTCTTACCTCAA
4	CGACCTGATCTGGAACATCAA
5	GTTGCTGATGGGTAGTACC

[0101] The following *Homo sapiens* PARP1 shRNA oligonucleotide sequences summarized in Table 2 were used in these experiments:

TABLE 2

Homo sapiens PARP1 shRNA Oligonucleotide Sequences

SEQ ID NO.:	Sequence
6	CTTCGTTAGAATGTCTGCCTTCTCGAGAAGGCAGACATTCTAACGAAGTTTTT
7	GCAGCTTCATAACCGAAGATTCTCGAGAATCTTCGGTTATGAAGCTGCTTTTT
8	CCGAGAAATCTCTTACCTCAACTCGAGTTGAGGTAAGAGATTTCTCGGTTTTT
9	CGACCTGATCTGGAACATCAACTCGAGTTGATGTTCCAGATCAGGTCGTTTTT
10	GTTGCTGATGGGTAGTACCTTCAAGAGAGGTACTACCCATCAGCAACTTTTT

[0102] The *Mus musculus* PARP1 target sequences summarized in Table 3 were identified in respect of these experiments and in relation to the shRNA oligonucleotide sequences outlined in Table 4 herein:

TABLE 3

Mus musculus PARP1 Target Sequences

SEQ ID NO.:	Sequence
11	GCACTTCATGAAGCTGTATGA
12	GCACAGTTATCGGCAGTAACA
13	GGAGGCAAGTTGACAGGATCT

TABLE 3 -continued

Mus musculus PARP1 Target Sequences

SEQ ID NO.:	Sequence
14	TCGACGTCAACTACGAGAAAC
15	GCCCTTGGAAACATGTATGAA

[0103] The following *Mus musculus* PARP1 shRNA oligonucleotide sequences summarized in Table 4 were used in these experiments:

TABLE 4

Mus musculus PARP1 shRNA Oligonucleotide Sequences

SEQ ID NO.:	Sequence
16	GCACTTCATGAAGCTGTATGACTCGAGTCATACAGCTTC ATGAAGTGCTTTTT
17	GCACAGTTATCGGCAGTAACACTCGAGTGTTACTGCCGA TAACTGTGCTTTTT
18	GGAGGCAAGTTGACAGGATCTCTCGAGAGATCCTGTCAA CTTGCCTCCTTTTT
19	TCGACGTCAACTACGAGAAACCTCGAGGTTTCTCGTAGT TGACGTCGATTTTT
20	GCCCTTGGAAACATGTATGAACTCGAGTTCATACATGTT TCCAAGGGCTTTTT

[0104] The *Homo sapiens* and *Mus musculus* PARP1 shRNA oligonucleotide sequences outlined in this Example were used in conjunction with the lentiviral vector system discussed herein.

[0105] An experimental therapeutic vector was designed as shown in FIG. **1**A (linear form), and FIGS. **1**C and **1**D (circularized forms). Referring to the circularized vector map shown in FIGS. **1**C and **1**D, the experimental therapeutic vector includes: a hybrid 5' long terminal repeat (RSV/5' LTR) (SEQ ID NOS: 21-22), a HIV gag (SEQ ID NO: 23), a RRE (Rev-response element) (SEQ ID NO: 24), a Env element (SEQ ID NO: 25), a cPPT (SEQ ID NO: 26), a H1 promoter (SEQ ID NO: 27), a shRNA targeting PARP1 (shPARP1) (SEQ ID NOS: 6-10), a EF1 promoter (SEQ ID NO: 28), a GFP element (SEQ ID NO: 29), a Woodchuck Post-Transcriptional Regulatory Element (WPRE) (SEQ ID NO: 30), and a 3' LTR delta U3 (SEQ ID NO: 31). The presence of GFP is for experimental purposes due to its usefulness in demonstrating transduction in in vitro and in vivo model systems.

[0106] Further, referring to circularized vector maps shown in FIGS. **1**E and **1**F, a therapeutic or lentiviral vector has been designed which includes: a hybrid 5' long terminal repeat (RSV/5' LTR) (SEQ ID NOS: 21-22), a HIV gag (SEQ ID NO: 23), a RRE (Rev-response element) (SEQ ID NO: 24), a Env element (SEQ ID NO: 25), a cPPT (SEQ ID NO: 26), a H1 promoter (SEQ ID NO: 27), a shRNA targeting PARP1 (shPARP1) (SEQ ID NOS: 6-10), a Woodchuck Post-Transcriptional Regulatory Element (WPRE) (SEQ ID NO: 30), and a 3' LTR delta U3 (SEQ ID NO: 31). The therapeutic or lentiviral vector detailed in FIGS. **1**E and **1**F does not contain GFP.

Example 3

shRNA-Mediated Decrease of PARP1 Protein Expression

[0107] shRNAs designed against *Homo sapiens* PARP1 were tested for their ability to downregulate PARP1 gene expression. The lentiviral vector containing human PARP1 shRNA was packaged as lentiviral particles. Lentiviral particles at a MOI of 1-10 were added to human U251 glioblastoma cells. After 48 hours, cells were lysed and PARP1 expression was measured by immunoblot analysis with a PARP1 specific antibody.

[0108] As shown in Table 5 below, five of the shRNAs designed against PARP1 showed an ability to downregulate PARP1 protein expression. Compared to a 100% control shRNA sequence: Sequence 6 (SEQ ID NO: 6) resulted in 57.1% of PARP1 protein expression; Sequence 7 (SEQ ID NO: 7) resulted in 45.8% of PARP1 protein expression; Sequence 8 (SEQ ID NO: 8) resulted in 47.2% of PARP1 protein expression; Sequence 9 (SEQ ID NO: 9) resulted in 48.8% of PARP1 protein expression; and Sequence 10 (SEQ ID NO: 10) resulted in 27.1% of PARP1 protein expression.

TABLE 5

shRNA-mediated downregulation of *Homo sapiens* PARP1

shRNA against *Homo sapiens* PARP1	Percentage protein expression (Control shRNA = 100%) after transduction with lentivirus expressing shRNA
Control shRNA Sequence (SEQ ID NO: 61)	100
Human PARP1 Sequence 6 (SEQ ID NO: 6)	57.1
Human PARP1 Sequence 7 (SEQ ID NO: 7)	45.8
Human PARP1 Sequence 8 (SEQ ID NO: 8)	47.2
Human PARP1 Sequence 9 (SEQ ID NO: 9)	48.8
Human PARP1 Sequence 10 (SEQ ID NO: 10)	27.1

shRNAs designed against *Mus musculus* PARP1 were tested for their ability to downregulate PARP1 gene expression. The lentiviral vector containing mouse PARP1 shRNA was packaged as lentiviral particles. Lentiviral particles at a MOI of 1-10 was added to mouse Hepal-6 hepatoma cells. After 48 hours, cells were lysed and PARP1 expression was measured by immunoblot analysis with a PARP1 specific antibody. As shown in Table 6 below, five of the shRNAs designed against PARP1 showed an ability to downregulate PARP1 protein expression. Compared to a 100% control shRNA sequence: Sequence 16 (SEQ ID NO: 16) resulted in 22.8% of PARP1 protein expression; Sequence 17 (SEQ ID NO: 17) resulted in 47.7% of PARP1 protein expression; Sequence 18 (SEQ ID NO: 18) resulted in 2% of PARP1 protein expression; Sequence 19 (SEQ ID NO:19) resulted in 0.2% of PARP1 protein expression; and Sequence 20 (SEQ ID NO: 20) resulted in 2% of PARP1 protein expression.

TABLE 6

shRNA-mediated downregulation of *Mus musculus* PARP1

shRNA against *Mus musculus* PARP1	Percentage protein expression (Control shRNA = 100%) after transduction with lentivirus expressing shRNA
Control shRNA Sequence (SEQ ID NO: 61)	100
Mouse PARP1 Sequence 16 (SEQ ID NO: 16)	22.8
Mouse PARP1 Sequence 17 (SEQ ID NO: 17)	47.7
Mouse PARP1 Sequence 18 (SEQ ID NO: 18)	2
Mouse PARP1 Sequence 19 (SEQ ID NO: 19)	0.2
Mouse PARP1 Sequence 20 (SEQ ID NO: 20)	2

[0109] PARP1 protein expression was found to be reduced in human and mouse cells following shRNA administration. Referring first to FIG. **2**, a reduction in PARP1 protein in U251 human glioblastoma cell lines is demonstrated following treatment with lentivirus vectors expressing shRNA. The cell line U251 contains measurable PARP1 protein in cell lysates as indicated in the lanes identified as shCon (i.e., a lentivirus vector containing an irrelevant shRNA sequence that does not affect PARP1 protein expression). Individual shRNA sequences 6-10 (as referred to in Table 2 herein) were cloned into lentivirus vectors, expressed as infectious virus particles and used to transduce U251 cells. 48 hours after transduction, cells were lysed, proteins were separated by polyacrylamide gel electrophoresis and detected by immunoblot assay using anti-PARP1 antibody (Cell Signaling Technology).

[0110] Still referring to FIG. **2**, Sequence 6 corresponds with lane shPARP1-1; Sequence 7 corresponds with lane shPARP1-2; Sequence 8 corresponds with lane shPARP1-3; Sequence 9 corresponds with lane shPARP1-4; and Sequence 10 corresponds with lane shPARP1-5. The housekeeping protein Actin was detected with Anti-Actin antibody (Sigma-Aldrich) to confirm that similar amounts of protein were analyzed in each lane of the gel. Sequence 10 was identified as being the most effective for reducing PARP1 protein in human U251 cells.

[0111] Turning to mouse cell experiments, and with reference to FIG. **3**, a reduction in PARP1 protein levels in Hepal-6 mouse hepatoma cells was observed following administration of lentivirus vectors expressing shRNAs. The cell line Hepal-6 contains measurable PARP1 protein in cell lysates as indicated in lanes identified as No infection (no lentivirus used) or shCon (lentivirus vector containing an irrelevant shRNA sequence that does not affect PARP1 protein expression). Individual shRNA constructs 16-20 (as referred to in Table 4 herein) were cloned into lentivirus vectors, expressed as infectious virus particles and used to transduce Hepal-6 cells. 48 hours after transduction, cells were lysed, proteins were separated by polyacrylamide gel electrophoresis and detected by immunoblot assay using anti-PARP1 antibody (Cell Signaling Technology). Still referring to FIG. **3**, Sequence 16 corresponds with lane shPARP1-1; Sequence 17 corresponds with lane shPARP1-2; Sequence 18 corresponds with lane shPARP1-3; Sequence 19 corresponds with lane shPARP1-4; and Sequence 20 corresponds with lane shPARP1-5. The housekeeping proteins Actin or Tubulin were detected with antibody reagents (Sigma-Aldrich) as controls for the amount of protein loaded in each lane of the gel. shRNA 16, 17 and 18 were potent for inhibiting PARP1 protein expression. Sequence 19 was identified as being most effective for reducing PARP1 protein in murine Hepal-6.

Example 4

Lentiviral Vector Transduction in Mouse Neurons

[0112] The lentiviral vector system outlined herein has been found to be capable of transduction in mouse neurons. With reference to FIG. **4**, wild-type mice were injected with mock (no lentivirus) in the left column of micrographs or LV-shPARP1 also expressing green fluorescence protein in the right column of micrographs, via a steel needle inserted into the substantia nigra region of the mouse brain. The LV-shPARP1-GFP was dosed at 0.1 ml containing approximately 1×10^8 transducing units. 14 days later, mice were sacrificed and the substantia nigra region was excised from the brain, fixed in formaldehyde, and embedded in paraffin. Thin sections were mounted on glass slides and visualized with a fluorescence microscope. TH+ neurons (expressing high levels of tyrosine hydroxylase) generally identify the substantia nigra region and appear red (or white in gray-scale photographs) in FIG. **4**. The middle panels depict cells that were transduced with mock (left column) or LV-shPARP1-GFP (see: green [or white in gray-scale photographs] staining in right column). Due to the high intensity of light emitted by GFP, indicating efficient transduction and transgene expression, positively transduced neurons appeared black in this figure and were not present, as expected, in the sham control (left column). The lower panels merge the TH+ neuron staining and GFP+ neuron staining from lentivirus transductions to demonstrate the presence of transduced cells within the substantia nigra including within TH+ neurons.

Example 5

Therapeutic Treatment of Neuronal Death Using Lentiviral Vector System

[0113] The chemical neurotoxin 1-Methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) causes severe and irreversible motor abnormalities in mice, and is widely used to model human PD. See, e.g., Kopin & Markey, 11 *Annu. Rev. Neurosci,* 81-96 (1988). Treating mice with MPTP lowers the levels of striatal dopamine and its metabolites, because drug neurotoxicity reduces the number of dopamine producing cells in the substantia nigra. The model has been used to test the protective effects of compounds including nitric oxide, which prevent neuronal death after MPTP exposure. See, e.g., Przedborski et al., 93 *Proc. Natl. Acad. Sci. USA.,* 44565-4571 (1996). This model can be employed to measure the potential for preventing death of dopaminergic neurons by pretreating mice with lentivirus vector designed to express a short hairpin RNA sequence (sh) that will reduce neuronal cell expression of PARP (LV-shPARP). The vector can be further modified to express the green fluorescence protein marker that will identify transduced cells (LV-shPARP-GFP) and is compared to a vector that does not express shPARP (LV-GFP).

[0114] Suspensions of LV-shPARP-GFP or LV-GFP are injected into the substantia nigra of healthy adult mice.

Doses are escalated until a toxic level is reached, which results in severe motor impairment or death of the mouse. Using the maximum tolerated dose, mice are treated with LV-shPARP-GFP or control vector. Two weeks later, sentinel animals from each group are sacrificed to confirm transduction of neurons in the substantia nigra. The remaining animals (in groups of 10) are treated with MPTP-HCl, 20 mg/kg dose in saline given four times via intraperitoneal injection with 2 hour intervals. Between 2 and 7 days later, groups of mice are sacrificed, the brain is removed, fixed and embedded in paraffin for sectioning. The substantia nigra region is identified by staining for tyrosine hydroxylase-expressing neurons (TH+) and transduced neurons are identified by expression of GFP. Therapeutic impact of LV-shPARP-GFP is determined by counting the numbers of TH+ or GFP+ neurons in substantia nigra from mice treated with LV-shPARP-GFP or control vector. MPTP is expected to destroy much of the substantia nigra TH+ cells and LV-shPARP-GFP is expected to protect these cells and preserve normal appearance of the substantia nigra. In additional groups of mice treated in the same way with both LV vectors and MPTP, the brains are removed at 7 days after MPTP dosing, the substantia nigra region is isolated by dissection and tissue is frozen at −80 degrees Celsius. Subsequently, the tissue specimens are thawed and dopamine is extracted according to published methods (see: Przedborski et al., infra). LV-shPARP-GFP is expected to preserve normal levels of dopamine production after MPTP treatment, and dopamine levels will be significantly higher in mice treated with LV-shPARP-GFP than mice treated with control vector.

Example 6

Lentiviral Targeting to Neurons using Variants of Envelope Glycoproteins

[0115] Properties of individual envelope glycoproteins impact tissue tropism and the efficiency of delivery of therapeutic genes to the sites of disease. To treat PD, a target for gene therapy is a TH+ cell of the substantia nigra. To optimize targeting to a TH+ cell, various envelope glycoproteins will be compared for their role in improving transduction efficiencies in the TH+ cells of the mouse substantia nigra. As described above in Example 1, an envelope plasmid has been designed and produced which contains the vesicular stomatitis virus G glycoprotein (VSV-G). This envelope plasmid can be compared to other designed envelope plasmids which, in place of VSV-G, includes FUG-C (N-terminal region of rabies virus glycoprotein), gp64 envelope glycoprotein from baculovirus, envelope glycoprotein from baboon endogenous virus or other suitable alternatives for packaging lentivirus particles. In each case, using the envelope plasmid variants, lentivirus vector stocks are produced, injected into mouse brains, and the efficiency of transduction into TH+ cells of the mouse substantia nigra is examined.

Example 7

Testing PARP Genes for Therapeutic Effect of PD

[0116] The studies described herein include a focus on PARP1 and how its modulation can be used to therapeutically treat PD. However, PARP1 is only 1 of approximately 16 closely related PARP genes with similar functions. Using the techniques for target identification, shRNA production and conversion into lentivirus-delivered miRNA as described herein, the other PARP genes can be tested for their ability to be effective therapeutic vectors in treating PD. Briefly, lentiviral vectors containing the other PARP genes can be injected into a mouse to test for PD correction using the methods, techniques and materials described herein.

Example 8

Method of Designing Synthetic miRNAs for Insertion into a Lentiviral Vector System

[0117] Target short-hairpin sequences that are 19-22 nucleotides long are chosen from a shRNA design program such as, for example, the Invitrogen Block-iT RNAi designer or the RNAi design program from the Broad Institute (MIT). Several sequences are tested for efficient knockdown of a particular gene, such as, for example, PARP. A shRNA sequence that decreases the target gene expression at least 80% is then inserted within a defined microRNA hairpin backbone. MicroRNA (miRNA) hairpin structures can be obtained from the miRBase.org website.

[0118] The chosen shRNA sequence is then inserted within the hairpin structure while leaving the loop sequence unchanged. The antisense shRNA sequence is inserted within the 5-prime sequence of the miRNA hairpin to become the seed sequence for gene targeting. The sense shRNA sequence is modified according to the particular miRNA hairpin structure chosen. As an example, nucleotides 9 and 10 of the sense strand are removed for the miR30 hairpin structure. A miR sequence containing a target sequence such as PARP and a backbone sequence are synthesized with BsrGI and NotI restriction sites by either MWG Operon or IDT. This sequence is inserted into the BsrGI and NotI sites of the miR-acceptor lentiviral vector.

Example 9

Treatment of Human Patients with PD

[0119] Twelve patients aged 35-75 years at least 5 years after initial diagnosis of PD receive bilateral, stereotactic, intraputaminal injections of LV-shPARP compositions (based, for example, on the lentiviral construct shown in FIG. **1**B) as described herein (cGMP grade) in a dose escalation study. The likely dose range is 10^8 transducing units of LV-shPARP in 5 ml of sterile saline [1 transducing unit is the amount of LV-shPARP required to achieve on average, 1 copy of the transgene integrated into the chromosome of a single target cell]. The upper range is expected to be approximately 10^{10} transducing units of LV-shPARP. Treated patients are followed for at least 1 year and up to 5 years for changes in locomotor status.

[0120] Changes in clinical status are determined using the Unified Parkinson's Disease Rating Scale, comparing LV-treated to off medication status for a matched group of patients with PD. Patients are also asked to record clinical status in terms of time without troubling dyskinesia, and may also undergo testing with the Purdue pegboard test of hand dexterity, and activities of daily living score. See, e.g., Marks Jr., et al., 9(12) *Lancet Neurol.,* 1164-72 (2010). Patient outcomes after LV-shPARP therapy are compared to previous gene therapy trials testing Adeno-associated virus delivery of glutamic acid decarboxylase gene or aromatic

L-amino acid decarboxylase to increase L-DOPA production or studies using Adeno-associated virus delivery of the neurotrophic growth factor neurturin. See, e.g., Kaplitt et al. 369 (9579) *Lancet Neurol.* 2097-105 (2007); see also Christine et al., 73(20) *Neurology,* 1662-9, (2009). It is rationally predicted that subjects receiving LV-shPARP compositions show improvements in PD and PD-related symptoms.

