Claims

1. A natural type miRNA, which is a single-stranded nucleic acid comprising X region and Y region,
wherein the 3'-terminus of said X region and the 5'-terminus of said Y region are linked via a linker region of a non-nucleotide structure,
said X region comprises (a) a guide strand sequence or (b) a passenger strand sequence of a mature miRNA,
when the X region comprises (a), said Y region comprises a passenger strand sequence of said mature miRNA,
when the X region comprises (b), said Y region comprises a guide strand sequence of said mature miRNA,
said X region further comprises an additional sequence,
said additional sequence has a length of 3 - 5 bases, and
said guide strand sequence and said passenger strand sequence form a double-stranded structure.

2. The natural type miRNA according to claim 1, wherein when said Y region and said X region are aligned, said Y region has an overhang on the 3'-terminus.

3. The natural type miRNA according to claim 2, wherein said overhang has a 0 - 4 base length.

4. The natural type miRNA according to any one of claims 1 to 3, wherein said X region comprises said guide strand or passenger strand sequence and an additional sequence, and said additional sequence is linked to the 3'-terminus of said guide strand or passenger strand sequence.

5. The natural type miRNA according to any one of claims 1 to 4, wherein said additional sequence is a base sequence selected from the group consisting of UAA, UGG, UCC, CAA, CGG, UAAU, UUAA, UUGG, UUUU, UAAUU, UCCGG, UUUUU, UUUUA, UUUAU, UUAUU, UAUUU, UUUAA, UUAUA, UAUUA, UUAAU, UAUAU, UUAAA, UAUAA, UAAUA, UAAAU, UAAAA, UUUGG, AUUAA, AUUUU, CUUAA, CUUUU, GUUAA and GUUUU.

6. The natural type miRNA according to any one of claims 1 to 5, wherein said X region has a length of 19 - 35 bases.

7. The natural type miRNA according to any one of claims 1 to 6, wherein said Y region has a length of 21 - 37 bases.

8. The natural type miRNA according to any one of claims 1 to 7, wherein a full-length is 40 - 68 base length.

9. The natural type miRNA according to any one of claims 1 to 8, wherein said linker region comprises at least one selected from the group consisting of an amino acid residue, a polyamine residue, and a polycarboxylic acid residue.

10. The natural type miRNA according to claim 9, wherein said linker region comprises a polycarboxylic acid residue.

11. The natural type miRNA according to claim 10, wherein said polycarboxylic acid residue is a terephthalic acid residue.

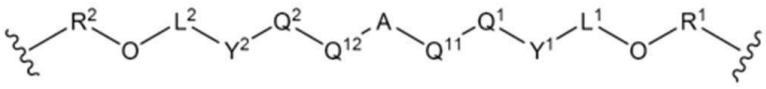
12. The natural type miRNA according to claim 9, wherein said linker region comprises an amino acid residue.

13. The natural type miRNA according to claim 12, wherein said amino acid residue is a glycine residue, a terephthalic acid amide residue, a proline residue or a lysine residue.

14. The natural type miRNA according to claim 12 or 13, wherein said amino acid residue comprises a plurality of amino acid residues linked to each other.

15. The natural type miRNA according to claim 14, wherein said plurality of amino acid residues are linked to form a residue of a glycine dimer or trimer.

16. The natural type miRNA according to any one of claims 1 to 15, wherein said linker residue is represented by the following chemical formula (I-0):



(I−0)

in said chemical formula (I-0),

Q^{11} and Q^{12} are each independently a single bond, CH_2 (a methylene group), NH (an imino group), C=O (a carbonyl group), C=S (a thiocarbonyl group), C=NH (an iminomethylene group), O, or S,

Q^1 and Q^2 are each independently a single bond, CH_2 (a methylene group), NH (an imino group), C=O (a carbonyl group), C=S (a thiocarbonyl group), C=NH (an iminomethylene group), O, or S,

