

WHAT IS CLAIMED IS:

1. A polypeptide comprising a first peptide comprising 3-10 amino acids from residues 1-10 of SEQ ID NO:01 linked to a second peptide comprising 3-13 amino acids from residues 244-400 of SEQ ID NO:02.
2. The polypeptide of claim 1, wherein the second peptide is from the microtubule binding region (MTBR) of tau (residues 244-372 of SEQ ID NO:02).
3. The polypeptide of claim 1, wherein the first peptide is N-terminal to the second peptide.
4. The polypeptide of claim 1, wherein the first peptide is C-terminal to the second peptide.
5. The polypeptide of any of claims 1 to 4, wherein:
 - (a) the first peptide comprises an amino acid sequence selected from the group consisting of
 - DAEFRHDSGY (SEQ ID NO:03),
 - DAEFRHDSG (SEQ ID NO:04),
 - DAEFRHDS (SEQ ID NO:05),
 - DAEFRHD (SEQ ID NO:06),
 - DAEFRH (SEQ ID NO:07),
 - DAEFR (SEQ ID NO:08),
 - DAEF (SEQ ID NO:09),
 - DAE (SEQ ID NO:10),
 - AEFRHDSGY (SEQ ID NO:11),
 - AEFRHDSG (SEQ ID NO:12),
 - AEFRHDS (SEQ ID NO:13),
 - AEFRHD (SEQ ID NO:14),
 - AEFRH (SEQ ID NO:15),
 - AEFR (SEQ ID NO:16),
 - AEF (SEQ ID NO:17),
 - EFRHDSGY (SEQ ID NO:18),

EFRHDSG (SEQ ID NO:19),
 EFRHDS (SEQ ID NO:20),
 EFRHD (SEQ ID NO:21),
 EFRH (SEQ ID NO:22),
 EFR (SEQ ID NO:23),
 FRHDSGY (SEQ ID NO:24),
 FRHDSG (SEQ ID NO:25),
 FRHDS (SEQ ID NO:26),
 FRHD (SEQ ID NO:27),
 FRH (SEQ ID NO:28),
 RHDSGY (SEQ ID NO:29),
 RHDSG (SEQ ID NO:30),
 RHDS (SEQ ID NO:31),
 RHD (SEQ ID NO:32),
 HDSGY (SEQ ID NO:33),
 HDSG (SEQ ID NO:34),
 HDS (SEQ ID NO:35),
 DSGY (SEQ ID NO:36),
 DSG (SEQ ID NO:37), and
 SGY (SEQ ID NO:38); and

(b) the second peptide comprises an amino acid sequence selected from the group consisting of

QIVYKPV (SEQ ID NO:39),
 QIVYKP (SEQ ID NO:40),
 QIVYKSV (SEQ ID NO:41),
 EIVYKSV (SEQ ID NO:42),
 QIVYKS (SEQ ID NO:83),
 EIVYKSP (SEQ ID NO:43),
 EIVYKS (SEQ ID NO:84),
 EIVYKPV (SEQ ID NO:44),
 EIVYKP (SEQ ID NO:85),
 IVYKSPV (SEQ ID NO:45),
 IVYK (SEQ ID NO:46),
 CNIKHVPG (SEQ ID NO:86),

CNIKHVP (SEQ ID NO:47),
 NIKHVP (SEQ ID NO:48),
 HVPGGG (SEQ ID NO:49),
 HVPGG (SEQ ID NO:50),
 HKPGGG (SEQ ID NO:51),
 HKPGG (SEQ ID NO:52),
 KHVPGGG (SEQ ID NO:53),
 KHVPGG (SEQ ID NO:54),
 HQPGGG (SEQ ID NO:55),
 HQPGG (SEQ ID NO:56),
 VKSKIGST (SEQ ID NO:801),
 SKIGSTEN (SEQ ID NO:817),
 TENLKHQP (SEQ ID NO:695),
 ENLKHQPG (SEQ ID NO:689),
 SKIGSTDNIKH (SEQ ID NO:985),
 SKIGSKDNIKH (SEQ ID NO:986),
 SKIGSLDNIKH (SEQ ID NO:988), and
 SEQ ID NO:146-996.

