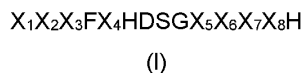


## Claims

1. A cyclic peptide comprising an amino acid sequence having the structure of formula (I) and variants thereof:



wherein:

- X<sub>1</sub> is absent or any amino acid; and
- X<sub>2</sub> is alanine or cysteine;
- X<sub>3</sub> is glutamic acid or cysteine;
- X<sub>4</sub> is arginine or cysteine;
- X<sub>5</sub> is tyrosine or cysteine;
- X<sub>6</sub> is glutamic acid or cysteine;
- X<sub>7</sub> is valine or cysteine; and
- X<sub>8</sub> is histidine or cysteine

wherein only one of X<sub>1</sub>, X<sub>2</sub>, X<sub>3</sub> and X<sub>4</sub> is cysteine and wherein only one of X<sub>5</sub>, X<sub>6</sub>, X<sub>7</sub> and X<sub>8</sub> is cysteine and the peptide is cyclized via the cysteine residue position at 1, 2, 3, or 5 and the cysteine residue at position 10, 11, 12 or 13.

2. A cyclic peptide according to claim 1 and variants thereof wherein:

X<sub>1</sub> is absence or any amino acid; and

wherein:

- a) X<sub>1</sub> is cysteine, X<sub>2</sub> is alanine, X<sub>3</sub> is glutamic acid, X<sub>4</sub> is arginine, X<sub>5</sub> is tyrosine, X<sub>6</sub> is glutamic acid, X<sub>7</sub> is histidine and X<sub>8</sub> is cysteine;
- b) X<sub>2</sub> is alanine, X<sub>3</sub> is cysteine, X<sub>4</sub> is arginine, X<sub>5</sub> is tyrosine, X<sub>6</sub> is glutamic acid, X<sub>7</sub> is cysteine and X<sub>8</sub> is histidine;
- c) X<sub>2</sub> is cysteine, X<sub>3</sub> is glutamic acid, X<sub>4</sub> is arginine, X<sub>5</sub> is tyrosine, X<sub>6</sub> is glutamic acid, X<sub>7</sub> is cysteine and X<sub>8</sub> is histidine;
- d) X<sub>2</sub> is cysteine, X<sub>3</sub> is glutamic acid, X<sub>4</sub> is arginine, X<sub>5</sub> is cysteine, X<sub>6</sub> is glutamic acid, X<sub>7</sub> is valine and X<sub>8</sub> is histidine;
- e) X<sub>2</sub> is cysteine, X<sub>3</sub> is glutamic acid, X<sub>4</sub> is arginine, X<sub>5</sub> is tyrosine, X<sub>6</sub> is glutamic acid, X<sub>7</sub> is valine and X<sub>8</sub> is cysteine;
- f) X<sub>2</sub> is cysteine, X<sub>3</sub> is glutamic acid, X<sub>4</sub> is arginine, X<sub>5</sub> is tyrosine, X<sub>6</sub> is cysteine, X<sub>7</sub> is valine and X<sub>8</sub> is histidine;
- g) X<sub>2</sub> is alanine, X<sub>3</sub> is cysteine, X<sub>4</sub> is arginine, X<sub>5</sub> is tyrosine, X<sub>6</sub> is cysteine, X<sub>7</sub> is valine and X<sub>8</sub> is histidine;
- h) X<sub>2</sub> is alanine, X<sub>3</sub> is glutamic acid, X<sub>4</sub> is cysteine, X<sub>5</sub> is tyrosine, X<sub>6</sub> is glutamic acid, X<sub>7</sub> is cysteine and X<sub>8</sub> is histidine;
- i) X<sub>2</sub> is alanine, X<sub>3</sub> is cysteine, X<sub>4</sub> is arginine, X<sub>5</sub> is cysteine, X<sub>6</sub> is glutamic acid, X<sub>7</sub> is histidine and X<sub>8</sub> is histidine; or

- j)  $X_2$  is alanine,  $X_3$  is cysteine,  $X_4$  is arginine,  $X_5$  is tyrosine,  $X_6$  is glutamic acid,  $X_7$  is histidine and  $X_8$  is cysteine;  
wherein the peptide is cyclized via the two cysteine residues.
3. A cyclic peptide according to claim 1 or 2 comprising an amino acid sequence or variant thereof selected from:
- a) DACFRHDSGYECHH wherein the peptide is a cyclized via the cysteine residues located at positions 3 and 12;
  - b) DACFRHDSGYEVCH wherein the peptide is a cyclized via the cysteine residues located at positions 3 and 13.
  - c) CAECFRHDSGYEVCH wherein the peptide is a cyclized via the cysteine residues located at positions 1 and 13;
  - d) DCEFRHDSGYECHH wherein the peptide is a cyclized via the cysteine residues located at positions 2 and 12;
  - e) DCEFRHDSGCEVHH wherein the peptide is a cyclized via the cysteine residues located at positions 2 and 10;
  - f) DCEFRHDSGYEVCH wherein the peptide is a cyclized via the cysteine residues located at positions 2 and 13;
  - g) DCEFRHDSGYCVHH wherein the peptide is a cyclized via the cysteine residues located at positions 2 and 11;
  - h) DACFRHDSGYCVHH wherein the peptide is a cyclized via the cysteine residues located at positions 3 and 11;
  - i) DAEFCHDSGYECHH wherein the peptide is a cyclized via the cysteine residues located at positions 5 and 12; and
  - j) DACFRHDSGCEVHH wherein the peptide is a cyclized via the cysteine residues located at positions 3 and 10.
4. A cyclic peptide according to any one of claims 1 or 2 wherein  $X_1$  is proline or aspartic acid.
5. A cyclic peptide according to any one of claims 1 to 4 wherein the peptide is cyclized via a bridge connecting the two cysteine residues.
6. A cyclic peptide according to any one of claims 1 to 5 wherein the peptide is cyclized via a bridge having the formula -S-S- or -S-CH<sub>2</sub>-S- between the two cysteine residues.
7. A cyclic peptide according to any one of claims 1 to 6 comprising:
- a) the amino acid sequence DACFRHDSGYECHH or variant thereof wherein the peptide is cyclized via the cysteine residues located at positions 3 and 12; or
  - b) the amino acid sequence DACFRHDSGYEVCH or variant thereof wherein the peptide is cyclized via the cysteine residues located at positions 3 and 13; or