Y^1 and Y^2 are each independently a single bond, CH_2, NH, O, or S;

L^1 is a single bond or an alkylene chain having n carbon atoms, and a hydrogen atom on an alkylene carbon atom may or may not be substituted with OH, OR^a, NH_2, NHR^a, NR^aR^b, SH, or SR^a, or,

L^1 is a polyether chain obtained by substituting at least one carbon atom on said alkylene chain with an oxygen atom,

provided that: when Y^1 is NH, O, or S, an atom bound to Y^1 in L^1 is carbon, an atom bound to OR^1 in L^1 is carbon, and oxygen atoms are not adjacent to each other;

L^2 is a single bond or an alkylene chain having m carbon atoms, and a hydrogen atom on an alkylene carbon atom may or may not be substituted with OH, OR^c, NH_2, NHR^c, NR^cR^d, SH, or SR^c, or

L^2 is a polyether chain obtained by substituting at least one carbon atom on said alkylene chain with an oxygen atom,

provided that: when Y^2 is NH, O, or S, an atom bound to Y^2 in L^2 is carbon, an atom bound to OR^2 in L^2 is carbon, and oxygen atoms are not adjacent to each other;

R^a, R^b, R^c, and R^d are each independently a substituent or a protecting group;

m is an integer in the range from 1 to 30;

n is an integer in the range from 1 to 30;

said regions X and Y are each linked to said linker residue via -OR^1- or -OR^2-,

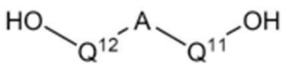
wherein R^1 and R^2 may or may not be present, and when they are present, R^1 and R^2 are each independently a nucleotide residue or said structure (I-0); and

A is any atomic group.

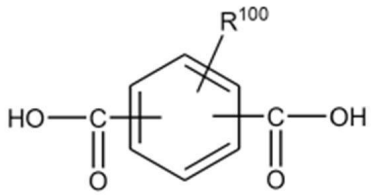
17. The natural type miRNA according to claim 16, wherein Q^{11} and Q^{12} in said chemical formula (I-0) are each a carbonyl group.

18. The natural type miRNA according to claim 17, wherein Q^{1} and Q^{2} in said chemical formula (I-0) are each an imino group.

19. The natural type miRNA according to claim 17, wherein the following chemical formula (Iα) has a structure represented by the following chemical formula (Iα2):



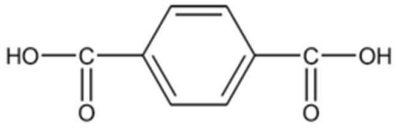
(Iα)



(Iα2)

in said chemical formula (Iα2),
R^{100} is any substituent, which may or may not be present, when it is present, it may be present singly or in plurality, and when it is present in plurality, they may be the same or different from each other.

20. The natural type miRNA according to claim 19, wherein said chemical formula (Iα2) has a structure represented by the following chemical formula (Iα3):

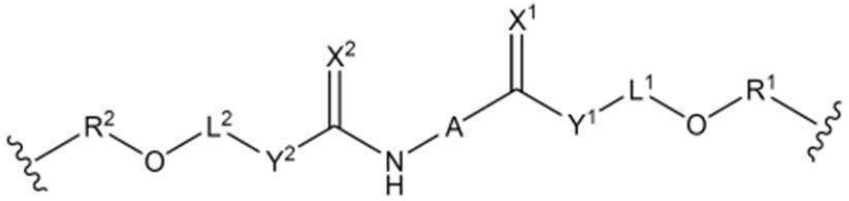


(Iα3) .

21. The natural type miRNA according to claim 16, wherein Q^{11} and Q^{12} in said chemical formula (I-0) are each an imino group.

22. The natural type miRNA according to claim 21, wherein Q^{1} and Q^{2} in said chemical formula (I-0) are each a carbonyl group.