[0121] The disclosure of the above example embodiments is intended to be illustrative, but not limiting, of the scope of the inventions, which are set forth in the following claims and their equivalents. Although exemplary embodiments of the inventions have been described in some detail for purposes of clarity of understanding, it will be apparent that certain changes and modifications can be practiced within the scope of the following claims. In the following claims, elements and/or steps do not imply any particular order of operation, unless explicitly stated in the claims or implicitly required by the disclosure.

Sequences

SEQ ID NO:	Description	Sequence
1	*Homo sapiens* PARP1 Target Sequence 1	CTTCGTTAGAATGTCTGCCTT
2	*Homo sapiens* PARP1 Target Sequence 2	GCAGCTTCATAACCGAAGATT
3	*Homo sapiens* PARP1 Target Sequence 3	CCGAGAAATCTCTTACCTCAA
4	*Homo sapiens* PARP1 Target Sequence 4	CGACCTGATCTGGAACATCAA
5	*Homo sapiens* PARP1 Target Sequence 5	GTTGCTGATGGGTAGTACC
6	*Homo sapiens* PARP1 shRNA Oligonucleotide Sequence 1	CTTCGTTAGAATGTCTGCCTTCTCGAGAAGGCAGACAT TCTAACGAAGTTTTT
7	*Homo sapiens* PARP1 shRNA Oligonucleotide Sequence 2	GCAGCTTCATAACCGAAGATTCTCGAGAATCTTCGGTT ATGAAGCTGCTTTTT
8	*Homo sapiens* PARP1 shRNA Oligonucleotide Sequence 3	CCGAGAAATCTCTTACCTCAACTCGAGTTGAGGTAAGA GATTTCTCGGTTTTT
9	*Homo sapiens* PARP1 shRNA Oligonucleotide Sequence 4	CGACCTGATCTGGAACATCAACTCGAGTTGATGTTCCA GATCAGGTCGTTTTT
10	*Homo sapiens* PARP1 shRNA Oligonucleotide Sequence 5	GTTGCTGATGGGTAGTACCTTCAAGAGAGGTACTACCC ATCAGCAACTTTTT
11	*Mus musculus* PARP1 Target Sequence 1	GCACTTCATGAAGCTGTATGA
12	*Mus musculus* PARP1 Target Sequence 2	GCACAGTTATCGGCAGTAACA
13	*Mus musculus* PARP1 Target Sequence 3	GGAGGCAAGTTGACAGGATCT
14	*Mus musculus* PARP1 Target Sequence 4	TCGACGTCAACTACGAGAAAC

-continued

Sequences

SEQ ID NO:	Description	Sequence
15	*Mus musculus* PARP1 Target Sequence 5	GCCCTTGGAAACATGTATGAA
16	*Mus musculus* PARP1 shRNA Oligonucleotide Sequence 1	GCACTTCATGAAGCTGTATGACTCGAGTCATACAGCTT CATGAAGTGCTTTTT
17	*Mus musculus* PARP1 shRNA Oligonucleotide Sequence 2	GCACAGTTATCGGCAGTAACACTCGAGTGTTACTGCCG ATAACTGTGCTTTTT
18	*Mus musculus* PARP1 shRNA Oligonucleotide Sequence 3	GGAGGCAAGTTGACAGGATCTCTCGAGAGATCCTGTC AACTTGCCTCCTTTTT
19	*Mus musculus* PARP1 shRNA Oligonucleotide Sequence 4	TCGACGTCAACTACGAGAAACCTCGAGGTTTCTCGTAG TTGACGTCGATTTTT
20	*Mus musculus* PARP1 shRNA Oligonucleotide Sequence 5	GCCCTTGGAAACATGTATGAACTCGAGTTCATACATGT TTCCAAGGGCTTTTT
21	*Rous Sarcoma* virus (RSV) promoter	GTAGTCTTATGCAATACTCTTGTAGTCTTGCAACATGGT AACGATGAGTTAGCAACATGCCTTACAAGGAGAGAAA AAGCACCGTGCATGCCGATTGGTGGAAGTAAGGTGGTA CGATCGTGCCTTATTAGGAAGGCAACAGACGGGTCTGA CATGGATTGGACGAACCACTGAATTGCCGCATTGCAGA GATATTGTATTTAAGTGCCTAGCTCGATACAATAAACG
22	5' Long terminal repeat (LTR)	GGTCTCTCTGGTTAGACCAGATCTGAGCCTGGGAGCTC TCTGGCTAACTAGGGAACCCACTGCTTAAGCCTCAATA AAGCTTGCCTTGAGTGCTTCAAGTAGTGTGTGCCCGTCT GTTGTGTGACTCTGGTAACTAGAGATCCCTCAGACCCTT TTAGTCAGTGTGGAAAATCTCTAGCA
23	Helper/Rev; HIV Gag; Viral capsid	ATGGGTGCGAGAGCGTCAGTATTAAGCGGGGGAGAAT TAGATCGATGGGAAAAAATTCGGTTAAGGCCAGGGGG AAAGAAAAAATATAAATTAAAACATATAGTATGGGCA AGCAGGGAGCTAGAACGATTCGCAGTTAATCCTGGCCT GTTAGAAACATCAGAAGGCTGTAGACAAATACTGGGA CAGCTACAACCATCCCTTCAGACAGGATCAGAAGAACT TAGATCATTATATAATACAGTAGCAACCCTCTATTGTGT GCATCAAAGGATAGAGATAAAAGACACCAAGGAAGCT TTAGACAAGATAGAGGAAGAGCAAAACAAAAGTAAGA AAAAAGCACAGCAAGCAGCAGCTGACACAGGACACAG CAATCAGGTCAGCCAAAATTACCCTATAGTGCAGAACA TCCAGGGGCAAATGGTACATCAGGCCATATCACCTAGA ACTTTAAATGCATGGGTAAAAGTAGTAGAAGAGAAGG CTTTCAGCCCAGAAGTGATACCCATGTTTTCAGCATTAT CAGAAGGAGCCACCCCACAAGATTTAAACACCATGCTA AACACAGTGGGGGGACATCAAGCAGCCATGCAAATGT TAAAAGAGACCATCAATGAGGAAGCTGCAGAATGGGA TAGAGTGCATCCAGTGCATGCAGGGCCTATTGCACCAG GCCAGATGAGAGAACCAAGGGGAAGTGACATAGCAGG AACTACTAGTACCCTTCAGGAACAAATAGGATGGATGA CACATAATCCACCTATCCCAGTAGGAGAAATCTATAAA AGATGGATAATCCTGGGATTAAATAAAATAGTAAGAAT GTATAGCCCTACCAGCATTCTGGACATAAGACAAGGAC CAAAGGAACCCTTTAGAGACTATGTAGACCGATTCTAT AAAACTCTAAGAGCCGAGCAAGCTTCACAAGAGGTAA AAAATTGGATGACAGAAACCTTGTTGGTCCAAAATGCG AACCCAGATTGTAAGACTATTTTAAAAGCATTGGGACC

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SEQ ID NO:	Description	Sequence
		AGGAGCGACACTAGAAGAAATGATGACAGCATGTCAG
		GGAGTGGGGGGACCCGGCCATAAAGCAAGAGTTTTGG
		CTGAAGCAATGAGCCAAGTAACAAATCCAGCTACCATA
		ATGATACAGAAAGGCAATTTTAGGAACCAAAGAAAGA
		CTGTTAAGTGTTTCAATTGTGGCAAAGAAGGGCACATA
		GCCAAAAATTGCAGGGCCCCTAGGAAAAAGGGCTGTT
		GGAAATGTGGAAAGGAAGGACACCAAATGAAAGATTG
		TACTGAGAGACAGGCTAATTTTTTTAGGGAAGATCTGGC
		CTTCCCACAAGGGAAGGCCAGGGAATTTTCTTCAGAGC
		AGACCAGAGCCAACAGCCCCACCAGAAGAGAGCTTCA
		GGTTTGGGGAAGAGACAACAACTCCCTCTCAGAAGCAG
		GAGCCGATAGACAAGGAACTGTATCCTTTAGCTTCCCT
		CAGATCACTCTTTGGCAGCGACCCCTCGTCACAATAA
24	Rev response element (RRE)	AGGAGCTTTGTTCCTTGGGTTCTTGGGAGCAGCAGGAA
		GCACTATGGGCGCAGCCTCAATGACGCTGACGGTACAG
		GCCAGACAATTATTGTCTGGTATAGTGCAGCAGCAGAA
		CAATTTGCTGAGGGCTATTGAGGCGCAACAGCATCTGT
		TGCAACTCACAGTCTGGGGCATCAAGCAGCTCCAGGCA
		AGAATCCTGGCTGTGGAAAGATACCTAAAGGATCAACA
		GCTCC
25	Envelope; VSV-G; Glycoprotein envelope-cell entry	ATGAAGTGCCTTTTGTACTTAGCCTTTTTATTCATTGGG
		GTGAATTGCAAGTTCACCATAGTTTTTCCACACAACCA
		AAAAGGAAACTGGAAAAATGTTCCTTCTAATTACCATT
		ATTGCCCGTCAAGCTCAGATTTAAATTGGCATAATGAC
		TTAATAGGCACAGCCTTACAAGTCAAAATGCCCAAGAG
		TCACAAGGCTATTCAAGCAGACGGTTGGATGTGTCATG
		CTTCCAAATGGGTCACTACTTGTGATTTCCGCTGGTATG
		GACCGAAGTATATAACACATTCCATCCGATCCTTCACT
		CCATCTGTAGAACAATGCAAGGAAAGCATTGAACAAA
		CGAAACAAGGAACTTGGCTGAATCCAGGCTTCCCTCCT
		CAAAGTTGTGGATATGCAACTGTGACGGATGCCGAAGC
		AGTGATTGTCCAGGTGACTCCTCACCATGTGCTGGTTG
		ATGAATACACAGGAGAATGGGTTGATTCACAGTTCATC
		AACGGAAAATGCAGCAATTACATATGCCCCACTGTCCA
		TAACTCTACAACCTGGCATTCTGACTATAAGGTCAAAG
		GGCTATGTGATTCTAACCTCATTTCCATGGACATCACCT
		TCTTCTCAGAGGACGGAGAGCTATCATCCCTGGGAAAG
		GAGGGCACAGGGTTCAGAAGTAACTACTTTGCTTATGA
		AACTGGAGGCAAGGCCTGCAAAATGCAATACTGCAAG
		CATTGGGGAGTCAGACTCCCATCAGGTGTCTGGTTCGA
		GATGGCTGATAAGGATCTCTTTGCTGCAGCCAGATTCC
		CTGAATGCCCAGAAGGGTCAAGTATCTCTGCTCCATCT
		CAGACCTCAGTGGATGTAAGTCTAATTCAGGACGTTGA
		GAGGATCTTGGATTATTCCCTCTGCCAAGAAACCTGGA
		GCAAAATCAGAGCGGGTCTTCCAATCTCTCCAGTGGAT
		CTCAGCTATCTTGCTCCTAAAAACCCAGGAACCGGTCC
		TGCTTTCACCATAATCAATGGTACCCTAAAATACTTTGA
		GACCAGATACATCAGAGTCGATATTGCTGCTCCAATCC
		TCTCAAGAATGGTCGGAATGATCAGTGGAACTACCACA
		GAAAGGGAACTGTGGGATGACTGGGCACCATATGAAG
		ACGTGGAAATTGGACCCAATGGAGTTCTGAGGACCAGT
		TCAGGATATAAGTTTCCTTTATACATGATTGGACATGGT
		ATGTTGGACTCCGATCTTCATCTTAGCTCAAAGGCTCAG
		GTGTTCGAACATCCTCACATTCAAGACGCTGCTTCGCA
		ACTTCCTGATGATGAGAGTTTATTTTTTGGTGATACTGG
		GCTATCCAAAAATCCAATCGAGCTTGTAGAAGGTTGGT
		TCAGTAGTTGGAAAAGCTCTATTGCCTCTTTTTTCTTTA
		TCATAGGGTTAATCATTGGACTATTCTTGGTTCTCCGAG
		TTGGTATCCATCTTTGCATTAAATTAAAGCACACCAAG
		AAAAGACAGATTTATACAGACATAGAGATGA
26	Central polypurine tract (cPPT)	TTTTAAAAGAAAAGGGGGGATTGGGGGGTACAGTGCA
		GGGGAAAGAATAGTAGACATAATAGCAACAGACATAC
		AAACTAAAGAATTACAAAAACAAATTACAAAATTCAA
		AATTTTA

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Sequences

SEQ ID NO:	Description	Sequence
27	Polymerase III shRNA promoters; H1 promoter	GAACGCTGACGTCATCAACCCGCTCCAAGGAATCGCGG GCCCAGTGTCACTAGGCGGGAACACCCAGCGCGCGTGC GCCCTGGCAGGAAGATGGCTGTGAGGGACAGGGGAGT GGCGCCCTGCAATATTTGCATGTCGCTATGTGTTCTGGG AAATCACCATAAACGTGAAATGTCTTTGGATTTGGGAA TCTTATAAGTTCTGTATGAGACCACTT
28	EF1	GCTCCGGTGCCCGTCAGTGGGCAGAGCGCACATCGCCC ACAGTCCCCGAGAAGTTGGGGGGAGGGGTCGGCAATT GAACGGGTGCCTAGAGAAGGTGGCGCGGGGTAAACTG GGAAAGTGATGTCGTGTACTGGCTCCGCCTTTTTCCCGA GGGTGGGGGAGAACCGTATATAAGTGCAGTAGTCGCC GTGAACGTTCTTTTTCGCAACGGGTTTGCCGCCAGAAC ACAGCTGAAGCTTCGAGGGGCTCGCATCTCTCCTTCAC GCGCCCGCCGCCCTACCTGAGGCCGCCATCCACGCCGG TTGAGTCGCGTTCTGCCGCCTCCCGCCTGTGGTGCCTCC TGAACTGCGTCCGCCGTCTAGGTAAGTTTAAAGCTCAG GTCGAGACCGGGCCTTTGTCCGGCGCTCCCTTGGAGCC TACCTAGACTCAGCCGGCTCTCCACGCTTTGCCTGACCC TGCTTGCTCAACTCTACGTCTTTGTTTCGTTTTCTGTTCT GCGCCGTTACAGATCCAAGCTGTGACCGGCGCCTAC
29	GFP	ATGGAGAGCGACGAGAGCGGCCTGCCCGCCATGGAGA TCGAGTGCCGCATCACCGGCACCCTGAACGGCGTGGAG TTCGAGCTGGTGGGCGGCGGAGAGGGCACCCCCAAGC AGGGCCGCATGACCAACAAGATGAAGAGCACCAAAGG CGCCCTGACCTTCAGCCCCTACCTGCTGAGCCACGTGA TGGGCTACGGCTTCTACCACTTCGGCACCTACCCCAGC GGCTACGAGAACCCCTTCCTGCACGCCATCAACAACGG CGGCTACACCAACACCCGCATCGAGAAGTACGAGGAC GGCGGCGTGCTGCACGTGAGCTTCAGCTACCGCTACGA GGCCGGCCGCGTGATCGGCGACTTCAAGGTGGTGGGCA CCGGCTTCCCCGAGGACAGCGTGATCTTCACCGACAAG ATCATCCGCAGCAACGCCACCGTGGAGCACCTGCACCC CATGGGCGATAACGTGCTGGTGGGCAGCTTCGCCCGCA CCTTCAGCCTGCGCGACGGCGGCTACTACAGCTTCGTG GTGGACAGCCACATGCACTTCAAGAGCGCCATCCACCC CAGCATCCTGCAGAACGGGGGCCCCATGTTCGCCTTCC GCCGCGTGGAGGAGCTGCACAGCAACACCGAGCTGGG CATCGTGGAGTACCAGCACGCCTTCAAGACCCCCATCG CCTTCGCCAGATCCCGCGCTCAGTCGTCCAATTCTGCCG TGGACGGCACCGCCGGACCCGGCTCCACCGGATCTCGC TAA
30	Long WPRE sequence	AATCAACCTCTGATTACAAAATTTGTGAAAGATTGACT GGTATTCTTAACTATGTTGCTCCTTTTACGCTATGTGGA TACGCTGCTTTAATGCCTTTGTATCATGCTATTGCTTCC CGTATGGCTTTCATTTTCTCCTCCTTGTATAAATCCTGG TTGCTGTCTCTTTATGAGGAGTTGTGGCCCGTTGTCAGG CAACGTGGCGTGGTGTGCACTGTGTTTGCTGACGCAAC CCCCACTGGTTGGGGCATTGCCACCACCTGTCAGCTCCT TTCCGGGACTTTCGCTTTCCCCCTCCCTATTGCCACGGC GGAACTCATCGCCGCCTGCCTTGCCCGCTGCTGGACAG GGGCTCGGCTGTTGGGCACTGACAATTCCGTGGTGTTG TCGGGGAAATCATCGTCCTTTCCTTGGCTGCTCGCCTGT GTTGCCACCTGGATTCTGCGCGGGACGTCCTTCTGCTAC GTCCCTTCGGCCCTCAATCCAGCGGACCTTCCTTCCCGC GGCCTGCTGCCGGCTCTGCGGCCTCTTCCGCGTCTTCGC CTTCGCCCTCAGACGAGTCGGATCTCCCTTTGGGCCGCC TCCCCGCCT
31	3' delta LTR	TGGAAGGGCTAATTCACTCCCAACGAAGATAAGATCTG CTTTTTGCTTGTACTGGGTCTCTCTGGTTAGACCAGATC TGAGCCTGGGAGCTCTCTGGCTAACTAGGGAACCCACT GCTTAAGCCTCAATAAAGCTTGCCTTGAGTGCTTCAAG TAGTGTGTGCCCGTCTGTTGTGTGACTCTGGTAACTAGA GATCCCTCAGACCCTTTTAGTCAGTGTGGAAAATCTCTA GCAGTAGTAGTTCATGTCA