6. The polypeptide of any of claims 1 to 5, wherein the first peptide and second peptide are linked by a cleavable linker.
7. The polypeptide of claim 6, wherein the cleavable linker comprises an amino acid sequence.
8. The polypeptide of claim 7, wherein the amino acid sequence comprises arginine-arginine (Arg-Arg), arginine-valine-arginine-arginine (Arg-Val-Arg-Arg (SEQ ID NO:69)), valine-citrulline (Val-Cit), valine-arginine (Val-Arg), valine-lysine (Val-Lys), valine-alanine (Val-Ala), phenylalanine-lysine (Phe-Lys), glycine-alanine-glycine-alanine (Gly-Ala-Gly-Ala; SEQ ID NO:80), alanine-glycine-alanine-glycine (Ala-Gly-Ala-Gly; SEQ ID NO:81), or lysine-glycine-lysine-glycine (Lys-Gly-Lys-Gly; SEQ ID NO:82).

9. The polypeptide of any of claims 1 to 8, further comprising a linker to a carrier at either a C-terminal portion of the polypeptide, or a N-terminal portion of the polypeptide.
10. The polypeptide of claim 9, wherein the linker comprises an amino acid sequence selected from the group consisting of GG, GGG, AA, AAA, KK, KKK, SS, SSS, GAGA (SEQ ID NO:80), AGAG (SEQ ID NO:81), and KGKG (SEQ ID NO:82).
11. The polypeptide of any of claims 1 to 10, wherein the polypeptide or linker to the carrier, if present, further comprises a C-terminal cysteine (C).
12. The polypeptide of any of claims 1 to 11, wherein the first peptide is DAEFRHD (SEQ ID NO:06), DAEFR (SEQ ID NO:08), or EFRHD (SEQ ID NO:21).
13. The polypeptide of claim 1, wherein the second peptide comprises 5-10 amino acids.
14. The polypeptide of claim 1, wherein the second peptide comprises the amino acid sequence
QIVYKPV (SEQ ID NO:39),
EIVYKSP (SEQ ID NO:43),
NIKHVP (SEQ ID NO:48),
VKSKIGST (SEQ ID NO:801),
SKIGSTEN (SEQ ID NO:817),
TENLKHQP (SEQ ID NO:695),
ENLKHQPG (SEQ ID NO:689),
SKIGSTDNIKH (SEQ ID NO:985),
SKIGSKDNIKH (SEQ ID NO:986), or
SKIGSLDNIKH (SEQ ID NO:988).
15. The polypeptide of claim 1, comprising an amino acid sequence of
DAEFRHDDRQIVYKPV (SEQ ID NO:57),
DAEFRHDDRREIVYKSV (SEQ ID NO:58),
DAEFRHDDRQIVYKPVGGC (SEQ ID NO:59),

DAEFRHDDRQIVYKPVC (SEQ ID NO:60), DAEFRHDDRQIVYKPVAAC (SEQ ID NO:61), DAEFRHDDRQIVYKPVKKC (SEQ ID NO:62), DAEFRHDDRREIVYKSPGGC (SEQ ID NO:63), DAEFRHDDRREIVYKSPAAC (SEQ ID NO:64), DAEFRHDDRREIVYKSPC (SEQ ID NO:65), DAEFRHDDRREIVYKSPKKC (SEQ ID NO:66), DAEFRHDDRNIKHVPGGC (SEQ ID NO:78), DAEFRHDDRNVKSKIGSTGGC (SEQ ID NO:997), DAEFRHDDRSKIGSTENGGC (SEQ ID NO:998), DAEFRHDDRRTENLKHQPGGC (SEQ ID NO:999), DAEFRHDDRRENLKHQPGGGC (SEQ ID NO:1000), DAEFRHDDRSKIGSKDNIKHGGC (SEQ ID NO:1001).

16. The polypeptide of claim 1, comprising the amino acid sequence of DAEFRHDDRQIVYKPVXXC (SEQ ID NO:70), wherein XX and C are independently optional and, if present, XX can be GG, AA, KK, SS, GAGA (SEQ ID NO:80), AGAG (SEQ ID NO:81), or KGKG (SEQ ID NO:82).

17. An immunotherapy composition, comprising the polypeptide of any of claims 1 to 16, wherein the polypeptide is linked to a carrier.

18. The immunotherapy composition of claim 17, wherein the carrier comprises serum albumins, immunoglobulin molecules, thyroglobulin, ovalbumin, tetanus toxoid (TT), diphtheria toxoid (DT), a genetically modified cross-reacting material (CRM) of diphtheria toxin, CRM197, meningococcal outer membrane protein complex (OMPC) and *H. influenzae* protein D (HiD), rEPA (*Pseudomonas aeruginosa* exotoxin A), KLH (keyhole limpet hemocyanin), and flagellin.

19. The immunotherapy composition of claim 18, wherein the carrier is CRM197 or diphtheria toxoid.

20. A pharmaceutical formulation comprising (a) the polypeptide of any one of claims 1 to 16 or the immunotherapy composition of any of claims 17 to 19 and (b) at least one adjuvant.

