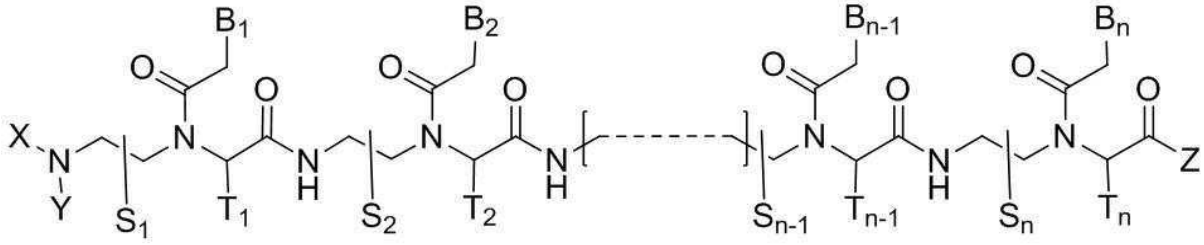
CLAIMS

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 14-mer pre-mRNA sequence of [(5' → 3') UGUACAGAUUGUCU] in the human tyrosinase pre-mRNA;

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

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

X and Y independently represent deuterido, hydrido [H], 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 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 radical, or substituted or non-substituted arylphosphonyl radical;

Z represents hydrido, 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 pharmaceutically acceptable 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 14-mer pre-mRNA sequence of [(5' → 3') UGUACAGAUUGUCU] in the human tyrosinase pre-mRNA;

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

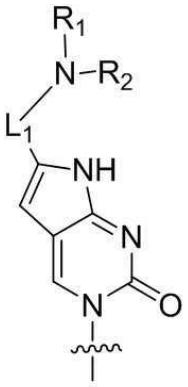
S_1, S_2, ⋯, S_{n-1}, S_n, T_1, T_2, ⋯, T_{n-1}, and T_n independently represent deuterido or hydrido radical;

X and Y independently represent deuterido, hydrido, formyl, aminocarbonyl, aminothiocarbonyl, substituted or non-substituted alkyl, substituted or non-substituted aryl, 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 radical, or substituted or non-substituted arylphosphonyl radical;

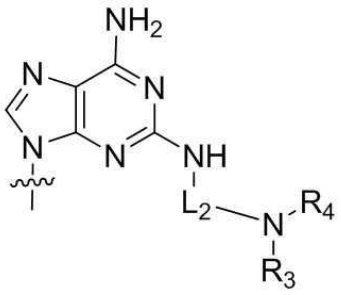
Z represents hydrido, hydroxy, substituted or non-substituted alkyloxy, substituted or non-substituted aryloxy, or substituted or non-substituted amino radical;

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;

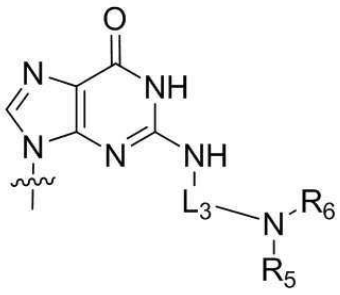
at least four of B_1, B_2, ⋯, B_{n-1}, and B_n are independently selected from unnatural nucleobases represented by **Formula II**, **Formula III**, or **Formula IV**:



Formula II



Formula III



Formula IV

wherein,

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;

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,

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-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 pharmaceutically acceptable salt thereof:

wherein,

n is an integer between 11 and 18;

the compound of **Formula I** possesses at least a 10-mer complementary overlap with the 14-mer pre-mRNA sequence of [(5' → 3') UGUACAGAUUGUCU] in the human tyrosinase pre-mRNA;

the compound of **Formula I** is fully complementary to the human tyrosinase pre-mRNA;

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

X and Y independently represent hydrido, substituted or non-substituted alkyl, substituted or non-substituted aryl, substituted or non-substituted alkylacyl, substituted or non-substituted arylacyl, substituted or non-substituted alkyloxycarbonyl, or substituted or non-substituted aryloxycarbonyl radical;

Z represents substituted or non-substituted amino 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;

at least four of 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**;

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;

Q_1 and Q_m are substituted or non-substituted methylene radical, and Q_m is directly linked to the basic amino group;

Q_2, Q_3, ⋯, and Q_{m-1} are independently selected from substituted or non-substituted methylene, oxygen, and amino radical; and,

m is an integer between 1 and 11.