23. The natural type miRNA according to any one of claims 1 to 3 and 6 to 10, wherein said linker region comprises an amino acid residue, and said amino acid residue is represented by the following chemical formula (I):



(I)

in said chemical formula (I),

X^1 and X^2 are each independently H_2, O, S or NH;

Y^1 and Y^2 are each independently a single bond, CH_2, NH, O or S;

L^1 is an alkylene chain having n carbon atoms, and a hydrogen atom on an alkylene carbon atom may or may not be substituted with OH, OR^a, NH_2, NHR^a, NR^aR^b, SH, or SR^a, or,

L^1 is a polyether chain obtained by substituting at least one carbon atom on said alkylene chain with an oxygen atom,

provided that: when Y^1 is NH, O, or S, an atom bound to Y^1 in L^1 is carbon, an atom bound to OR^1 in L^1 is carbon, and oxygen atoms are not adjacent to each other;

L^2 is an alkylene chain having m carbon atoms, and a hydrogen atom on an alkylene carbon atom may or may not be substituted with OH, OR^c, NH_2, NHR^c, NR^cR^d, SH, or SR^c, or

L^2 is a polyether chain obtained by substituting at least one carbon atom on said alkylene chain with an oxygen atom,

provided that: when Y^2 is NH, O, or S, an atom bound to Y^2 in L^2 is carbon, an atom bound to OR^2 in L^2 is carbon, and oxygen atoms are not adjacent to each other;

R^a, R^b, R^c, and R^d are each independently a substituent or a protecting group;

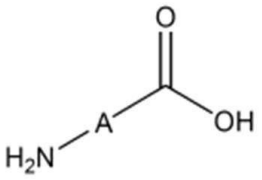
m is an integer in the range from 0 to 30;

n is an integer in the range from 0 to 30;

said regions X and Y are each linked to said amino acid residue via $-OR^1-$ or $-OR^2-$,

wherein R^1 and R^2 may or may not be present, and when they are present, R^1 and R^2 are each independently a nucleotide residue or

said structure (I); and
A is any atomic group, provided that the following chemical formula (Ia) is an amino acid or peptide:



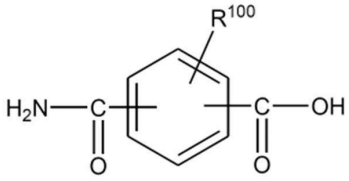
(Ia)

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24. The natural type miRNA according to claim 23, wherein said amino acid in said amino acid residue is at least one of a natural amino acid and an artificial amino acid.

25. The natural type miRNA according to claim 24, wherein said natural amino acid is an amino acid that constitutes a protein.

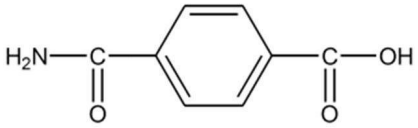
26. The natural type miRNA according to claim 23 or 24, wherein said amino acid in said amino acid residue is at least one kind selected from the group consisting of glycine, α-alanine, arginine, asparagine, aspartic acid, cysteine, cystine, glutamine, glutamic acid, histidine, isoleucine, leucine, lysine, hydroxylysine, methionine, phenylalanine, serine, threonine, tyrosine, valine, proline, 4-hydroxyproline, tryptophan, β-alanine, 1-amino-2-carboxycyclopentane, aminobenzoic acid, aminopyridinecarboxylic acid and amino acid represented by the following chemical formula (Ia2), and optionally further has a substituent or a protecting group:



(Ia2)

in said chemical formula (Ia2),
R^{100} is any substituent, which may or may not be present, when it is present, it may be present singly or in plurality, and when it is present in plurality, they may be the same or different from each other.

