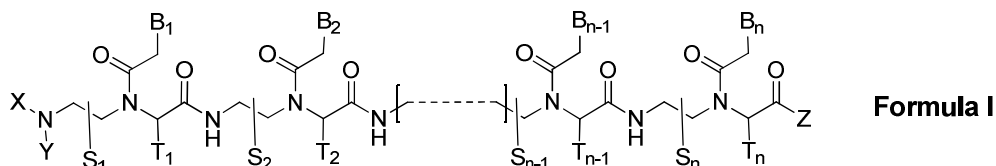


CLAIMS

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



wherein,

n is an integer between 10 and 25;

the compound of **Formula I** possesses at least a 10-mer complementary overlap with a 14-mer pre-mRNA sequence of [(5' → 3') AUCCCAGGGUAACA] in the human SNAP25 pre-mRNA;

the compound of **Formula I** is fully complementary to the human SNAP25 pre-mRNA, or partially complementary to the human SNAP25 pre-mRNA with one or two mismatches;

S₁, S₂, ..., S_{n-1}, S_n, T₁, T₂, ..., T_{n-1}, and T_n independently represent deuterido [D], hydrido [H], substituted or non-substituted alkyl, or substituted or non-substituted aryl radical;

X and Y independently represent hydrido, formyl [H-C(=O)-], aminocarbonyl [NH₂-C(=O)-], aminothiocabonyl [NH₂-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 alkylaminothiocabonyl, substituted or non-substituted arylaminothiocabonyl, substituted or non-substituted alkyloxythiocabonyl, substituted or non-substituted aryloxythiocabonyl, 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;

B₁, B₂, ..., 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 B₁, B₂, ..., 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 25;

the compound of **Formula I** possesses at least a 10-mer complementary overlap with a 14-mer pre-mRNA sequence of [(5' → 3') AUCCCAGGGUAACA] in the human SNAP25 pre-mRNA;

the compound of **Formula I** is fully complementary to the human SNAP25 pre-mRNA, or partially complementary to the human SNAP25 pre-mRNA with one or two mismatches;

S₁, S₂, ..., S_{n-1}, S_n, T₁, T₂, ..., T_{n-1}, and T_n independently represent deuterido, hydrido, substituted or non-substituted alkyl, or substituted or non-substituted aryl radical;

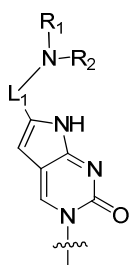
X and Y independently represent hydrido, formyl, aminocarbonyl, aminothiocarbonyl, substituted or non-substituted alkyl, substituted or non-substituted aryl, substituted or non-substituted alkylacyl, substituted or non-substituted arylacyl, substituted or non-substituted alkyloxycarbonyl, substituted 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;

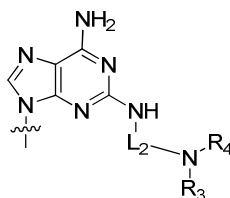
Z represents hydrido, hydroxy, substituted or non-substituted alkyloxy, substituted or non-substituted aryloxy, substituted or non-substituted amino, substituted or non-substituted alkyl, or substituted or non-substituted aryl radical;

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

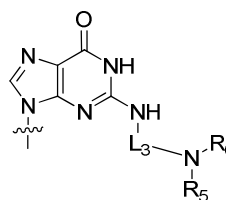
at least four of $B_1, B_2, \dots, B_{n-1}$, and B_n are independently selected from unnatural nucleobases represented by **Formula II**, **Formula III**, or **Formula IV**:



Formula II



Formula III

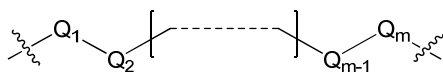


Formula IV

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 ($-\text{CH}_2-$) radical, and Q_m is directly linked to the basic amino group;

$Q_2, Q_3, \dots$, 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 pharmaceutical salt thereof:

wherein,

n is an integer between 11 and 21;

the compound of **Formula I** possesses at least a 10-mer complementary overlap with a 14-mer pre-mRNA sequence of [(5' $\rightarrow$ 3') AUCCCAGGGUAACA] in the human SNAP25 pre-mRNA;

the compound of **Formula I** is fully complementary to the human SNAP25 pre-mRNA, or partially complementary to the human SNAP25 pre-mRNA with one or two mismatches;