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Sequences

SEQ ID NO:	Description	Sequence
32	Helper/Rev; CMV early (CAG) enhancer; Enhance Transcription	TAGTTATTAATAGTAATCAATTACGGGGTCATTAGTTCA TAGCCCATATATGGAGTTCCGCGTTACATAACTTACGG TAAATGGCCCGCCTGGCTGACCGCCCAACGACCCCCGC CCATTGACGTCAATAATGACGTATGTTCCCATAGTAAC GCCAATAGGGACTTTCCATTGACGTCAATGGGTGGACT ATTTACGGTAAACTGCCCACTTGGCAGTACATCAAGTG TATCATATGCCAAGTACGCCCCCTATTGACGTCAATGA CGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGA CCTTATGGGACTTTCCTACTTGGCAGTACATCTACGTAT TAGTCATC
33	Helper/Rev; Chicken beta actin (CAG) promoter; Transcription	GCTATTACCATGGGTCGAGGTGAGCCCCACGTTCTGCT TCACTCTCCCCATCTCCCCCCCCTCCCCACCCCCAATTT TGTATTTATTTATTTTTTAATTATTTTGTGCAGCGATGG GGGCGGGGGGGGGGGGGGCGCGCGCCAGGCGGGGCGG GGCGGGGCGAGGGGCGGGGCGGGGCGAGGCGGAGAG GTGCGGCGGCAGCCAATCAGAGCGGCGCGCTCCGAAA GTTTCCTTTTATGGCGAGGCGGCGGCGGCGGCCCT ATAAAAAGCGAAGCGCGCGGCGGGCG
34	Helper/Rev; Chicken beta actin intron; Enhance gene expression	GGAGTCGCTGCGTTGCCTTCGCCCCGTGCCCCGCTCCGC GCCGCCTCGCGCCGCCCGCCCCGGCTCTGACTGACCGC GTTACTCCCACAGGTGAGCGGGCGGGACGGCCCTTCTC CTCCGGGCTGTAATTAGCGCTTGGTTTAATGACGGCTC GTTTCTTTTCTGTGGCTGCGTGAAAGCCTTAAAGGGCTC CGGGAGGGCCCTTTGTGCGGGGGGGAGCGGCTCGGGG GGTGCGTGCGTGTGTGTGTGCGTGGGGAGCGCCGCGTG CGGCCCGCGCTGCCCGGCGGCTGTGAGCGCTGCGGGCG CGGCGCGGGGCTTTGTGCGCTCCGCGTGTGCGCGAGGG GAGCGCGGCCGGGGGCGGTGCCCCGCGGTGCGGGGGG GCTGCGAGGGGAACAAAGGCTGCGTGCGGGGTGTGTG CGTGGGGGGGTGAGCAGGGGGTGTGGGCGCGGCGGTC GGGCTGTAACCCCCCCCTGCACCCCCCTCCCCGAGTTG CTGAGCACGGCCCGGCTTCGGGTGCGGGGCTCCGTGCG GGGCGTGGCGCGGGGCTCGCCGTGCCGGGCGGGGGGT GGCGGCAGGTGGGGGTGCCGGGCGGGGCGGGGCCGCC TCGGGCCGGGGAGGGCTCGGGGGAGGGGCGCGGCGGC CCCGGAGCGCCGGCGGCTGTCGAGGCGCGGCGAGCCG CAGCCATTGCCTTTTATGGTAATCGTGCGAGAGGGCGC AGGGACTTCCTTTGTCCCAAATCTGGCGGAGCCGAAAT CTGGGAGGCGCCGCCGCACCCCCTCTAGCGGGCGCGGG CGAAGCGGTGCGGCGCCGGCAGGAAGGAAATGGGCGG GGAGGGCCTTCGTGCGTCGCCGCGCCGCCGTCCCCTTC TCCATCTCCAGCCTCGGGGCTGCCGCAGGGGGACGGCT GCCTTCGGGGGGGACGGGGCAGGGCGGGGTTCGGCTTC TGGCGTGTGACCGGCGG
35	Helper/Rev; HIV Pol; Protease and reverse transcriptase	ATGAATTTGCCAGGAAGATGGAAACCAAAAATGATAG GGGGAATTGGAGGTTTTATCAAAGTAGGACAGTATGAT CAGATACTCATAGAAATCTGCGGACATAAAGCTATAGG TACAGTATTAGTAGGACCTACACCTGTCAACATAATTG GAAGAAATCTGTTGACTCAGATTGGCTGCACTTTAAAT TTTCCCATTAGTCCTATTGAGACTGTACCAGTAAAATTA AAGCCAGGAATGGATGGCCCAAAAGTTAAACAATGGC CATTGACAGAAGAAAAAATAAAAGCATTAGTAGAAAT TTGTACAGAAATGGAAAAGGAAGGAAAAATTTCAAAA ATTGGGCCTGAAAATCCATACAATACTCCAGTATTTGC CATAAAGAAAAAAGACAGTACTAAATGGAGAAAATTA GTAGATTTCAGAGAACTTAATAAGAGAACTCAAGATTT CTGGGAAGTTCAATTAGGAATACCACATCCTGCAGGGT TAAAACAGAAAAAATCAGTAACAGTACTGGATGTGGG CGATGCATATTTTTCAGTTCCCTTAGATAAAGACTTCAG GAAGTATACTGCATTTACCATACCTAGTATAAACAATG AGACACCAGGGATTAGATATCAGTACAATGTGCTTCCA CAGGGATGGAAAGGATCACCAGCAATATTCCAGTGTAG CATGACAAAAATCTTAGAGCCTTTTAGAAAACAAAATC CAGACATAGTCATCTATCAATACATGGATGATTTGTAT GTAGGATCTGACTTAGAAATAGGGCAGCATAGAACAA AAATAGAGGAACTGAGACAACATCTGTTGAGGTGGGG

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SEQ ID NO:	Description	Sequence
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		GGACAGTACAGCCTATAGTGCTGCCAGAAAAGGACAG
		CTGGACTGTCAATGACATACAGAAATTAGTGGGAAAAT
		TGAATTGGGCAAGTCAGATTTATGCAGGGATTAAAGTA
		AGGCAATTATGTAAACTTCTTAGGGGAACCAAAGCACT
		AACAGAAGTAGTACCACTAACAGAAGAAGCAGAGCTA
		GAACTGGCAGAAAACAGGGAGATTCTAAAAGAACCGG
		TACATGGAGTGTATTATGACCCATCAAAAGACTTAATA
		GCAGAAATACAGAAGCAGGGGCAAGGCCAATGGACAT
		ATCAAATTTATCAAGAGCCATTTAAAAATCTGAAAACA
		GGAAAATATGCAAGAATGAAGGGTGCCCACACTAATG
		ATGTGAAACAATTAACAGAGGCAGTACAAAAAATAGC
		CACAGAAAGCATAGTAATATGGGGAAAGACTCCTAAA
		TTTAAATTACCCATACAAAAGGAAACATGGGAAGCATG
		GTGGACAGAGTATTGGCAAGCCACCTGGATTCCTGAGT
		GGGAGTTTGTCAATACCCCTCCCTTAGTGAAGTTATGGT
		ACCAGTTAGAGAAAGAACCCATAATAGGAGCAGAAAC
		TTTCTATGTAGATGGGGCAGCCAATAGGGAAACTAAAT
		TAGGAAAAGCAGGATATGTAACTGACAGAGGAAGACA
		AAAAGTTGTCCCCCTAACGGACACAACAAATCAGAAG
		ACTGAGTTACAAGCAATTCATCTAGCTTTGCAGGATTC
		GGGATTAGAAGTAAACATAGTGACAGACTCACAATATG
		CATTGGGAATCATTCAAGCACAACCAGATAAGAGTGAA
		TCAGAGTTAGTCAGTCAAATAATAGAGCAGTTAATAAA
		AAAGGAAAAAGTCTACCTGGCATGGGTACCAGCACAC
		AAAGGAATTGGAGGAAATGAACAAGTAGATGGGTTGG
		TCAGTGCTGGAATCAGGAAAGTACTA
36	Helper Rev; HIV Integrase; Integration of viral RNA	TTTTTAGATGGAATAGATAAGGCCCAAGAAGAACATGA
		GAAATATCACAGTAATTGGAGAGCAATGGCTAGTGATT
		TTAACCTACCACCTGTAGTAGCAAAAGAAATAGTAGCC
		AGCTGTGATAAATGTCAGCTAAAAGGGGAAGCCATGC
		ATGGACAAGTAGACTGTAGCCCAGGAATATGGCAGCTA
		GATTGTACACATTTAGAAGGAAAAGTTATCTTGGTAGC
		AGTTCATGTAGCCAGTGGATATATAGAAGCAGAAGTAA
		TTCCAGCAGAGACAGGGCAAGAAACAGCATACTTCCTC
		TTAAAATTAGCAGGAAGATGGCCAGTAAAAACAGTAC
		ATACAGACAATGGCAGCAATTTCACCAGTACTACAGTT
		AAGGCCGCCTGTTGGTGGGCGGGGATCAAGCAGGAATT
		TGGCATTCCCTACAATCCCCAAAGTCAAGGAGTAATAG
		AATCTATGAATAAAGAATTAAAGAAAATTATAGGACA
		GGTAAGAGATCAGGCTGAACATCTTAAGACAGCAGTAC
		AAATGGCAGTATTCATCCACAATTTTAAAAGAAAAGGG
		GGGATTGGGGGGTACAGTGCAGGGGAAAGAATAGTAG
		ACATAATAGCAACAGACATACAAACTAAAGAATTACA
		AAAACAAATTACAAAAATTCAAAATTTTCGGGTTTATT
		ACAGGGACAGCAGAGATCCAGTTTGGAAAGGACCAGC
		AAAGCTCCTCTGGAAAGGTGAAGGGGCAGTAGTAATA
		CAAGATAATAGTGACATAAAAGTAGTGCCAAGAAGAA
		AAGCAAAGATCATCAGGGATTATGGAAAACAGATGGC
		AGGTGATGATTGTGTGGCAAGTAGACAGGATGAGGATT
		AA
37	Helper/Rev; HIV Rev; Nuclear export and stabilize viral mRNA	ATGGCAGGAAGAAGCGGAGACAGCGACGAAGAACTCC
		TCAAGGCAGTCAGACTCATCAAGTTTCTCTATCAAAGC
		AACCCACCTCCCAATCCCGAGGGGACCCGACAGGCCCG
		AAGGAATAGAAGAAGAAGGTGGAGAGAGAGACAGAG
		ACAGATCCATTCGATTAGTGAACGGATCCTTAGCACTT
		ATCTGGGACGATCTGCGGAGCCTGTGCCTCTTCAGCTA
		CCACCGCTTGAGAGACTTACTCTTGATTGTAACGAGGA
		TTGTGGAACTTCTGGGACGCAGGGGGTGGGAAGCCCTC
		AAATATTGGTGGAATCTCCTACAATATTGGAGTCAGGA
		GCTAAAGAATAG
38	Helper/Rev; Rabbit beta globin poly A; RNA stability	AGATCTTTTTCCCTCTGCCAAAAATTATGGGGACATCAT
		GAAGCCCCTTGAGCATCTGACTTCTGGCTAATAAAGGA
		AATTTATTTTCATTGCAATAGTGTGTTGGAATTTTTTGT
		GTCTCTCACTCGGAAGGACATATGGGAGGGCAAATCAT
		TTAAAACATCAGAATGAGTATTTGGTTTAGAGTTTGGC

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SEQ ID NO:	Description	Sequence
		AACATATGCCATATGCTGGCTGCCATGAACAAAGGTGG
		CTATAAAGAGGTCATCAGTATATGAAACAGCCCCCTGC
		TGTCCATTCCTTATTCCATAGAAAAGCCTTGACTTGAGG
		TTAGATTTTTTTTTATATTTTGTTTTGTGTTATTTTTTTCTT
		TAACATCCCTAAAATTTTCCTTACATGTTTTACTAGCCA
		GATTTTTCCTCCTCTCCTGACTACTCCCAGTCATAGCTG
		TCCCTCTTCTCTTATGAAGATC
39	Envelope; CMV promoter; Transcription	ACATTGATTATTGACTAGTTATTAATAGTAATCAATTAC
		GGGGTCATTAGTTCATAGCCCATATATGGAGTTCCGCG
		TTACATAACTTACGGTAAATGGCCCGCCTGGCTGACCG
		CCCAACGACCCCCGCCCATTGACGTCAATAATGACGTA
		TGTTCCCATAGTAACGCCAATAGGGACTTTCCATTGAC
		GTCAATGGGTGGAGTATTTACGGTAAACTGCCCACTTG
		GCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCC
		TATTGACGTCAATGACGGTAAATGGCCCGCCTGGCATT
		ATGCCCAGTACATGACCTTATGGGACTTTCCTACTTGGC
		AGTACATCTACGTATTAGTCATCGCTATTACCATGGTGA
		TGCGGTTTTGGCAGTACATCAATGGGCGTGGATAGCGG
		TTTGACTCACGGGGATTTCCAAGTCTCCACCCCATTGAC
		GTCAATGGGAGTTTGTTTTGGCACCAAAATCAACGGGA
		CTTTCCAAAATGTCGTAACAACTCCGCCCCATTGACGC
		AAATGGGCGGTAGGCGTGTACGGTGGGAGGTCTATATA
		AGC
40	Envelope; Beta globin intron; Enhance gene expression	GTGAGTTTGGGGACCCTTGATTGTTCTTTCTTTTTCGCT
		ATTGTAAAATTCATGTTATATGGAGGGGGCAAAGTTTT
		CAGGGTGTTGTTTAGAATGGGAAGATGTCCCTTGTATC
		ACCATGGACCCTCATGATAATTTTGTTTCTTTCACTTTC
		TACTCTGTTGACAACCATTGTCTCCTCTTATTTTCTTTTC
		ATTTTCTGTAACTTTTTCGTTAAACTTTAGCTTGCATTTG
		TAACGAATTTTTAAATTCACTTTTGTTTATTTGTCAGAT
		TGTAAGTACTTTCTCTAATCACTTTTTTTTCAAGGCAAT
		CAGGGTATATTATATTGTACTTCAGCACAGTTTTAGAG
		AACAATTGTTATAATTAAATGATAAGGTAGAATATTTC
		TGCATATAAATTCTGGCTGGCGTGGAAATATTCTTATTG
		GTAGAAACAACTACACCCTGGTCATCATCCTGCCTTTCT
		CTTTATGGTTACAATGATATACACTGTTTGAGATGAGG
		ATAAAATACTCTGAGTCCAAACCGGGCCCCTCTGCTAA
		CCATGTTCATGCCTTCTTCTCTTTCCTACAG
41	Primer	TAAGCAGAATTCATGAATTTGCCAGGAAGAT
42	Primer	CCATACAATGAATGGACACTAGGCGGCCGCACGAAT
43	Gag, Pol, Integrase fragment	GAATTCATGAATTTGCCAGGAAGATGGAAACCAAAAAT
		GATAGGGGGAATTGGAGGTTTTATCAAAGTAAGACAGT
		ATGATCAGATACTCATAGAAATCTGCGGACATAAAGCT
		ATAGGTACAGTATTAGTAGGACCTACACCTGTCAACAT
		AATTGGAAGAAATCTGTTGACTCAGATTGGCTGCACTT
		TAAATTTTCCCATTAGTCCTATTGAGACTGTACCAGTAA
		AATTAAAGCCAGGAATGGATGGCCCAAAAGTTAAACA
		ATGGCCATTGACAGAAGAAAAAATAAAAGCATTAGTA
		GAAATTTGTACAGAAATGGAAAAGGAAGGAAAAATTT
		CAAAAATTGGGCCTGAAAATCCATACAATACTCCAGTA
		TTTGCCATAAAGAAAAAAGACAGTACTAAATGGAGAA
		AATTAGTAGATTTCAGAGAACTTAATAAGAGAACTCAA
		GATTTCTGGGAAGTTCAATTAGGAATACCACATCCTGC
		AGGGTTAAAACAGAAAAAATCAGTAACAGTACTGGAT
		GTGGGCGATGCATATTTTTCAGTTCCCTTAGATAAAGA
		CTTCAGGAAGTATACTGCATTTACCATACCTAGTATAA
		ACAATGAGACACCAGGGATTAGATATCAGTACAATGTG
		CTTCCACAGGGATGGAAAGGATCACCAGCAATATTCCA
		GTGTAGCATGACAAAAATCTTAGAGCCTTTTAGAAAAC
		AAAATCCAGACATAGTCATCTATCAATACATGGATGAT
		TTGTATGTAGGATCTGACTTAGAAATAGGGCAGCATAG
		AACAAAAATAGAGGAACTGAGACAACATCTGTTGAGG
		TGGGGATTTACCACACCAGACAAAAAACATCAGAAAG
		AACCTCCATTCCTTTGGATGGGTTATGAACTCCATCCTG
		ATAAATGGACAGTACAGCCTATAGTGCTGCCAGAAAAG

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SEQ ID NO:	Description	Sequence
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		AAAATTGAATTGGGCAAGTCAGATTTATGCAGGGATTA
		AAGTAAGGCAATTATGTAAACTTCTTAGGGGAACCAAA
		GCACTAACAGAAGTAGTACCACTAACAGAAGAAGCAG
		AGCTAGAACTGGCAGAAAACAGGGAGATTCTAAAAGA
		ACCGGTACATGGAGTGTATTATGACCCATCAAAAGACT
		TAATAGCAGAAATACAGAAGCAGGGGCAAGGCCAATG
		GACATATCAAATTTATCAAGAGCCATTTAAAAATCTGA
		AAACAGGAAAGTATGCAAGAATGAAGGGTGCCCACAC
		TAATGATGTGAAACAATTAACAGAGGCAGTACAAAAA
		ATAGCCACAGAAAGCATAGTAATATGGGGAAAGACTC
		CTAAATTTAAATTACCCATACAAAAGGAAACATGGGAA
		GCATGGTGGACAGAGTATTGGCAAGCCACCTGGATTCC
		TGAGTGGGAGTTTGTCAATACCCCTCCCTTAGTGAAGTT
		ATGGTACCAGTTAGAGAAAGAACCCATAATAGGAGCA
		GAAACTTTCTATGTAGATGGGGCAGCCAATAGGGAAAC
		TAAATTAGGAAAAGCAGGATATGTAACTGACAGAGGA
		AGACAAAAAGTTGTCCCCCTAACGGACACAACAAATCA
		GAAGACTGAGTTACAAGCAATTCATCTAGCTTTGCAGG
		ATTCGGGATTAGAAGTAAACATAGTGACAGACTCACAA
		TATGCATTGGGAATCATTCAAGCACAACCAGATAAGAG
		TGAATCAGAGTTAGTCAGTCAAATAATAGAGCAGTTAA
		TAAAAAAGGAAAAAGTCTACCTGGCATGGGTACCAGC
		ACACAAAGGAATTGGAGGAAATGAACAAGTAGATAAA
		TTGGTCAGTGCTGGAATCAGGAAAGTACTATTTTTAGA
		TGGAATAGATAAGGCCCAAGAAGAACATGAGAAATAT
		CACAGTAATTGGAGAGCAATGGCTAGTGATTTTAACCT
		ACCACCTGTAGTAGCAAAAGAAATAGTAGCCAGCTGTG
		ATAAATGTCAGCTAAAAGGGGAAGCCATGCATGGACA
		AGTAGACTGTAGCCCAGGAATATGGCAGCTAGATTGTA
		CACATTTAGAAGGAAAAGTTATCTTGGTAGCAGTTCAT
		GTAGCCAGTGGATATATAGAAGCAGAAGTAATTCCAGC
		AGAGACAGGGCAAGAAACAGCATACTTCCTCTTAAAAT
		TAGCAGGAAGATGGCCAGTAAAAACAGTACATACAGA
		CAATGGCAGCAATTTCACCAGTACTACAGTTAAGGCCG
		CCTGTTGGTGGGCGGGGATCAAGCAGGAATTTGGCATT
		CCCTACAATCCCCAAAGTCAAGGAGTAATAGAATCTAT
		GAATAAAGAATTAAAGAAAATTATAGGACAGGTAAGA
		GATCAGGCTGAACATCTTAAGACAGCAGTACAAATGGC
		AGTATTCATCCACAATTTTAAAAGAAAAGGGGGGATTG
		GGGGGTACAGTGCAGGGGAAAGAATAGTAGACATAAT
		AGCAACAGACATACAAACTAAAGAATTACAAAAACAA
		ATTACAAAAATTCAAAATTTTCGGGTTTATTACAGGGA
		CAGCAGAGATCCAGTTTGGAAAGGACCAGCAAAGCTC
		CTCTGGAAAGGTGAAGGGGCAGTAGTAATACAAGATA
		ATAGTGACATAAAAGTAGTGCCAAGAAGAAAAGCAAA
		GATCATCAGGGATTATGGAAAACAGATGGCAGGTGAT
		GATTGTGTGGCAAGTAGACAGGATGAGGATTAA
44	DNA Fragment containing Rev, RRE and rabbit beta globin poly A	TCTAGAATGGCAGGAAGAAGCGGAGACAGCGACGAAG
		AGCTCATCAGAACAGTCAGACTCATCAAGCTTCTCTAT
		CAAAGCAACCCACCTCCCAATCCCGAGGGGACCCGACA
		GGCCCGAAGGAATAGAAGAAGAAGGTGGAGAGAGAG
		ACAGAGACAGATCCATTCGATTAGTGAACGGATCCTTG
		GCACTTATCTGGGACGATCTGCGGAGCCTGTGCCTCTTC
		AGCTACCACCGCTTGAGAGACTTACTCTTGATTGTAAC
		GAGGATTGTGGAACTTCTGGGACGCAGGGGGTGGGAA
		GCCCTCAAATATTGGTGGAATCTCCTACAATATTGGAG
		TCAGGAGCTAAAGAATAGAGGAGCTTTGTTCCTTGGGT
		TCTTGGGAGCAGCAGGAAGCACTATGGGCGCAGCGTCA
		ATGACGCTGACGGTACAGGCCAGACAATTATTGTCTGG
		TATAGTGCAGCAGCAGAACAATTTGCTGAGGGCTATTG
		AGGCGCAACAGCATCTGTTGCAACTCACAGTCTGGGGC
		ATCAAGCAGCTCCAGGCAAGAATCCTGGCTGTGGAAAG
		ATACCTAAAGGATCAACAGCTCCTAGATCTTTTTCCCTC
		TGCCAAAAATTATGGGGACATCATGAAGCCCCTTGAGC
		ATCTGACTTCTGGCTAATAAAGGAAATTTATTTTCATTG
		CAATAGTGTGTTGGAATTTTTTGTGTCTCTCACTCGGAA
		GGACATATGGGAGGGCAAATCATTTAAAACATCAGAAT
		GAGTATTTGGTTTAGAGTTTGGCAACATATGCCATATG