4. The peptide nucleic acid derivative according to claim 3, or a pharmaceutically acceptable salt thereof:

wherein,

n is an integer between 11 and 16;

the compound of **Formula I** possesses at least a 10-mer complementary overlap with the 14-mer pre-mRNA sequence of [(5' → 3') UGUACAGAUUGUCU] in the human tyrosinase pre-mRNA;

the compound of **Formula I** is fully complementary to the human tyrosinase pre-mRNA;

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

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

Z represents substituted or non-substituted amino 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;

at least four of 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**;

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;

Q_1 and Q_m are methylene radical, and Q_m is directly linked to the basic amino group;

Q_2, Q_3, ⋯, and Q_{m-1} are independently selected from methylene, oxygen, and amino radical; and,

m is an integer between 1 and 9.

5. The peptide nucleic acid derivative according to claim 4, or a pharmaceutically acceptable salt thereof:

wherein,

n is an integer between 11 and 16;

the compound of **Formula I** possesses at least a 10-mer complementary overlap with the 14-mer pre-mRNA sequence of [(5' ⟶ 3') UGUACAGAUUGUCU] in the human tyrosinase pre-mRNA;

the compound of **Formula I** is fully complementary to the human tyrosinase pre-mRNA;

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

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

Z represents substituted or non-substituted amino 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;

at least four of 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**;

R_1, R_3, and R_5 are hydrido radical, and R_2, R_4, and R_6 independently represent hydrido, or substituted or non-substituted alkyl radical;

Q_1 and Q_m are methylene radical, and Q_m is directly linked to the basic amino group;

Q_2, Q_3, ⋯, and Q_{m-1} are independently selected from methylene, oxygen radical; and,

m is an integer between 1 and 9.

6. The peptide nucleic acid derivative according to claim 5, or a pharmaceutically acceptable salt thereof:

wherein,

n is an integer between 11 and 16;

the compound of **Formula I** possesses at least a 10-mer complementary overlap with the 14-mer pre-mRNA sequence of [(5' → 3') UGUACAGAUUGUCU] in the human tyrosinase pre-mRNA;

the compound of **Formula I** is fully complementary to the human tyrosinase pre-mRNA;

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

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

Z represents substituted or non-substituted amino radical;

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

at least five of 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**;

R_1, R_2 , R_3, R_4, R_5, and R_6 are hydrido radical;

Q_1 and Q_m are methylene radical, and Q_m is directly linked to the basic amino group;

Q_2, Q_3, ⋯, and Q_{m-1} are independently selected from methylene, and oxygen radical; and,

m is an integer between 1 and 9.

7. The peptide nucleic acid derivative according to claim 6, or a pharmaceutically acceptable salt thereof:

wherein,

n is an integer between 11 and 16;

the compound of **Formula I** possesses at least a 10-mer complementary overlap with the 14-mer pre-mRNA sequence of [(5' → 3') UGUACAGAUUGUCU] in the human tyrosinase pre-mRNA;

the compound of **Formula I** is fully complementary to the human tyrosinase pre-mRNA;

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

X is hydrido radical;

Y represents substituted or non-substituted alkylacyl, or substituted or non-substituted alkyloxycarbonyl radical;

Z represents substituted or non-substituted amino radical;

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

at least five of 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**;

R_1, R_2, R_3, R_4, R_5, and R_6 are hydrido radical;

L_1 represents $-(CH_2)_2-O-(CH_2)_2-$, $-CH_2-O-(CH_2)_2-$, $-CH_2-O-(CH_2)_3-$, $-CH_2-O-(CH_2)_4-$, or $-CH_2-O-(CH_2)_5-$ with the right end is directly linked to the basic amino group; and,

L_2 and L_3 are independently selected from $-(CH_2)_2-O-(CH_2)_2-$, $-(CH_2)_3-O-(CH_2)_2-$, $-(CH_2)_2-O-(CH_2)_3-$, $-(CH_2)_2-$, $-(CH_2)_3-$, $-(CH_2)_4-$, $-(CH_2)_5-$, $-(CH_2)_6-$, $-(CH_2)_7-$, and $-(CH_2)_8-$ with the right end is directly linked to the basic amino group.

