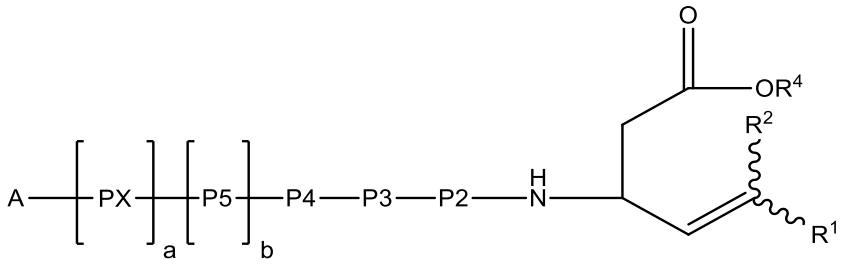
CLAIMS

1. A compound of Formula I:



I

in which

a is 0 or 1;

b is 0 or 1 provided that when b is 0, a is 0;

A is

1) H,

2) C_1-C_6 alkyl,

3) aryl,

4) heteroaryl,

5) heterocyclyl,

6) R^3-OC(O)-;

7) R^3-$S(O)_2$-; or

8) $PhCH_2OC(O)$-

P2, P3, P4, and, when present, P5 and PX, are any (D) or (L) amino acid residue;

the line "–" when located between P2, P3, P4, P5 or PX represents a peptide bond or a peptidomimetic bond;

the wavy line represents either cis or trans orientation of R^1 and R^2;

R^1 is

1) SO_2R^5,

2) SO_3R^5; or

3) SOR^5,

in which R^5 is C_1-C_6 alkyl, aryl, or heterocylyl**;**

R^2 is

1) H,

2) halogen,

3) haloaklyl,

4) C_1-C_6 alkyl, or

5) C_3-C_7 cycloalkyl;

R^3 is

1) C_1-C_6 alkyl,

2) aryl,

3) heteroaryl, or

4) heterocyclyl;

R^4 is

1) H, or

2) C_1–C_6 alkyl;

R^5 is

1) H,

2) C_1-C_6 alkyl,

3) C_2-C_6 alkene,

4) C_3-C_7 cycloalkyl,

5) aryl,

6) heteroaryl,

7) heterocyclyl, or

8) any optionally protected (D) or (L) amino acid residue;

R^6 is

1) any (D) or (L) amino acid residue,

2) C_1-C_6 alkyl,

3) C_3-C_7 cycloalkyl,

4) aryl,

5) heteroaryl, or

6) heterocyclyl,

in which the alkyl or the cycloalkyl are optionally substituted with one or more **R^{10}** substituents; and in which the aryl, heteroaryl or heterocyclyl are optionally substituted with one or more **R^{20}** substituents;

R^7 and R^8 are independently selected from:

1) H,

2) C_1–C_6 alkyl,

3) C_3–C_7 cycloalkyl,

4) haloalkyl,

5) aryl,

6) heteroaryl, or

7) heterocyclyl,

in which the alkyl and the cycloalkyl are optionally substituted with one or more R^{10} substituents, and the aryl, the heteroaryl and the heterocyclyl are optionally substituted with one or more R^{20} substituents;

R^9 is

1) H,

2) C_1-C_6 alkyl,

3) C_3-C_7 cycloalkyl,

4) aryl,

5) heteroaryl, or

6) heterocyclyl,

in which the alkyl or the cycloalkyl are optionally substituted with one or more **R^{10}** substituents; and in which the aryl, heteroaryl or heterocyclyl are optionally substituted with one or more **R^{20}** substituents;

R^{10} is independently selected from:

1) halogen,

2) C_1–C_6 alkyl,

3) C_3–C_7 cycloalkyl,

4) haloalkyl,

5) aryl,

6) heteroaryl,

7) heterocyclyl,

8) OR^9,

9) $S(O)_mR^9$,

10) NR^7R^8 ,

11) COR^9,

12) $C(O)OR^9$,

13) $OC(O)R^9$,

14) $SC(O)R^9$,

15) $CONR^7R^8$, or

16) $S(O)_2NR^7R^8$;

R^{20} is independently selected from:

1) halogen,

2) NO_2,

3) CN,

4) C_1-C_6 alkyl,

5) haloalkyl,

6) C_3-C_7 cycloalkyl,

7) OR^7,

8) NR^7R^8,

9) SR^7,

10) aryl,

11) heteroaryl,

12) heterocyclyl,

13) SO_2R^5,

14) SO_3R^5,

15) SOR^5,

16) $SONHR^5$,

17) SO_2NHR^5,

18) PO_3R^5,

19) $PO(OR^5)_2$,

20) $PO(OR^5)$,

21) COR^7,

22) CO_2R^7,

23) $S(O)_mR^7$,

24) $CONR^7R^8$, or

25) $S(O)_2NR^7R^8$,

in which the alkyl and the cycloalkyl are optionally substituted with one or more R^6 substituents; and in which the aryl, the heteroaryl, or the heterocyclyl are optionally substituted with one or more R^{30};

