[0011] Functional improvement in patients suffering from DMD and other muscular dystrophies requires gene restoration at an early stage of disease. There is a need for treatments that increase muscle strength and protect against muscle injury in patients suffering from DMD.

SUMMARY

[0012] The present invention is directed to gene therapy vectors, e.g. AAV, expressing the micro-dystrophin gene to skeletal muscles including diaphragm and cardiac muscle to protect muscle fibers from injury, increase muscle strength and reduce and/or prevent fibrosis

[0013] The disclosure provides for therapies and approaches for increasing muscular force and/or increasing muscle mass using gene therapy vectors to deliver micro-dystrophin to address the gene defect observed in DMD. As shown in Example 2, treatment with micro-dystrophin gene therapy resulted in a greater muscle force *in vivo*. Furthermore, delivery of micro-dystrophin gene therapy intramuscularly and systemically showed delivery of dystrophin to the muscles in mice models *in vivo*.

[0013a] In one aspect, the present disclosure refers to a recombinant AAVrh74 vector comprising in the 5' to 3´ direction an inverted terminal repeat (ITR), an MHCK7 muscle-specific control element, a chimeric intron sequence having nucleotides 1046-1195 of SEQ ID NO: 3, the nucleotide sequence of SEQ ID NO: 1, a poly A tail, and an ITR. In another aspect, the present invention refers to a recombinant AAVrh74 vector comprising in the 5' to 3´ direction an inverted terminal repeat (ITR), an MHCK7 muscle-specific control element, a chimeric intron, the nucleotide sequence of SEQ ID NO: 1, a poly A tail 3´ having nucleotides 4787 to 4842 of SEQ ID NO: 3, and an ITR. In another aspect, the present disclosure refers to a composition comprising the recombinant AAVrh74 vector as disclosed herein, and a pharmaceutically acceptable carrier. In another aspect, there is provided the use of a recombinant AAVrh74 vector as disclosed herein or a composition disclosed herein for the preparation of a medicament for treatment of muscular dystrophy in a subject in need thereof. In yet another aspect, there is provided the use of a recombinant AAVrh74 vector as disclosed herein or a composition as disclosed herein for the preparation of a medicament for reducing or preventing fibrosis in a subject suffering from muscular dystrophy.

[0014] In one example, the disclosure provides for a rAAV vector comprising a muscle specific control element nucleotide sequence, and a nucleotide sequence encoding the micro-dystrophin protein. For example, the nucleotide sequence encodes a functional micro-dystrophin protein, wherein the nucleotide is, e.g., at least 65%, at least 70%, at least 75%, at least 80%, 81%, 82%,

CLAIMS

What is claimed:

1. A recombinant AAVrh74 vector comprising in the 5’ to 3′ direction an inverted terminal repeat (ITR), an MHCK7 muscle-specific control element, a chimeric intron sequence having nucleotides 1046-1195 of SEQ ID NO: 3, the nucleotide sequence of SEQ ID NO: 1, a polyA tail, and an ITR.

2. A recombinant AAVrh74 vector comprising in the 5’ to 3′ direction an inverted terminal repeat (ITR), an MHCK7 muscle-specific control element, a chimeric intron, the nucleotide sequence of SEQ ID NO: 1, a poly A tail 3′ having nucleotides 4787 to 4842 of SEQ ID NO: 3, and an ITR.

3. A composition comprising the recombinant AAVrh74 vector of claim 1 or 2 and a pharmaceutically acceptable carrier.

4. Use of the recombinant AAVrh74 vector of claim 1 or 2, or the composition of claim 3, for the preparation of a medicament for the treatment of muscular dystrophy in a subject in need thereof.

5. Use of the recombinant AAVrh74 vector of claim 1 or 2 or the composition of claim 3, for the preparation of a medicament for reducing or preventing fibrosis in a subject suffering from muscular dystrophy.

6. The use of claim 4 or 5 wherein the subject is suffering from Duchenne muscular dystrophy.

7. The use of any one of claims 4-6 wherein the medicament is formulated for intramuscular injection or intravenous injection.

8. The use of any one of claims 4-6 wherein the medicament is formulated for systemic administration.

9. The use of claim 8, wherein the medicament is formulated for parenteral administration by injection, infusion, or implantation.