

CLAIMS

1. A recombinant polynucleotide, wherein the recombinant polynucleotide comprises a first nucleotide sequence, wherein the first nucleotide sequence consists of:
 - (a) the nucleotide sequence of SEQ ID NO: 6; or
 - (b) a biologically equivalent nucleotide sequence that is at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to the nucleotide sequence of SEQ ID NO: 6 across its full length of SEQ ID NO: 6.
2. A recombinant polynucleotide, wherein the recombinant polynucleotide comprises a second nucleotide sequence, wherein the second nucleotide sequence consists of:
 - (a) the nucleotide sequence of SEQ ID NO: 8; or
 - (b) a biologically equivalent nucleotide sequence that is at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to the nucleotide sequence of SEQ ID NO: 8 across its full length of SEQ ID NO: 8.
3. The recombinant polynucleotide of claim 1 or 2, further comprising one or more additional nucleotides comprising a selection marker, an origin of replication (ORI), and an untranslated region (UTR).
4. A dual adeno-associated viral (AAV) vector system comprising:
 - (a) a first AAV vector, wherein the first AAV vector comprises the recombinant polynucleotide of claim 1; and
 - (b) a second AAV vector, wherein the second AAV vector comprises the recombinant polynucleotide of claim 2.
5. The dual adeno-associated viral (AAV) vector system of claim 4, wherein the molar ratio of first and second rAAV vectors is between about 100:1-1:100, about 10:1-1:10, about 2:1-1:2, or about 1:1.
6. An adeno-associated viral (AAV) vector comprising:
 - a polynucleotide encoding a first fragment of a functional human dysferlin (hDYSF) protein, wherein the polynucleotide consists of:
 - i. the nucleotide sequence of SEQ ID NO: 6; or

- ii. a biologically equivalent nucleotide sequence that is at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to the nucleotide sequence of SEQ ID NO: 6 across the full length of SEQ ID NO: 6.
- 7. The AAV vector according to claim 6, further comprising one or more additional polynucleotides selected from a selection marker, an untranslated region (UTR), and an origin of replication (ORI).
- 8. An adeno-associated viral (AAV) vector comprising:
 - a polynucleotide encoding a second fragment of a functional human dysferlin (hDYSF) protein, wherein the polynucleotide consists of:
 - i. the nucleotide sequence of SEQ ID NO: 8; or
 - ii. a biologically equivalent nucleotide sequence that is at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to the nucleotide sequence of SEQ ID NO: 8 across the full length of SEQ ID NO: 8.
- 9. The AAV vector according to claim 8, further comprising one or more polynucleotides selected from a selection marker, an origin of replication (ORI), and an untranslated region (UTR).
- 10. The dual adeno-associated viral (AAV) vector system of claim 4 or 5, and the AAV vector of any one of claims 6-9, wherein the AAV vector is 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) a plasmid comprising the recombinant polynucleotide of any one of claims 1-3;
 - (b) an adenovirus helper plasmid; and
 - (c) a rep-cap plasmid.
- 12. An adeno-associated viral (AAV) packaging system comprising:
 - (a) a plasmid comprising the recombinant polynucleotide of any one of claims 1-3;
 - and

- (b) an adenovirus helper plasmid.
13. The adeno-associated viral packaging system of claim 11 or 12, wherein the adenovirus helper plasmid comprises pHELP plasmid.
14. A method for producing an adeno-associated viral (AAV) vector, comprising contacting a packaging cell with the plasmid comprising the AAV packaging system of claim 11.
15. The method of claim 14, wherein the cell is a host cell.
16. The method according to claim 15, wherein the host cells is a mammalian host cell.
17. The method according to claim 15 or 16 wherein the host cell is HEK293.
18. A method for producing an adeno-associated viral (AAV) vector, comprising contacting a packaging cell line with a plasmid comprising the recombinant polynucleotide of any one of claims 1-3, wherein the packaging cell line expresses an adeno-associated viral rep and cap genes.
19. A cell comprising the recombinant polynucleotide of any one of claims 1-3.
20. The AAV packaging system of any one of claims 11-13 or the method of any one of claims 14-18, wherein the plasmid comprises a polynucleotide that is at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to SEQ ID NO: 18 or 19.
21. The AAV packaging system of any one of claims 11-13 or the method of any one of claims 14-18, wherein the plasmid comprises a polynucleotide of SEQ ID NO: 18 or 19.
22. Use of a composition in the manufacture of a medicament to treat a dysferlinopathy in a subject in need thereof, wherein the composition comprises:
- an effective amount of a first polynucleotide, wherein the first polynucleotide is the recombinant polynucleotide of claim 1; and
 - an effective amount of a second polynucleotide, wherein the second polynucleotide is the recombinant polynucleotide of claim 2.

23. The use of claim 22, wherein the first polynucleotide and/or second polynucleotide are for intramuscular or intravenous administration.
24. The use of claim 22 or 23, wherein the first and second polynucleotides are for simultaneous or sequential administration.
25. Use of a composition in the manufacture of a medicament to treat a dysferlinopathy in a subject in need thereof, wherein the composition comprises:
- a. an effective amount of a first adeno-associated viral (AAV) vector, wherein the first AAV vector is the AAV vector of claim 6; and
 - b. an effective amount of a second AAV vector, wherein the second AAV vector is the AAV vector of claim 8.
26. The use of claim 25, wherein the first AAV vector and/or second AAV vector is for intramuscular or intravenous administration.
27. The use of claim 25 or 26, wherein the first and second AAV vectors are for simultaneous or sequential administration.
28. Use of a composition in the manufacture of a medicament to treat a dysferlinopathy in a subject in need thereof, wherein the composition comprises an effective amount of the AAV dual vector system of claim 4 or 5.
29. The use of any one of claims 25-28, wherein the effective amount of the first AAV vector is between about 1×10^6 - 1×10^{16} vg/kg, about 1×10^8 - 1×10^{15} vg/kg, or about 1×10^{10} - 1×10^{14} vg/kg.
30. A recombinant polynucleotide encoding a human dysferlin (hDYSF) protein, wherein the recombinant polynucleotide sequence comprises a nucleotide sequence of SEQ ID NO: 20 or a nucleotide sequence that is at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to the nucleotide sequence of SEQ ID NO: 20 across the full length of SEQ ID NO: 20.
31. The recombinant polynucleotide of claim 30, wherein the recombinant polynucleotide sequence comprises a nucleotide sequence of SEQ ID NO: 20.

32. The use of any one of claims 22-29, wherein dysferlinopathy is limb girdle muscular dystrophy type 2B (LGMD2B) or Miyoshi myopathy.