

CLAIMS

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



(I)

5 in which:

X_1 is absent or any amino acid; and

X_2 is alanine or cysteine;

X_3 is glutamic acid or cysteine;

X_4 is arginine;

10 X_5 is tyrosine or cysteine;

X_6 is glutamic acid;

X_7 is valine or cysteine; and

X_8 is histidine or cysteine

15 in which only one of X_1 , X_2 and X_3 is cysteine and in which only one of X_5 , X_7 and X_8 is cysteine and the peptide is cyclized via the cysteine residue position at 1, 2 or 3, and the cysteine residue at position 10, 12 or 13.

2. A cyclic peptide according to Claim 1, in which:

X_1 is absent or any amino acid; and

in which:

20 (a) X_1 is cysteine, X_2 is alanine, X_3 is glutamic acid, X_4 is arginine, X_5 is tyrosine, X_6 is glutamic acid, X_7 is valine and X_8 is cysteine;

(b) X_2 is alanine, X_3 is cysteine, X_4 is arginine, X_5 is tyrosine, X_6 is glutamic acid, X_7 is cysteine and X_8 is histidine;

25 (c) X_2 is cysteine, X_3 is glutamic acid, X_4 is arginine, X_5 is tyrosine, X_6 is glutamic acid, X_7 is cysteine and X_8 is histidine;

(d) X₂ is cysteine, X₃ is glutamic acid, X₄ is arginine, X₅ is cysteine, X₆ is glutamic acid, X₇ is valine and X₈ is histidine;

(e) X₂ is cysteine, X₃ is glutamic acid, X₄ is arginine, X₅ is tyrosine, X₆ is glutamic acid, X₇ is valine and X₈ is cysteine;

5 (f) X₂ is alanine, X₃ is cysteine, X₄ is arginine, X₅ is cysteine, X₆ is glutamic acid, X₇ is valine and X₈ is histidine; or

(g) X₂ is alanine, X₃ is cysteine, X₄ is arginine, X₅ is tyrosine, X₆ is glutamic acid, X₇ is valine and X₈ is cysteine;

in which the peptide is cyclized via the two cysteine residues.

10 3. A cyclic peptide according to Claim 1 or 2 comprising an amino acid sequence selected from:

(a) DACFRHDSGYECHH in which the peptide is a cyclized via the cysteine residues located at positions 3 and 12;

15 (b) DACFRHDSGYEVCH in which the peptide is a cyclized via the cysteine residues located at positions 3 and 13.

(c) CAEFRHDSGYEVCH in which the peptide is a cyclized via the cysteine residues located at positions 1 and 13;

d) DCEFRHDSGYECHH in which the peptide is a cyclized via the cysteine residues located at positions 2 and 12;

20 (e) DCEFRHDSGCEVHH in which the peptide is a cyclized via the cysteine residues located at positions 2 and 10;

(f) DCEFRHDSGYEVCH in which the peptide is a cyclized via the cysteine residues located at positions 2 and 13; and

25 (g) DACFRHDSGCEVHH in which the peptide is a cyclized via the cysteine residues located at positions 3 and 10.

4. A cyclic peptide according to Claims 1 or 2, in which X₁ is proline or aspartic acid.

5. A cyclic peptide according to any preceding claim, in which the peptide is cyclized via a bridge connecting the two cysteine residues.

6. A cyclic peptide according to any preceding claim, in which the peptide is cyclized via a bridge having the formula -S-S- or -S-CH₂-S- between the two cysteine residues.
7. A cyclic peptide according to any preceding claim, comprising:
 - (a) the amino acid sequence DACFRHDSGYECHH in which the peptide is cyclized via the cysteine residues located at positions 3 and 12; or
 - (b) the amino acid sequence DACFRHDSGYEVCH in which the peptide is cyclized via the cysteine residues located at positions 3 and 13; or
 - (c) the amino acid sequence CAEFRHDSGYEVCH in which the peptide is a cyclized via the cysteine residues located at positions 1 and 13
8. A cyclic peptide according to any preceding claim, comprising:
 - (a) the amino acid sequence DACFRHDSGYECHH in which the peptide is a cyclic peptide formed by the bridge having the formula -S-CH₂-S- between the two cysteine residues at positions 3 and 12; or
 - (b) the amino acid sequence DACFRHDSGYEVCH in which the peptide is a cyclic peptide formed by the bridge having the formula -S-CH₂-S- between the two cysteine residues at positions 3 and 13; or
 - (c) the amino acid sequence CAEFRHDSGYEVCH in which the peptide is a cyclic peptide formed by the bridge having the formula -S-CH₂-S- between the two cysteine residues at positions 1 and 13.
9. A cyclic peptide according to any preceding claim, consisting of:
 - (a) the amino acid sequence DACFRHDSGYECHH in which the peptide is a cyclic peptide formed by the bridge having the formula -S-CH₂-S- between the two cysteine residues at positions 3 and 12; or
 - (b) the amino acid sequence DACFRHDSGYEVCH in which the peptide is a cyclic peptide formed by the bridge having the formula -S-CH₂-S- between the two cysteine residues at positions 3 and 13; or
 - (c) the amino acid sequence CAEFRHDSGYEVCH in which the peptide is a cyclic peptide formed by the bridge having the formula -S-CH₂-S- between the two cysteine residues at positions 1 and 13.

10. A cyclic peptide according to any preceding claim, comprising the amino acid sequence DACFRHDSGYECHH in which the peptide is a cyclic peptide formed by the bridge having the formula -S-CH₂-S- between the cysteine residues at positions 3 and 12.
11. A pharmaceutical composition comprising a cyclic peptide according to any preceding
5 claim and a pharmaceutically acceptable carrier.
12. A pharmaceutical composition according to Claim 11, further comprising an adjuvant.
13. Use of a cyclic peptide according to any of Claims 1 to 10 or a composition according to Claim 11 or 12 in the preparation of a medicament for the treatment of Alzheimer's disease.
14. Use of a cyclic peptide according to any of Claims 1 to 10 or a composition according to
10 Claim 11 or 12 in the preparation of a medicament for inducing an immune response in a subject.
15. Use according to Claim 14, in which the immune response produces antibodies against amyloid beta in the form of low molecular weight amyloid-beta oligomers.
16. A cyclic polypeptide according to any of Claims 1 to 10 for use in treating Alzheimer's
15 disease.
17. A method of producing a cyclic peptide according to any of Claims 1 to 10, comprising the steps of:
 - (a) synthesizing a linear peptide comprising the sequence of a peptide as defined in any of Claims 1 to 10; and
 - 20 (b) cyclizing the linear peptide via the cysteine residue to obtain a cyclic peptide according to any of Claims 1 to 10.
18. A method for generating an antibody that specifically recognizes low molecular weight oligomers of amyloid beta comprising:
 - 25 (a) immunizing an animal with a cyclic peptide according to any of Claims 1 to 10; and
 - (b) obtaining the antibodies generated by the immunization in step (a).