R^{30} is

1) NO_2,

2) C_2-C_6 alkene-$\mathbf{R^{20}}$,

3) SO_2R^5,

4) SOR^5,

5) $SONHR^5$,

6) SO_2NHR^5,

7) CN,

8) CO_2R^5,

9) COR^5,

10) PO_3R^5,

11) $PO(OR^5)_2$, or

12) $PO(OR^5)$;

or a pharmaceutically acceptable salt thereof.

2. A compound according to Claim 1, in which A is H.

3. A compound according to Claim 1, in which A is $PhCH_2OC(O)$-.

4. A compound according to Claim 1, in which R^4 is H, CH_3 or CH_3CH_2.

5. A compound according to Claim 1, in which R^4 is H.

6. A compound according to Claim 1, in which a and b are both 0.

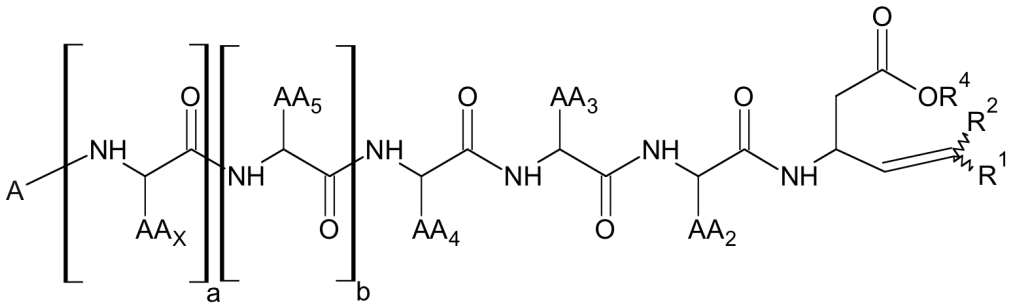
7. A compound according to Claim 1, in which a is 0 and b is 1.

8. A compound according to Claim 1, in which R^1 is in the trans configuration.

9. A compound according to Claim 1, in which R^2 is H or Cl.

10. A compound according to Claim 1, in which R^2 is Cl.

11. A compound of Formula IA



IA

in which

a is 0 or 1;

b is 0 or 1 provided that when b is 0, a is 0;

A is

1) H,

2) C_1-C_6 alkyl,

3) aryl,

4) heteroaryl,

5) heterocyclyl,

6) R^3-OC(O)-,

7) R^3-$S(O)_2$-, or

8) $PhCH_2OC(O)$-

AA_2 is an amino acid side chain of Val, Leu, Pro, Met, Ala, Thr, His, Ser, Lys, Trp or Ile, and in which the carbon bearing AA_2 is of the (R) or (S) configuration;

AA_3 is an amino acid side chain of Trp, Tyr, Ala, Asp, Gln, Glu, Phe, Ser, Thr, Val, Gly, Leu, His, or Ile; or AA_3 is phenylglycine, indanylglycine, or Ala-(2'-quinolyl), and in which the carbon bearing AA_3 is of the (R) or (S) configuration;

AA_4 is an amino acid side chain of Asp, Ile, Leu, Glu, Ala, Val, Tyr, Trp, Phe, or Pro, and in which the carbon bearing AA_4 is of the (R) or (S) configuration;

AA_5, when present, is an amino acid side chain of Val or Leu, and in which the carbon bearing AA_5 is of the (R) or (S) configuration;

AA_X, when present, is an amino acid side chain of any D or L amino acid residue and in which the carbon bearing AA_x is of the (R) or (S) configuration;

the wavy line represents either cis or trans orientation of R^1 and R^2;

R^1 is

1) SO_2R^5,

2) SO_3R^5; or

3) SOR^5,

in which R^5 is C_1-C_6 alkyl, aryl, or heterocylyl;

R^2 is

1) H,

2) halogen,

3) haloaklyl,

4) C_1-C_6 alkyl, or

5) C_3-C_7 cycloalkyl;

R^3 is

1) C_1-C_6 alkyl,

2) aryl,

3) heteroaryl, or

4) heterocyclyl;

R^4 is

1) H, or

2) C_1–C_6 alkyl;