8. The peptide nucleic acid derivative according to claim 1, which is selected from the group of peptide nucleic acid derivatives provided below, or a pharmaceutically acceptable salt thereof:

(N⟶C) Fethoc-CA(5)G-ACA(5)-ATC(1O2)-TG(6)T-A(5)-NH_2;

(N⟶C) Fethoc-AC(1/2)A(5)-GA(5)C-AA(5)T-CTG(6)-C(1/2)C-NH_2;

(N⟶C) Ac-CA(5)G-ACA(5)-ATC(1O2)-TG(6)T-A(5)-NH_2;

(N⟶C) Benzoyl-CA(5)G-ACA(5)-ATC(1O2)-TG(6)T-A(5)-NH_2;

(N⟶C) Piv-CA(5)G-ACA(5)-ATC(1O2)-TG(6)T-A(5)-NH_2;

(N⟶C) Methyl-CA(5)G-ACA(5)-ATC(1O2)-TG(6)T-A(5)-NH_2;

(N⟶C) n-Propyl-CA(5)G-ACA(5)-ATC(1O2)-TG(6)T-A(5)-NH_2;

(N⟶C) Fmoc-CA(5)G-ACA(5)-ATC(1O2)-TG(6)T-A(5)-NH_2;

(N⟶C) p-Toluenesulfonyl-CA(5)G-ACA(5)-ATC(1O2)-TG(6)T-A(5)-NH_2;

(N⟶C) H-Lys-CA(5)G-ACA(5)-ATC(1O2)-TG(6)T-A(5)-NH_2;

(N⟶C) Fethoc-Lys-Gly-CA(5)G-ACA(5)-ATC(1O2)-TG(6)T-A(5)-NH_2;

(N⟶C) Fethoc-CA(5)G-ACA(5)-ATC(1O2)-TG(6)T-A(5)-Lys-NH_2;

(N⟶C) Fethoc-Val-Gly-CA(5)G-ACA(5)-ATC(1O2)-TG(6)T-A(5)-NH_2;

(N⟶C) Ac-Arg-CA(5)G-ACA(5)-ATC(1O2)-TG(6)T-A(5)-NH_2;

(N⟶C) Benzyl-CA(5)G-ACA(5)-ATC(1O2)-TG(6)T-A(5)-NH_2;

(N⟶C) Phenyl-CA(5)G-ACA(5)-ATC(1O2)-TG(6)T-A(5)-NH_2;

(N⟶C)
[N-(2-Phenylethyl)amino]carbonyl-CA(5)G-ACA(5)-ATC(1O2)-TG(6)T-A(5)-NH_2;

(N⟶C) Benzoyl-Leu-CA(5)G-ACA(5)-ATC(1O2)-TG(6)T-A(5)-NH_2;

(N⟶C) Piv-Lys-CA(5)G-ACA(5)-ATC(1O2)-TG(6)T-A(5)-Val-NH_2;

(N⟶C) Fethoc-CA(7)G-AC(2O2)A-A(4)TC(1O2)-TG(6)T-A-NH_2;

(N⟶C) Fethoc-CTG(6)-ACA(5)-ATC(1O2)-TG(6)T-A(5)-NH_2;

(N⟶C) Fethoc-CA(5)G-ATA(5)-ATC(1O2)-TG(5)T-A(5)-NH_2;

(N⟶C) Fethoc-TA(5)G-ACA(5)-ATC(1O2)-TG(6)T-A(5)-NH_2;

(N⟶C) Fethoc-TCA(3)-GAC(1O5)-A(5)AT-C(1O2)TG(5)-TA(5)-NH_2;

(N⟶C) Fethoc-CA(5)G-ACA(5)-ATC(1O2)-TG(6)T-A(5)C-NH_2;

(N⟶C) Fethoc-AG(6)A-CA(5)A-TC(1O2)T-G(6)TA(5)-C-NH_2;

(N⟶C) Fethoc-AG(6)A-CA(5)A-TC(1O2)T-G(6)TA(5)-CA(2O2)A-NH_2;

(N⟶C) Fethoc-AC(1O2)A-GA(6)C-AA(6)T-CTG(6)-TA(6)C(1O2)-AA(6)-NH_2;

(N⟶C) Fethoc-AC(1O3)T-GA(6)C-TA(6)T-CTG(6)-TAC(1O5)-A(4)A-NH_2;

(N⟶C) Fethoc-GA(6)C-AA(6)T-CTG(6)-TA(6)C(1O2)-AA(6)-NH_2;

(N⟶C) Fethoc-AC(1O2)A-GA(6)C-AA(6)T-CTG(6)-TA(6)C-A(5)AA(2O2)-A-NH_2;

(N⟶C) Fethoc-AA(6)T-CTG(6)-TA(6)C-A(5)AA(2O2)-A-NH_2;

