CLAIMS

What is claimed is:

1. A method for treating or preventing myotonic dystrophy type 1 (DM1) in an individual in need thereof comprising: systemically administering to the individual a therapeutically effective amount of a cationic peptide-linked morpholino antisense oligonucleotide comprising a sequence complementary to at least 3 polyCUG repeat sequences in a 3' untranslated region (UTR) of a dystrophia myotonica protein kinase (DMPK) RNA transcript target, wherein administration of the cationic peptide-linked morpholino antisense oligonucleotide relieves at least one symptom of DM1 in at least two muscles.

2. The method of claim 1, wherein the cationic peptide is 8-30 amino acid residues in length and comprises one or more subsequences selected from the group consisting of RXR, RX, RB, and RBR, wherein R is arginine, B is β-alanine, and each X is independently — NH—$(CHR^1)_n$—C(O)—,wherein n is 4-6 and each R^1 is independently H or methyl such that at most two R^1s are methyl.

3. The method of claim 2, wherein the cationic peptide comprises the amino acid sequence $Ac(RXRRBR)_2XB$-.

4. The method of claim 2, wherein the cationic peptide comprises the amino acid sequence $Ac(RXR)_4XB$-.

5. The method of any one of claims 1-4, wherein the cationic peptide-linked morpholino antisense oligonucleotide comprises the sequence 5' – $(AGC)_n$ – 3', 5' – $(GCA)_n$ – 3', or 5' – $(CAG)_n$ – 3', wherein n is any of about 5-25.

6. The method of claim 5, wherein the cationic peptide-linked morpholino antisense oligonucleotide further comprises 1 to 2 additional morpholino nucleotides on the 5' and/or the 3' end of the oligonucleotide.

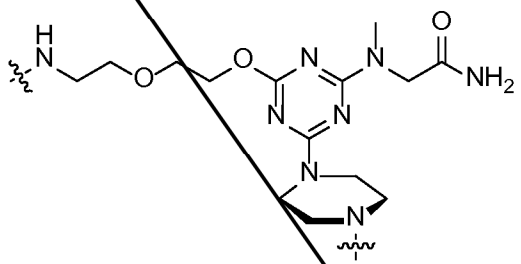
7. The method of claim 5, wherein the cationic peptide-linked morpholino antisense oligonucleotide comprises the sequence: 5' - AGCAGCAGCAGCAGCAGCAGCA – 3'.

8. The method of claim 7, wherein the cationic peptide-linked morpholino antisense oligonucleotide further comprises a 5' amine modification.

9. The method of any one of claims 1-8, wherein the cationic peptide-linked morpholino antisense oligonucleotide is a phosphorodiamidate cationic peptide-linked morpholino antisense oligonucleotide.

10. The method of any one of claims 1-9, wherein the cationic peptide is separated from the morpholino antisense oligonucleotide by a spacer moiety linked at the 5' end of the morpholino antisense oligonucleotide.

11. The method of claim 10, wherein the spacer moiety comprises



12. The method of any one of claims 1-11, wherein the muscles are skeletal muscles, smooth muscles, and/or cardiac muscle.

13. The method of any one of claims 1-12, wherein the cationic peptide-linked morpholino antisense oligonucleotide penetrates into cells of the tibialis anterior muscle, the quadriceps muscle, and/or the gastrocnemius muscle.

14. The method of any one of claims 1-13, wherein said at least one symptom of DM1 is myotonia.

15. The method of any one of claims 1-14, wherein said at least one symptom of DM1 is aggregation of musclebind-like-1 (MBNL-1) protein in ribonuclear foci within myonuclei.

16. The method of any one of claims 1-15, wherein said at least one symptom of DM1 is abnormal splicing of at least one RNA transcript in muscle cells.

17. The method of claim 16, wherein said at least one RNA transcript is selected from the group consisting of: Serca-1, m-Titin, Zasp, and CIC-1.

18. The method of any one of claims 1-17, wherein systemic administration of the cationic peptide-linked morpholino antisense oligonucleotide is performed intravenously, intraperitoneally, or subcutaneously.

19. The method of any one of claims 1-18, wherein the cationic peptide-linked morpholino antisense oligonucleotide is administered to the individual weekly.

20. The method of any one of claims 1-19, wherein the cationic peptide-linked morpholino antisense oligonucleotide is administered to the individual for at least one week.

21. The method of any one of claims 1-20, wherein the cationic peptide-linked morpholino antisense oligonucleotide is administered with a pharmaceutically acceptable excipient.

