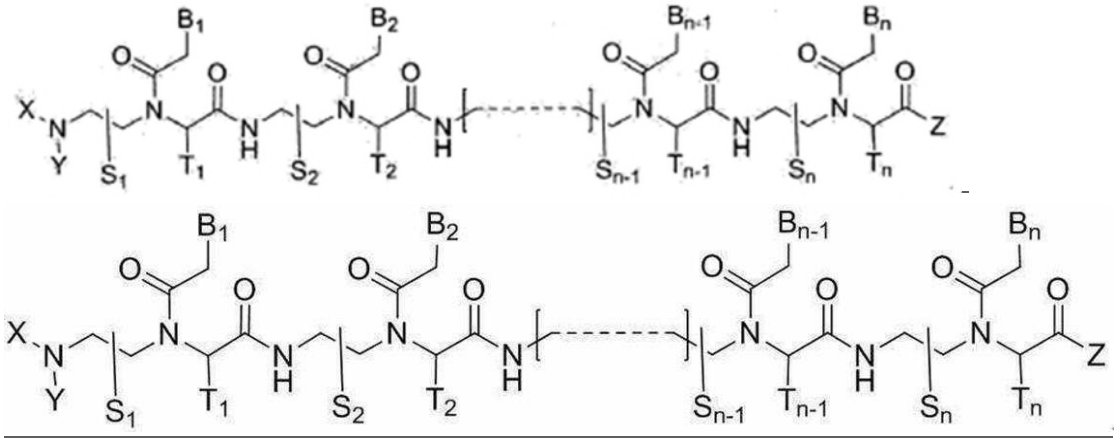
Claims

1. A peptide nucleic acid derivative represented by **Formula I**, or a pharmaceutically acceptable salt thereof:

[Formula I]



wherein,

n is an integer between 10 and 21;

the compound of **Formula I** possesses at least a 10-mer complementary overlap with the 16-mer pre-mRNA sequence of [(5' → 3') CAUAUAUGGUGAGUAU] in the human MMP-1 pre-mRNA;

the compound of **Formula I** is fully complementary to the human MMP-1 pre-mRNA, or partially complementary to the human MMP-1 pre-mRNA with one or two mismatches;

S_1, S_2, ···, S_{n-1}, S_n, T_1, T_2, ···, T_{n-1}, and T_n independently represent hydrido, deuterido, substituted or non-substituted alkyl, or substituted or non-substituted aryl radical;

X and Y independently represent hydrido, deuterido, formyl [H-C(=O)-], aminocarbonyl [NH_2-C(=O)-], aminothiocarbonyl [NH_2-C(=S)-], substituted or non-substituted alkyl, substituted or non-substituted aryl, substituted or non-substituted alkyloxy, substituted or non-substituted aryloxy, substituted or non-substituted alkylacyl, substituted or non-substituted arylacyl, substituted or non-substituted alkyloxycarbonyl, substituted or non-substituted aryloxycarbonyl, substituted or non-substituted alkylaminocarbonyl, substituted or non-substituted arylaminocarbonyl, substituted or non-substituted alkylaminothiocarbonyl, substituted or non-substituted arylaminothiocarbonyl, substituted or non-substituted alkyloxythiocarbonyl, substituted or non-substituted aryloxythiocarbonyl,

substituted or non-substituted alkylsulfonyl, substituted or non-substituted arylsulfonyl, substituted or non-substituted alkylphosphonyl, or substituted or non-substituted arylphosphonyl radical;

Z represents hydrido, deuterido, hydroxy, substituted or non-substituted alkyloxy, substituted or non-substituted aryloxy, substituted or non-substituted amino, substituted or non-substituted alkyl, or substituted or non-substituted aryl radical;

B_1, B_2, ⋯, B_{n-1}, and B_n are independently selected from natural nucleobases including adenine, thymine, guanine, cytosine and uracil, and unnatural nucleobases; and,

at least four of B_1, B_2, ⋯, B_{n-1}, and B_n are independently selected from unnatural nucleobases with a substituted or non-substituted amino radical covalently linked to the nucleobase moiety.

