

CLAIMS

1. A nucleic acid comprising an adeno-associated virus (AAV) expression cassette, wherein the AAV expression cassette comprises, from 5' to 3':

a 5' inverted terminal repeat (ITR);

a human Arc gene promoter (hArcMin);

a Rett Syndrome-associated gene; and

a 3' ITR;

wherein the hArcMin comprises a nucleic acid sequence of SEQ ID NO: 12, or a sequence at least 95% identical thereto.

2. The nucleic acid of claim 1, wherein the promoter drives expression of the Rett-syndrome-associated gene.

3. The nucleic acid of claim 1, wherein the promoter further comprises a cyclic AMP response element (CRE), a serum response element (SRE), a synaptic activity response element (SARE), a MEF2 response element, or a combination thereof.

4. The nucleic acid of claim 3, wherein the promoter further comprises at least one synaptic activity response element (SARE).

5. The nucleic acid of claim 4, wherein the synaptic activity response element (SARE) is a human synaptic activity response element (hSARE) and comprises a nucleic acid sequence of SEQ ID NO: 11, or a sequence at least 95% identical thereto.

6. The nucleic acid of claim 5, wherein the promoter comprises the nucleic acid sequence of SEQ ID NO: 6, or a sequence at least 95% identical thereto.

7. The nucleic acid of claim 5, wherein the promoter comprises the nucleic acid sequence of SEQ ID NO: 16, or a sequence at least 95% identical thereto.

8. The nucleic acid of claim 1, wherein the Rett-syndrome-associated gene encodes brain-derived neurotrophic factor (BDNF), insulin-like growth factor 1 (IGF1), methyl-CpG-binding protein 2 (MECP2), Huntingtin protein, Huntington-associated protein 1, Orthodenticle homeobox 2 (OTX-2), FXRD Domain Containing Ion Transport Regulator 1 (FXRD1), Neurexin-2-alpha (NRXN2), or Protein Kinase C Gamma (PRKCG).

9. The nucleic acid of claim 1, wherein at least one of the 5' ITR and the 3' ITR is isolated or derived from the genome of AAV1, AAV2, AAV3, AAV4, AAV5, AAV6, AAV7, AAV8, AAV9, AAV10, AAV11, AAV12, AAVrh8, AAVrh10, AAVrh32.33, AAVrh74, Avian AAV or Bovine AAV.

10. The nucleic acid of claim 1, wherein the 5' ITR comprises the sequence of SEQ ID NO: 1, or the 3' ITR comprises the sequence of SEQ ID NO: 2, or a combination thereof.
11. The nucleic acid of claim 1, wherein the AAV cassette comprises one of the following located between the Rett-syndrome-associated gene and the 3' ITR: (a) a brain-derived neurotrophic factor (BDNF) short 3' UTR, (b) a BDNF long 3' UTR, or (c) a polyadenylation signal.
12. The nucleic acid of claim 11, wherein the AAV cassette comprises a BDNF short 3' UTR, and wherein the BDNF short 3' UTR comprises a nucleic acid sequence of SEQ ID NO: 8, or a sequence at least 95% identical thereto.
13. The nucleic acid of claim 11, wherein the AAV cassette comprises a BDNF long 3' UTR, and wherein the BDNF long 3' UTR comprises a nucleic acid sequence of SEQ ID NO: 10, or a sequence at least 95% identical thereto.
14. The nucleic acid of claim 11, wherein the polyadenylation signal is a polyadenylation signal isolated or derived from one or more of the following genes: simian virus 40 (SV40), rBG, α -globin, β -globin, human collagen, human growth hormone (hGH), polyoma virus, human growth hormone (hGH) or bovine growth hormone (bGH).
15. The nucleic acid of claim 14, wherein the AAV cassette comprises a bGH polyadenylation signal and wherein the bGH polyadenylation signal comprises a nucleic acid sequence of SEQ ID NO: 9, or a sequence at least 90% identical thereto.
16. The nucleic acid of claim 1, wherein the AAV expression cassette comprises one of the following: (a) a nucleic acid sequence of SEQ ID NO: 3, or a sequence at least 95% identical thereto; (b) a nucleic acid sequence of SEQ ID NO: 4 or a sequence at least 95% identical thereto; or (c) a nucleic acid sequence of SEQ ID NO: 5 or a sequence at least 95% identical thereto.
17. A composition, comprising: (a) the nucleic acid of claim 1; and (b) a pharmaceutically acceptable carrier.
18. The nucleic acid of claim 1, wherein the hArcMin promoter comprises a nucleic acid sequence of SEQ ID NO: 12.
19. The nucleic acid of claim 5, wherein the human synaptic activity response element (hSARE) comprises a nucleic acid sequence of SEQ ID NO: 11.
20. The nucleic acid of claim 6, wherein the promoter comprises the nucleic acid sequence of SEQ ID NO: 6.
21. The nucleic acid of claim 7, wherein the promoter comprises the nucleic acid sequence of SEQ ID NO: 16.
22. The nucleic acid of claim 12, wherein the BDNF short 3' UTR comprises a nucleic acid sequence of SEQ ID NO: 8.

23. The nucleic acid of claim 13, wherein the BDNF long 3' UTR comprises a nucleic acid sequence of SEQ ID NO: 10.

24. The nucleic acid of claim 15, wherein the bGH polyadenylation signal comprises a nucleic acid sequence of SEQ ID NO: 9.

25. The nucleic acid of claim 16, wherein the AAV expression cassette comprises one of the following: (a) a nucleic acid sequence of SEQ ID NO: 3; (b) a nucleic acid sequence of SEQ ID NO: 4; or (c) a nucleic acid sequence of SEQ ID NO: 5.