

CLAIMS

1. A recombinant AAV (rAAV) vector comprising an AAV capsid and a gene expression cassette comprising a polynucleotide sequence encoding γ -sarcoglycan under the transcriptional control of a promoter, wherein the polynucleotide sequence comprises a nucleotide sequence at least 95% identical to SEQ ID NO: 1 or SEQ ID NO: 3.
2. The rAAV vector of claim 1, wherein the gene expression cassette is flanked by one or more AAV inverted terminal repeats.
3. The rAAV vector of claim 1, wherein the polynucleotide sequence encoding γ -sarcoglycan comprises the nucleotide sequence set forth in SEQ ID NO: 1.
4. The rAAV vector according to any one of claims 1 to 3, wherein the rAAV vector comprises a self-complementary AAV vector genome.
5. The rAAV vector according to any one of claims 1 to 4, wherein the rAAV vector comprises a genome lacking AAV rep and cap DNA.
6. The rAAV vector of any one of claims 1 to 5, wherein the vector is of the serotype AAV1, AAV2, AAV4, AAV5, AAV6, AAV7, AAV8, AAV9, AAV10, AAV11, AAV12, AAV13 or AAV rh74.
7. The rAAV vector of claim 6, wherein the rAAV vector is of the serotype AAV rh74 and wherein the rAAV vector comprises an AAV rh.74 capsid.
8. The rAAV vector of claim claim 7, wherein the AAV rh.74 capsid comprises the amino acid sequence set forth in SEQ ID NO: 10.
9. The rAAV vector of any one of claims 1 to 8, wherein the genome of the rAAV vector comprises a muscle-specific control element and wherein the polynucleotide sequence is operably linked to the muscle-specific control element.
10. The rAAV vector of claim 9, wherein the muscle-specific control element is selected from the group consisting of human skeletal actin gene element, cardiac actin gene element, myocyte-specific enhancer binding factor mef, muscle creatine kinase (MCK), truncated MCK (tMCK), myosin heavy chain (MHC), MHCK7, C5-12, murine creatine kinase enhancer element, skeletal fast-twitch troponin c gene element, slow-

twitch cardiac troponin c gene element, the slow-twitch troponin i gene element, hypoxia-inducible nuclear factors, steroid-inducible element, and glucocorticoid response element (gre).

11. The rAAV vector of claim 10, wherein the muscle-specific control element is truncated MCK (tMCK).

12. The rAAV vector of any one of claims 1 to 11, wherein the promoter is MHCK7.

13. The rAAV vector of claim 12, wherein the MHCK promoter comprises the nucleotide sequence set forth in SEQ ID NO: 4.

14. The rAAV vector of any one of claims 1 to 13, wherein the genome rAAV vector comprising the nucleotide sequence set forth in SEQ ID NO: 5.

15. The rAAV vector of any one of claims 1 to 14, wherein the polynucleotide sequence encoding γ -sarcoglycan encodes an amino acid sequence that is at least 95% identical, at least 99% identical, or 100% identical to SEQ ID NO: 2.

16. A composition comprising the rAAV vector of any one of claims 1 to 15, optionally comprising a pharmaceutically acceptable carrier.

17. The composition of claims 16, comprising Lactated Ringer's Solution (LRS).

18. Use of the rAAV vector of claims 1-15 or the composition of claim 16 or 17 for the manufacture of a medicament for:

treating γ -sarcoglycanopathy in a subject;

increasing muscular force, muscle endurance, and/or muscle mass in a subject;

reducing fibrosis in a subject;

reducing contraction-induced injury in a subject;

treating muscular dystrophy in a subject suffering from muscular dystrophy;

reducing degenerating fibers or necrotic fibers in a subject suffering from muscular dystrophy;

reducing inflammation in a subject suffering from muscular dystrophy;

elevating creatine kinase levels in a subject suffering from muscular dystrophy;

treating myofiber atrophy and hypertrophy in a subject suffering from muscular dystrophy;

decreasing dystrophic calcification in a subject suffering from muscular dystrophy;

decreasing fatty infiltration in a subject; and/or

decreasing central nucleation in a subject.

19. Use of the rAAV vector of claims 1-15 or the composition of claim 16 or 17 for the manufacture of a medicament for treating limb-girdle muscular dystrophy.

20. The use according to claim 19, wherein the limb-girdle muscular dystrophy is limb-girdle muscular dystrophy type 2C.

21. Use of the rAAV vector of claims 1-15 or the composition of claim 16 or 17, is formulated for use intramuscularly or intravenously.

22. The use according to any one of claims 1 to 22, is formulated for use systemically.

23. The use according to any one of claims 1 to 23, is formulated for use parentally.

24. The use according to any one of claims 18 to 23, wherein the use increases muscular force, muscle endurance, and/or muscle mass of one or more muscles of the subject.

25. The use according to claim 24, wherein the one or more muscles is selected from the group consisting of heart, diaphragm, upper legs, lower legs, pelvic girdle shoulder, and arm.

26. The use according to claim 24 or claim 25, wherein muscular force, muscle endurance, and/or muscle mass is increased at least about 5%, at least about 10%, at least about 15%, at least about 20%, at least about 50%, or at least about 80% compared to an untreated control subject.

27. A host cell, comprising an rAAV vector of any one of claims 1 to 15.

28. A host cell, comprising a polynucleotide sequence comprising a nucleotide sequence at least 95% identical to SEQ ID NO: 1.

29. The host cell of claim 28, wherein the polynucleotide sequence comprises the nucleotide sequence set forth in SEQ ID NO: 1.
30. A host cell, comprising a polynucleotide sequence comprising a nucleotide sequence at least 95% identical to SEQ ID NO: 3.
31. The host cell of claim 30, wherein the polynucleotide sequence comprises the nucleotide sequence set forth in SEQ ID NO: 3.
32. The host cell of any one of claims 28-31, wherein the polynucleotide sequence encodes an amino acid sequence that is at least 95% identical, at least 99% identical, or 100% identical to SEQ ID NO: 2.
33. The host cell of any one of claims 28-32, wherein the cell is a mammalian cell.
34. A combination therapy, comprising the composition of any one of claims 17-16 and a corticosteroid.
35. A kit, comprising the composition of any one of claims 16-17 and a corticosteroid or the combination therapy of claim 28.
36. The kit of claim 29, comprising a corticosteroid.