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Sequences

SEQ ID NO:	Description	Sequence
		CTGGCTGCCATGAACAAAGGTGGCTATAAAGAGGTCAT
		CAGTATATGAAACAGCCCCCTGCTGTCCATTCCTTATTC
		CATAGAAAAGCCTTGACTTGAGGTTAGATTTTTTTTATA
		TTTTGTTTTGTGTTATTTTTTTCTTTAACATCCCTAAAAT
		TTTCCTTACATGTTTTACTAGCCAGATTTTTCCTCCTCTC
		CTGACTACTCCCAGTCATAGCTGTCCCTCTTCTCTTATG
		AAGATCCCTCGACCTGCAGCCCAAGCTTGGCGTAATCA
		TGGTCATAGCTGTTTCCTGTGTGAAATTGTTATCCGCTC
		ACAATTCCACACAACATACGAGCCGGAAGCATAAAGT
		GTAAAGCCTGGGGTGCCTAATGAGTGAGCTAACTCACA
		TTAATTGCGTTGCGCTCACTGCCCGCTTTCCAGTCGGGA
		AACCTGTCGTGCCAGCGGATCCGCATCTCAATTAGTCA
		GCAACCATAGTCCCGCCCCTAACTCCGCCCATCCCGCC
		CCTAACTCCGCCCAGTTCCGCCCATTCTCCGCCCCATGG
		CTGACTAATTTTTTTTATTTATGCAGAGGCCGAGGCCGC
		CTCGGCCTCTGAGCTATTCCAGAAGTAGTGAGGAGGCT
		TTTTTGGAGGCCTAGGCTTTTGCAAAAAGCTAACTTGTT
		TATTGCAGCTTATAATGGTTACAAATAAAGCAATAGCA
		TCACAAATTTCACAAATAAAGCATTTTTTTCACTGCATT
		CTAGTTGTGGTTTGTCCAAACTCATCAATGTATCTTATC
		AGCGGCCGCCCCGGG
45	DNA fragment containing the CAG enhancer/promoter/ intron sequence	ACGCGTTAGTTATTAATAGTAATCAATTACGGGGTCAT
		TAGTTCATAGCCCATATATGGAGTTCCGCGTTACATAA
		CTTACGGTAAATGGCCCGCCTGGCTGACCGCCCAACGA
		CCCCCGCCCATTGACGTCAATAATGACGTATGTTCCCAT
		AGTAACGCCAATAGGGACTTTCCATTGACGTCAATGGG
		TGGACTATTTACGGTAAACTGCCCACTTGGCAGTACAT
		CAAGTGTATCATATGCCAAGTACGCCCCCTATTGACGT
		CAATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGT
		ACATGACCTTATGGGACTTTCCTACTTGGCAGTACATCT
		ACGTATTAGTCATCGCTATTACCATGGGTCGAGGTGAG
		CCCCACGTTCTGCTTCACTCTCCCCATCTCCCCCCCCTC
		CCCACCCCCAATTTTGTATTTATTTATTTTTTTAATTATTT
		TGTGCAGCGATGGGGGCGGGGGGGGGGGGGCGCGCG
		CCAGGCGGGGCGGGGCGGGGCGAGGGGCGGGGCGGGG
		CGAGGCGGAGAGGTGCGGCGGCAGCCAATCAGAGCGG
		CGCGCTCCGAAAGTTTCCTTTTATGGCGAGGCGGCGGC
		GGCGGCGGCCCTATAAAAAGCGAAGCGCGCGGCGGGC
		GGGAGTCGCTGCGTTGCCTTCGCCCCGTGCCCCGCTCC
		GCGCCGCCTCGCGCCGCCCGCCCCGGCTCTGACTGACC
		GCGTTACTCCCACAGGTGAGCGGGCGGGACGGCCCTTC
		TCCTCCGGGCTGTAATTAGCGCTTGGTTTAATGACGGCT
		CGTTTCTTTTCTGTGGCTGCGTGAAAGCCTTAAAGGGCT
		CCGGGAGGGCCCTTTGTGCGGGGGGGAGCGGCTCGGG
		GGGTGCGTGCGTGTGTGTGTGCGTGGGGAGCGCCGCGT
		GCGGCCCGCGCTGCCCGGCGGCTGTGAGCGCTGCGGGC
		GCGGCGCGGGGCTTTGTGCGCTCCGCGTGTGCGCGAGG
		GGAGCGCGGCCGGGGGCGGTGCCCCGCGGTGCGGGGG
		GGCTGCGAGGGGAACAAAGGCTGCGTGCGGGGTGTGT
		GCGTGGGGGGGTGAGCAGGGGGTGTGGGCGCGGCGGT
		CGGGCTGTAACCCCCCCCTGCACCCCCCTCCCCGAGTT
		GCTGAGCACGGCCCGGCTTCGGGTGCGGGGCTCCGTGC
		GGGGCGTGGCGCGGGGCTCGCCGTGCCGGGCGGGGGG
		TGGCGGCAGGTGGGGGTGCCGGGCGGGGCGGGGCCGC
		CTCGGGCCGGGGAGGGCTCGGGGGAGGGGCGCGGCGG
		CCCCGGAGCGCCGGCGGCTGTCGAGGCGCGGCGAGCC
		GCAGCCATTGCCTTTTATGGTAATCGTGCGAGAGGGCG
		CAGGGACTTCCTTTGTCCCAAATCTGGCGGAGCCGAAA
		TCTGGGAGGCGCCGCCGCACCCCCTCTAGCGGGCGCGG
		GCGAAGCGGTGCGGCGCCGGCAGGAAGGAAATGGGCG
		GGGAGGGCCTTCGTGCGTCGCCGCGCCGCCGTCCCCTT
		CTCCATCTCCAGCCTCGGGGCTGCCGCAGGGGGACGGC
		TGCCTTCGGGGGGGACGGGGCAGGGCGGGGTTCGGCTT
		CTGGCGTGTGACCGGCGGGAATTC
46	DNA fragment containing VSV-G	GAATTCATGAAGTGCCTTTTGTACTTAGCCTTTTTATTC
		ATTGGGGTGAATTGCAAGTTCACCATAGTTTTTCCACAC
		AACCAAAAAGGAAACTGGAAAAATGTTCCTTCTAATTA
		CCATTATTGCCCGTCAAGCTCAGATTTAAATTGGCATA

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SEQ ID NO:	Description	Sequence
		Sequences
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		AAGAGTCACAAGGCTATTCAAGCAGACGGTTGGATGTG
		TCATGCTTCCAAATGGGTCACTACTTGTGATTTCCGCTG
		GTATGGACCGAAGTATATAACACATTCCATCCGATCCT
		TCACTCCATCTGTAGAACAATGCAAGGAAAGCATTGAA
		CAAACGAAACAAGGAACTTGGCTGAATCCAGGCTTCCC
		TCCTCAAAGTTGTGGATATGCAACTGTGACGGATGCCG
		AAGCAGTGATTGTCCAGGTGACTCCTCACCATGTGCTG
		GTTGATGAATACACAGGAGAATGGGTTGATTCACAGTT
		CATCAACGGAAAATGCAGCAATTACATATGCCCCACTG
		TCCATAACTCTACAACCTGGCATTCTGACTATAAGGTC
		AAAGGGCTATGTGATTCTAACCTCATTTCCATGGACAT
		CACCTTCTTCTCAGAGGACGGAGAGCTATCATCCCTGG
		GAAAGGAGGGCACAGGGTTCAGAAGTAACTACTTTGCT
		TATGAAACTGGAGGCAAGGCCTGCAAAATGCAATACTG
		CAAGCATTGGGGAGTCAGACTCCCATCAGGTGTCTGGT
		TCGAGATGGCTGATAAGGATCTCTTTGCTGCAGCCAGA
		TTCCCTGAATGCCCAGAAGGGTCAAGTATCTCTGCTCC
		ATCTCAGACCTCAGTGGATGTAAGTCTAATTCAGGACG
		TTGAGAGGATCTTGGATTATTCCCTCTGCCAAGAAACC
		TGGAGCAAAATCAGAGCGGGTCTTCCAATCTCTCCAGT
		GGATCTCAGCTATCTTGCTCCTAAAAACCCAGGAACCG
		GTCCTGCTTTCACCATAATCAATGGTACCCTAAAATACT
		TTGAGACCAGATACATCAGAGTCGATATTGCTGCTCCA
		ATCCTCTCAAGAATGGTCGGAATGATCAGTGGAACTAC
		CACAGAAAGGGAACTGTGGGATGACTGGGCACCATAT
		GAAGACGTGGAAATTGGACCCAATGGAGTTCTGAGGA
		CCAGTTCAGGATATAAGTTTCCTTTATACATGATTGGAC
		ATGGTATGTTGGACTCCGATCTTCATCTTAGCTCAAAGG
		CTCAGGTGTTCGAACATCCTCACATTCAAGACGCTGCTT
		CGCAACTTCCTGATGATGAGAGTTTATTTTTTGGTGATA
		CTGGGCTATCCAAAAATCCAATCGAGCTTGTAGAAGGT
		TGGTTCAGTAGTTGGAAAAGCTCTATTGCCTCTTTTTTC
		TTTATCATAGGGTTAATCATTGGACTATTCTTGGTTCTC
		CGAGTTGGTATCCATCTTTGCATTAAATTAAAGCACAC
		CAAGAAAAGACAGATTTATACAGACATAGAGATGAGA
		ATTC
47	Rev; RSV promoter; Transcription	ATGGCAGGAAGAAGCGGAGACAGCGACGAAGAACTCC
		TCAAGGCAGTCAGACTCATCAAGTTTCTCTATCAAAGC
		AACCCACCTCCCAATCCCGAGGGGACCCGACAGGCCCG
		AAGGAATAGAAGAAGAAGGTGGAGAGAGAGACAGAG
		ACAGATCCATTCGATTAGTGAACGGATCCTTAGCACTT
		ATCTGGGACGATCTGCGGAGCCTGTGCCTCTTCAGCTA
		CCACCGCTTGAGAGACTTACTCTTGATTGTAACGAGGA
		TTGTGGAACTTCTGGGACGCAGGGGGTGGGAAGCCCTC
		AAATATTGGTGGAATCTCCTACAATATTGGAGTCAGGA
		GCTAAAGAATAG
48	RSV promoter and HIV Rev	CAATTGCGATGTACGGGCCAGATATACGCGTATCTGAG
		GGGACTAGGGTGTGTTTAGGCGAAAAGCGGGGCTTCGG
		TTGTACGCGGTTAGGAGTCCCCTCAGGATATAGTAGTT
		TCGCTTTTGCATAGGGAGGGGGAAATGTAGTCTTATGC
		AATACACTTGTAGTCTTGCAACATGGTAACGATGAGTT
		AGCAACATGCCTTACAAGGAGAGAAAAAGCACCGTGC
		ATGCCGATTGGTGGAAGTAAGGTGGTACGATCGTGCCT
		TATTAGGAAGGCAACAGACAGGTCTGACATGGATTGGA
		CGAACCACTGAATTCCGCATTGCAGAGATAATTGTATT
		TAAGTGCCTAGCTCGATACAATAAACGCCATTTGACCA
		TTCACCACATTGGTGTGCACCTCCAAGCTCGAGCTCGTT
		TAGTGAACCGTCAGATCGCCTGGAGACGCCATCCACGC
		TGTTTTGACCTCCATAGAAGACACCGGGACCGATCCAG
		CCTCCCCTCGAAGCTAGCGATTAGGCATCTCCTATGGC
		AGGAAGAAGCGGAGACAGCGACGAAGAACTCCTCAAG
		GCAGTCAGACTCATCAAGTTTCTCTATCAAAGCAACCC
		ACCTCCCAATCCCGAGGGGACCCGACAGGCCCGAAGG
		AATAGAAGAAGAAGGTGGAGAGAGAGACAGAGACAG
		ATCCATTCGATTAGTGAACGGATCCTTAGCACTTATCTG
		GGACGATCTGCGGAGCCTGTGCCTCTTCAGCTACCACC
		GCTTGAGAGACTTACTCTTGATTGTAACGAGGATTGTG

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SEQ ID NO:	Description	Sequence
		GAACTTCTGGGACGCAGGGGGTGGGAAGCCCTCAAAT ATTGGTGGAATCTCCTACAATATTGGAGTCAGGAGCTA AAGAATAGTCTAGA
49	Promoter; PGK	GGGGTTGGGGTTGCGCCTTTTCCAAGGCAGCCCTGGGT TTGCGCAGGGACGCGGCTGCTCTGGGCGTGGTTCCGGG AAACGCAGCGGCGCCGACCCTGGGTCTCGCACATTCTT CACGTCCGTTCGCAGCGTCACCCGGATCTTCGCCGCTA CCCTTGTGGGCCCCCGGCGACGCTTCCTGCTCCGCCCC TAAGTCGGGAAGGTTCCTTGCGGTTCGCGGCGTGCCGG ACGTGACAAACGGAAGCCGCACGTCTCACTAGTACCCT CGCAGACGGACAGCGCCAGGGAGCAATGGCAGCGCGC CGACCGCGATGGGCTGTGGCCAATAGCGGCTGCTCAGC AGGGCGCGCCGAGAGCAGCGGCCGGGAAGGGGCGGTG CGGGAGGCGGGGTGTGGGGCGGTAGTGTGGGCCCTGTT CCTGCCCGCGCGGTGTTCCGCATTCTGCAAGCCTCCGG AGCGCACGTCGGCAGTCGGCTCCCTCGTTGACCGAATC ACCGACCTCTCTCCCCAG
50	Promoter; UbC	GCGCCGGGTTTTGGCGCCTCCCGCGGGCGCCCCCCTCC TCACGGCGAGCGCTGCCACGTCAGACGAAGGGCGCAG GAGCGTTCCTGATCCTTCCGCCCGGACGCTCAGGACAG CGGCCCGCTGCTCATAAGACTCGGCCTTAGAACCCCAG TATCAGCAGAAGGACATTTTAGGACGGGACTTGGGTGA CTCTAGGGCACTGGTTTTCTTTCCAGAGAGCGGAACAG GCGAGGAAAAGTAGTCCCTTCTCGGCGATTCTGCGGAG GGATCTCCGTGGGGCGGTGAACGCCGATGATTATATAA GGACGCGCCGGGTGTGGCACAGCTAGTTCCGTCGCAGC CGGGATTTGGGTCGCGGTTCTTGTTTGTGGATCGCTGTG ATCGTCACTTGGTGAGTTGCGGGCTGCTGGGCTGGCCG GGGCTTTCGTGGCCGCCGGGCCGCTCGGTGGGACGGAA GCGTGTGGAGAGACCGCCAAGGGCTGTAGTCTGGGTCC GCGAGCAAGGTTGCCCTGAACTGGGGGTTGGGGGGAG CGCACAAAATGGCGGCTGTTCCCGAGTCTTGAATGGAA GACGCTTGTAAGGCGGGCTGTGAGGTCGTTGAAACAAG GTGGGGGGCATGGTGGGCGGCAAGAACCCAAGGTCTT GAGGCCTTCGCTAATGCGGGAAAGCTCTTATTCGGGTG AGATGGGCTGGGGCACCATCTGGGGACCCTGACGTGAA GTTTGTCACTGACTGGAGAACTCGGGTTTGTCGTCTGGT TGCGGGGGCGGCAGTTATGCGGTGCCGTTGGGCAGTGC ACCCGTACCTTTGGGAGCGCGCGCCTCGTCGTGTCGTG ACGTCACCCGTTCTGTTGGCTTATAATGCAGGGTGGGG CCACCTGCCGGTAGGTGTGCGGTAGGCTTTTCTCCGTCG CAGGACGCAGGGTTCGGGCCTAGGGTAGGCTCTCCTGA ATCGACAGGCGCCGGACCTCTGGTGAGGGGAGGGATA AGTGAGGCGTCAGTTTCTTTGGTCGGTTTTATGTACCTA TCTTCTTAAGTAGCTGAAGCTCCGGTTTTGAACTATGCG CTCGGGGTTGGCGAGTGTGTTTTGTGAAGTTTTTTAGGC ACCTTTTGAAATGTAATCATTTGGGTCAATATGTAATTT TCAGTGTTAGACTAGTAAA
51	Poly A; SV40	GTTTATTGCAGCTTATAATGGTTACAAATAAAGCAATA GCATCACAAATTTCACAAATAAAGCATTTTTTTCACTGC ATTCTAGTTGTGGTTTGTCCAAACTCATCAATGTATCTT ATCA
52	Poly A; bGH	GACTGTGCCTTCTAGTTGCCAGCCATCTGTTGTTTGCCC CTCCCCCGTGCCTTCCTTGACCCTGGAAGGTGCCACTCC CACTGTCCTTTCCTAATAAAATGAGGAAATTGCATCGC ATTGTCTGAGTAGGTGTCATTCTATTCTGGGGGGTGGG GTGGGGCAGGACAGCAAGGGGGAGGATTGGGAAGACA ATAGCAGGCATGCTGGGGATGCGGTGGGCTCTATGG
53	Envelope; RD114	ATGAAACTCCCAACAGGAATGGTCATTTTATGTAGCCT AATAATAGTTCGGGCAGGGTTTGACGACCCCCGCAAGG CTATCGCATTAGTACAAAAACAACATGGTAAACCATGC GAATGCAGCGGAGGGCAGGTATCCGAGGCCCCACCGA ACTCCATCCAACAGGTAACTTGCCCAGGCAAGACGGCC TACTTAATGACCAACCAAAAATGGAAATGCAGAGTCAC TCCAAAAAATCTCACCCCTAGCGGGGGAGAACTCCAGA

