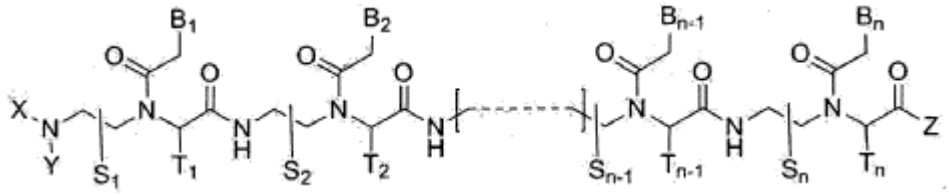
Claims

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 l6-mer pre-mRNA sequence of [(5' - 3') CAUAUAUGGUGAGUAU] in the human MMP-l pre-mRNA;

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

Si, S_2, · · · , S_{n-i}, S_n, Ti, T_2, · · , T_n-i, 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(=0)-],

aminocarbonyl [NH_2-C(=0)-], 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;

$B_]$, B_2, · - · , B_{n-i}, and B_n are independently selected from natural nucleobases including adenine, thymine, guanine, cytosine and uracil, and unnatural nucleobases; and, at least four of Bi, B_2, · · · , B_{n-i}, 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 ¦⟶ sesses at least a lO-mer complementary overlap with the 16-mer pre-mRNA sequence of [(5'
3') CAUAUAUGGUGAGUAU] in the human MMP-l pre-mRNA;

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

Si, S_2, · · · , S_{n-i}, S_n, Ti, T_2, · - , T_{n-i}, and T_n independently represent hydrido, deuterido radical;

X and Y independently represent hydrido, deuterido, formyl [H-C(=0)-],

aminocarbonyl [NH_2-C(=0)-], 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

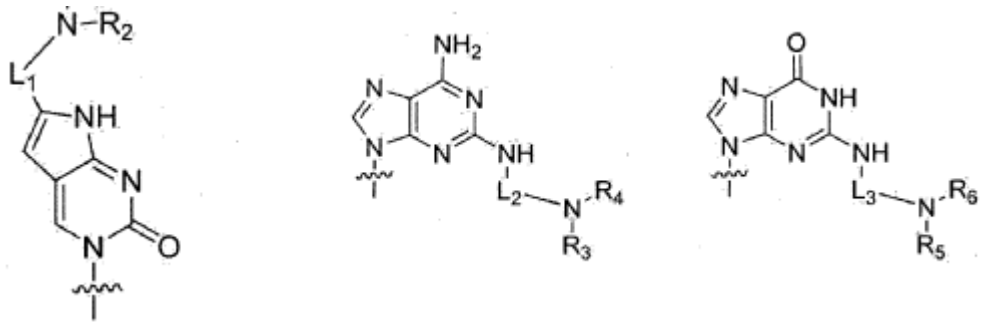
alkyloxythiocarbonyl, substituted or non-substituted aryloxythiocarbonyl, substituted or non-substituted alkylsulfonyl, substituted or non-substituted arylsulfonyl, substituted or non-substituted alkylphosphonyl, or substituted or non-substituted arylphosphonyl radical;

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

Bi, B , — · , B_{n-i}, 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_2, · · , B_{n-i}, and B_n are independently selected from unnatural nucleobases represented by Formula II, Formula III, or Formula IV:

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

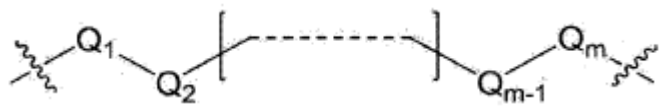


wherein,

Ri, R_2, R_3, R4, R_5 and R_6 are independently selected from hydrido and substituted or non-substituted alkyl radical;

Li , 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 and Q_m are substituted or non-substituted methylene (-CH_2-) radical, and Q_m is directly linked to the basic amino group;

Q2, Q_3, · · , and Q_{m-i} 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 and 16;

the compound of Formula I possesses at least a lO-mer complementary overlap with

the 16-mer pre-mRNA sequence of [(5' — 3') CAUAUAUGGUGAGUAU] in the human MMP-l pre-mRNA;

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

Si, S_2, · · · , S_{n-i}, S_n, Tu T_2, , T_{n-i}, 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_2, · , B_{n-i}, 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_2, ⋯ , B_{n-i}, and B_n are independently selected from unnatural nucleobases represented by Formula II, Formula III, or Formula IV;

Ri, R_2, R_3, R4, R_5 and R_6 are hydrido radical;

Qi and Q_m are methylene radical, and Q_m is directly linked to the basic amino group;

Q_2, Q3, · , and Q_{m-i} 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 1 and 16;

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

the compound of Formula I is fully complementary to the human MMP-l pre-mRNA; Si, S_2, · · · , S_n-i, S_n, Ti, T_2, · · , T_{n-i}, and T_n are hydrido radical;

X is hydrido radical;

Y represents substituted or non- substituted alkyloxycarbonyl radical;

Z represents substituted or non-substituted amino radical;

Bi, B_2, · ·· , B_{n-i}, 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_2, ⋯ , B_{n-i}, and B_n are independently selected from unnatural nucleobases represented by Formula II, Formula III, or Formula IV;

Ri , R_2, R_3, R_4, R_5 and R_6 are hydrido radical;

Li represents $-(CH_2)_2-0-(CH_2)_2-$, $-CH_2-0-(CH_2)_2-$, $-CH_2-0-(CH_2)_3-$, $-CH_2-0-(CH_2)_4-$, or $-CH_2-0-(CH_2)_5-$ with the right end is directly linked to the basic amino group; and,

L_2 and L_3 are independently selected from $-(CH_2)_2-0-(CH_2)_2-$, $-(CH_2)_3-0-(CH_2)_2-$, $-(CH_2)_2-0-(CH_2)_3-$, $-(CH_2)_2-$, $-(CH_2)_3-$, $-(CH_2)_4-$, $-(CH_2)_5-$, $-(CH_2)_6-$, $-(CH_2)$, and $-(CH_2)_8-$ 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:

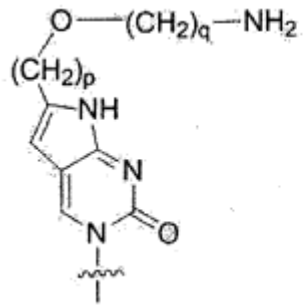
(N C) Fethoc-TA(6)C-TCA(6)-CC(102) A(6)-TA(6)T-A(6)T-NH_2

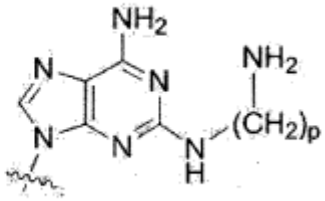
wherein,

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]





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-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 with the human MMP-l gene transcription in a subject.

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 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 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.