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.

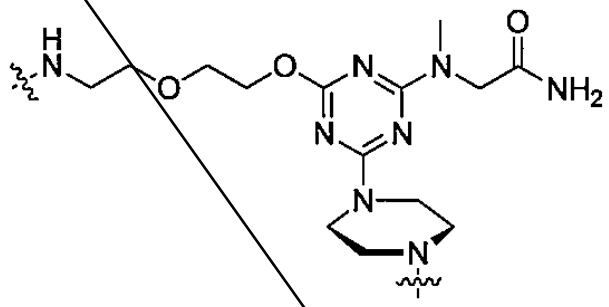
7. The use of claim 5, wherein the cationic peptide-linked morpholino antisense oligonucleotide comprises the sequence: 5’- AGCAGCAGCAGCAGCAGCAGCAGCA – 3’.

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



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 R A 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.

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 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, and wherein a systemic 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 comprises the amino acid sequence $Ac(RXRRBR)_2XB$-.

3. The use of claim 1, wherein the cationic peptide comprises the amino acid sequence $Ac(RXR)_4XB$-.

4. The use of any one of claims 1-3, 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.

5. The use of claim 4, 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.

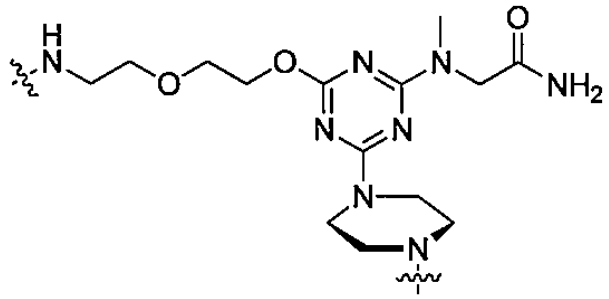
6. The use of claim 4, wherein the cationic peptide-linked morpholino antisense oligonucleotide comprises the sequence: 5’- AGCAGCAGCAGCAGCAGCAGCAGCA – 3’.

7. The use of claim 6, wherein the cationic peptide-linked morpholino antisense oligonucleotide further comprises a 5' amine modification.

8. The use of any one of claims 1-7, wherein the cationic peptide-linked morpholino antisense oligonucleotide is a phosphorodiamidate cationic peptide-linked morpholino antisense oligonucleotide.

9. The use of any one of claims 1-8, 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.

10. The use of claim 9, wherein the spacer moiety comprises



11. The use of any one of claims 1-10, wherein the muscles are skeletal muscles, smooth muscles, and/or cardiac muscle.

12. The use of any one of claims 1-11, wherein the cationic peptide-linked morpholino antisense oligonucleotide penetrates into cells of the tibialis anterior muscle, the quadriceps muscle, and/or the gastrocnemius muscle.

13. The use of any one of claims 1-12, wherein said at least one symptom of DM1 is myotonia.

14. The use of any one of claims 1-13, wherein said at least one symptom of DM1 is aggregation of musclebind-like-1 (MBNL-1) protein in ribonuclear foci within myonuclei.

15. The use of any one of claims 1-14, wherein said at least one symptom of DM1 is abnormal splicing of at least one R A transcript in muscle cells.

16. The use of claim 15, wherein said at least one RNA transcript is selected from the group consisting of: Serca-1, m-Titin, Zasp, and CIC-1.

17. The use of any one of claims 1-16, wherein the systemic administration of the cationic peptide-linked morpholino antisense oligonucleotide is performed intravenously, intraperitoneally, or subcutaneously.

18. The use of any one of claims 1-17, wherein the cationic peptide-linked morpholino antisense oligonucleotide is administered to the individual weekly.

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

20. The use of any one of claims 1 -19, wherein the cationic peptide-linked morpholino antisense oligonucleotide is administered with a pharmaceutically acceptable excipient.

21. The use of any one of claims 1-20, wherein the individual is a human.