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Sequences	
SEQ ID NO: Description	Sequence
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	TCTTGTTATACTGAATACCGGCAATGCAGGGCGAATAA
	TAAGACATACTACACGGCCACCTTGCTTAAAATACGGT
	CTGGGAGCCTCAACGAGGTACAGATATTACAAAACCCC
	AATCAGCTCCTACAGTCCCCTTGTAGGGGCTCTATAAA
	TCAGCCCGTTTGCTGGAGTGCCACAGCCCCCATCCATA
	TCTCCGATGGTGGAGGACCCCTCGATACTAAGAGAGTG
	TGGACAGTCCAAAAAAGGCTAGAACAAATTCATAAGG
	CTATGCATCCTGAACTTCAATACCACCCCTTAGCCCTGC
	CCAAAGTCAGAGATGACCTTAGCCTTGATGCACGGACT
	TTTGATATCCTGAATACCACTTTTAGGTTACTCCAGATG
	TCCAATTTTAGCCTTGCCCAAGATTGTTGGCTCTGTTTA
	AAACTAGGTACCCCTACCCCTCTTGCGATACCCACTCCC
	TCTTTAACCTACTCCCTAGCAGACTCCCTAGCGAATGCC
	TCCTGTCAGATTATACCTCCCCTCTTGGTTCAACCGATG
	CAGTTCTCCAACTCGTCCTGTTTATCTTCCCCTTTCATTA
	ACGATACGGAACAAATAGACTTAGGTGCAGTCACCTTT
	ACTAACTGCACCTCTGTAGCCAATGTCAGTAGTCCTTTA
	TGTGCCCTAAACGGGTCAGTCTTCCTCTGTGGAAATAA
	CATGGCATACACCTATTTACCCCAAAACTGGACAGGAC
	TTTGCGTCCAAGCCTCCCTCCTCCCCGACATTGACATCA
	TCCCGGGGGATGAGCCAGTCCCCATTCCTGCCATTGAT
	CATTATATACATAGACCTAAACGAGCTGTACAGTTCAT
	CCCTTTACTAGCTGGACTGGGAATCACCGCAGCATTCA
	CCACCGGAGCTACAGGCCTAGGTGTCTCCGTCACCCAG
	TATACAAAATTATCCCATCAGTTAATATCTGATGTCCAA
	GTCTTATCCGGTACCATACAAGATTTACAAGACCAGGT
	AGACTCGTTAGCTGAAGTAGTTCTCCAAAATAGGAGGG
	GACTGGACCTACTAACGGCAGAACAAGGAGGAATTTGT
	TTAGCCTTACAAGAAAAATGCTGTTTTTATGCTAACAA
	GTCAGGAATTGTGAGAAACAAAATAAGAACCCTACAA
	GAAGAATTACAAAAACGCAGGGAAAGCCTGGCATCCA
	ACCCTCTCTGGACCGGGCTGCAGGGCTTTCTTCCGTACC
	TCCTACCTCTCCTGGGACCCCTACTCACCCTCCTACTCA
	TACTAACCATTGGGCCATGCGTTTTCAATCGATTGGTCC
	AATTTGTTAAAGACAGGATCTCAGTGGTCCAGGCTCTG
	GTTTTGACTCAGCAATATCACCAGCTAAAACCCATAGA
	GTACGAGCCATGA
54 Envelope; GALV	ATGCTTCTCACCTCAAGCCCGCACCACCTTCGGCACCA
	GATGAGTCCTGGGAGCTGGAAAAGACTGATCATCCTCT
	TAAGCTGCGTATTCGGAGACGGCAAAACGAGTCTGCA
	GAATAAGAACCCCCACCAGCCTGTGACCCTCACCTGGC
	AGGTACTGTCCCAAACTGGGGACGTTGTCTGGGACAAA
	AAGGCAGTCCAGCCCCTTTGGACTTGGTGGCCCTCTCT
	TACACCTGATGTATGTGCCCTGGCGGCCGGTCTTGAGT
	CCTGGGATATCCCGGGATCCGATGTATCGTCCTCTAAA
	AGAGTTAGACCTCCTGATTCAGACTATACTGCCGCTTA
	TAAGCAAATCACCTGGGGAGCCATAGGGTGCAGCTAC
	CCTCGGGCTAGGACCAGGATGGCAAATTCCCCCTTCTA
	CGTGTGTCCCCGAGCTGGCCGAACCCATTCAGAAGCTA
	GGAGGTGTGGGGGGCTAGAATCCCTATACTGTAAAGA
	ATGGAGTTGTGAGACCACGGGTACCGTTTATTGGCAAC
	CCAAGTCCTCATGGGACCTCATAACTGTAAAATGGGAC
	CAAAATGTGAAATGGGAGCAAAAATTTCAAAAGTGTG
	AACAAACCGGCTGGTGTAACCCCCTCAAGATAGACTTC
	ACAGAAAAAGGAAAACTCTCCAGAGATTGGATAACGG
	AAAAAACCTGGGAATTAAGGTTCTATGTATATGGACAC
	CCAGGCATACAGTTGACTATCCGCTTAGAGGTCACTAA
	CATGCCGGTTGTGGCAGTGGGCCCAGACCCTGTCCTTG
	CGGAACAGGGACCTCCTAGCAAGCCCCTCACTCTCCCT
	CTCTCCCCACGGAAAGCGCCGCCCACCCCTCTACCCCC
	GGCGGCTAGTGAGCAAACCCCTGCGGTGCATGGAGAA
	ACTGTTACCCTAAACTCTCCGCCTCCCACCAGTGGCGA
	CCGACTCTTTGGCCTTGTGCAGGGGGCCTTCCTAACCTT
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gcgacactag aagaaatgat gacagcatgt cagggagtgg ggggacccgg ccataaagca 1080

agagttttgg ctgaagcaat gagccaagta acaaatccag ctaccataat gatacagaaa 1140

ggcaatttta ggaaccaaag aaagactgtt aagtgtttca attgtggcaa agaagggcac 1200

atagccaaaa attgcagggc ccctaggaaa aagggctgtt ggaaatgtgg aaaggaagga 1260

caccaaatga aagattgtac tgagagacag gctaatttttt tagggaagat ctggccttcc 1320

cacaagggaa ggccagggaa ttttcttcag agcagaccag agccaacagc cccaccagaa 1380

gagagcttca ggtttgggga agagacaaca actccctctc agaagcagga gccgatagac 1440

aaggaactgt atcctttagc ttccctcaga tcactctttg gcagcgaccc ctcgtcacaa 1500

-continued

taa 1503

<210> SEQ ID NO 24
<211> LENGTH: 233
<212> TYPE: DNA
<213> ORGANISM: Human Immunodeficiency Virus

<400> SEQUENCE: 24

aggagctttg ttccttgggt tcttgggagc agcaggaagc actatgggcg cagcctcaat 60

gacgctgacg gtacaggcca gacaattatt gtctggtata gtgcagcagc agaacaattt 120

gctgagggct attgaggcgc aacagcatct gttgcaactc acagtctggg gcatcaagca 180

gctccaggca agaatcctgg ctgtggaaag atacctaaag gatcaacagc tcc 233

<210> SEQ ID NO 25
<211> LENGTH: 1519
<212> TYPE: DNA
<213> ORGANISM: Vesicular Stomatitis Indiana Virus

<400> SEQUENCE: 25

atgaagtgcc ttttgtactt agccttttta ttcattgggg tgaattgcaa gttcaccata 60

gtttttccac acaaccaaaa aggaaactgg aaaaatgttc cttctaatta ccattattgc 120

ccgtcaagct cagatttaaa ttggcataat gacttaatag gcacagcctt acaagtcaaa 180

atgcccaaga gtcacaaggc tattcaagca gacggttgga tgtgtcatgc ttccaaatgg 240

gtcactactt gtgatttccg ctggtatgga ccgaagtata taacacattc catccgatcc 300

ttcactccat ctgtagaaca atgcaaggaa agcattgaac aaacgaaaca aggaacttgg 360

ctgaatccag gcttccctcc tcaaagttgt ggatatgcaa ctgtgacgga tgccgaagca 420

gtgattgtcc aggtgactcc tcaccatgtg ctggttgatg aatacacagg agaatgggtt 480

gattcacagt tcatcaacgg aaaatgcagc aattacatat gccccactgt ccataactct 540

acaacctggc attctgacta taaggtcaaa gggctatgtg attctaacct catttccatg 600

gacatcacct tcttctcaga ggacggagag ctatcatccc tgggaaagga gggcacaggg 660

ttcagaagta actactttgc ttatgaaact ggaggcaagg cctgcaaaat gcaatactgc 720

aagcattggg gagtcagact cccatcaggt gtctggttcg agatggctga taaggatctc 780

tttgctgcag ccagattccc tgaatgccca gaagggtcaa gtatctctgc tccatctcag 840

acctcagtgg atgtaagtct aattcaggac gttgagagga tcttggatta ttccctctgc 900

caagaaacct ggagcaaaat cagagcgggt cttccaatct ctccagtgga tctcagctat 960

cttgctccta aaaacccagg aaccggtcct gctttcacca taatcaatgg taccctaaaa 1020

tactttgaga ccagatacat cagagtcgat attgctgctc caatcctctc aagaatggtc 1080

ggaatgatca gtggaactac cacagaaagg gaactgtggg atgactgggc accatatgaa 1140

gacgtggaaa ttggacccaa tggagttctg aggaccagtt caggatataa gtttccttta 1200

tacatgattg gacatggtat gttggactcc gatcttcatc ttagctcaaa ggctcaggtg 1260

ttcgaacatc ctcacattca agacgctgct tcgcaacttc ctgatgatga gagtttattt 1320

tttggtgata ctgggctatc caaaaatcca atcgagcttg tagaaggttg gttcagtagt 1380

tggaaaagct ctattgcctc ttttttcttt atcatagggt taatcattgg actattcttg 1440

gttctccgag ttggtatcca tctttgcatt aaattaaagc acaccaagaa aagacagatt 1500

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tatacagaca tagagatga 1519

<210> SEQ ID NO 26
<211> LENGTH: 118
<212> TYPE: DNA
<213> ORGANISM: Rous Sarcoma virus

<400> SEQUENCE: 26

ttttaaaaga aaaggggga ttgggggta cagtgcaggg gaaagaatag tagacataat 60

agcaacagac atacaaacta aagaattaca aaaacaaatt acaaaattca aaatttta 118

<210> SEQ ID NO 27
<211> LENGTH: 217
<212> TYPE: DNA
<213> ORGANISM: Rous Sarcoma virus

<400> SEQUENCE: 27

gaacgctgac gtcatcaacc cgctccaagg aatcgcgggc ccagtgtcac taggcgggaa 60

cacccagcgc gcgtgcgccc tggcaggaag atggctgtga gggacagggg agtggcgccc 120

tgcaatattt gcatgtcgct atgtgttctg ggaaatcacc ataaacgtga aatgtctttg 180

gatttgggaa tcttataagt tctgtatgag accactt 217

<210> SEQ ID NO 28
<211> LENGTH: 532
<212> TYPE: DNA
<213> ORGANISM: Rous Sarcoma virus

<400> SEQUENCE: 28

gctccggtgc ccgtcagtgg gcagagcgca catcgcccac agtccccgag aagttggggg 60

gaggggtcgg caattgaacg ggtgcctaga gaaggtggcg cggggtaaac tgggaaagtg 120

atgtcgtgta ctggctccgc ctttttcccg agggtggggg agaaccgtat ataagtgcag 180

tagtcgccgt gaacgttctt tttcgcaacg ggtttgccgc cagaacacag ctgaagcttc 240

gaggggctcg catctctcct tcacgcgccc gccgccctac ctgaggccgc catccacgcc 300

ggttgagtcg cgttctgccg cctcccgcct gtggtgcctc ctgaactgcg tccgccgtct 360

aggtaagttt aaagctcagg tcgagaccgg gcctttgtcc ggcgctccct tggagcctac 420

ctagactcag ccggctctcc acgctttgcc tgaccctgct tgctcaactc tacgtctttg 480

tttcgttttc tgttctgcgc cgttacagat ccaagctgtg accggcgcct ac 532

<210> SEQ ID NO 29
<211> LENGTH: 759
<212> TYPE: DNA
<213> ORGANISM: Aequorea victoria

<400> SEQUENCE: 29

atggagagcg acgagagcgg cctgcccgcc atggagatcg agtgccgcat caccggcacc 60

ctgaacggcg tggagttcga gctggtgggc ggcggagagg gcacccccaa gcagggccgc 120

atgaccaaca agatgaagag caccaaaggc gccctgacct tcagccccta cctgctgagc 180

cacgtgatgg gctacggctt ctaccacttc ggcacctacc ccagcggcta cgagaacccc 240

ttcctgcacg ccatcaacaa cggcggctac accaacaccc gcatcgagaa gtacgaggac 300

ggcggcgtgc tgcacgtgag cttcagctac cgctacgagg ccggccgcgt gatcggcgac 360

-continued

ttcaaggtgg tgggcaccgg cttccccgag gacagcgtga tcttcaccga caagatcatc 420

cgcagcaacg ccaccgtgga gcacctgcac cccatgggcg ataacgtgct ggtgggcagc 480

ttcgcccgca ccttcagcct gcgcgacggc ggctactaca gcttcgtggt ggacagccac 540

atgcacttca agagcgccat ccaccccagc atcctgcaga acgggggccc catgttcgcc 600

ttccgccgcg tggaggagct gcacagcaac accgagctgg gcatcgtgga gtaccagcac 660

gccttcaaga cccccatcgc cttcgccaga tcccgcgctc agtcgtccaa ttctgccgtg 720

gacggcaccg ccggacccgg ctccaccgga tctcgctaa 759

<210> SEQ ID NO 30
<211> LENGTH: 590
<212> TYPE: DNA
<213> ORGANISM: Woodchuck hepatitis B virus

<400> SEQUENCE: 30

aatcaacctc tgattacaaa atttgtgaaa gattgactgg tattcttaac tatgttgctc 60

cttttacgct atgtggatac gctgctttaa tgcctttgta tcatgctatt gcttcccgta 120

tggctttcat tttctcctcc ttgtataaat cctggttgct gtctctttat gaggagttgt 180

ggcccgttgt caggcaacgt ggcgtggtgt gcactgtgtt tgctgacgca acccccactg 240

gttggggcat tgccaccacc tgtcagctcc tttccgggac tttcgctttc cccctcccta 300

ttgccacggc ggaactcatc gccgcctgcc ttgcccgctg ctggacaggg gctcggctgt 360

tgggcactga caattccgtg gtgttgtcgg ggaaatcatc gtcctttcct tggctgctcg 420

cctgtgttgc cacctggatt ctgcgcggga cgtccttctg ctacgtccct tcggccctca 480

atccagcgga ccttccttcc cgcggcctgc tgccggctct gcggcctctt ccgcgtcttc 540

gccttcgccc tcagacgagt cggatctccc tttgggccgc ctccccgcct 590

<210> SEQ ID NO 31
<211> LENGTH: 250
<212> TYPE: DNA
<213> ORGANISM: Human Immunodeficiency Virus

<400> SEQUENCE: 31

tggaagggct aattcactcc caacgaagat aagatctgct ttttgcttgt actgggtctc 60

tctggttaga ccagatctga gcctgggagc tctctggcta actagggaac ccactgctta 120

agcctcaata aagcttgcct tgagtgcttc aagtagtgtg tgcccgtctg ttgtgtgact 180

ctggtaacta gagatccctc agacccttt agtcagtgtg gaaaatctct agcagtagta 240

gttcatgtca 250

<210> SEQ ID NO 32
<211> LENGTH: 352
<212> TYPE: DNA
<213> ORGANISM: artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Helper/Rev CMV early (CAG) enhancer DNA construct

<400> SEQUENCE: 32

tagttattaa tagtaatcaa ttacggggtc attagttcat agcccatata tggagttccg 60

cgttacataa cttacggtaa atggcccgcc tggctgaccg cccaacgacc cccgcccatt 120

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gacgtcaata atgacgtatg ttcccatagt aacgccaata gggactttcc attgacgtca 180

atgggtggac tatttacggt aaactgccca cttggcagta catcaagtgt atcatatgcc 240

aagtacgccc cctattgacg tcaatgacgg taaatggccc gcctggcatt atgcccagta 300

catgacctta tgggactttc ctacttggca gtacatctac gtattagtca tc 352

<210> SEQ ID NO 33
<211> LENGTH: 290
<212> TYPE: DNA
<213> ORGANISM: artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Helper/Rev Chicken beta actin (CAG) promoter DNA construct

<400> SEQUENCE: 33

gctattacca tgggtcgagg tgagccccac gttctgcttc actctcccca tctccccccc 60

ctccccaccc ccaattttgt atttatttat tttttaatta ttttgtgcag cgatgggggc 120

gggggggggg ggggcgcgcg ccaggcgggg cggggcgggg cgaggggcgg ggcggggcga 180

ggcggagagg tgcggcggca gccaatcaga gcggcgcgct ccgaaagttt ccttttatgg 240

cgaggcggcg gcggcggcgg ccctataaaa agcgaagcgc gcggcgggcg 290

<210> SEQ ID NO 34
<211> LENGTH: 960
<212> TYPE: DNA
<213> ORGANISM: artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Helper/Rev Chicken beta actin intron DNA construct

