

CLAIMS:

1. A recombinant AAV (rAAV) for delivery of a gene product to a patient in need thereof which specifically represses expression of the gene product in dorsal root ganglia (DRG), said rAAV comprising an AAV capsid having packaged therein a vector genome, wherein the vector genome comprises:
 - (a) a coding sequence for the gene product under the control of regulatory sequences that direct expression of the gene product in a cell containing the vector genome; and
 - (b) at least eight miR target sequences, wherein each target sequence is specific for miR-183 or miR-182, and wherein the at least eight miR target sequences are operably linked to the 3' end of the coding sequence.
2. The rAAV according claim 1, wherein the at least eight miR target sequences comprise at least five, at least six, at least seven, or at least eight target sequences specific for miR-183.
3. The rAAV according claim 1, wherein the at least eight miR target sequences comprise at least five, at least six, at least seven, or at least eight target sequences specific for miR-182.
4. The rAAV according to any one of claims 1 to 3, wherein the at least eight miR target sequences comprise at least four target sequences specific for miR-183 and/or at least four target sequences specific for miR-182.
5. The rAAV according to claim 1, wherein the at least eight miR target sequences comprise four target sequences specific for miR-183 and four target sequences specific for miR-182.
6. The rAAV according to any one of claims 1 to 5, wherein the expression cassette comprises a 3' UTR having at least eight miR target sequences.
7. The rAAV according to any one of claims 1 to 6, wherein the least eight miR target sequences are in a 3' UTR that is 200 to 1200 nucleotides in length.

8. The rAAV according to any one of claims 1 to 7, wherein the at least eight miR target sequences are continuous or are separated by a spacer of 1 to 10 nucleotides, wherein the spacer is not a miRNA target sequence.
9. The rAAV according to any one of claims 1 to 8, wherein the 5' end of the first of the at least eight miR target sequences is within 20 nucleotides from the 3' end of the gene coding sequence.
10. The rAAV according to any one of claims 1 to 8, wherein the 5' end of the first of the at least eight miR target sequences is at least 100 nucleotides from the 3' end of the gene coding sequence.
11. The rAAV according to any one of claims 1 to 10, wherein the vector genome further comprises at least one target sequence specific for miR-183 or miR-182 in a 5' UTR.
12. The rAAV according to any one of claims 1 to 11, wherein each of the at least eight target sequences comprises
 - (a) AGTGAATTCTACCAGTGCCATA (SEQ ID NO: 1); or
 - (b) AGTGTGAGTTCTACCATTGCCAAA (SEQ ID NO: 3).
13. The rAAV according to any one of claims 1 to 12, wherein the at least eight miR target sequences are continuous and not separated by a spacer.
14. The rAAV according to any one of claims 1 to 13, wherein each of the at least eight miR target sequences are separated by a spacer and each spacer is independently selected from one or more of (i) GGAT (SEQ ID NO: 5); (ii) CACGTG (SEQ ID NO: 6); or (iii) GCATGC (SEQ ID NO: 7).
15. The rAAV according to any one of claims 1 to 14, wherein a spacer is located between each of the at least eight miR target sequences and 3' to the first miRNA target sequence and/or 5' to the last miR target sequence.
16. The rAAV according to any one of claim 1 to 15, wherein the vector genome comprises a tissue-specific promoter.

17. The rAAV according to any one of claim 1 to 16, wherein the vector genome comprises a central nervous system-specific promoter, a muscle-specific promoter, a cardiac-specific promoter, or a liver-specific promoter.
18. The rAAV according to any one of claims 1 to 15, wherein the vector genome comprises a constitutive promoter.
19. A composition for gene delivery which specifically represses expression of a gene product in dorsal root ganglia (DRG), comprising an expression cassette that is a nucleic acid sequence comprising:
- (a) a coding sequence for the gene product under the control of regulatory sequences that direct expression of the gene product in a cell containing the expression cassette; and
 - (b) at least eight miR target sequences, wherein each target sequence is specific for miR-183 or miR-182, and wherein the at least eight miR target sequences are operably linked to the 3' end of the coding sequence.
20. The composition according to claim 19, wherein the at least eight miR target sequences comprise at least five, at least six, at least seven, or at least eight target sequences specific for miR-183.
21. The composition according to claim 19, wherein the at least eight miR target sequences comprise at least five, at least six, at least seven, or at least eight target sequences specific for miR-182.
22. The composition according to any one of claims 19 to 21, wherein the at least eight miR target sequences comprise at least four target sequences specific for miR-183 and/or at least four target sequences specific for miR-182.
23. The composition according to any one of claims 19 to 22, wherein at least eight miR target sequences comprise four target sequences specific for miR-183 and four target sequences specific for miR-182.
24. The composition according to any one of claims 19 to 23, wherein the expression cassette comprises a 3' UTR having at least eight miR target sequences.
25. The composition according to claim 24, wherein the 3' UTR having at least eight miR target sequences is 200 to 1200 nucleotides in length.