21. The pharmaceutical formulation of claim 20, wherein the adjuvant is selected from the group consisting of aluminum hydroxide, aluminum phosphate, aluminum sulfate, 3 De-O-acylated monophosphoryl lipid A (MPL), QS-21, TQL1055, QS-18, QS-17, QS-7, Complete Freund's Adjuvant (CFA), Incomplete Freund's Adjuvant (IFA), oil in water emulsions (such as squalene or peanut oil), CpG, polyglutamic acid, polylysine, AddaVax™, MF59®, and combinations thereof.
22. The pharmaceutical formulation of claim 21, wherein the adjuvant comprises a liposomal formulation.
23. The pharmaceutical formulation of claim 22, comprising a multiple antigen presenting system (MAP).
24. The pharmaceutical formulation of claim 23, wherein the MAP comprises one or more of a Lys-based dendritic scaffold, helper T-cell epitopes, immune stimulating lipophilic moieties, cell penetrating peptides, radical induced polymerization, self-assembling nanoparticles as antigen-presenting platforms and gold nanoparticles.
25. An immunotherapy composition, comprising a first peptide sequence comprising 3-10 amino acid residues from the first ten N-terminal residues of SEQ ID NO:01 and a second peptide sequence comprising 3-13 amino acids from residues 244-400 of SEQ ID NO:02.
26. The immunotherapy composition of claim 25, wherein:
- (a) the first peptide sequence comprises an amino acid sequence selected from the group consisting of
 - DAEFRHDSGY (SEQ ID NO:03),
 - DAEFRHDSG (SEQ ID NO:04),
 - DAEFRHDS (SEQ ID NO:05),
 - DAEFRHD (SEQ ID NO:06),
 - DAEFRH (SEQ ID NO:07),
 - DAEFR (SEQ ID NO:08),
 - DAEF (SEQ ID NO:09),

DAE (SEQ ID NO:10),
 AEFRHDSGY (SEQ ID NO:11),
 AEFRHDSG (SEQ ID NO:12),
 AEFRHDS (SEQ ID NO:13),
 AEFRHD (SEQ ID NO:14),
 AEFRH (SEQ ID NO:15),
 AEFR (SEQ ID NO:16),
 AEF (SEQ ID NO:17),
 EFRHDSGY (SEQ ID NO:18),
 EFRHDSG (SEQ ID NO:19),
 EFRHDS (SEQ ID NO:20),
 EFRHD (SEQ ID NO:21),
 EFRH (SEQ ID NO:22),
 EFR (SEQ ID NO:23),
 FRHDSGY (SEQ ID NO:24),
 FRHDSG (SEQ ID NO:25),
 FRHDS (SEQ ID NO:26),
 FRHD (SEQ ID NO:27),
 FRH (SEQ ID NO:28),
 RHDSGY (SEQ ID NO:29),
 RHDSG (SEQ ID NO:30),
 RHDS (SEQ ID NO:31),
 RHD (SEQ ID NO:32),
 HDSGY (SEQ ID NO:33),
 HDSG (SEQ ID NO:34),
 HDS (SEQ ID NO:35),
 DSGY (SEQ ID NO:36),
 DSG (SEQ ID NO:37), and
 SGY (SEQ ID NO:38); and

(b) the second peptide sequence comprises an amino acid sequence
 selected from the group consisting of

QIVYKPV (SEQ ID NO:39),
 QIVYKP (SEQ ID NO:40),
 QIVYKSV (SEQ ID NO:41),

QIVYKS (SEQ ID NO:83),
 EIVYKSP (SEQ ID NO:43),
 EIVYKS (SEQ ID NO:84),
 EIVYKPV (SEQ ID NO:44),
 EIVYKP (SEQ ID NO:85),
 IVYKSPV (SEQ ID NO:45),
 IVYK (SEQ ID NO:46),
 CNIKHVPG (SEQ ID NO:86),
 CNIKHVP (SEQ ID NO:47),
 NIKHVP (SEQ ID NO:48),
 HVPGGG (SEQ ID NO:49),
 HVPGG (SEQ ID NO:50),
 HKPGGG (SEQ ID NO:51),
 HKPGG (SEQ ID NO:52),
 KHVPGGG SEQ ID NO:53),
 KHVPGG (SEQ ID NO:54),
 HQPGGG (SEQ ID NO:55),
 HQPGG (SEQ ID NO:56),
 VKSKIGST (SEQ ID NO:801),
 SKIGSTEN (SEQ ID NO:817),
 TENLKHQP (SEQ ID NO:695),
 ENLKHQPG (SEQ ID NO:689),
 SKIGSTDNIKH (SEQ ID NO:985),
 SKIGSKDNIKH (SEQ ID NO:986),
 SKIGSLDNIKH (SEQ ID NO:988), and
 SEQ ID NO:146-996

wherein each of the first peptide sequence and the second peptide sequence may optionally comprise a C-terminal cysteine.