<400> SEQUENCE: 34

ggagtcgctg cgttgccttc gccccgtgcc ccgctccgcg ccgcctcgcg ccgcccgccc 60

cggctctgac tgaccgcgtt actcccacag gtgagcgggc gggacggccc ttctcctccg 120

ggctgtaatt agcgcttggt ttaatgacgg ctcgtttctt ttctgtggct gcgtgaaagc 180

cttaaagggc tccgggaggg ccctttgtgc ggggggggagc ggctcggggg gtgcgtgcgt 240

gtgtgtgtgc gtggggagcg ccgcgtgcgg cccgcgctgc ccggcggctg tgagcgctgc 300

gggcgcggcg cggggctttg tgcgctccgc gtgtgcgcga ggggagcgcg gccgggggcg 360

gtgccccgcg gtgcgggggg gctgcgaggg gaacaaaggc tgcgtgcggg gtgtgtgcgt 420

ggggggggtga gcagggggtg tgggcgcggc ggtcgggctg taacccccccc ctgcaccccc 480

ctccccgagt tgctgagcac ggcccggctt cgggtgcggg gctccgtgcg gggcgtggcg 540

cggggctcgc cgtgccgggc gggggggtggc ggcaggtggg ggtgccgggc ggggcggggc 600

cgcctcgggc cggggagggc tcgggggagg ggcgcggcgg ccccggagcg ccggcggctg 660

tcgaggcgcg gcgagccgca gccattgcct tttatggtaa tcgtgcgaga gggcgcaggg 720

acttcctttg tcccaaatct ggcggagccg aaatctggga ggcgccgccg cacccccctct 780

agcgggcgcg ggcgaagcgg tgcggcgccg gcaggaagga aatgggcggg gagggccttc 840

gtgcgtcgcc gcgccgccgt ccccttctcc atctccagcc tcggggctgc cgcaggggga 900

cggctgcctt cgggggggac ggggcagggc ggggttcggc ttctggcgtg tgaccggcgg 960

<210> SEQ ID NO 35
<211> LENGTH: 1872
<212> TYPE: DNA

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<213> ORGANISM: artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Helper/Rev HIV Pol DNA construct

<400> SEQUENCE: 35

atgaatttgc caggaagatg gaaaccaaaa atgatagggg gaattggagg ttttatcaaa 60

gtaggacagt atgatcagat actcatagaa atctgcggac ataaagctat aggtacagta 120

ttagtaggac ctacacctgt caacataatt ggaagaaatc tgttgactca gattggctgc 180

actttaaatt ttcccattag tcctattgag actgtaccag taaaattaaa gccaggaatg 240

gatggcccaa aagttaaaca atggccattg acagaagaaa aaataaaagc attagtagaa 300

atttgtacag aaatggaaaa ggaaggaaaa atttcaaaaa ttgggcctga aaatccatac 360

aatactccag tatttgccat aaagaaaaaa gacagtacta aatggagaaa attagtagat 420

ttcagagaac ttaataagag aactcaagat ttctgggaag ttcaattagg aataccacat 480

cctgcagggt taaaacagaa aaaatcagta acagtactgg atgtgggcga tgcatatttt 540

tcagttccct tagataaaga cttcaggaag tatactgcat ttaccatacc tagtataaac 600

aatgagacac cagggattag atatcagtac aatgtgcttc cacagggatg gaaaggatca 660

ccagcaatat tccagtgtag catgacaaaa atcttagagc cttttagaaa acaaaatcca 720

gacatagtca tctatcaata catggatgat ttgtatgtag gatctgactt agaaatagggg 780

cagcatagaa caaaaataga ggaactgaga caacatctgt tgaggtgggg atttaccaca 840

ccagacaaaa aacatcagaa agaacctcca ttcctttgga tgggttatga actccatcct 900

gataaatgga cagtacagcc tatagtgctg ccagaaaagg acagctggac tgtcaatgac 960

atacagaaat tagtgggaaa attgaattgg gcaagtcaga tttatgcagg gattaaagta 1020

aggcaattat gtaaacttct taggggaacc aaagcactaa cagaagtagt accactaaca 1080

gaagaagcag agctagaact ggcagaaaac agggagattc taaaagaacc ggtacatgga 1140

gtgtattatg acccatcaaa agacttaata gcagaaatac agaagcaggg gcaaggccaa 1200

tggacatatc aaatttatca agagccattt aaaaatctga aaacaggaaa atatgcaaga 1260

atgaagggtg cccacactaa tgatgtgaaa caattaacag aggcagtaca aaaaatagcc 1320

acagaaagca tagtaatatg gggaaagact cctaaattta aattacccat acaaaaggaa 1380

acatgggaag catggtggac agagtattgg caagccacct ggattcctga gtgggagttt 1440

gtcaataccc ctcccttagt gaagttatgg taccagttag agaaagaacc cataatagga 1500

gcagaaactt tctatgtaga tggggcagcc aatagggaaa ctaaattagg aaaagcagga 1560

tatgtaactg acagaggaag acaaaaagtt gtccccctaa cggacacaac aaatcagaag 1620

actgagttac aagcaattca tctagctttg caggattcgg gattagaagt aaacatagtg 1680

acagactcac aatatgcatt gggaatcatt caagcacaac cagataagag tgaatcagag 1740

ttagtcagtc aaataataga gcagttaata aaaaaggaaa aagtctacct ggcatgggta 1800

ccagcacaca aaggaattgg aggaaatgaa caagtagatg ggttggtcag tgctggaatc 1860

aggaaagtac ta 1872

<210> SEQ ID NO 36
<211> LENGTH: 867
<212> TYPE: DNA
<213> ORGANISM: artificial sequence
<220> FEATURE:

-continued

<223> OTHER INFORMATION: Helper Rev HIV Integrase DNA construct

<400> SEQUENCE: 36

tttttagatg gaatagataa ggcccaagaa gaacatgaga aatatcacag taattggaga 60

gcaatggcta gtgattttaa cctaccacct gtagtagcaa aagaaatagt agccagctgt 120

gataaatgtc agctaaaagg ggaagccatg catggacaag tagactgtag cccaggaata 180

tggcagctag attgtacaca tttagaagga aaagttatct tggtagcagt tcatgtagcc 240

agtggatata tagaagcaga agtaattcca gcagagacag ggcaagaaac agcatacttc 300

ctcttaaaat tagcaggaag atggccagta aaaacagtac atacagacaa tggcagcaat 360

ttcaccagta ctacagttaa ggccgcctgt tggtgggcgg ggatcaagca ggaatttggc 420

attccctaca atccccaaag tcaaggagta atagaatcta tgaataaaga attaaagaaa 480

attataggac aggtaagaga tcaggctgaa catcttaaga cagcagtaca aatggcagta 540

ttcatccaca attttaaaag aaaaggggg attgggggt acagtgcagg ggaaagaata 600

gtagacataa tagcaacaga catacaaact aaagaattac aaaaacaaat tacaaaaatt 660

caaaattttc gggtttatta cagggacagc agagatccag tttggaaagg accagcaaag 720

ctcctctgga aaggtgaagg ggcagtagta atacaagata atagtgacat aaaagtagtg 780

ccaagaagaa aagcaaagat catcagggat tatggaaaac agatggcagg tgatgattgt 840

gtggcaagta gacaggatga ggattaa 867

<210> SEQ ID NO 37
<211> LENGTH: 351
<212> TYPE: DNA
<213> ORGANISM: artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Helper/Rev HIV Rev DNA construct

<400> SEQUENCE: 37

atggcaggaa gaagcggaga cagcgacgaa gaactcctca aggcagtcag actcatcaag 60

tttctctatc aaagcaaccc acctcccaat cccgagggga cccgacaggc ccgaaggaat 120

agaagaagaa ggtggagaga gagacagaga cagatccatt cgattagtga acggatcctt 180

agcacttatc tgggacgatc tgcggagcct gtgcctcttc agctaccacc gcttgagaga 240

cttactcttg attgtaacga ggattgtgga acttctggga cgcaggggt gggaagccct 300

caaatattgg tggaatctcc tacaatattg gagtcaggag ctaaagaata g 351

<210> SEQ ID NO 38
<211> LENGTH: 448
<212> TYPE: DNA
<213> ORGANISM: artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Helper/Rev Rabbit beta globin poly A DNA
construct

<400> SEQUENCE: 38

agatcttttt ccctctgcca aaaattatgg ggacatcatg aagccccttg agcatctgac 60

ttctggctaa taaaggaaat ttattttcat tgcaatagtg tgttggaatt ttttgtgtct 120

ctcactcgga aggacatatg ggagggcaaa tcatttaaaa catcagaatg agtatttggt 180

ttagagtttg gcaacatatg ccatatgctg gctgccatga acaaaggtgg ctataaagag 240

gtcatcagta tatgaaacag ccccctgctg tccattcctt attccataga aaagccttga 300

-continued

cttgaggtta gatttttttt atattttgtt ttgtgttatt tttttcttta acatccctaa 360

aattttcctt acatgtttta ctagccagat ttttcctcct ctcctgacta ctcccagtca 420

tagctgtccc tcttctctta tgaagatc 448

<210> SEQ ID NO 39
<211> LENGTH: 577
<212> TYPE: DNA
<213> ORGANISM: Cytomegalovirus

<400> SEQUENCE: 39

acattgatta ttgactagtt attaatagta atcaattacg gggtcattag ttcatagccc 60

atatatggag ttccgcgtta cataacttac ggtaaatggc ccgcctggct gaccgcccaa 120

cgacccccgc ccattgacgt caataatgac gtatgttccc atagtaacgc caatagggac 180

tttccattga cgtcaatggg tggagtattt acggtaaact gcccacttgg cagtacatca 240

agtgtatcat atgccaagta cgccccctat tgacgtcaat gacggtaaat ggcccgcctg 300

gcattatgcc cagtacatga ccttatggga ctttcctact tggcagtaca tctacgtatt 360

agtcatcgct attaccatgg tgatgcggtt ttggcagtac atcaatgggc gtggatagcg 420

gtttgactca cggggatttc caagtctcca ccccattgac gtcaatggga gtttgttttg 480

gcaccaaaat caacgggact ttccaaaatg tcgtaacaac tccgccccat tgacgcaaat 540

gggcggtagg cgtgtacggt gggaggtcta tataagc 577

<210> SEQ ID NO 40
<211> LENGTH: 573
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 40

gtgagtttgg ggacccttga ttgttctttc tttttcgcta ttgtaaaatt catgttatat 60

ggaggggggca aagttttcag ggtgttgttt agaatgggaa gatgtccctt gtatcaccat 120

ggaccctcat gataattttg tttctttcac tttctactct gttgacaacc attgtctcct 180

cttattttct tttcattttc tgtaactttt tcgttaaact ttagcttgca tttgtaacga 240

atttttaaat tcacttttgt ttatttgtca gattgtaagt actttctcta atcacttttt 300

tttcaaggca atcagggtat attatattgt acttcagcac agttttagag aacaattgtt 360

ataattaaat gataaggtag aatatttctg catataaatt ctggctggcg tggaaatatt 420

cttattggta gaaacaacta caccctggtc atcatcctgc ctttctcttt atggttacaa 480

tgatatacac tgtttgagat gaggataaaa tactctgagt ccaaaccggg cccctctgct 540

aaccatgttc atgccttctt ctctttccta cag 573

<210> SEQ ID NO 41
<211> LENGTH: 31
<212> TYPE: DNA
<213> ORGANISM: artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Primer DNA fragment

<400> SEQUENCE: 41

taagcagaat tcatgaattt gccaggaaga t 31

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<210> SEQ ID NO 42
<211> LENGTH: 36
<212> TYPE: DNA
<213> ORGANISM: artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Primer DNA fragment

<400> SEQUENCE: 42

ccatacaatg aatggacact aggcggccgc acgaat 36

<210> SEQ ID NO 43
<211> LENGTH: 2745
<212> TYPE: DNA
<213> ORGANISM: artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Gag, Pol, Integrase DNA fragment

<400> SEQUENCE: 43

gaattcatga atttgccagg aagatggaaa ccaaaaatga tagggggaat tggaggtttt 60

atcaaagtaa gacagtatga tcagatactc atagaaatct gcggacataa agctataggt 120

acagtattag taggacctac acctgtcaac ataattggaa gaaatctgtt gactcagatt 180

ggctgcactt taaattttcc cattagtcct attgagactg taccagtaaa attaaagcca 240

ggaatggatg gcccaaaagt taaacaatgg ccattgacag aagaaaaaat aaaagcatta 300

gtagaaattt gtacagaaat ggaaaaggaa ggaaaaattt caaaaattgg gcctgaaaat 360

ccatacaata ctccagtatt tgccataaag aaaaaagaca gtactaaatg gagaaaatta 420

gtagatttca gagaacttaa taagagaact caagatttct gggaagttca attaggaata 480

ccacatcctg cagggttaaa acagaaaaaa tcagtaacag tactggatgt gggcgatgca 540

tatttttcag ttcccttaga taaagacttc aggaagtata ctgcatttac catacctagt 600

ataaacaatg agacaccagg gattagatat cagtacaatg tgcttccaca gggatggaaa 660

ggatcaccag caatattcca gtgtagcatg acaaaaatct tagagccttt tagaaaacaa 720

aatccagaca tagtcatcta tcaatacatg gatgatttgt atgtaggatc tgacttagaa 780

atagggcagc atagaacaaa aatagaggaa ctgagacaac atctgttgag gtggggattt 840

accacaccag acaaaaaaca tcagaaagaa cctccattcc tttggatggg ttatgaactc 900

catcctgata aatggacagt acagcctata gtgctgccag aaaaggacag ctggactgtc 960

aatgacatac agaaattagt gggaaaattg aattgggcaa gtcagattta tgcagggatt 1020

aaagtaaggc aattatgtaa acttcttagg ggaaccaaag cactaacaga agtagtacca 1080

ctaacagaag aagcagagct agaactggca gaaaacaggg agattctaaa agaaccggta 1140

catggagtgt attatgaccc atcaaaagac ttaatagcag aaatacagaa gcaggggcaa 1200

ggccaatgga catatcaaat ttatcaagag ccatttaaaa atctgaaaac aggaaagtat 1260

gcaagaatga agggtgccca cactaatgat gtgaaacaat taacagaggc agtacaaaaa 1320

atagccacag aaagcatagt aatatgggga aagactccta aatttaaatt acccatacaa 1380

aaggaaacat gggaagcatg gtggacagag tattggcaag ccacctggat tcctgagtgg 1440

gagtttgtca ataccctcc cttagtgaag ttatggtacc agttagagaa agaacccata 1500

ataggagcag aaactttcta tgtagatggg gcagccaata gggaaactaa attaggaaaa 1560

gcaggatatg taactgacag aggaagacaa aaagttgtcc ccctaacgga cacaacaaat 1620

cagaagactg agttacaagc aattcatcta gctttgcagg attcgggatt agaagtaaac 1680

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atagtgacag actcacaata tgcattggga atcattcaag cacaaccaga taagagtgaa 1740

tcagagttag tcagtcaaat aatagagcag ttaataaaaa aggaaaaagt ctacctggca 1800

tgggtaccag cacacaaagg aattggagga aatgaacaag tagataaatt ggtcagtgct 1860

ggaatcagga aagtactatt tttagatgga atagataagg cccaagaaga acatgagaaa 1920

tatcacagta attggagagc aatggctagt gattttaacc taccacctgt agtagcaaaa 1980

gaaatagtag ccagctgtga taaatgtcag ctaaaagggg aagccatgca tggacaagta 2040

gactgtagcc caggaatatg gcagctagat tgtacacatt tagaaggaaa agttatcttg 2100

gtagcagttc atgtagccag tggatatata gaagcagaag taattccagc agagacaggg 2160

caagaaacag catacttcct cttaaaatta gcaggaagat ggccagtaaa aacagtacat 2220

acagacaatg gcagcaattt caccagtact acagttaagg ccgcctgttg gtgggcgggg 2280

atcaagcagg aatttggcat tccctacaat ccccaaagtc aaggagtaat agaatctatg 2340

aataaagaat taaagaaaat tataggacag gtaagagatc aggctgaaca tcttaagaca 2400

gcagtacaaa tggcagtatt catccacaat tttaaaagaa aaggggggat tgggggggtac 2460

agtgcagggg aaagaatagt agacataata gcaacagaca tacaaactaa agaattacaa 2520

aaacaaatta caaaaattca aaattttcgg gtttattaca gggacagcag agatccagtt 2580

tggaaaggac cagcaaagct cctctggaaa ggtgaagggg cagtagtaat acaagataat 2640

agtgacataa aagtagtgcc aagaagaaaa gcaaagatca tcagggatta tggaaaacag 2700

atggcaggtg atgattgtgt ggcaagtaga caggatgagg attaa 2745

<210> SEQ ID NO 44
<211> LENGTH: 1586
<212> TYPE: DNA
<213> ORGANISM: artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Rev, RRE and rabbit beta globin poly A DNA fragment

<400> SEQUENCE: 44

tctagaatgg caggaagaag cggagacagc gacgaagagc tcatcagaac agtcagactc 60

atcaagcttc tctatcaaag caacccacct cccaatcccg aggggacccg acaggcccga 120

aggaatagaa gaagaaggtg gagagagaga cagagacaga tccattcgat tagtgaacgg 180

atccttggca cttatctggg acgatctgcg gagcctgtgc ctcttcagct accaccgctt 240

gagagactta ctcttgattg taacgaggat tgtggaactt ctgggacgca gggggtggga 300

agccctcaaa tattggtgga atctcctaca atattggagt caggagctaa agaatagagg 360

agctttgttc cttgggttct tgggagcagc aggaagcact atgggcgcag cgtcaatgac 420

gctgacggta caggccagac aattattgtc tggtatagtg cagcagcaga acaatttgct 480

gagggctatt gaggcgcaac agcatctgtt gcaactcaca gtctggggca tcaagcagct 540

ccaggcaaga atcctggctg tggaaagata cctaaaggat caacagctcc tagatctttt 600

tccctctgcc aaaaattatg gggacatcat gaagcccctt gagcatctga cttctggcta 660

ataaaggaaa tttattttca ttgcaatagt gtgttggaat tttttgtgtc tctcactcgg 720

aaggacatat gggagggcaa atcatttaaa acatcagaat gagtatttgg tttagagttt 780

ggcaacatat gccatatgct ggctgccatg aacaaaggtg gctataaaga ggtcatcagt 840

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atatgaaaca gccccctgct gtccattcct tattccatag aaaagccttg acttgaggtt 900

agatttttt tatattttgt tttgtgttat ttttttcttt aacatcccta aaattttcct 960

tacatgtttt actagccaga tttttcctcc tctcctgact actcccagtc atagctgtcc 1020

ctcttctctt atgaagatcc ctcgacctgc agcccaagct tggcgtaatc atggtcatag 1080

ctgtttcctg tgtgaaattg ttatccgctc acaattccac acaacatacg agccggaagc 1140

ataaagtgta aagcctgggg tgcctaatga gtgagctaac tcacattaat tgcgttgcgc 1200

tcactgcccg ctttccagtc gggaaacctg tcgtgccagc ggatccgcat ctcaattagt 1260

cagcaaccat agtcccgccc ctaactccgc ccatcccgcc cctaactccg cccagttccg 1320

cccattctcc gccccatggc tgactaattt tttttattta tgcagaggcc gaggccgcct 1380

cggcctctga gctattccag aagtagtgag gaggcttttt tggaggccta ggcttttgca 1440

aaaagctaac ttgtttattg cagcttataa tggttacaaa taaagcaata gcatcacaaa 1500

tttcacaaat aaagcatttt tttcactgca ttctagttgt ggtttgtcca aactcatcaa 1560

tgtatcttat cagcggccgc cccggg 1586

<210> SEQ ID NO 45
<211> LENGTH: 1614
<212> TYPE: DNA
<213> ORGANISM: artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: CAG enhancer/promoter/intron sequence DNA fragment

