Claims

[Claim 1]

An antisense oligomer which is selected from the group consisting of (a) to (d) below:

(a) an antisense oligomer comprising a base sequence of SEQ ID NO: 4 or 5;

(b) an antisense oligomer which comprises a base sequence having deletion, substitution, insertion and/or addition of 1 to 5 base(s) in the base sequence of SEQ ID NO: 4 or 5, and has an activity to induce skipping of exon 50 in the human dystrophin gene;

(c) an antisense oligomer which comprises a base sequence having at least 80% sequence identity to a base sequence of SEQ ID NO: 4 or 5 and has an activity to induce skipping of exon 50 in the human dystrophin gene; and

(d) an antisense oligomer that hybridizes under stringent conditions to an oligonucleotide consisting of a base sequence complementary to the base sequence of SEQ ID NO: 4 or 5 and has an activity to induce skipping of exon 50 in the human dystrophin gene,

or a pharmaceutically acceptable salt or hydrate thereof.

[Claim 2]

An antisense oligomer which is selected from the group consisting of (e) to (h) below:

(e) an antisense oligomer which consists of a base sequence of SEQ ID NO: 4 or 5;

(f) an antisense oligomer which consists of a base sequence having deletion and/or substitution of 1 to 5 base(s) in the base sequence of SEQ ID NO: 4 or 5, and has an activity to induce skipping of exon 50 in the human dystrophin gene;

(g) an antisense oligomer which consists of a base sequence having at least 80% sequence identity to a base sequence of SEQ ID NO: 4 or 5 and has an activity to induce skipping of exon 50 in the human dystrophin gene; and

(h) an antisense oligomer that hybridizes under high stringent conditions to an oligonucleotide consisting of a base sequence complementary to the base sequence of SEQ ID NO: 4 or 5 and has an activity to induce skipping of exon 50 in the human dystrophin gene,

or a pharmaceutically acceptable salt or hydrate thereof.

[Claim 3]

The antisense oligomer or the pharmaceutically acceptable salt or hydrate thereof according to claim 1, wherein the antisense oligomer is

an antisense oligomer which comprises a base sequence having at least 90% sequence identity to a base sequence of SEQ ID NO: 4 or 5 and has an activity to induce skipping of exon 50 in the human dystrophin gene.

[Claim 4]

The antisense oligomer or the pharmaceutically acceptable salt or hydrate thereof according to any one of claims 1 to 3, wherein the antisense oligomer is an oligonucleotide.

[Claim 5]

The antisense oligomer or the pharmaceutically acceptable salt or hydrate thereof according to claim 4, wherein the sugar moiety and/or the phosphate bond moiety of at least one nucleotide constituting the oligonucleotide are/is modified.

[Claim 6]

The antisense oligomer or the pharmaceutically acceptable salt or hydrate thereof according to claim 4 or 5, wherein the sugar moiety of at least one nucleotide constituting the oligonucleotide is a ribose in which the 2'-OH group is replaced by any one selected from the group consisting of OR, R, R'OR, SH, SR, NH_2, NHR, NR_2, N_3, CN, F, Cl, Br and I (wherein R is an alkyl or an aryl and R' is an alkylene).

[Claim 7]

The antisense oligomer or the pharmaceutically acceptable salt or hydrate thereof according to any one of claims 4 to 6, wherein the phosphate bond moiety of at least one nucleotide constituting the oligonucleotide is any one selected from the group consisting of a phosphorothioate bond, a phosphorodithioate bond, an alkylphosphonate bond, a phosphoramidate bond and a boranophosphate bond.

[Claim 8]

The antisense oligomer or the pharmaceutically acceptable salt or hydrate thereof according to any one of claims 1 to 3, wherein the antisense oligomer is a morpholino oligomer.

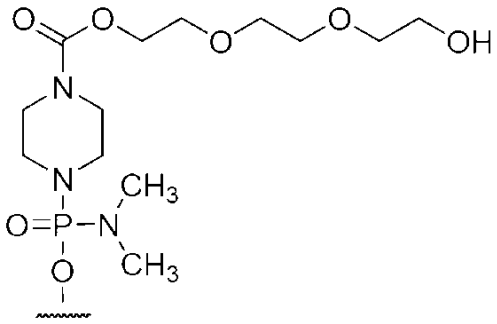
[Claim 9]

The antisense oligomer or the pharmaceutically acceptable salt or hydrate thereof according to claim 8, wherein the antisense oligomer is a phosphorodiamidate morpholino oligomer.

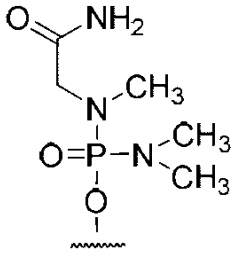
[Claim 10]

The antisense oligomer or the pharmaceutically acceptable salt or hydrate thereof according to claim 8 or 9, wherein the 5' end is any one of chemical formulae (1) to (3) below:

[Formula 1]



（1）



（2）



（3）

[Claim 11]

The antisense oligomer or the pharmaceutically acceptable salt or hydrate thereof according to any one of claims 1 to 10, wherein the length of the antisense oligomer is 19 or 20 bases.

[Claim 12]

A pharmaceutical composition for the treatment of muscular dystrophy, comprising the antisense oligomer or the pharmaceutically acceptable salt or hydrate thereof according to any one of claims 1 to 11.

[Claim 13]

The pharmaceutical composition according to claim 12, further comprising a pharmaceutically acceptable carrier.

[Claim 14]

The pharmaceutical composition according to claim 12 or 13 for being administered to a patient with muscular dystrophy, wherein the patient is a patient having a mutation that is amenable to exon 50 skipping in the dystrophin gene.

[Claim 15]

The pharmaceutical composition according to claim 14, wherein the patient has the dystrophin gene that has at least a frameshift mutation caused by deletion of an exon in the vicinity of exon 50 and in which the amino acid reading frame is corrected by exon 50 skipping.

[Claim 16]

The pharmaceutical composition according to claim 14 or 15, wherein the patient has a frameshift mutation caused by deletions of exons 51, 51-53, 51-55, or 51-57 in the dystrophin gene.

[Claim 17]

The pharmaceutical composition according to any one of claims 14 to 16, wherein the patient is a human.

[Claim 18]

Use of the antisense oligomer or the pharmaceutically acceptable salt or hydrate thereof according to any one of claims 1 to 11 in the manufacture of a medicament for the treatment of muscular dystrophy.

[Claim 19]

A method for treatment of muscular dystrophy, which comprises administering to a patient with muscular dystrophy an effective amount of the antisense oligomer or the pharmaceutically acceptable salt or hydrate thereof according to any one of claims 1 to 11, or the pharmaceutical composition according to any one of claims 12 to 16.

[Claim 20]

The method for treatment according to claim 19, wherein the patient is a human.

[Claim 21]

The antisense oligomer or the pharmaceutically acceptable salt or hydrate thereof according to any one of claims 1 to 11, or the pharmaceutical composition according to any one of claims 12 to 16 for use in the treatment of muscular dystrophy.

[Claim 22]

The antisense oligomer or the pharmaceutically acceptable salt or hydrate thereof, or the pharmaceutical composition according to claim 21, wherein in the treatment, a patient with muscular dystrophy is a human.