22. The method of any one of claims 1-21, wherein the individual is a human.

CLAIMS

What is claimed is:

1. Use of an effective amount of a cationic peptide-linked morpholino antisense oligonucleotide comprising a sequence complementary to at least 3 polyCUG repeat sequences in a 3' untranslated region (UTR) of a dystrophia myotonica protein kinase (DMPK) RNA transcript target for the manufacture of a medicament for treating or preventing myotonic dystrophy type 1 (DM1) in an individual in need thereof, wherein administration of the cationic peptide-linked morpholino antisense oligonucleotide relieves at least one symptom of DM1 in at least two muscles.

2. The use of claim 1, wherein the cationic peptide is 8-30 amino acid residues in length and comprises one or more subsequences selected from the group consisting of RXR, RX, RB, and RBR, wherein R is arginine, B is β-alanine, and each X is independently —NH—$(CHR^1)_n$—C(O)—,wherein n is 4-6 and each R^1 is independently H or methyl such that at most two R^1s are methyl.

3. The use of claim 2, wherein the cationic peptide comprises the amino acid sequence $Ac(RXRRBR)_2XB$-.

4. The use of claim 2, wherein the cationic peptide comprises the amino acid sequence $Ac(RXR)_4XB$-.

5. The use of any one of claims 1-4, wherein the cationic peptide-linked morpholino antisense oligonucleotide comprises the sequence 5' – $(AGC)_n$ – 3', 5' – $(GCA)_n$ – 3', or 5' – $(CAG)_n$ – 3', wherein n is any of about 5-25.

6. The use of claim 5, wherein the cationic peptide-linked morpholino antisense oligonucleotide further comprises 1 to 2 additional morpholino nucleotides on the 5' and/or the 3' end of the oligonucleotide.

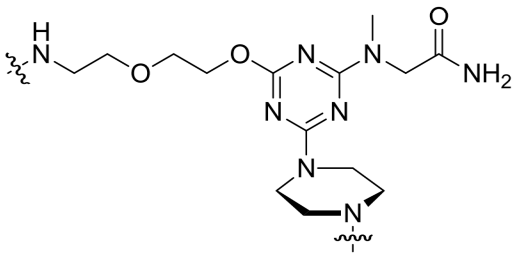
7. The use of claim 5, wherein the cationic peptide-linked morpholino antisense oligonucleotide comprises the sequence: 5' - AGCAGCAGCAGCAGCAGCAGCAGCA – 3'.

8. The use of claim 7, wherein the cationic peptide-linked morpholino antisense oligonucleotide further comprises a 5' amine modification.

9. The use of any one of claims 1-8, wherein the cationic peptide-linked morpholino antisense oligonucleotide is a phosphorodiamidate cationic peptide-linked morpholino antisense oligonucleotide.

10. The use of any one of claims 1-9, wherein the cationic peptide is separated from the morpholino antisense oligonucleotide by a spacer moiety linked at the 5' end of the morpholino antisense oligonucleotide.

11. The use of claim 10, wherein the spacer moiety comprises



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12. The use of any one of claims 1-11, wherein the muscles are skeletal muscles, smooth muscles, and/or cardiac muscle.

13. The use of any one of claims 1-12, wherein the cationic peptide-linked morpholino antisense oligonucleotide penetrates into cells of the tibialis anterior muscle, the quadriceps muscle, and/or the gastrocnemius muscle.

14. The use of any one of claims 1-13, wherein said at least one symptom of DM1 is myotonia.

15. The use of any one of claims 1-14, wherein said at least one symptom of DM1 is aggregation of musclebind-like-1 (MBNL-1) protein in ribonuclear foci within myonuclei.

16. The use of any one of claims 1-15, wherein said at least one symptom of DM1 is abnormal splicing of at least one RNA transcript in muscle cells.

17. The use of claim 16, wherein said at least one RNA transcript is selected from the group consisting of: Serca-1, m-Titin, Zasp, and CIC-1.

18. The use of any one of claims 1-17, wherein systemic administration of the cationic peptide-linked morpholino antisense oligonucleotide is performed intravenously, intraperitoneally, or subcutaneously.

19. The use of any one of claims 1-18, wherein the cationic peptide-linked morpholino antisense oligonucleotide is administered to the individual weekly.

20. The use of any one of claims 1-19, wherein the cationic peptide-linked morpholino antisense oligonucleotide is administered to the individual for at least one week.

21. The use of any one of claims 1-20, wherein the cationic peptide-linked morpholino antisense oligonucleotide is administered with a pharmaceutically acceptable excipient.

22. The use of any one of claims 1-21, wherein the individual is a human.