<400> SEQUENCE: 45

acgcgttagt tattaatagt aatcaattac ggggtcatta gttcatagcc catatatgga 60

gttccgcgtt acataactta cggtaaatgg cccgcctggc tgaccgccca acgacccccg 120

cccattgacg tcaataatga cgtatgttcc catagtaacg ccaataggga ctttccattg 180

acgtcaatgg gtggactatt tacggtaaac tgcccacttg gcagtacatc aagtgtatca 240

tatgccaagt acgccccta ttgacgtcaa tgacggtaaa tggcccgcct ggcattatgc 300

ccagtacatg accttatggg actttcctac ttggcagtac atctacgtat tagtcatcgc 360

tattaccatg ggtcgaggtg agccccacgt tctgcttcac tctccccatc tccccccct 420

ccccaccccc aattttgtat ttatttattt tttaattatt ttgtgcagcg atgggggcgg 480

gggggggggg ggcgcgcgcc aggcggggcg gggcggggcg aggggcgggg cggggcgagg 540

cggagaggtg cggcggcagc caatcagagc ggcgcgctcc gaaagtttcc ttttatggcg 600

aggcggcggc ggcggcggcc ctataaaaag cgaagcgcgc ggcgggcggg agtcgctgcg 660

ttgccttcgc cccgtgcccc gctccgcgcc gcctcgcgcc gcccgccccg gctctgactg 720

accgcgttac tcccacaggt gagcgggcgg gacggcccct ctcctccggg ctgtaattag 780

cgcttggttt aatgacggct cgtttctttt ctgtggctgc gtgaaagcct taaagggctc 840

cgggagggcc ctttgtgcgg gggggagcgg ctcgggggggt gcgtgcgtgt gtgtgtgcgt 900

ggggagcgcc gcgtgcggcc cgcgctgccc ggcggctgtg agcgctgcgg gcgcggcgcg 960

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gcgggggggc tgcgagggga acaaaggctg cgtgcggggt gtgtgcgtgg gggggtgagc 1080

agggggtgtg ggcgcggcgg tcgggctgta acccccccct gcacccccct ccccgagttg 1140

ctgagcacgg cccggcttcg ggtgcggggc tccgtgcggg gcgtggcgcg gggctcgccg 1200

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tgccgggcgg ggggtggcgg caggtggggg tgccgggcgg ggcggggccg cctcgggccg 1260

gggagggctc gggggagggg cgcggcggcc ccggagcgcc ggcggctgtc gaggcgcggc 1320

gagccgcagc cattgccttt tatggtaatc gtgcgagagg gcgcagggac ttcctttgtc 1380

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gccgccgtcc ccttctccat ctccagcctc ggggctgccg caggggacg gctgccttcg 1560

gggggacgg ggcagggcgg ggttcggctt ctggcgtgtg accggcggga attc 1614

<210> SEQ ID NO 46
<211> LENGTH: 1531
<212> TYPE: DNA
<213> ORGANISM: Vesicular Stomatitis Indiana Virus

<400> SEQUENCE: 46

gaattcatga agtgcctttt gtacttagcc tttttattca ttggggtgaa ttgcaagttc 60

accatagttt ttccacacaa ccaaaaagga aactggaaaa atgttccttc taattaccat 120

tattgcccgt caagctcaga tttaaattgg cataatgact taataggcac agccttacaa 180

gtcaaaatgc ccaagagtca caaggctatt caagcagacg gttggatgtg tcatgcttcc 240

aaatgggtca ctacttgtga tttccgctgg tatggaccga agtatataac acattccatc 300

cgatccttca ctccatctgt agaacaatgc aaggaaagca ttgaacaaac gaaacaagga 360

acttggctga atccaggctt ccctcctcaa agttgtggat atgcaactgt gacggatgcc 420

gaagcagtga ttgtccaggt gactcctcac catgtgctgg ttgatgaata cacaggagaa 480

tgggttgatt cacagttcat caacggaaaa tgcagcaatt acatatgccc cactgtccat 540

aactctacaa cctggcattc tgactataag gtcaaagggc tatgtgattc taacctcatt 600

tccatggaca tcaccttctt ctcagaggac ggagagctat catccctggg aaaggagggc 660

acagggttca gaagtaacta ctttgcttat gaaactggag gcaaggcctg caaaatgcaa 720

tactgcaagc attggggagt cagactccca tcaggtgtct ggttcgagat ggctgataag 780

gatctctttg ctgcagccag attccctgaa tgcccagaag ggtcaagtat ctctgctcca 840

tctcagacct cagtggatgt aagtctaatt caggacgttg agaggatctt ggattattcc 900

ctctgccaag aaacctggag caaaatcaga gcgggtcttc caatctctcc agtggatctc 960

agctatcttg ctcctaaaaa cccaggaacc ggtcctgctt tcaccataat caatggtacc 1020

ctaaaatact ttgagaccag atacatcaga gtcgatattg ctgctccaat cctctcaaga 1080

atggtcggaa tgatcagtgg aactaccaca gaaagggaac tgtgggatga ctgggcacca 1140

tatgaagacg tggaaattgg acccaatgga gttctgagga ccagttcagg atataagttt 1200

cctttataca tgattggaca tggtatgttg gactccgatc ttcatcttag ctcaaaggct 1260

caggtgttcg aacatcctca cattcaagac gctgcttcgc aacttcctga tgatgagagt 1320

ttatttttttg gtgatactgg gctatccaaa aatccaatcg agcttgtaga aggttggttc 1380

agtagttgga aaagctctat tgcctctttt ttctttatca tagggttaat cattggacta 1440

ttcttggttc tccgagttgg tatccatctt tgcattaaat taaagcacac caagaaaaga 1500

cagatttata cagacataga gatgagaatt c 1531

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<210> SEQ ID NO 47
<211> LENGTH: 351
<212> TYPE: DNA
<213> ORGANISM: Rous Sarcoma Virus

<400> SEQUENCE: 47

atggcaggaa gaagcggaga cagcgacgaa gaactcctca aggcagtcag actcatcaag 60

tttctctatc aaagcaaccc acctcccaat cccgagggga cccgacaggc ccgaaggaat 120

agaagaagaa ggtggagaga gagacagaga cagatccatt cgattagtga acggatcctt 180

agcacttatc tgggacgatc tgcggagcct gtgcctcttc agctaccacc gcttgagaga 240

cttactcttg attgtaacga ggattgtgga acttctggga cgcaggggt gggaagccct 300

caaatattgg tggaatctcc tacaatattg gagtcaggag ctaaagaata g 351

<210> SEQ ID NO 48
<211> LENGTH: 884
<212> TYPE: DNA
<213> ORGANISM: artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Rous Sarcoma Virus (RSV) promoter and Human Immunodeficiency Virus (HIV) Rev DNA fragment

<400> SEQUENCE: 48

caattgcgat gtacgggcca gatatacgcg tatctgaggg gactagggtg tgtttaggcg 60

aaaagcgggg cttcggttgt acgcggttag gagtcccctc aggatatagt agtttcgctt 120

ttgcataggg agggggaaat gtagtcttat gcaatacact tgtagtcttg caacatggta 180

acgatgagtt agcaacatgc cttacaagga gagaaaaagc accgtgcatg ccgattggtg 240

gaagtaaggt ggtacgatcg tgccttatta ggaaggcaac agacaggtct gacatggatt 300

ggacgaacca ctgaattccg cattgcagag ataattgtat ttaagtgcct agctcgatac 360

aataaacgcc atttgaccat tcaccacatt ggtgtgcacc tccaagctcg agctcgttta 420

gtgaaccgtc agatcgcctg gagacgccat ccacgctgtt ttgacctcca tagaagacac 480

cgggaccgat ccagcctccc ctcgaagcta gcgattaggc atctcctatg gcaggaagaa 540

gcggagacag cgacgaagaa ctcctcaagg cagtcagact catcaagttt ctctatcaaa 600

gcaacccacc tcccaatccc gaggggaccc gacaggcccg aaggaataga agaagaaggt 660

ggagagagag acagagacag atccattcga ttagtgaacg gatccttagc acttatctgg 720

gacgatctgc ggagcctgtg cctcttcagc taccaccgct tgagagactt actcttgatt 780

gtaacgagga ttgtggaact tctgggacgc agggggtggg aagccctcaa atattggtgg 840

aatctcctac aatattggag tcaggagcta aagaatagtc taga 884

<210> SEQ ID NO 49
<211> LENGTH: 511
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 49

ggggttgggg ttgcgccttt tccaaggcag ccctgggttt gcgcagggac gcggctgctc 60

tgggcgtggt tccgggaaac gcagcggcgc cgaccctggg tctcgcacat tcttcacgtc 120

cgttcgcagc gtcacccgga tcttcgccgc tacccttgtg ggccccccgg cgacgcttcc 180

tgctccgccc ctaagtcggg aaggttcctt gcggttcgcg gcgtgccgga cgtgacaaac 240

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ggaagccgca cgtctcacta gtaccctcgc agacggacag cgccagggag caatggcagc 300

gcgccgaccg cgatgggctg tggccaatag cggctgctca gcagggcgcg ccgagagcag 360

cggccgggaa ggggcggtgc gggaggcggg gtgtggggcg gtagtgtggg ccctgttcct 420

gcccgcgcgg tgttccgcat tctgcaagcc tccggagcgc acgtcggcag tcggctccct 480

cgttgaccga atcaccgacc tctctcccca g 511

<210> SEQ ID NO 50
<211> LENGTH: 1162
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 50

gcgccgggtt ttggcgcctc ccgcgggcgc ccccctcctc acggcgagcg ctgccacgtc 60

agacgaaggg cgcaggagcg ttcctgatcc ttccgcccgg acgctcagga cagcggcccg 120

ctgctcataa gactcggcct tagaacccca gtatcagcag aaggacattt taggacggga 180

cttgggtgac tctagggcac tggttttctt tccagagagc ggaacaggcg aggaaaagta 240

gtcccttctc ggcgattctg cggagggatc tccgtggggc ggtgaacgcc gatgattata 300

taaggacgcg ccgggtgtgg cacagctagt tccgtcgcag ccgggatttg ggtcgcggtt 360

cttgtttgtg gatcgctgtg atcgtcactt ggtgagttgc gggctgctgg gctggccggg 420

gctttcgtgg ccgccgggcc gctcggtggg acggaagcgt gtggagagac cgccaagggc 480

tgtagtctgg gtccgcgagc aaggttgccc tgaactgggg gttgggggga gcgcacaaaa 540

tggcggctgt tcccgagtct tgaatggaag acgcttgtaa ggcgggctgt gaggtcgttg 600

aaacaaggtg gggggcatgg tgggcggcaa gaacccaagg tcttgaggcc ttcgctaatg 660

cgggaaagct cttattcggg tgagatgggc tggggcacca tctggggacc ctgacgtgaa 720

gtttgtcact gactggagaa ctcgggtttg tcgtctggtt gcgggggcgg cagttatgcg 780

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gccggacctc tggtgagggg agggataagt gaggcgtcag tttctttggt cggttttatg 1020

tacctatctt cttaagtagc tgaagctccg gttttgaact atgcgctcgg ggttggcgag 1080

tgtgttttgt gaagtttttt aggcaccttt tgaaatgtaa tcatttgggt caatatgtaa 1140

ttttcagtgt tagactagta aa 1162

<210> SEQ ID NO 51
<211> LENGTH: 120
<212> TYPE: DNA
<213> ORGANISM: Simian virus 40

<400> SEQUENCE: 51

gtttattgca gcttataatg gttacaaata aagcaatagc atcacaaatt tcacaaataa 60

agcatttttt tcactgcatt ctagttgtgg tttgtccaaa ctcatcaatg tatcttatca 120

<210> SEQ ID NO 52
<211> LENGTH: 227
<212> TYPE: DNA
<213> ORGANISM: Bos taurus

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<400> SEQUENCE: 52

gactgtgcct tctagttgcc agccatctgt tgtttgcccc tcccccgtgc cttccttgac 60

cctggaaggt gccactccca ctgtccttttc ctaataaaat gaggaaattg catcgcattg 120

tctgagtagg tgtcattcta ttctgggggg tggggtgggg caggacagca agggggagga 180

ttgggaagac aatagcaggc atgctgggga tgcggtgggc tctatgg 227

<210> SEQ ID NO 53
<211> LENGTH: 1695
<212> TYPE: DNA
<213> ORGANISM: Feline Endogenous Virus

<400> SEQUENCE: 53

atgaaactcc caacaggaat ggtcatttta tgtagcctaa taatagttcg ggcagggttt 60

gacgaccccc gcaaggctat cgcattagta caaaaacaac atggtaaacc atgcgaatgc 120

agcggagggc aggtatccga ggccccaccg aactccatcc aacaggtaac ttgcccaggc 180

aagacggcct acttaatgac caaccaaaaa tggaaatgca gagtcactcc aaaaaatctc 240

acccctagcg ggggagaact ccagaactgc ccctgtaaca ctttccagga ctcgatgcac 300

agttcttgtt atactgaata ccggcaatgc agggcgaata ataagacata ctacacggcc 360

accttgctta aaatacggtc tgggagcctc aacgaggtac agatattaca aaaccccaat 420

cagctcctac agtccccttg taggggctct ataaatcagc ccgtttgctg gagtgccaca 480

gcccccatcc atatctccga tggtggagga cccctcgata ctaagagagt gtggacagtc 540

caaaaaaggc tagaacaaat tcataaggct atgcatcctg aacttcaata ccacccctta 600

gccctgccca aagtcagaga tgaccttagc cttgatgcac ggacttttga tatcctgaat 660

accacttta ggttactcca gatgtccaat tttagccttg cccaagattg ttggctctgt 720

ttaaaactag gtacccctac ccctcttgcg atacccactc cctctttaac ctactcccta 780

gcagactccc tagcgaatgc ctcctgtcag attatacctc ccctcttggt tcaaccgatg 840

cagttctcca actcgtcctg tttatcttcc cctttcatta acgatacgga acaaatagac 900

ttaggtgcag tcacctttac taactgcacc tctgtagcca atgtcagtag tcctttatgt 960

gccctaaacg ggtcagtctt cctctgtgga aataacatgg catacaccta tttaccccaa 1020

aactggacag gactttgcgt ccaagcctcc ctcctccccg acattgacat catcccgggg 1080

gatgagccag tccccattcc tgccattgat cattatatac atagacctaa acgagctgta 1140

cagttcatcc ctttactagc tggactggga atcaccgcag cattcaccac cggagctaca 1200

ggcctaggtg tctccgtcac ccagtataca aaattatccc atcagttaat atctgatgtc 1260

caagtcttat ccggtaccat acaagattta caagaccagg tagactcgtt agctgaagta 1320

gttctccaaa ataggagggg actggaccta ctaacggcag aacaaggagg aatttgttta 1380

gccttacaag aaaaatgctg tttttatgct aacaagtcag gaattgtgag aaacaaaata 1440

agaaccctac aagaagaatt acaaaaacgc agggaaagcc tggcatccaa ccctctctgg 1500

accgggctgc agggctttct tccgtacctc ctacctctcc tgggacccct actcaccctc 1560

ctactcatac taaccattgg gccatgcgtt ttcaatcgat tggtccaatt tgttaaagac 1620

aggatctcag tggtccaggc tctggttttg actcagcaat atcaccagct aaaacccata 1680

gagtacgagc catga 1695

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<210> SEQ ID NO 54
<211> LENGTH: 2013
<212> TYPE: DNA
<213> ORGANISM: Gibbon Ape Leukemia Virus

<400> SEQUENCE: 54

atgcttctca cctcaagccc gcaccacctt cggcaccaga tgagtcctgg gagctggaaa 60

agactgatca tcctcttaag ctgcgtattc ggagacggca aaacgagtct gcagaataag 120

aacccccacc agcctgtgac cctcacctgg caggtactgt cccaaactgg ggacgttgtc 180

tgggacaaaa aggcagtcca gccccctttgg acttggtggc cctctcttac acctgatgta 240

tgtgccctgg cggccggtct tgagtcctgg gatatcccgg gatccgatgt atcgtcctct 300

aaaagagtta gacctcctga ttcagactat actgccgctt ataagcaaat cacctgggga 360

gccatagggt gcagctaccc tcgggctagg accaggatgg caaattcccc cttctacgtg 420

tgtccccgag ctggccgaac ccattcagaa gctaggaggt gtgggggggct agaatcccta 480

tactgtaaag aatggagttg tgagaccacg ggtaccgttt attggcaacc caagtcctca 540

tgggacctca taactgtaaa atgggaccaa aatgtgaaat gggagcaaaa atttcaaaag 600

tgtgaacaaa ccggctggtg taacccccctc aagatagact tcacagaaaa aggaaaactc 660

tccagagatt ggataacgga aaaaacctgg gaattaaggt tctatgtata tggacaccca 720

ggcatacagt tgactatccg cttagaggtc actaacatgc cggttgtggc agtgggccca 780

gaccctgtcc ttgcggaaca gggacctcct agcaagcccc tcactctccc tctctcccca 840

cggaaagcgc cgcccacccc tctacccccg gcggctagtg agcaaacccc tgcggtgcat 900

ggagaaactg ttaccctaaa ctctccgcct cccaccagtg gcgaccgact ctttggcctt 960

gtgcaggggg ccttcctaac cttgaatgct accaacccag gggccactaa gtcttgctgg 1020

ctctgtttgg gcatgagccc cccttattat gaagggatag cctcttcagg agaggtcgct 1080

tatacctcca accatacccg atgccactgg ggggcccaag gaaagcttac cctcactgag 1140

gtctccggac tcgggtcatg catagggaag gtgcctctta cccatcaaca tctttgcaac 1200

cagaccttac ccatcaattc ctctaaaaac catcagtatc tgctcccctc aaaccatagc 1260

tggtgggcct gcagcactgg cctcaccccc tgcctctcca cctcagtttt taatcagtct 1320

aaagacttct gtgtccaggt ccagctgatc ccccgcatct attaccattc tgaagaaacc 1380

ttgttacaag cctatgacaa atcacccccc aggtttaaaa gagagcctgc ctcacttacc 1440

ctagctgtct tcctggggtt agggattgcg gcaggtatag gtactggctc aaccgcccta 1500

attaaagggc ccatagacct ccagcaaggc ctaaccagcc tccaaatcgc cattgacgct 1560

gacctccggg cccttcagga ctcaatcagc aagctagagg actcactgac ttccctatct 1620

gaggtagtac tccaaaatag gagaggcctt gacttactat tccttaaaga aggaggcctc 1680

tgcgcggccc taaaagaaga gtgctgtttt tatgtagacc actcaggtgc agtacgagac 1740

tccatgaaaa aacttaaaga aagactagat aaaagacagt tagagcgcca gaaaaaccaa 1800

aactggtatg aagggtggtt caataactcc ccttggttta ctaccctact atcaaccatc 1860

gctgggcccc tattgctcct ccttttgtta ctcactcttg ggccctgcat catcaataaa 1920

ttaatccaat tcatcaatga taggataagt gcagtcaaaa ttttagtcct tagacagaaa 1980

tatcagaccc tagataacga ggaaaacctt taa 2013

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<210> SEQ ID NO 55
<211> LENGTH: 1530
<212> TYPE: DNA
<213> ORGANISM: Rabies virus

