3:1124-1132; U.S. Patent. No. 5,786,211; U.S. Patent No. 5,871,982; and U.S. Patent. No. 6,258,595. The foregoing documents are hereby incorporated by reference in their entirety herein, with particular emphasis on those sections of the documents relating to rAAV production.

[0048] The invention thus provides packaging cells that produce replication-deficient, infectious rAAV. In one embodiment packaging cells may be stably transformed cancer cells such as HeLa cells, 293 cells and PerC.6 cells (a cognate 293 line). In another embodiment, packaging cells are cells that are not transformed cancer cells such as low passage 293 cells (human fetal kidney cells transformed with E1 of adenovirus), MRC-5 cells (human fetal fibroblasts), WI-38 cells (human fetal fibroblasts), Vero cells (monkey kidney cells) and FRhL-2 cells (rhesus fetal lung cells).

[0049] Thus, in another aspect, the invention provides rAAV such as rAAV9 (*i.e.*, replication-deficient, infectious encapsidated rAAV9 particles) comprising a rAAV genome of the invention. The genomes of the rAAV lack AAV rep and cap DNA, that is, there is no AAV rep or cap DNA between the ITRs of the genomes. In some embodiments, the rAAV genome is a self-complementary genome. In some embodiments, the rAAV genome is a single-stranded genome.

[0050] rAAV are provided such as a self-complementary AAV9 (scAAV9) named "AVXS-201." Its gene cassette (nucleotides 151-2558 of the AVXS-201 genome set out in SEQ ID NO: 1) has, in sequence, a 549bp promoter fragment (SEQ ID NO: 2) (nucleotides 74085586-74086323 of NC_000086.7 in the reverse orientation) from the mouse *MECP2* gene, an SV40 intron, a human MECP2B cDNA (SEQ ID NO: 3) (CCDS Database #CCDS48193.1), and a synthetic polyadenylation signal sequence (SEQ ID NO: 4). The gene cassette is flanked by a mutant AAV2 inverted terminal repeat (ITR) and a wild type AAV2 inverted terminal repeat that together enable packaging of self-complementary AAV genomes. The genome lacks AAV rep and cap DNA, that is, there is no AAV rep or cap DNA between the ITRs of the genome.

[0051] rAAV are provided such as a scAAV9 named "scAAV9.738.Mecp2." Its gene cassette (nucleotides 198-2890 of the scAAV9.738.Mecp2 genome set out in SEQ ID NO: 5) has, in sequence, a 738bp promoter fragment (SEQ ID NO: 6) (nucleotides 74085586-74086323 of NC_000086.7 in the reverse orientation) from the mouse *MECP2* gene, an SV40 intron, a mouse MECP2α cDNA (SEQ ID NO: 7) (CCDS Database #CCDS41016.1), and a polyadenylation signal sequence from the bovine growth hormone gene. The gene cassette is flanked by a mutant AAV2 inverted terminal repeat (ITR) and a wild type AAV2 inverted terminal repeat that together enable packaging of self-complementary AAV

CLAIMS

1. A recombinant adeno-associated virus (rAAV) vector comprising a gene cassette comprising a promoter consisting of the polynucleotide sequence of SEQ ID NO: 2, an SV40 intron, a polynucleotide sequence encoding a methyl-CpG-binding protein 2 (MECP2) and a synthetic polyadenylation signal sequence, wherein the gene cassette is flanked by a mutant AAV2 inverted terminal repeat and a wild type inverted terminal repeat.

2. The rAAV vector of claim 1, wherein the rAAV vector is self-complementary (scAAV).

3. The rAAV vector of claim 1 or 2, wherein the rAAV is rAAV9.

4. The rAAV9 vector of claim 3, wherein the polynucleotide sequence encoding MECP2 comprises the polynucleotide sequence of SEQ ID NO: 3.

5. The rAAV vector of any one of claims 1-3, wherein the rAAV comprises nucleotides 151-2558 of SEQ ID NO: 1.

6. The rAAV vector of any one of claims 1-5, wherein the polyadenylation signal sequence comprises the polynucleotide sequence of SEQ ID NO: 4.

7. A virus comprising the viral vector of any one of claims 1-6.

8. The virus of claim 7, further comprising one or more capsid proteins.

9. A pharmaceutical composition comprising the rAAV vector of any one of claims 1-6 or the virus of any one of claims 7-8.

10. The pharmaceutical composition of claim 9, wherein the composition is formulated for intrathecal (IT) administration.

11. The pharmaceutical composition of any one of claims 9-10 for use in treating Rett syndrome.

12. The pharmaceutical composition according to claim 11, administered by intrathecal (IT) administration.

13. The pharmaceutical composition of claim 11 or 12, wherein the use further comprising a non-ionic, low-osmolar contrast agent to the patient.

14. The pharmaceutical composition of claim 13, wherein the non-ionic, low-osmolar contrast agent comprises one or more of iobitridol, iohexol, iomeprol, iopamidol, iopentol, iopromide, ioversol, and ioxilan.

15. The pharmaceutical composition of claim 14, wherein the non-ionic, low-osmolar contrast agent comprises iohexol.

16. Use of an rAAV vector of any one of claims 1-6, the virus of any one of claims 7-8, or the pharmaceutical composition of any one of claims 9-10 for the preparation of medicament for treating Rett syndrome.

17. The use of claim 16, wherein the medicament is formulated for intrathecal (IT) administration.

18. The use of claim 16 or 17, wherein the medicament further comprises a non-ionic, low-osmolar contrast agent to the patient.

19. The use of claim 18, wherein the non-ionic, low-osmolar contrast agent comprises one or more of iobitridol, iohexol, iomeprol, iopamidol, iopentol, iopromide, ioversol, and ioxilan.

20. The use of claim 19, wherein the non-ionic, low-osmolar contrast agent comprises iohexol.

21. Use of an i) rAAV vector of any one of claims 1-6, the virus of any one of claims 7-8, or the pharmaceutical composition of any one of claims 9-10, and ii) a non-ionic, low-osmolar contract agent in the manufacture of a medicament for combination therapy of Rett syndrome.