27. The immunotherapy composition of any one of claims 25-26, wherein the at least one of the first peptide and the second peptide further comprise a linker to a carrier at either a C-terminal portion of the polypeptide, or a N-terminal portion of the polypeptide.

28. The immunotherapy composition of claim 27, wherein the linker comprises an amino acid sequence selected from the group consisting of GG, GGG, AA, AAA, KK, KKK, SS, SSS, GAGA (SEQ ID NO:80), AGAG (SEQ ID NO:81), and KGKG (SEQ ID NO:82).

29. The immunotherapy composition of claim 28, wherein the linker to the carrier may optionally comprise a C-terminal cysteine (C).

30. The immunotherapy composition of any one of claims 25-29, wherein the carrier comprises serum albumins, immunoglobulin molecules, thyroglobulin, ovalbumin, tetanus toxoid (TT), diphtheria toxoid (DT), a genetically modified cross-reacting material (CRM) of diphtheria toxin, CRM197, meningococcal outer membrane protein complex (OMPC) and *H. influenzae* protein D (HiD), rEPA (*Pseudomonas aeruginosa* exotoxin A), KLH (keyhole limpet hemocyanin), and flagellin.

31. The immunotherapy composition of any one of claims 25-30, further comprising a multiple antigen presenting system (MAP).

32. The immunotherapy composition of claim 31, wherein the MAP comprises one or more of a Lys-based dendritic scaffold, helper T-cell epitopes, immune stimulating lipophilic moieties, cell penetrating peptides, radical induced polymerization, self-assembling nanoparticles as antigen-presenting platforms and gold nanoparticles.

33. A pharmaceutical formulation comprising the immunotherapy composition of any of claims 25 to 32 and at least one adjuvant.

34. The pharmaceutical formulation of claim 33, wherein the adjuvant is selected from the group consisting of aluminum hydroxide, aluminum phosphate, aluminum sulfate, 3 De-O-acylated monophosphoryl lipid A (MPL), QS-21, TQL1055, QS-18, QS-17, QS-7, Complete Freund's Adjuvant (CFA), Incomplete Freund's Adjuvant (IFA), oil in water emulsions (such as squalene or peanut oil), CpG, polyglutamic acid, polylysine, AddaVax™, MF59®, and combinations thereof.

35. A nucleic acid comprising a nucleic acid sequence encoding a polypeptide of any one of claims 1 to 16 or the immunotherapy composition of claims 25-29.
36. A nucleic acid immunotherapy composition comprising the nucleic acid of claim 35 and at least one adjuvant.
37. Use of the immunotherapy composition of any of claims 17-19 and 25-32, or the pharmaceutical formulation of any of claims 20-24 and 33-34, in the manufacture of a medicament for treating or effecting prophylaxis of Alzheimer's disease.
38. Use of the immunotherapy composition of any of claims 17-19 and 25-32, or the pharmaceutical formulation of any of claims 20-24 and 33-34, in the manufacture of a medicament for inhibiting or reducing aggregation of at least one of A β and tau in a subject having or at risk of developing Alzheimer's disease.
39. Use of the nucleic acid immunotherapy composition of claim 36 in the manufacture of a medicament for treating or effecting prophylaxis of Alzheimer's disease in a subject.
40. Use of the nucleic acid immunotherapy composition of claim 36 in the manufacture of a medicament for inhibiting or reducing aggregation of at least one of A β and tau in a subject having or at risk of developing Alzheimer's disease.
41. An immunization kit comprising the immunotherapy composition of any of claims 17-19 and 25-32.
42. The kit of claim 41, further comprising an adjuvant.
43. The kit of claim 42, wherein the immunotherapy composition is in a first container and the adjuvant is in a second container.
44. A kit comprising the nucleic acid immunotherapy composition of claim 36.
45. The kit of claim 44, further comprising an adjuvant.

46. The kit of claim 45, wherein the nucleic acid immunotherapy composition is in a first container and the adjuvant is in a second container.

47. The immunotherapy composition of any of claims 17-19 and 25-32, or the pharmaceutical formulation of any of claims 20-24 and 33-34, or the nucleic acid immunotherapy composition of claim 36, for use in therapy.