$S_1, S_2, \dots, S_{n-1}, S_n, T_1, T_2, \dots, T_{n-1}$, 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, substituted or non-substituted aryloxycarbonyl, substituted or non-substituted alkylaminocarbonyl, substituted or non-substituted arylaminocarbonyl, substituted or non-substituted alkylsulfonyl, or substituted or non-substituted arylsulfonyl radical;

Z represents substituted or non-substituted amino radical;

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

at least four of $B_1, B_2, \dots, B_{n-1}$, 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;

$Q_2, Q_3, \dots$, 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 2, or a pharmaceutical salt thereof:

wherein,

n is an integer between 11 and 19;

the compound of **Formula I** possesses at least a 10-mer complementary overlap with a 14-mer pre-mRNA sequence of [(5' $\rightarrow$ 3') AUCCCAGGGUAACA] in the human SNAP25 pre-mRNA;

the compound of **Formula I** is fully complementary to the human SNAP25 pre-mRNA;

$S_1, S_2, \dots, S_{n-1}, S_n, T_1, T_2, \dots, T_{n-1}$, 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, substituted or non-substituted alkylaminocarbonyl, substituted or non-substituted alkylsulfonyl, or substituted or non-substituted arylsulfonyl radical;

Z represents substituted or non-substituted amino radical;

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

at least four of $B_1, B_2, \dots, B_{n-1}$, 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;

$Q_2, Q_3, \dots$, 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 2, or a pharmaceutical salt thereof:

wherein,

n is an integer between 11 and 19;

the compound of **Formula I** possesses at least a 10-mer complementary overlap with a 14-mer pre-mRNA sequence of [(5' → 3') AUCCCAGGGUAACA] in the human SNAP25 pre-mRNA;

the compound of **Formula I** is fully complementary to the human SNAP25 pre-mRNA;

S₁, S₂, ..., S_{n-1}, S_n, T₁, T₂, ..., 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, or substituted or non-substituted alkyloxycarbonyl radical;

Z represents substituted or non-substituted amino radical;

B₁, B₂, ..., 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 B₁, B₂, ..., B_{n-1}, and B_n are independently selected from unnatural nucleobases represented by **Formula II**, **Formula III**, or **Formula IV**;

R₁, R₃, and R₅ are hydrido radical, and R₂, R₄, and R₆ independently represent hydrido, or substituted or non-substituted alkyl radical;

Q₁ and Q_m are methylene radical, and Q_m is directly linked to the basic amino group;

Q₂, Q₃, ..., and Q_{m-1} are independently selected from methylene, oxygen radical; and,

m is an integer between 1 and 8.

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

wherein,

n is an integer between 11 and 19;

the compound of **Formula I** possesses at least a 10-mer complementary overlap with a 14-mer pre-mRNA sequence of [(5' → 3') AUCCCAGGGUAACA] in the human SNAP25 pre-mRNA;

the compound of **Formula I** is fully complementary to the human SNAP25 pre-mRNA;

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

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

Z represents substituted or non-substituted amino radical;

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

at least five of $B_1, B_2, \dots, B_{n-1},$ 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;

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

and,

m is an integer between 1 and 8.

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

wherein,

n is an integer between 11 and 19;

the compound of **Formula I** possesses at least a 10-mer complementary overlap with a 14-mer pre-mRNA sequence of [(5' → 3') AUCCCAGGGUAACA] in the human SNAP25 pre-mRNA;

the compound of **Formula I** is fully complementary to the human SNAP25 pre-mRNA;

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

X is hydrido radical;

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

Z represents substituted or non-substituted amino radical;

B₁, B₂, ..., B_{n-1}, and B_n are independently selected from adenine, thymine, guanine, cytosine, and unnatural nucleobases;

at least five of B₁, B₂, ..., B_{n-1}, and B_n are independently selected from unnatural nucleobases represented by **Formula II**, **Formula III**, or **Formula IV**;

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

L₁ represents -(CH₂)₂-O-(CH₂)₂-, -CH₂-O-(CH₂)₂-, -CH₂-O-(CH₂)₃-, -CH₂-O-(CH₂)₄-, or -CH₂-O-(CH₂)₅- with the right end is directly linked to the basic amino group; and,