- c) . the amino acid sequence CAEFRHDSGYEVCH or variant thereof wherein the peptide is a cyclized via the cysteine residues located at positions 1 and 13
8. A cyclic peptide according to any one of claims 1 to 7 comprising:
- a) the amino acid sequence DACFRHDSGYECHH or variant thereof wherein the peptide is a cyclic peptide formed by the bridge having the formula -S-CH<sub>2</sub>-S- between the two cysteine residues at positions 3 and 12; or
  - b) the amino acid sequence DACFRHDSGYEVCH or variant thereof wherein the peptide is a cyclic peptide formed by the bridge having the formula -S-CH<sub>2</sub>-S- between the two cysteine residues at positions 3 and 13; or
  - c) the amino acid sequence CAEFRHDSGYEVCH or variant thereof wherein the peptide is a cyclic peptide formed by the bridge having the formula -S-CH<sub>2</sub>-S- between the two cysteine residues at positions 1 and 13.
9. A cyclic peptide according to any one of claims 1 to 8 consisting of:
- a) the amino acid sequence DACFRHDSGYECHH or variant thereof wherein the peptide is a cyclic peptide formed by the bridge having the formula -S-CH<sub>2</sub>-S- between the two cysteine residues at positions 3 and 12; or
  - b) the amino acid sequence DACFRHDSGYEVCH or variant thereof wherein the peptide is a cyclic peptide formed by the bridge having the formula -S-CH<sub>2</sub>-S- between the two cysteine residues at positions 3 and 13; or
  - c) the amino acid sequence CAEFRHDSGYEVCH or variant thereof wherein the peptide is a cyclic peptide formed by the bridge having the formula -S-CH<sub>2</sub>-S- between the two cysteine residues at positions 1 and 13.
10. A cyclic peptide comprising an amino acid sequence having at least 85% sequence identity with:
- a) the amino acid sequence DACFRHDSGYECHH or variant thereof wherein the peptide comprises the cysteine residues at positions 3 and 12 via which the peptide is cyclised and the phenylalanine residue at position 4; or
  - b) the amino acid sequence DACFRHDSGYEVCH or variant thereof wherein the peptide comprises the cysteine residues at positions 3 and 13 via which the peptide is cyclised and the phenylalanine residue at position 4; or
  - c) the amino acid sequence CAEFRHDSGYEVCH or variant thereof wherein the peptide comprises the cysteine residues at positions 1 and 13 via which the peptide is cyclised and the phenylalanine residue at position 4.
11. A cyclic peptide according to any one of claims 1 to 10 comprising the amino acid sequence DACFRHDSGYECHH or variant thereof wherein the peptide is a cyclic peptide formed by the bridge having the formula -S-CH<sub>2</sub>-S- between the cysteine residues at positions 3 and 12.

12. A pharmaceutical composition comprising the cyclic peptide according to any one of claims 1 to 11 and a pharmaceutically acceptable carrier.
13. A pharmaceutical composition according to claim 12 further comprising an adjuvant.
14. A method of treating a neurodegenerative disease comprising administering a cyclic peptide according to any one of claims 1 to 11 or a composition according to any one of claims 12 or 13 to an individual in need thereof.
15. A method according to claim 14 wherein the neurodegenerative disease is Alzheimer's disease.
16. A method for inducing an immune response in a subject comprising administering a cyclic peptide according to any one of claims 1 to 11 or a composition according to any one of claims 12 or 13 to the subject
17. A method according to claim 16 wherein the immune response produces antibodies against amyloid beta in the form of low molecular weight amyloid-beta oligomers.
18. A cyclic polypeptide according to any one of claims 1 to 11 to for use in treating a neurodegenerative disease.
19. A cyclic peptide for use according to claim 18 wherein the neurodegenerative disease is Alzheimer's disease.
20. A method of producing a cyclic peptide according to any one of claims 1 to 11 comprising the steps of:
  - (a) synthesizing a linear peptide comprising the sequence of the peptide as defined in any one of claims 1 to 11; and
  - (b) cyclizing the linear peptide via the cysteine residue to obtain the cyclic peptide according to any one of claims 1 to 11.
21. A method for the generating an antibody that specifically recognizes low molecular weight oligomers of amyloid beta comprising:
  - (a) immunizing an animal with a cyclic peptide or variant thereof according to any of claims 1-11; and
  - (b) obtaining the antibodies generated by the immunization in step (a).