R^5 is

1) H,

2) C_1-C_6 alkyl,

3) C_2-C_6 alkene,

4) C_3-C_7 cycloalkyl,

5) aryl,

6) heteroaryl,

7) heterocyclyl, or

8) any optionally protected (D) or (L) amino acid residue;

R^6 is

1) any (D) or (L) amino acid residue,

2) C_1-C_6 alkyl,

3) C_3-C_7 cycloalkyl,

4) aryl,

5) heteroaryl, or

6) heterocyclyl,

in which the alkyl or the cycloalkyl are optionally substituted with one or more **R^{10}** substituents; and in which the aryl, heteroaryl or heterocyclyl are optionally substituted with one or more **R^{20}** substituents;

R^7 and R^8 are independently selected from:

1) H,

2) C_1–C_6 alkyl,

3) C_3–C_7 cycloalkyl,

4) haloalkyl,

5) aryl,

6) heteroaryl, or

7) heterocyclyl,

in which the alkyl and the cycloalkyl are optionally substituted with one or more R^{10} substituents, and the aryl, the heteroaryl and the heterocyclyl are optionally substituted with one or more R^{20} substituents;

R^9 is

1) H,

2) C_1-C_6 alkyl,

3) C_3-C_7 cycloalkyl,

4) aryl,

5) heteroaryl, or

6) heterocyclyl,

in which the alkyl or the cycloalkyl are optionally substituted with one or more $\mathbf{R^{10}}$ substituents; and in which the aryl, heteroaryl or heterocyclyl are optionally substituted with one or more $\mathbf{R^{20}}$ substituents;

R^{10} is independently selected from:

1) halogen,

2) C_1–C_6 alkyl,

3) C_3–C_7 cycloalkyl,

4) haloalkyl,

5) aryl,

6) heteroaryl,

7) heterocyclyl,

8) OR^9,

9) $S(O)_mR^9$,

10) NR^7R^8 ,

11) COR^9,

12) $C(O)OR^9$,

13) $OC(O)R^9$,

14) $SC(O)R^9$,

15) $CONR^7R^8$, or

16) $S(O)_2NR^7R^8$;

R^{20} is independently selected from:

1) halogen,

2) NO_2,

3) CN,

4) C_1-C_6 alkyl,

5) haloalkyl,

6) C_3-C_7 cycloalkyl,

7) OR^7,

8) NR^7R^8,

9) SR^7,

10) aryl,

11) heteroaryl,

12) heterocyclyl,

13) SO_2R^5,

14) SO_3R^5,

15) SOR^5,

16) $SONHR^5$,

17) SO_2NHR^5,

18) PO_3R^5,

19) $PO(OR^5)_2$,

20) $PO(OR^5)$,

21) COR^7,

22) CO_2R^7,

23) $S(O)_mR^7$,

24) $CONR^7R^8$, or

25) $S(O)_2NR^7R^8$,

in which the alkyl and the cycloalkyl are optionally substituted with one or more R^6 substituents; and in which the aryl, the heteroaryl, or the heterocyclyl are optionally substituted with one or more R^{30}**;**

R^{30} is

1) NO_2,

2) C_2-C_6 alkene-$\mathbf{R^{20}}$,

3) SO_2R^5,

4) SOR^5,

5) $SONHR^5$,

6) SO_2NHR^5,

7) CN,

8) CO_2R^5,

9) COR^5,

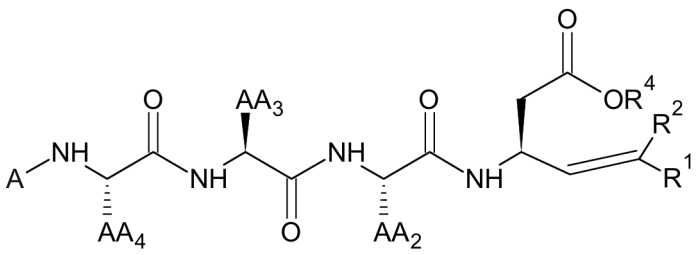
10) PO_3R^5,

11) $PO(OR^5)_2$, or

12) $PO(OR^5)$;

or a pharmaceutically acceptable salt, or the compound is labeled with a detectable label or an affinity tag thereof.

