CLAIMS

1. An Aβ peptide analogue comprising:

an N-terminal domain corresponding to positions 1-18 of SEQ ID NO:1;

a middle domain corresponding to positions 19-24 of SEQ ID NO:1; and

a C-terminal domain corresponding to positions 25-42 of SEQ ID NO:1, and including a modification comprising:

deletion of 1-13 amino acids; or

at least one of:

a C-terminus modification comprising an amide, N-alkyl amide, cysteamide, ester, aldehyde, hydrazide or hydroxamic acid; and

a C-terminal domain substitution comprising an amino acid, an amino acid analogue, or both.

2. The Aβ peptide analogue of claim 1, wherein the N-terminal domain has at least 85% identity to positions 1-18 of SEQ ID NO:1

3. The Aβ peptide analogue of claim 1, wherein the middle domain has at least 85% identity to positions 19-24 of SEQ ID NO:1.

4. The Aβ peptide analogue of claim 1, wherein the C-terminal domain substitution comprises one or more prolines, one or more charged amino acids, one or more polar amino acids, or any combination thereof.

5. The Aβ peptide analogue of claim 1, wherein the C-terminal domain substitution comprises one or more amino acid analogues selected from 3-hydroxyproline, 4-hydroxyproline, selenocysteine, pyroglutamic acid, carboxyglutamic acid, octenyl alanine, pyrrolysine, palmitoyl aspartate, D-amino acids including D-proline, β-amino acids, γ-amino acids, homo-amino acids, β-homo-amino acids, α-methyl amino acids, N-methyl amino acids, N-ethyl amino acids, N-alkylated amino acid derivatives (preferably with 1, 2 or 3 carbons in the alkyl moiety), peptoid substituents, pyruvic acid derivatives, branched-

chain amino acid derivatives, nitro amino acid derivatives, halogenated amino acid derivatives, ring-substituted amino acid derivatives, aromatic amino acid derivatives, linear core amino acids, hydroxylated amino acid derivatives, cyclic amino acids, bicyclic amino acids, 3-amino-3-aryl-propionic acids, 3-amino-4-aryl-butyric acids, amino acids with aromatic spacers, alicyclic amino acids, α-phenylglycine derivatives.

6. The Aβ peptide analogue of claim 1, wherein the Aβ peptide analogue comprises an increased half-life in cerebrospinal fluid (CSF) relative to wild type Aβ42 peptide, wherein the half-life is at least about 10 min, at least about 20 min, at least about 30 min, at least about 40 min, at least about 50 min, at least about 1 hours, at least about 5 hours, at least about 10 hours, at least about 1 day, at least about 10 days, at least about 60 days, at least about 10 weeks, or at least about 50 weeks.

7. The Aβ peptide analogue of claim 1, wherein the Aβ peptide analogue comprises an increased protease resistance relative to wild type Aβ42 peptide.

8. The Aβ peptide analogue of claim 1, wherein the Aβ peptide analogue has a decreased propensity for beta-sheet stacking and amyloid formation relative to wild type Aβ42 peptide.

9. The Aβ peptide analogue of claim 1, wherein the Aβ peptide analogue comprises increased solubility in a liquid medium relative to wild type Aβ42 peptide, preferably wherein the solubility is at least about 1 mg/ml, more preferably at least about 5 mg/ml and most preferably at least about 50 mg/ml.

10. The Aβ peptide analogue of claim 1, wherein the Aβ peptide analogue performs a function of wild type Aβ42 peptide to at least 50% of the level performed by wild type Aβ42 peptide, preferably wherein the function comprises inducing α7 nicotinic acetylcholine receptor (α7nAChR) mediated Ca^{2+} influx.

11. The Aβ peptide analogue of claim 1, wherein the Aβ peptide analogue is selected from the group consisting of SEQ ID NOS:190-1660.

12. The Aβ peptide analogue of claim 1, comprising (N-(4-aminobutyl)glycine) at position 34, position 35, or both, preferably wherein the Aβ peptide analogue is selected from the group consisting of SEQ ID NOS:203, 417, 623, 829, 1035, 1241, 1447 and 1649.

13. The Aβ peptide analogue of claim 1, comprising (N-(2-carboxyethyl)glycine) at position 34, position 35, or both, preferably wherein the Aβ peptide analogue is selected from the group consisting of SEQ ID NOS:204, 418, 624, 830, 1034, 1242, 1448 and 1650.

14. The Aβ peptide analogue of claim 1, wherein the Aβ peptide analogue is selected from:
the group consisting of SEQ ID NOS:300, 514, 720, 926, 1132, 1338 and 1544;
the group consisting of SEQ ID NOS:402, 616, 822, 1028, 1234, 1440 and 1646;
the group consisting of SEQ ID NOS:301, 515, 721, 927, 1133, 1339 and 1545;
the group consisting of SEQ ID NOS:302, 516, 722, 928, 1134, 1340 and 1546;
the group consisting of SEQ ID NOS:303, 517, 723, 929, 1135, 1341 and 1547;
the group consisting of SEQ ID NOS:304, 518, 724, 930, 1136, 1342 and 1548;
the group consisting of SEQ ID NOS:305, 519, 725, 931, 1137, 1343 and 1549;
the group consisting of SEQ ID NOS:306, 520, 726, 932, 1138, 1344 and 1550;
the group consisting of SEQ ID NOS:307, 521, 727, 933, 1139, 1345 and 1551;
the group consisting of SEQ ID NOS:308, 522, 728, 934, 1140, 1346 and 1552;
the group consisting of SEQ ID NOS:309, 523, 729, 935, 1141, 1347 and 1553;
the group consisting of SEQ ID NOS:310, 524, 730, 936, 1142, 1348 and 1554;
the group consisting of SEQ ID NOS:311, 525, 731, 937, 1143, 1349 and 1555; or
the group consisting of SEQ ID NOS:400, 614, 820, 1026, 1232, 1438 and 1644.

15. An Aβ peptide analogue comprising:
an N-terminal domain corresponding to positions 1-18 of SEQ ID NO:1;
a middle domain corresponding to positions 19-24 of SEQ ID NO:1; and

a C-terminal domain corresponding to positions 25-42 of SEQ ID NO:1, and including a modification comprising:

deletion of 1-13 amino acids; or

at least one of:

a C-terminus modification comprising an amide, N-alkyl amide, cysteamide, ester, aldehyde, hydrazide or hydroxamic acid; and

a C-terminal domain substitution comprising an amino acid, an amino acid analogue, or both,

for use in therapy.