CLAIMS

1. An isolated and purified nucleotide sequence, comprising:

(a) a micro-dystrophin gene encoding a protein comprising:

an amino-terminal actin-binding domain;

a β-dystroglycan binding domain; and

a spectrin-like repeat domain, comprising at least four spectrin-like repeats, in which two of the at least four spectrin-like repeats comprise a neuronal nitric oxide synthase binding domain; and

(b) a regulatory cassette which is selected from the group consisting of a CK8 promoter and a cardiac troponin T (cTnT) promoter.

2. An isolated and purified nucleotide sequence according to Claim 1, in which the at least four spectrin-like repeats include spectrin-like repeat 1 (SR1), spectrin-like repeat 16 (SR16), spectrin-like repeat 17 (SR17), and spectrin-like repeat 24 (SR24); and/or

in which the protein encoded by the micro-dystrophin gene further comprises at least a portion of a hinge domain;

optionally in which the hinge domain is selected from at least one of a Hinge 1 domain, a Hinge 2 domain, a Hinge 3 domain, a Hinge 4 domain, and a hinge-like domain.

3. An isolated and purified nucleotide sequence, comprising:

a micro-dystrophin gene encoding a protein comprising:

an amino-terminal actin-binding domain; and

at least two spectrin-like repeats that are directly coupled to each other, in which the at least two spectrin-like repeats that are directly coupled to each other are selected from at least one of spectrin-like repeat 1 directly coupled to spectrin-like repeat 2, spectrin-like repeat 2 directly coupled to spectrin-like repeat 3, spectrin-like repeat 1 directly coupled to spectrin-like repeat 16, spectrin-like repeat 17 directly coupled to spectrin-like repeat 23, spectrin-like repeat 17 directly coupled to spectrin-like repeat 24, and spectrin-like repeat 23 directly coupled to spectrin-like repeat 24; or

an isolated and purified nucleotide sequence, comprising:

a micro-dystrophin gene encoding a protein comprising, in order:

a Hinge 1 domain (H1);

a spectrin-like repeat 1 (SR1);

a spectrin-like repeat 16 (SR16);

a spectrin-like repeat 17 (SR17);

a spectrin-like repeat 24 (SR24); and

a Hinge 4 domain (H4); and optionally

in which the H1 is directly coupled to the SR1; or

in which the SR 1 is directly coupled to the SR16; or

in which the SR16 is directly coupled to the SR17; or

in which the SR 17 is directly coupled to the SR24; or

in which the SR24 is directly coupled to the H4; or

in which the protein encoded by the micro-dystrophin gene further comprises between the SR1 and the SR16, in order, a spectrin-like repeat 2 (SR2) and a spectrin-like repeat 3 (SR3), optionally in which the SR1 is directly coupled to the SR2 and the SR2 is further coupled to the SR3; or

in which the H1 is directly coupled to the SR1, the SR1 is directly coupled to the SR16, the SR16 is directly coupled to the SR17, the SR17 is directly coupled to the SR23, the SR23 is directly coupled to the SR24, and the SR24 is directly coupled to the H4.

4. A pharmaceutical composition, comprising:

an isolated and purified nucleotide sequence according to any of Claims 1 to 4; and

a delivery vehicle; or comprising:

a micro-dystrophin gene comprising the nucleic acid sequence of SEQ ID NO: 16; and

an adeno-associated virus (AAV) vector or a recombinant adeno-associated virus (rAAV) vector; or comprising:

a micro-dystrophin gene encoding a protein, in which the protein comprises the amino acid sequence of SEQ ID NO: 4; and

an adeno-associated virus (AAV) vector or a recombinant adeno-associated virus (rAAV) vector; or comprising:

a micro-dystrophin gene comprising the nucleic acid sequence of SEQ ID NO: 18; and

an adeno-associated virus (AAV) vector or a recombinant adeno-associated virus (rAAV) vector; or comprising:

a micro-dystrophin gene encoding a protein, in which the protein comprises the amino acid sequence of SEQ ID NO: 5; and

an adeno-associated virus (AAV) vector or a recombinant adeno-associated virus (rAAV) vector; or

a pharmaceutical composition for the treatment or prophylactic treatment of muscular dystrophy, comprising:

a micro-dystrophin gene comprising the nucleic acid sequence of SEQ ID NO: 16 or SEQ ID NO: 18; and

an adeno-associated virus (AAV) vector or a recombinant adeno-associated virus (rAAV) vector, in which a serotype of the AAV vector or the rAAV vector is selected from at least one of serotype 6, serotype 8, and serotype 9.

5. A pharmaceutical composition according to Claim 5, in which a serotype of the AAV vector or the rAAV vector is selected from at least one of serotype 6, serotype 8, and serotype 9.

6. A pharmaceutical composition for use in treating or prophylactically treating a subject having muscular dystrophy comprising a micro-dystrophin gene operably coupled to a regulatory cassette; or comprising:

a micro-dystrophin gene comprising the nucleic acid sequence of SEQ ID NO: 16 or SEQ ID NO: 18; and

an adeno-associated virus (AAV) vector or a recombinant adeno-associated virus (rAAV) vector, in which a serotype of the AAV vector or the rAAV vector is selected from at least one of serotype 6, serotype 8, and serotype 9; or

a pharmaceutical composition for use in the treatment or prophylactic treatment of muscular dystrophy, comprising:

a micro-dystrophin gene comprising the nucleic acid sequence of SEQ ID NO: 16 or SEQ ID NO: 18; and

an adeno-associated virus (AAV) vector or a recombinant adeno-associated virus (rAAV) vector, in which a serotype of the AAV vector or the rAAV vector is selected from at least one of serotype 6, serotype 8, and serotype 9.

7. An isolated and purified nucleotide sequence according to Claim 1 or 2, or a pharmaceutical composition for use according to Claim 6, in which the regulatory cassette is configured to express the micro-dystrophin gene such that a level of expression of the micro-dystrophin gene is at least 100-fold higher in striated muscle cells than the level of expression of the micro-dystrophin gene in non-muscle cells.