2. The peptide nucleic acid derivative according to claim 1, or a pharmaceutical salt thereof:

wherein,

n is an integer between 10 and 21;

the compound of **Formula I** possesses at least a 10-mer complementary overlap with the 16-mer pre-mRNA sequence of [(5'- → - → 3') CAUAUAUGGUGAGUAU] in the human MMP-1 pre-mRNA;

the compound of **Formula I** is fully complementary to the human MMP-1 pre-mRNA, or partially complementary to the human MMP-1 pre-mRNA with one or two mismatches;

S_1, S_2, ⋯, S_{n-1}, S_n, T_1, T_2, ⋯, T_{n-1}, and T_n independently represent hydrido, deuterido radical;

X and Y independently represent hydrido, deuterido, formyl [H-C(=O)-], aminocarbonyl [NH_2-C(=O)-], aminothiocarbonyl [NH_2-C(=S)-], substituted or non-substituted alkyl, substituted or non-substituted aryl, substituted or non-substituted alkyloxy, substituted or non-substituted aryloxy, substituted or non-substituted alkylacyl, substituted or non-substituted arylacyl, substituted or non-substituted alkyloxycarbonyl, substituted or non-substituted aryloxycarbonyl, substituted or non-substituted alkylaminocarbonyl, substituted or

non-substituted arylaminocarbonyl, substituted or non-substituted alkylaminothiocarbonyl, substituted or non-substituted arylaminothiocarbonyl, substituted or non-substituted

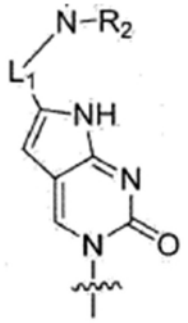
_alkyloxythiocarbonyl, substituted or non-substituted aryloxythiocarbonyl, substituted or non-substituted alkylsulfonyl, substituted or non-substituted arylsulfonyl, substituted or non-substituted alkylphosphonyl, or substituted or non-substituted arylphosphonyl radical;

Z represents hydrido, hydroxy, substituted or non-substituted alkyloxy, substituted or non-substituted aryloxy, or substituted or non-substituted amino radical;

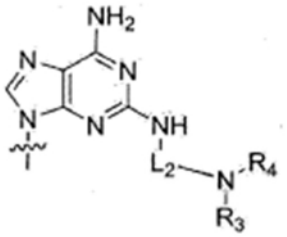
~~Bi, B , ···~~B_1, B_2, ···, B_{n-1}, and B_n are independently selected from natural nucleobases including adenine, thymine, guanine, cytosine and uracil, and unnatural nucleobases;

at least four of ~~Bi~~B_1, B_2, ···, B_{n-1}, and B_n are independently selected from unnatural nucleobases represented by **Formula II**, **Formula III**, or **Formula IV**:

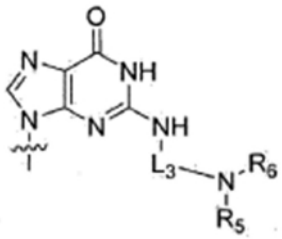
~~[Formula II] [Formula III] [Formula IV]~~



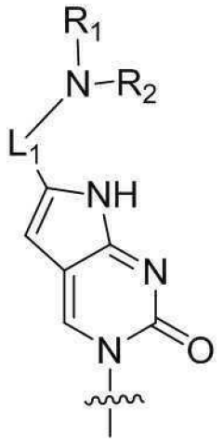
[Formula II]

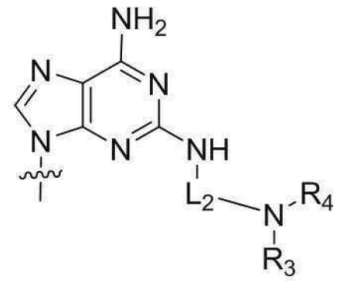


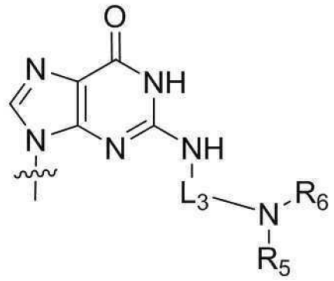
[Formula III]



[Formula IV]