26. The composition according to any one of claims 19 to 25, wherein the at least eight miR target sequences are continuous or are separated by a spacer of 1 to 10 nucleotides, wherein the spacer is not a miR target sequence.
27. The composition according to any one of claims 19 to 26, wherein the 5' end of the first of the at least eight miR target sequences is within 20 nucleotides from the 3' end of the gene coding sequence.
28. The composition according to any one of claims 19 to 26, wherein the 5' end of the first of the at least eight miR target sequences is at least 100 nucleotides from the 3' end of the gene coding sequence.
29. The composition according to any one of claims 19 to 28, wherein the expression cassette further comprises at least one target sequence specific for miR-183 or miR-182 in a 5' UTR.
30. The composition according to any one of claims 19 to 29, wherein each of the at least eight target sequences comprises
- (a) AGTGAATTCTACCAGTGCCATA (SEQ ID NO: 1); or
 - (b) AGTGTGAGTTCTACCATTGCCAAA (SEQ ID NO: 3).
31. The composition according to any one of claims 19 to 30, wherein the at least eight miR target sequences are continuous and not separated by spacers.
32. The composition according to any one of claims 19 to 30, wherein each of the at least eight miR target sequences are separated by a spacer and each spacer is independently selected from one or more of (i) GGAT (SEQ ID NO: 5); (ii) CACGTG (SEQ ID NO: 6); or (iii) GCATGC (SEQ ID NO: 7).
33. The composition according to any one of claims 26 to 30 or 32, wherein the spacers between each of the at least eight miRNA target sequences are the same.
34. The composition according to any one of claims 19 to 33, wherein the expression cassette is carried by a viral vector that is a recombinant parvovirus, a recombinant lentivirus, a recombinant retrovirus, or a recombinant adenovirus.

35. The composition according to any one of claims 19 to 33, wherein the expression cassette is carried by a non-viral vector that is naked DNA, naked RNA, an inorganic particle, a lipid particle, a polymer-based vector, or a chitosan-based formulation.
36. A pharmaceutical composition comprising the rAAV according to any one of claims 1 to 18 or the expression cassette according to any one of claims 19 to 35 and a formulation buffer suitable for delivery via intracerebroventricular, intrathecal, intracisternal, or intravenous injection.
37. A method for repressing expression of a gene product in DRG neurons in a patient, said method comprising delivering the rAAV according to any one of claims 1 to 18, the composition according to any one of claims 19 to 35, or the pharmaceutical composition according to claim 36 to the patient.
38. A method for modulating neuronal degeneration and/or decreasing secondary dorsal spinal cord axonal degeneration following intrathecal or systemic gene therapy administration to a patient, said method comprising delivering the rAAV according to any one of claims 1 to 18, the composition according to any one of claims 19 to 35, or the pharmaceutical composition according to claim 36 to the patient.
39. The rAAV according to any one of claims 1 to 18, the composition according to any one of claims 19 to 35, or the pharmaceutical composition according to claim 36 for use in gene delivery, wherein expression of the delivered gene product is repressed in DRG neurons of the patient.
40. Use the rAAV according to any one of claims 1 to 18, the composition according to any one of claims 19 to 35, or the pharmaceutical composition according to claim 36 for delivering a transgene to a patient, wherein expression of the delivered transgene is repressed in DRG neurons of the patient.