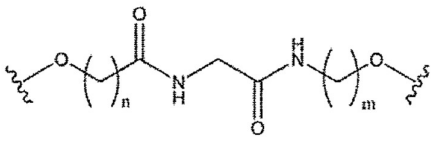
27. The natural type miRNA according to claim 26, wherein said chemical formula (Ia2) has a structure represented by the following chemical formula (Ia3):



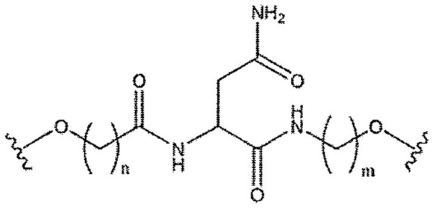
(Ia3)

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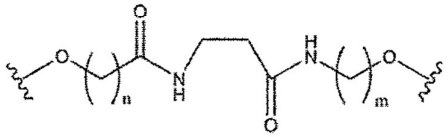
28. The natural type miRNA according to claim 16 or 23, wherein said chemical formula (I-0) or (I) has a structure of the following chemical formulae (I-1) - (I-7) and, in the following chemical formulae (I-1) - (I-7), n is an integer of 0 - 30, and m is an integer of 0 – 30:



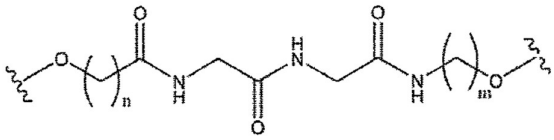
(I－1)



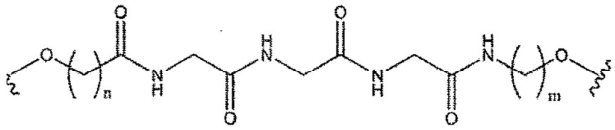
(I－2)



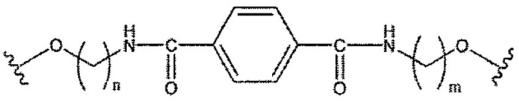
(I－3)



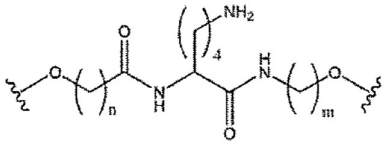
(I－4)



(I－5)



(I－6)



(I－7)

29. The natural type miRNA according to claim 28, wherein, in said chemical formula (I-1), n=11 and m=12, or n=5 and m=4.

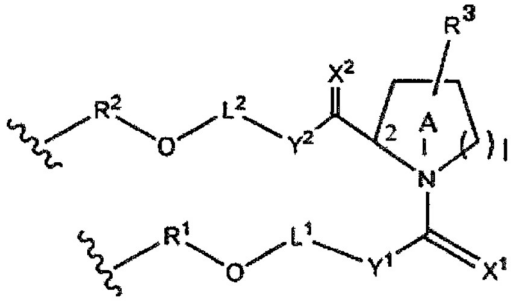
30. The natural type miRNA according to claim 28, wherein, in said chemical formula (I-4), n=5 and m=4.

31. The natural type miRNA according to claim 28, wherein, in said chemical formula (I-6), n=4 and m=4.

32. The natural type miRNA according to claim 28, wherein, in said chemical formula (I-7), n=5 and m=4.

33. The natural type miRNA according to any one of claims 1 to 9, 12 and 13, wherein a non-nucleotide structure of said linker region comprises at least one of a pyrrolidine skeleton and a piperidine skeleton.

34. The natural type miRNA according to any one of claims 1 to 8, wherein said non-nucleotide structure is represented by the following formula (II):



... (II)

wherein,

X^1 and X^2 are each independently H_2, O, S, or NH;

Y^1 and Y^2 are each independently a single bond, CH_2, NH, O, or S;

R^3 is a hydrogen atom or a substituent which is bonded to C-3, C-4, C-5 or C-6 on ring A,

L^1 is an alkylene chain having n atoms, and a hydrogen atom on an alkylene carbon atom may or may not be substituted with OH, OR^a, NH_2, NHR^a, NR^aR^b, SH, or SR^a, or,