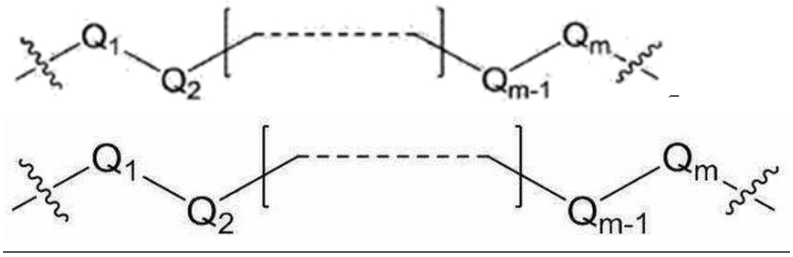
wherein,

~~Ri~~R_1, R_2, R_3, R_4, R_5 and R_6 are independently selected from hydrido and substituted or non-substituted alkyl radical;

~~Li~~ L_1, L_2 and L_3 are a covalent linker represented by **Formula V** covalently linking

the basic amino group to the nucleobase moiety:_

[Formula V]



wherein,

~~Qi~~Q_1 and Q_{m-}_are substituted or non-substituted methylene (-CH_2-) radical, and Q_{m-}_is directly linked to the basic amino group;

Q_2, Q_3, ~~···~~···, and Q_{m-i-1} are independently selected from substituted or non-substituted methylene, oxygen (-O-), sulfur (-S-), and substituted or non-substituted amino radical [-N(H)-, or -N(substituent)-]; and,

_____m is an integer between 1 and 15.

3.–____The peptide nucleic acid derivative according to claim 2, or a pharmaceutical salt thereof:

wherein,

n is an integer between ~~1 1~~11 and 16;

the compound of **Formula I** possesses at least a ~~lO~~10-mer complementary overlap with _the 16-mer pre-mRNA sequence of [(5' —→ 3') CAUAUAUGGUGAGUAU] in the human MMP-~~l~~1 pre-mRNA;

the compound of **Formula I** is fully complementary to the human MMP-~~l~~1 pre-mRNA;

~~Si~~S_1, S_2, ~~···~~···, S_{n-i1}, S_n, ~~Tu~~T_1, T_2, ···, T_{n-i1}, and T_{n-}_are hydrido radical;

X and Y independently represent hydrido, substituted or non-substituted alkylacyl, or substituted or non-substituted alkyloxycarbonyl radical;

Z represents substituted or non-substituted amino radical;

~~Bi~~B_1, B_2, ~~···~~···, B_{n-i1}, and B_{n-}_are independently selected from natural nucleobases including-_adenine,-_thymine,-_guanine,-_cytosine-_and-_uracil, and unnatural nucleobases;

at least five of ~~Bi~~B_1, B_2, ~~···~~···, B_{n-i1}, and B_{n-}_are independently selected from unnatural nucleobases represented by **Formula II**, **Formula III**, or **Formula IV**;

RiR1, R2, R3, R4, R5- and R6- are hydrido radical;

QiQ1 and Qm- are methylene radical, and Qm- is directly linked to the basic amino group;

Q2, Q3, ---, and Qm-i-1 are independently selected from methylene and oxygen radical; and,

m is an integer between 1 and 9.

4.–____The peptide nucleic acid derivative according to claim 3, or a pharmaceutical salt thereof:

wherein,

n is an integer between 1 111 and 16;

the compound of **Formula I** possesses at least a lO10-mer complementary overlap with the 16-mer pre-mRNA sequence of [(5' ⊛⟶ 3') CAUAUAUGGUGAGUAU] in the human MMP-l1 pre-mRNA;

the compound of **Formula I** is fully complementary to the human MMP-l1 pre-mRNA; Si

S1, S2, ----, Sn-i1, Sn, TiT1, T2, ---, Tn-i1, and Tn- are hydrido radical;

X is hydrido radical;

Y represents substituted or non--substituted alkyloxycarbonyl radical;

Z represents substituted or non-substituted amino radical;

BiB1, B2, ---, Bn-i1, and Bn- are independently selected from natural nucleobases including- adenine,- thymine,- guanine,- cytosine- and- uracil, and unnatural nucleobases;

at least five of BiB1, B2, ---, Bn-i1, and Bn- are independently selected from unnatural nucleobases represented by **Formula II**, **Formula III**, or **Formula IV**;

Ri R1, R2, R3, R4, R5- and R6- are hydrido radical;

LiL1 represents -(CH2)2-0O-(CH2)2-, -CH2-0O-(CH2)2-, -CH2-0O-(CH2)3-, -CH2-0O-(CH2)4-, or -CH2-0O-(CH2)5- with the right end is directly linked to the basic amino group; and,

L2- and L3- are independently selected from -(CH2)2-0O-(CH2)2-, -(CH2)3-0O-(CH2)2-, -(CH2)2-0O-(CH2)3-, -(CH2)2-, -(CH2)3-, -(CH2)4-, -(CH2)5-, -(CH2)6-, -(CH2)-7-, and -(CH2)8- with the right end is directly linked to the basic amino group.