L₂ and L₃ are independently selected from -(CH₂)₂-, -(CH₂)₃-, -(CH₂)₄-, -(CH₂)₅-, -(CH₂)₆-, -(CH₂)₇-, -(CH₂)₈-, -(CH₂)₂-O-(CH₂)₂-, -(CH₂)₃-O-(CH₂)₂-, and -(CH₂)₂-O-(CH₂)₃- 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-A(6)TT-TG(6)T-TA(6)C-CC(1O2)T-GG(6)G-A(6)-NH₂;

(N → C) Fethoc-A(6)TC-TG(6)T-TA(6)C-CC(1O2)T-GG(6)G-A(6)-NH₂;

(N → C) Piv-A(6)TT-TG(6)T-TA(6)C-CC(1O2)T-GG(6)G-A(6)-NH₂;

(N → C) Fethoc-A(6)TT-TG(6)T-TA(2O2)C-CC(1O2)T-GG(5)G-A(5)-NH₂;

(N → C) Fmoc-Lys-A(6)TT-TG(6)T-TA(6)C-CC(1O2)T-GG(6)G-A(6)-NH₂;

(N → C) Fethoc-TG(5)T-TA(6)C-C(1O2)CT-GG(5)G-A(5)-NH₂;

(N → C) Fethoc-TG(5)T-TA(6)C-C(1O2)CT-GG(5)T-A(5)-NH₂;

(N → C) Fethoc-TG(5)T-TA(6)C-C(1O3)CT-GG(5)G-A(5)-NH₂;

(N → C) Fethoc-Lys-Leu-TG(5)T-TA(5)C-CC(1O2)T-GG(5)G-A(2O2)T-Lys-NH₂;

(N → C) H-TG(5)T-TA(5)C-CC(1O2)T-GG(3)G-A(5)T-NH₂;

(N → C) Benzoyl-TG(5)T-TA(6)C-C(1O3)CT-GG(5)G-A(5)-Val-Lys-NH₂;

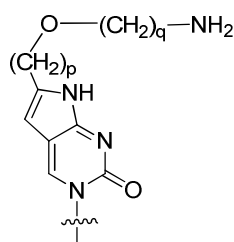
(N → C) Benzoyl-TG(5)T-TA(5)C-CC(1O3)T-GG(5)G-A(5)T-NH₂;

(N → C) n-Hexanoyl-TG(5)T-TA(8)C-CC(1O2)T-GG(5)G-A(5)T-NH₂;