L^1 is a polyether chain obtained by substituting at least one carbon atom on said alkylene chain with an oxygen atom,

provided that: when Y^1 is NH, O, or S, an atom bound to Y^1 in L^1 is carbon, an atom bound to OR^1 in L^1 is carbon, and oxygen atoms are not adjacent to each other;

L^2 is an alkylene chain having m atoms, and a hydrogen atom on an alkylene carbon atom may or may not be substituted with OH, OR^c, NH_2, NHR^c, NR^cR^d, SH, or SR^c, or
L^2 is a polyether chain obtained by substituting at least one carbon atom on said alkylene chain with an oxygen atom,
provided that: when Y^2 is NH, O, or S, an atom bound to Y^2 in L^2 is carbon, an atom bound to OR^2 in L^2 is carbon, and oxygen atoms are not adjacent to each other;
R^a, R^b, R^c, and R^d are each independently a substituent or a protecting group;
l is 1 or 2;
m is an integer in the range from 0 to 30;
n is an integer in the range from 0 to 30; and
in ring A, one carbon atom other than said C-2 on ring A may be substituted by nitrogen, oxygen or sulfur, and may contain, in said ring A, a carbon-carbon double bond or a carbon-nitrogen double bond,
said regions (X) and (Y) are each linked to said non-nucleotide structure via $-OR^1-$ or $-OR^2-$,
wherein R^1 and R^2 may or may not be present, and when they are present, R^1 and R^2 are each independently a nucleotide residue or said structure (I).

35. The natural type miRNA according to any one of claims 1 to 34, wherein said X region comprises a guide strand sequence of a mature miRNA selected from the group consisting of hsa-miR-34a or hsa-let-7a.

36. The natural type miRNA according to claim 35, wherein said mature miRNA is hsa-miR-34a.

37. The natural type miRNA according to claim 36, wherein the nucleotide sequence of the natural type miRNA according to claim 1 is a nucleotide sequence selected from the group consisting of SEQ ID NO: 14 - 17.

38. The natural type miRNA according to claim 36, wherein the nucleotide sequence of the natural type miRNA according to claim 1 is a nucleotide sequence selected from the group consisting of SEQ

ID NO: 34 - 43.

39. The natural type miRNA according to claim 35, wherein said mature miRNA is hsa-let-7a.

40. The natural type miRNA according to claim 39, wherein the nucleotide sequence of the natural type miRNA according to claim 1 is a nucleotide sequence of SEQ ID NO: 23 or 24.

41. The natural type miRNA according to claim 39, wherein the nucleotide sequence of the natural type miRNA according to claim 1 is a nucleotide sequence of SEQ ID NO: 32.

42. The natural type miRNA according to any one of claims 1 to 34, wherein said X region comprises a passenger strand sequence of a mature miRNA of hsa-miR-29b.

43. The natural type miRNA according to claim 42, wherein the nucleotide sequence of the natural type miRNA according to claim 1 is a nucleotide sequence of SEQ ID NO: 28 or 29.

44. The natural type miRNA according to claim 42, wherein the nucleotide sequence of the natural type miRNA according to claim 1 is a nucleotide sequence selected from the group consisting of SEQ ID NO: 33 and 44 - 81.

45. A composition for inhibiting expression of a target gene, comprising the natural type miRNA according to any one of claims 1 to 44.

46. A pharmaceutical composition comprising the natural type miRNA according to any one of claims 1 to 44.

47. A method for inhibiting expression of a target gene, comprising using the natural type miRNA according to any one of claims 1 to 44 in vitro.

48. The method according to claim 47, comprising a step of administering said natural type miRNA to a cell or a tissue.

49. A single-stranded nucleic acid for use in the treatment of a disease, which is the natural type miRNA according to any one of claims 1 to 44, wherein said guide strand sequence of said natural type miRNA is a guide strand sequence of a mature miRNA that inhibits expression of a gene involved in said disease.