(N⟶C) Fethoc-AC(1O2)A-GA(6)C-AA(6)T-CTG(6)-TA(6)C-A(5)AA(2O3)-A-NH_2;

(N⟶C) Fethoc-GC(1O4)T-AC(1O2)A-GA(4)C-AAT-CTG(6)-TA(6)C-NH_2;

(N⟶C) Fethoc-GC(1O2)T-A(3)CA-GA(4)C-AAT-C(1O2)TG-NH_2;

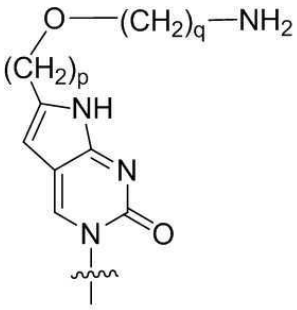
(N⟶C) Fethoc-GC(1O2)T-A(3)CA-G(2O2)AC-A(5)AT-C(1O2)TG-NH_2; and

(N⟶C) Fethoc-GC(1O2)T-A(3)CA-GA(4)C-A(2O2)AT-C(1O2)TG-NH_2:

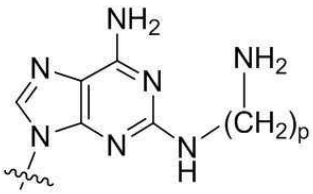
wherein,

A, G, T, and C are PNA monomers with a natural nucleobase of adenine, guanine, thymine, and cytosine, respectively;

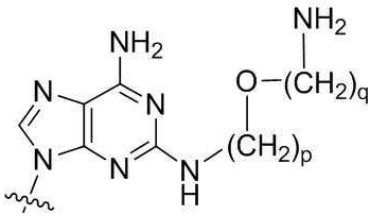
C(pOq), A(p), A(pOq), G(p), and G(pOq) are PNA monomers with an unnatural nucleobase represented by **Formula VI**, **Formula VII**, **Formula VIII**, **Formula IX**, and **Formula X**, respectively;



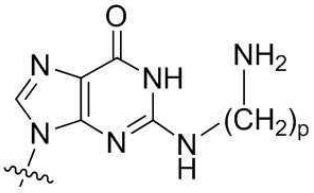
Formula VI



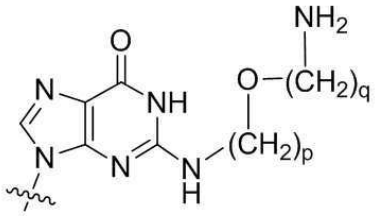
Formula VII



Formula VII



Formula IX



Formula X

wherein,

p and q are integers; and,

the abbreviations for the N- and C-terminus substituents are as specifically described as follows: "Fmoc-" is the abbreviation for "[(9-fluorenyl)methyloxy]carbonyl-"; "Fethoc-" for "[2-(9-fluorenyl)ethyl-1-oxy]carbonyl"; "Ac-" for "acetyl-"; "Benzoyl-" for "benzenecabonyl-"; "Piv-" for "pivalyl-"; "Methyl-" for "methyl-"; "n-Propyl-" for "1-(n-propyl)-"; "H-" for "hydrido-" group; "p-Toluenesulfonyl" for "(4-methylbenzene)-1-sulfonyl-"; "-Lys-" for amino acid residue "lysine"; "-Val-" for amino acid residue "valine"; "-Leu-" for amino acid residue "leucine"; "-Arg-" for amino acid residue "arginine"; "-Gly-" for amino acid residue "glycine"; "[N-(2-Phenylethyl)amino]carbonyl-" for "[N-1-(2-phenylethyl)amino]carbonyl-"; "Benzyl-" for "1-(phenyl)methyl-"; "Phenyl-" for "phenyl-"; "Me-" for "methyl-"; and "-NH_2" for non-subsituted "-amino" group.

9. A pharmaceutical composition for treating diseases or conditions involving the expression of the human tyrosinase gene, comprising the peptide nucleic acid derivative or the pharmaceutically acceptable salt thereof according to claim 1.

10. A pharmaceutical composition for treating hyper-pigmentation, comprising

the peptide nucleic acid derivative or the pharmaceutically acceptable salt thereof according to claim 1.

11. The peptide nucleic acid derivative or a pharmaceutically acceptable salt thereof according to claim 1 for use in treating diseases or conditions involving the expression of the human tyrosinase gene.

12. Use of the peptide nucleic acid derivative or a pharmaceutically acceptable salt thereof according to claim 1 in the manufacture of a medicament for the treatment of hyper-pigmentation.