

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 muscle-specific promoter, wherein the polynucleotide sequence comprises a nucleotide sequence of 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 rAAV vector comprises a nucleotide sequence of SEQ ID NO: 3.
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 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 element, muscle creatine kinase (MCK), truncated MCK (tMCK) promoter, myosin heavy chain (MHC) element, MHCK7 promoter, 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) promoter.

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

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 of 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 in the manufacture of a medicament for:

treating γ -sarcoglycanopathy in a subject;

increasing muscular force, muscle endurance, and/or muscle mass in a subject suffering from γ -sarcoglycanopathy;

reducing fibrosis in a subject suffering from γ -sarcoglycanopathy;

reducing contraction-induced injury in a subject suffering from γ -sarcoglycanopathy; and/or

treating limb-girdle muscular dystrophy type 2C in a subject suffering from muscular dystrophy, wherein the rAAV vector is of the serotype AAV rh74.

19. Use of the rAAV vector of claims 1-15 or the composition of claim 16 or 17 in the manufacture of a medicament for treating limb-girdle muscle dystrophy type 2C, wherein the

medicament is to be administered systematically, parentally, intramuscularly or intravenously.

20. The use according to claim 19, wherein the medicament is to be administered systemically.

21. The use according to claim 19, wherein the medicament is to be administered parentally.

22. The use according to any one of claims 18 to 21, wherein the use increases muscular force, muscle endurance, and/or muscle mass of one or more muscles of the subject.

23. The use according to claim 22, wherein the one or more muscles is selected from the group consisting of heart, diaphragm, upper legs, lower legs, pelvic girdle shoulder, and arm.

24. The use according to claim 22 or 23, wherein muscular force, muscle endurance, and/or muscle mass is increased at least 5%, at least 10%, at least 15%, at least 20%, at least 50%, or at least 80% compared to an untreated control subject.

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

26. A host cell, comprising a polynucleotide sequence comprising a nucleotide sequence of SEQ ID NO: 1.

27. A host cell, comprising a polynucleotide sequence comprising a nucleotide sequence of SEQ ID NO: 3.

28. The host cell of any one of claims 25-27, wherein the polynucleotide sequence encodes an amino acid sequence of SEQ ID NO: 2.

29. The host cell of any one of claims 25-28, wherein the cell is a mammalian cell, a bacterial cell, or a yeast cell.

30. A kit, comprising the composition of any one of claims 16-17 and a corticosteroid.