<400> SEQUENCE: 55

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ttccccattt acacgatacc agacgaactt ggtccctgga gccctattga catacaccat 120

ctcagctgtc caaataacct ggttgtggag gatgaaggat gtaccaacct gtccgagttc 180

tcctacatgg aactcaaagt gggatacatc tcagccatca aagtgaacgg gttcacttgc 240

acaggtgttg tgacagaggc agagacctac accaactttg ttggttatgt cacaaccaca 300

ttcaagagaa agcatttccg ccccacccca gacgcatgta gagccgcgta taactggaag 360

atggccggtg accccagata tgaagagtcc ctacacaatc catacccga ctaccactgg 420

cttcgaactg taagaaccac caaagagtcc ctcattatca tatccccaag tgtgacagat 480

ttggacccat atgacaaatc ccttcactca agggtcttcc ctggcggaaa gtgctcagga 540

ataacggtgt cctctaccta ctgctcaact aaccatgatt acaccatttg gatgcccgag 600

aatccgagac caaggacacc ttgtgacatt tttaccaata gcagagggaa gagagcatcc 660

aacgggaaca agacttgcgg ctttgtggat gaaagaggcc tgtataagtc tctaaaagga 720

gcatgcaggc tcaagttatg tggagttctt ggacttagac ttatggatgg aacatgggtc 780

gcgatgcaaa catcagatga gaccaaatgg tgccctccag atcagttggt gaatttgcac 840

gactttcgct cagacgagat cgagcatctc gttgtggagg agttagttaa gaaaagagag 900

gaatgtctgg atgcattaga gtccatcatg accaccaagt cagtaagttt cagacgtctc 960

agtcacctga gaaaacttgt cccagggttt ggaaaagcat ataccatatt caacaaaacc 1020

ttgatggagg ctgatgctca ctacaagtca gtccggacct ggaatgagat catcccctca 1080

aaagggtgtt tgaaagttgg aggaaggtgc catcctcatg tgaacggggt gtttttcaat 1140

ggtataatat tagggcctga cgaccatgtc ctaatcccag agatgcaatc atccctcctc 1200

cagcaacata tggagttgtt ggaatcttca gttatccccc tgatgcaccc cctggcagac 1260

ccttctacag ttttcaaaga aggtgatgag gctgaggatt ttgttgaagt tcacctcccc 1320

gatgtgtaca aacagatctc aggggttgac ctgggtctcc cgaactgggg aaagtatgta 1380

ttgatgactg caggggccat gattggcctg gtgttgatat tttccctaat gacatggtgc 1440

agagttggta tccatctttg cattaaatta aagcacacca agaaaagaca gatttataca 1500

gacatagaga tgaaccgact tggaaagtaa 1530

<210> SEQ ID NO 56
<211> LENGTH: 1497
<212> TYPE: DNA
<213> ORGANISM: Lymphocytic Choriomeningitis Virus

<400> SEQUENCE: 56

atgggtcaga ttgtgacaat gtttgaggct ctgcctcaca tcatcgatga ggtgatcaac 60

attgtcatta ttgtgcttat cgtgatcacg ggtatcaagg ctgtctacaa ttttgccacc 120

tgtgggatat tcgcattgat cagtttccta cttctggctg gcaggtcctg tggcatgtac 180

ggtcttaagg gacccgacat ttacaaagga gtttaccaat ttaagtcagt ggagtttgat 240

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atcagtatgg ggacttctgg actagaattg accttcacca atgattccat catcagtcac 360

aacttttgca atctgacctc tgccttcaac aaaaagacct ttgaccacac actcatgagt 420

atagtttcga gcctacacct cagtatcaga gggaactcca actataaggc agtatcctgc 480

gacttcaaca atggcataac catccaatac aacttgacat tctcagatcg acaaagtgct 540

cagagccagt gtagaacctt cagaggtaga gtcctagata tgtttagaac tgccttcggg 600

gggaaatata tgaggagtgg ctggggctgg acaggctcag atggcaagac cacctggtgt 660

agccagacga gttaccaata cctgattata caaaatagaa cctgggaaaa ccactgcaca 720

tatgcaggtc cttttgggat gtccaggatt ctcctttccc aagagaagac taagttcttc 780

actaggagac tagcgggcac attcacctgg actttgtcag actcttcagg ggtggagaat 840

ccaggtggtt attgcctgac caaatggatg attcttgctg cagagcttaa gtgtttcggg 900

aacacagcag ttgcgaaatg caatgtaaat catgatgccg aattctgtga catgctgcga 960

ctaattgact acaacaaggc tgctttgagt aagttcaaag aggacgtaga atctgccttg 1020

cacttattca aaacaacagt gaattctttg atttcagatc aactactgat gaggaaccac 1080

ttgagagatc tgatgggggt gccatattgc aattactcaa agttttggta cctagaacat 1140

gcaaagaccg gcgaaactag tgtccccaag tgctggcttg tcaccaatgg ttcttactta 1200

aatgagaccc acttcagtga tcaaatcgaa caggaagccg ataacatgat tacagagatg 1260

ttgaggaagg attacataaa gaggcagggg agtacccccc tagcattgat ggaccttctg 1320

atgttttcca catctgcata tctagtcagc atcttcctgc accttgtcaa aataccaaca 1380

cacaggcaca taaaaggtgg ctcatgtcca aagccacacc gattaaccaa caaaggaatt 1440

tgtagttgtg gtgcatttaa ggtgcctggt gtaaaaaccg tctggaaaag acgctga 1497

<210> SEQ ID NO 57
<211> LENGTH: 1692
<212> TYPE: DNA
<213> ORGANISM: Fowl Plague virus

<400> SEQUENCE: 57

atgaacactc aaatcctggt tttcgccctt gtggcagtca tccccacaaa tgcagacaaa 60

atttgtcttg gacatcatgc tgtatcaaat ggcaccaaag taaacacact cactgagaga 120

ggagtagaag ttgtcaatgc aacggaaaca gtggagcgga caaacatccc caaaatttgc 180

tcaaaaggga aaagaaccac tgatcttggc caatgcggac tgttagggac cattaccgga 240

ccacctcaat gcgaccaatt tctagaattt tcagctgatc taataatcga gagacgagaa 300

ggaaatgatg tttgttaccc ggggaagttt gttaatgaag aggcattgcg acaaatcctc 360

agaggatcag gtgggattga caaagaaaca atgggattca catatagtgg aataaggacc 420

aacggaacaa ctagtgcatg tagaagatca gggtcttcat tctatgcaga aatggagtgg 480

ctcctgtcaa atacagacaa tgctgctttc ccacaaatga caaaatcata caaaaacaca 540

aggagagaat cagctctgat agtctgggga atccaccatt caggatcaac caccgaacag 600

accaaactat atgggagtgg aaataaactg ataacagtcg ggagttccaa atatcatcaa 660

tcttttgtgc cgagtccagg aacacgaccg cagataaatg gccagtccgg acggattgat 720

tttcattggt tgatcttgga tcccaatgat acagttactt ttagtttcaa tggggctttc 780

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atagctccaa atcgtgccag cttcttgagg ggaaagtcca tggggatcca gagcgatgtg 840

caggttgatg ccaattgcga aggggaatgc taccacagtg gagggactat aacaagcaga 900

ttgccttttc aaaacatcaa tagcagagca gttggcaaat gcccaagata tgtaaaacag 960

gaaagtttat tattggcaac tgggatgaag aacgttcccg aaccttccaa aaaaaggaaa 1020

aaaagaggcc tgtttggcgc tatagcaggg tttattgaaa atggttggga aggtctggtc 1080

gacgggtggt acggtttcag gcatcagaat gcacaaggag aaggaactgc agcagactac 1140

aaaagcaccc aatcggcaat tgatcagata accggaaagt taaatagact cattgagaaa 1200

accaaccagc aatttgagct aatagataat gaattcactg aggtggaaaa gcagattggc 1260

aatttaatta actggaccaa agactccatc acagaagtat ggtcttacaa tgctgaactt 1320

cttgtggcaa tggaaaacca gcacactatt gatttggctg attcagagat gaacaagctg 1380

tatgagcgag tgaggaaaca attaagggaa aatgctgaag aggatggcac tggttgcttt 1440

gaaatttttc ataaatgtga cgatgattgt atggctagta taaggaacaa tacttatgat 1500

cacagcaaat acagagaaga agcgatgcaa aatagaatac aaattgaccc agtcaaattg 1560

agtagtggct acaaagatgt gatactttgg tttagcttcg gggcatcatg ctttttgctt 1620

cttgccattg caatgggcct tgttttcata tgtgtgaaga acggaaacat gcggtgcact 1680

atttgtatat aa 1692

<210> SEQ ID NO 58
<211> LENGTH: 1266
<212> TYPE: DNA
<213> ORGANISM: Ross River Virus

<400> SEQUENCE: 58

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gattgcgggg acgggtactt ctgctatagc ccagttgcta tcgaggagat ccgagatgag 120

gcgtctgatg gcatgcttaa gatccaagtc tccgcccaaa taggtctgga caaggcaggc 180

acccacgccc acacgaagct ccgatatatg gctggtcatg atgttcagga atctaagaga 240

gattccttga gggtgtacac gtccgcagcg tgctccatac atgggacgat gggacacttc 300

atcgtcgcac actgtccacc aggcgactac ctcaaggttt cgttcgagga cgcagattcg 360

cacgtgaagg catgtaaggt ccaatacaag cacaatccat tgccggtggg tagagagaag 420

ttcgtggtta gaccacactt tggcgtagag ctgccatgca cctcatacca gctgacaacg 480

gctcccaccg acgaggagat tgacatgcat acaccgccag atataccgga tcgcaccctg 540

ctatcacaga cggcgggcaa cgtcaaaata acagcaggcg gcaggactat caggtacaac 600

tgtacctgcg gccgtgacaa cgtaggcact accagtactg acaagaccat caacacatgc 660

aagattgacc aatgccatgc tgccgtcacc agccatgaca aatggcaatt tacctctcca 720

tttgttccca gggctgatca gacagctagg aaaggcaagg tacacgttcc gttccctctg 780

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ctgacgccag gagcggtggt accgttgaca ctggggctgc tttgctgcgc accgagggcg 1260

aatgca 1266

<210> SEQ ID NO 59
<211> LENGTH: 1266
<212> TYPE: DNA
<213> ORGANISM: Murine Leukemia virus

<400> SEQUENCE: 59

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gcgtctgatg gcatgcttaa gatccaagtc tccgcccaaa taggtctgga caaggcaggc 180

acccacgccc acacgaagct ccgatatatg gctggtcatg atgttcagga atctaagaga 240

gattccttga gggtgtacac gtccgcagcg tgctccatac atgggacgat gggacacttc 300

atcgtcgcac actgtccacc aggcgactac ctcaaggttt cgttcgagga cgcagattcg 360

cacgtgaagg catgtaaggt ccaatacaag cacaatccat tgccggtggg tagagagaag 420

ttcgtggtta gaccacactt tggcgtagag ctgccatgca cctcatacca gctgacaacg 480

gctcccaccg acgaggagat tgacatgcat acaccgccag atataccgga tcgcaccctg 540

ctatcacaga cggcgggcaa cgtcaaaata acagcaggcg gcaggactat caggtacaac 600

tgtacctgcg gccgtgacaa cgtaggcact accagtactg acaagaccat caacacatgc 660

aagattgacc aatgccatgc tgccgtcacc agccatgaca aatggcaatt tacctctcca 720

tttgttccca gggctgatca gacagctagg aaaggcaagg tacacgttcc gttccctctg 780

actaacgtca cctgccgagt gccgttggct cgagcgccgg atgccaccta tggtaagaag 840

gaggtgaccc tgagattaca cccagatcat ccgacgctct tctcctatag gagtttagga 900

gccgaaccgc acccgtacga ggaatgggtt gacaagttct ctgagcgcat catcccagtg 960

acggaagaag ggattgagta ccagtggggc aacaacccgc cggtctgcct gtgggcgcaa 1020

ctgacgaccg agggcaaacc ccatggctgg ccacatgaaa tcattcagta ctattatgga 1080

ctataccccg ccgccactat tgccgcagta tccggggcga gtctgatggc cctcctaact 1140

ctggcggcca catgctgcat gctggccacc gcgaggagaa agtgcctaac accgtacgcc 1200

ctgacgccag gagcggtggt accgttgaca ctggggctgc tttgctgcgc accgagggcg 1260

aatgca 1266

<210> SEQ ID NO 60
<211> LENGTH: 2030
<212> TYPE: DNA
<213> ORGANISM: Ebola virus

<400> SEQUENCE: 60

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agcacattac aggttagtga tgtcgacaaa ctggtttgcc gtgacaaact gtcatccaca 180

aatcaattga gatcagttgg actgaatctc gaagggaatg gagtggcaac tgacgtgcca 240

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tctgcaacta aaagatgggg cttcaggtcc ggtgtcccac caaaggtggt caattatgaa 300

gctggtgaat gggctgaaaa ctgctacaat cttgaaatca aaaaacctga cgggagtgag 360

tgtctaccag cagcgccaga cgggattcgg ggcttccccc ggtgccggta tgtgcacaaa 420

gtatcaggaa cgggaccgtg tgccggagac tttgccttcc acaaagaggg tgctttcttc 480

ctgtatgacc gacttgcttc cacagttatc taccgaggaa cgactttcgc tgaaggtgtc 540

gttgcatttc tgatactgcc ccaagctaag aaggacttct tcagctcaca ccccttgaga 600

gagccggtca atgcaacgga ggacccgtct agtggctact attctaccac aattagatat 660

caagctaccg gttttggaac caatgagaca gagtatttgt tcgaggttga caatttgacc 720

tacgtccaac ttgaatcaag attcacacca cagtttctgc tccagctgaa tgagacaata 780

tatacaagtg ggaaaaggag caataccacg ggaaaactaa tttggaaggt caaccccgaa 840

attgatacaa caatcgggga gtgggccttc tgggaaacta aaaaaacctc actagaaaaa 900

ttcgcagtga agagttgtct ttcacagctg tatcaaacag agccaaaaac atcagtggtc 960

agagtccggc gcgaacttct tccgacccag ggaccaacac aacaactgaa gaccacaaaa 1020

tcatggcttc agaaaattcc tctgcaatgg ttcaagtgca cagtcaagga agggaagctg 1080

cagtgtcgca tctgacaacc cttgccacaa tctccacgag tcctcaaccc cccacaacca 1140

aaccaggtcc ggacaacagc acccacaata cacccgtgta taaacttgac atctctgagg 1200

caactcaagt tgaacaacat caccgcagaa cagacaacga cagcacagcc tccgacactc 1260

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acaacaacac tcatcaccaa gataccggag aagagagtgc cagcagcggg aagctaggct 1440

taattaccaa tactattgct ggagtcgcag gactgatcac aggcgggagg agagctcgaa 1500

gagaagcaat tgtcaatgct caacccaaat gcaaccctaa tttacattac tggactactc 1560

aggatgaagg tgctgcaatc ggactggcct ggataccata tttcgggcca gcagccgagg 1620

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tggccaacga gacgactcaa gctcttcaac tgttcctgag agccacaacc gagctacgca 1740

ccttttcaat cctcaaccgt aaggcaattg atttcttgct gcagcgatgg ggcggcacat 1800

gccacatttt gggaccggac tgctgtatcg aaccacatga ttggaccaag aacataacag 1860

acaaaattga tcagattatt catgattttg ttgataaaac ccttccggac caggggggaca 1920

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<210> SEQ ID NO 61
<211> LENGTH: 49
<212> TYPE: DNA
<213> ORGANISM: artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Control shRNA sequence

<400> SEQUENCE: 61

gccgctttgt aggatagagc tcgagctcta tcctacaaag cggcttttt 49

What is claimed is:

1. A lentiviral vector system for expressing a lentiviral particle, the system comprising:

a. a therapeutic vector comprising a shRNA for inhibiting PARP expression;

b. an envelope plasmid comprising a neuron-specific sequence for targeting the shRNA to a neuron; and

c. at least one helper plasmid comprising gag, pol, and rev genes, wherein when the therapeutic vector, the envelope plasmid and the at least one helper plasmid are transfected into a packaging cell line, a neuron-specific lentiviral particle capable of inhibiting PARP expression is produced by the packaging cell line.

2. The lentiviral vector system of claim **1**, wherein the shRNA comprises a PARP-specific shRNA.

3. The lentiviral vector system of claim **1**, wherein the shRNA comprises a PARP1-specific shRNA.

4. The lentiviral vector system of claim **1**, wherein the shRNA comprises a shRNA having at least 80%, or at least 85%, or at least 90%, or at least 95% sequence identity with any one of SEQ ID NOs: 6-10.

5. The lentiviral vector system of claim **1**, wherein the shRNA comprises any one of SEQ ID NOs: 6-10.

6. The lentiviral vector system of claim **1**, wherein the neuron-specific sequence encodes VSV-G, FUG-C, or gp64, or a variant thereof.

7. The lentiviral vector system of claim **1**, wherein the neuron-specific sequence encodes VSV-G or a variant thereof.

8. The lentiviral vector system of claim **1**, wherein the neuron-specific sequence encodes a protein that improves transduction into a neuron.

9. The lentiviral vector system of claim **1**, wherein the neuron-specific sequence encodes a protein that improves transduction into a TH+ neuron.

10. A lentiviral particle produced by a packaging cell and capable of infecting a cell, the lentiviral particle comprising:

a. an envelope protein capable of infecting the cell; and

b. a shRNA for inhibiting PARP expression.

11. The lentiviral particle of claim **10**, wherein the cell comprises a neuron.

12. The lentiviral particle of claim **10**, wherein the cell comprises a TH+ neuron.

13. The lentiviral particle of claim **10**, wherein the shRNA comprises a PARP-specific shRNA.

14. The lentiviral particle of claim **10**, wherein the shRNA comprises a PARP1-specific shRNA.

15. The lentiviral particle of claim **10**, wherein the shRNA comprises a shRNA having at least 80%, or at least 85%, or at least 90%, or at least 95% sequence identity with any one of SEQ ID NOs: 6-10.

16. The lentiviral particle of claim **10**, wherein the shRNA comprises any one of SEQ ID NOs: 6-10.

17. A method of treating a subject suffering from Parkinson's disease, the method comprising administering to the subject a lentiviral particle, wherein the lentiviral particle comprises:

a. an envelope protein capable of infecting a cell in the subject; and

b. a shRNA for inhibiting PARP expression.

18. The method of claim **17**, wherein the cell comprises a neuron.

19. The method of claim **17**, wherein the cell comprises a TH+ neuron.

20. The method of claim **17**, wherein the shRNA comprises a PARP-specific shRNA.

21. The method of claim **17**, wherein the shRNA comprises a PARP1-specific shRNA.

22. The method of claim **17**, wherein the shRNA comprises a shRNA having at least 80%, or at least 85%, or at least 90%, or at least 95% sequence identity with any one of SEQ ID NOs: 6-10.

23. The method of claim **17**, wherein the shRNA comprises any one of SEQ ID NOs: 6-10.

24. The method of claim **17**, further comprising a second therapeutic regimen.

25. The method of claim **17**, further comprising a second therapeutic regime, wherein the second therapeutic regimen comprises ablative surgical intervention, neural stimulation, L-DOPA administration, or dopamine agonist administration.

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