12. A compound according to Claim 11, which conforms to Formula IIA



IIA

in which

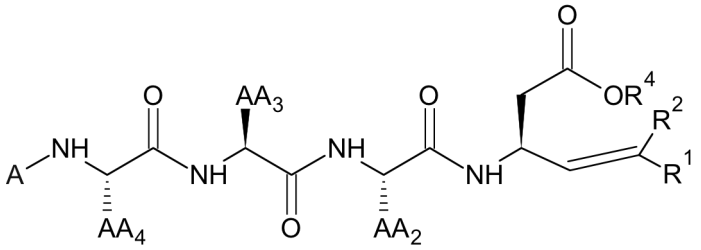
AA_2 is the amino acid side chain of Val, Leu, Pro, Met, Ala, Thr, His, Ser or Lys;

AA_3 is the amino acid side chain of Trp, Tyr, Ala, Asp, Gln, Phe, Ser, Thr, Val, Gly, Leu, Glu; or AA_3 is phenylglycine, indanylglycine, or Ala-(2'-quinolyl);

AA_4 is the amino acid side chain of Asp;

and in which A, R^1, R^2 and R^4 are as defined in Claim 11.

13. A compound according to Claim 11, which conforms to Formula IIA



IIA

in which

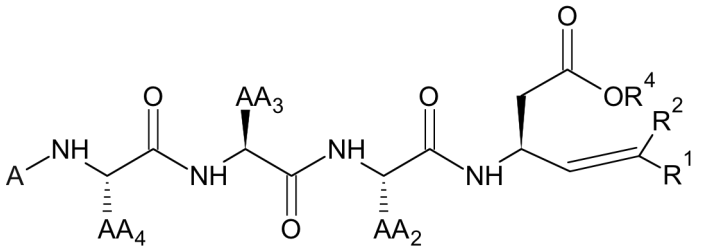
AA_2 is the amino acid side chain of Thr, His, Val, Trp, Ile or Ala;

AA_3 is the amino acid side chain of Glu or AA_3 is Ala-(2'-quinolyl);

AA_4 is the amino acid side chain of Ile, Leu, Glu, Asp, Ala, Pro or Val;

and in which A, R^1, R^2 and R^4 are as defined in Claim 11.

14. A compound according to Claim 11, which includes compounds of Formula IIA



IIA

in which

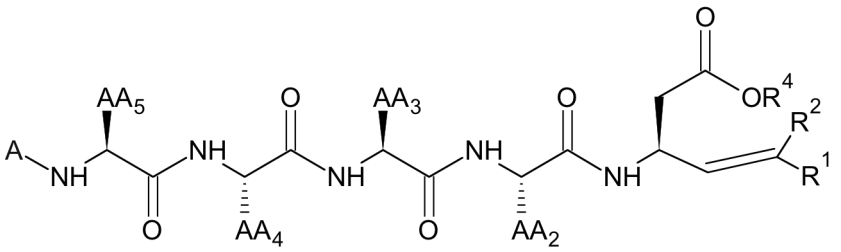
AA_2 is the amino acid side chain of Ile, Val, Ala, Thr or His;

AA_3 is the amino acid side chain of Glu, Gln, Asp, Ala, Gly, Thr, Val, Trp; or AA_3 is phenylglycine or indanylglycine;

AA_4 is the amino acid side chain of Val, Tyr, Trp, Phe or Asp;

and in which A, R^1, R^2 and R^4 are as defined in Claim 11.

15. A compound according to Claim 11, which includes compounds of Formula IIIA



IIIA

in which

AA_2 is the amino acid side chain of Ala, Ser, Lys or Val;

AA_3 is the amino acid side chain of Val, Glu, Thr, or Gln;

AA_4 is the amino acid side chain of Asp, or Leu;

AA_5 is the amino acid side chain of Val or Leu;

and in which A, R^1, R^2 and R^4 are as defined in Claim 11.

16. An Intermediate compound selected from the group consisting of: compound #4, compound #12, compound #16 and compound #20.

17. A pharmaceutical composition comprising a compound according to Claim 1 or 11 and one or more pharmaceutically acceptable carriers.

18. A pharmaceutical composition according to Claim 17, in which the pharmaceutically acceptable salt is one that allows the compound to penetrate cells.

19. A pharmaceutical composition for treating, or reducing the risk of developing a disease in a subject in need thereof, comprising an effective amount of a compound according to any of Claims 1 to 15.

20. Use of a compound according to any of Claims 1 to 15 for the manufacture of a medication for preventing and/or treating of excessive apoptosis or an apoptosis-mediated disease in a subject in need thereof.

21. Use of a compound according to any of Claims 1 to 15 for the manufacture of a medication for preventing and/or treating of Huntington's disease or Alzheimer's disease in a subject in need thereof.

22. A compound according to Claim 1, in which P4 is a natural alpha amino acid.

23. Use according to Claim 20 or 21, in which the disease is Alzheimer's disease.