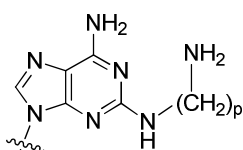
$(N \rightarrow C)$ n-Propyl-TG(5)T-TA(6)C-C(103)CT-GG(5)G-A(5)-NH₂;
 $(N \rightarrow C)$ Ac-TG(5)T-TA(6)C-C(103)CT-GG(5)G-A(5)-NH₂;
 $(N \rightarrow C)$ [N-(2-Phenylethyl)amino]carbonyl-TG(5)T-TA(4)C-CC(102)T-GG(5)G-A(5)T-NH₂;
 $(N \rightarrow C)$ n-Propyl-TG(202)T-TA(5)C-CC(202)T-GG(5)G-A(5)T-NH₂;
 $(N \rightarrow C)$ FAM-HEX-HEX-TG(202)T-TA(5)C-CC(202)T-GG(5)G-A(5)T-NH₂;
 $(N \rightarrow C)$ n-Propyl-TG(202)T-TA(5)C-CC(202)T-GG(5)G-A(5)T-Arg-NH₂;
 $(N \rightarrow C)$ n-Benzoyl-Gly-TG(202)T-TA(5)C-CC(202)T-GG(5)G-A(5)T-NH₂;
 $(N \rightarrow C)$ N-Me-N-Phenyl-TG(5)T-TA(5)C-CC(105)T-GG(5)G-A(5)T-NH₂;
 $(N \rightarrow C)$ p-Toluenesulfonyl-TG(203)T-TA(5)C-CC(102)T-GG(5)G-A(5)T-Lys-NH₂;
 $(N \rightarrow C)$ Fethoc-TG(5)T-TA(6)C-C(102)CT-GG(5)G-A(6)T-NH₂;
 $(N \rightarrow C)$ Bezenesulfonyl-TG(5)T-TA(203)C-CC(105)T-GG(5)G-A(6)T-NH₂;
 $(N \rightarrow C)$ Phenyl-TG(5)T-TA(6)C-C(102)CT-GG(5)G-A(6)T-NH₂;
 $(N \rightarrow C)$ Fethoc-TG(5)G-TA(5)C-C(102)CT-TG(5)G-A(5)T-NH₂;
 $(N \rightarrow C)$ Fethoc-TG(5)T-AA(5)C-CC(102)T-GG(5)T-A(5)T-NH₂;
 $(N \rightarrow C)$ Fethoc-TG(6)T-TA(3)C-CC(105)T-GG(6)G-A(3)T-NH₂;
 $(N \rightarrow C)$ Fethoc-G(5)TT-A(5)CC(102)-CTG-G(5)GA(5)-TC(102)-NH₂;
 $(N \rightarrow C)$ Benzyl-G(5)TT-A(5)CC(102)-CTG-G(5)GA(5)-TC(102)-NH₂;
 $(N \rightarrow C)$ Fethoc-GTT-A(3)CC(105)-CTG(6)-GGA(3)-TC(105)-NH₂;
 $(N \rightarrow C)$ Fethoc-TA(5)C-C(102)CT(105)-GG(5)G-A(5)TC-C(102)A-NH₂;
 $(N \rightarrow C)$ Fmoc-Leu-TA(4)C-C(103)CT-GG(5)G-A(4)TC-C(103)A-NH₂;
 $(N \rightarrow C)$ Fethoc-C(102)AT-TTG(6)-TTA(5)-CCC(102)-TG(6)-NH₂;
 $(N \rightarrow C)$ Fethoc-CA(6)T-TTG(5)-TTA(5)-CCC(102)-TG(5)-NH₂;
 $(N \rightarrow C)$ Fethoc-A(6)TT-TG(5)T-TA(5)C-C(102)CT-G(5)-NH₂;
 $(N \rightarrow C)$ Fethoc-CA(6)T-CA(6)T-TTG(5)-TTA(5)-CCC(102)-TG(5)-NH₂;
 $(N \rightarrow C)$ Fethoc-A(5)TT-TG(5)T-TA(5)C-CC(102)T-GG(5)G-A(5)-NH₂;
 $(N \rightarrow C)$ Fethoc-A(6)TT-TG(5)T-TA(6)C-C(102)CT-GG(5)G-A(5)-NH₂; and,
 $(N \rightarrow C)$ Fethoc-A(6)TT-TG(5)T-TA(6)C-C(102)CT-G(5)G-NH₂;
 wherein,

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

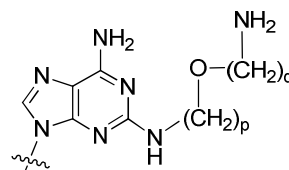
C(pOq), A(p), A(pOq), G(p), and G(pOq) are PNA monomers with an unnatural nucleobase represented by **Formula VI**, **Formula VII**, **Formula VIII**, **Formula IX**, and **Formula X**, respectively;



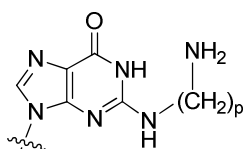
Formula VI



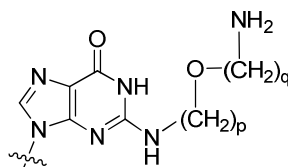
Formula VII



Formula VIII



Formula IX



Formula X

wherein,

p and q are integers; and,

the abbreviations for the N- and C-terminus substituents are specifically defined 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-"; "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-"; "-HEX-" for "6-amino-1-hexanoyl-", "FAM-" for "5, or 6-fluorescein-carbonyl- (isomeric mixture)", and "-NH₂" for non-substituted "-amino" group.

9. A peptide nucleic acid derivative of any one of claims 1-8, for use in the treatment of a disease or condition by down-regulating the expression of the human SNAP25 gene.

10. Use of a peptide nucleic acid derivative of any one of claims 1-8 in the manufacture of a medicament for the treatment of facial wrinkles.

11. The use of claim 10, wherein the medicament is for topical administration.

12. A method of cosmetically treating or reducing facial wrinkles of a subject comprising administering to the subject a peptide nucleic acid derivative of any one of claims 1-8.

13. The method of claim 12, wherein the peptide nucleic acid derivative is administered topically.

14. A peptide nucleic acid derivative of any one of claims 1-8, for use in therapy.

15. A peptide nucleic acid derivative of any one of claims 1-8, for use in the treatment of facial wrinkles.