5.–____The peptide nucleic acid derivative according to claim 4, which is a peptide nucleic acid derivative provided below, or a pharmaceutically acceptable salt thereof:

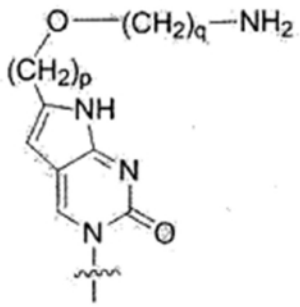
(N-→C) Fethoc-TA(6)C-TCA(6)-CC(-102)-1O2)A(6)-TA(6)T-A(6)T-NH_2

wherein,

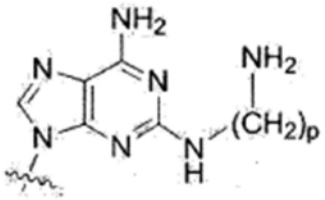
A, T, and C are monomers of peptide nucleic acid with a natural nucleobase of-_adenine,-_thymine, and-_cytosine, respectively;

C(pOq) and A(p) are monomers of peptide nucleic acid with an unnatural nucleobase represented by **Formula VI** and **Formula VII**, respectively;

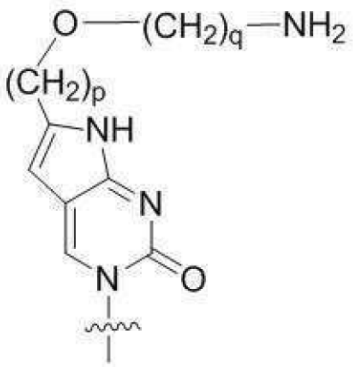
~~[Formula VI] [Formula VII]~~

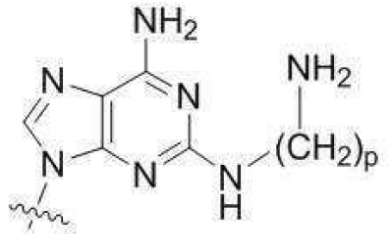


[Formula VI]



[Formula VII]





_____wherein,

p and q are integers and p is 1 or 6, and q is 2; and,

_____"Fethoc-" is the abbreviation for "[2-(9-fluorenyl)ethyl-~~l~~1-oxy]carbonyl".

6. The peptide nucleic acid derivative according to claim 1, or a pharmaceutically acceptable salt thereof for use in a method to treat diseases or conditions associated directly with the human MMP-l gene transcription in a subject- through downregulation of the human MMP-l gene transcription.

7. The peptide nucleic acid derivative according to claim 1, or a pharmaceutically acceptable salt thereof for use in a method to treat skin aging in a subject.

8. A pharmaceutical composition for treating diseases or conditions associated ~~with~~directly with human MMP-l gene transcription through downregulation of the human MMP-l gene transcription, comprising the peptide nucleic acid derivative according to claim 1, or a pharmaceutically acceptable salt thereof.

9. A cosmetic composition for treating diseases or conditions associated ~~with~~directly with human MMP-l gene transcription through downregulation of the human MMP-l gene transcription, comprising the peptide nucleic acid derivative according to claim 1, or a pharmaceutically acceptable salt thereof.

10. A pharmaceutical composition for treating skin aging, comprising the peptide nucleic acid derivative according to claim 1, or a pharmaceutically acceptable salt thereof.

11. A cosmetic composition for treating skin aging, comprising the peptide nucleic acid derivative according to claim 1, or a pharmaceutically acceptable salt thereof.

~~12. Use of the peptide nucleic acid derivative according to claim 1, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament to treat diseases or conditions associated with the human MMP-l gene transcription in a subject.~~

~~13. Use of the peptide nucleic acid derivative according to claim 1, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament to treat skin aging in a subject.~~