

CLAIMS

1. A dual adeno-associated viral (AAV) vector system comprising:
 - (a) a first AAV vector, wherein the first AAV vector comprises a first recombinant polynucleotide comprising a fragment of a human dysferlin (hDYSF) gene, wherein the fragment consists of the nucleotide sequence of SEQ ID NO: 1; and
 - (b) a second AAV vector, wherein the second AAV vector comprises a second recombinant polynucleotide comprising a fragment of a human dysferlin (hDYSF) gene, wherein the fragment consists of the nucleotide sequence of SEQ ID NO: 2.
2. The dual AAV vector system of claim 1, wherein the first recombinant polynucleotide further comprises one or more additional nucleotide sequences selected from: an inverted terminal repeat (ITR), a promoter, an intron, a selection marker, an origin of replication (ORI), and an untranslated region (UTR).
3. The dual AAV vector system of claim 1 or 2, wherein the second recombinant polynucleotide further comprises one or more additional nucleotide sequences selected from: an intron, a UTR, an ORI, a selection marker, an ITR, and a polyadenylation (poly A) signal.
4. The dual AAV vector system of claim 2 or 3, wherein the ITR is an AAV ITR.
5. The dual AAV vector system of claim 2, wherein the promoter is a muscle-specific promoter.
6. The dual AAV vector system of claim 5, wherein the muscle-specific promoter is MHCK7.
7. The dual AAV vector system of any one of claims 1-6, wherein the first recombinant polynucleotide comprises the nucleotide sequence of SEQ ID NO: 6.
8. The dual AAV vector system of any one of claims 1-7, wherein the second recombinant polynucleotide comprises the nucleotide sequence of SEQ ID NO: 8.

9. The dual AAV vector system of any one of claims 1-8, wherein the molar ratio of first and second AAV vectors is between 100:1-1:100, 10:1-1:10, 2:1-1:2, or 1:1.
10. The dual AAV vector system of any one of claims 1-9, wherein the first and second AAV vectors are AAV-1, AAV-2, AAV-3, AAV-4, AAV-5, AAV-6, AAV-7, AAV-8, AAV-9, AAV-10, AAV-11, AAV-12, AAV-13, AAVrh.10, AAVrh.20, AAVrh.74 or a recombinant AAV.
11. An adeno-associated viral (AAV) packaging system comprising:
 - (a) (i) a first plasmid comprising a first recombinant polynucleotide comprising a fragment of a human dysferlin (hDYSF) gene, wherein the fragment consists of the nucleotide sequence of SEQ ID NO: 1; or (ii) a second plasmid comprising a second recombinant polynucleotide comprising a fragment of a hDYSF gene, wherein the fragment consists of the nucleotide sequence of SEQ ID NO: 2; and
 - (b) an adenovirus helper plasmid.
12. The AAV packaging system of claim 11, further comprising a rep-cap plasmid.
13. The AAV packaging system of claim 11 or 12, wherein the adenovirus helper plasmid comprises a pHELP plasmid.
14. A method for producing an AAV vector, comprising contacting a packaging cell with the AAV packaging system of any one of claims 11-13.
15. The method of claim 14, wherein the cell is a host cell.
16. The method according to claim 15, wherein the host cell is a mammalian host cell.
17. The method according to claim 15 or 16, wherein the host cell is HEK293.
18. A cell comprising the dual AAV vector system of any one of claims 1-10.
19. The AAV packaging system of any one of claims 11-13 or the method of any one of claims 14-17, wherein the first plasmid comprising a first recombinant polynucleotide comprises the nucleotide sequence of SEQ ID NO: 18 and the second plasmid comprising a second recombinant polynucleotide comprises the nucleotide sequence of SEQ ID NO: 19.

20. Use of an effective amount of the dual AAV vector system of any one of claims 1-10 in the manufacture of a medicament to treat a dysferlinopathy in a subject in need thereof.
21. The use of claim 20, wherein the first AAV vector and/or second AAV vector are for intramuscular or intravenous administration.
22. The use of claim 20 or 21, wherein the first and second AAV vectors are for simultaneous or sequential administration.
23. The use of any one of claims 20-22, wherein the effective amount of the first AAV vector is between 1×10^6 - 1×10^{16} vg/kg, 1×10^8 - 1×10^{15} vg/kg, or 1×10^{10} - 1×10^{14} vg/kg.
24. A recombinant polynucleotide encoding a human dysferlin (hDYSF) protein, wherein the recombinant polynucleotide sequence comprises a nucleotide sequence of SEQ ID NO: 20.
25. The use of any one of claims 20-23, wherein dysferlinopathy is limb girdle muscular dystrophy type 2B (LGMD2B) or Miyoshi myopathy.