(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
25 November 2021 (25.11.2021)

WIPO | PCT

(10) International Publication Number
WO 2021/236809 A3

(51) International Patent Classification:
A61K 38/12 (2006.01) *C07K 7/06* (2006.01)
A61P 25/28 (2006.01) *C07K 7/64* (2006.01)
C07K 19/00 (2006.01) *A61K 39/39* (2006.01)

(21) International Application Number:
PCT/US2021/033222

(22) International Filing Date:
19 May 2021 (19.05.2021)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

63/027,150	19 May 2020 (19.05.2020)	US
63/062,903	07 August 2020 (07.08.2020)	US
63/140,917	24 January 2021 (24.01.2021)	US

(71) Applicant: **OTHAIR PROTHENA LIMITED** [IE/IE]; 77 Sir John Rogerson's Quay, Block C, Grand Canal Docklands, Dublin 2, D02 VK60 (IE).

(72) Inventors; and

(71) Applicants: **BARBOUR, Robin** [US/US]; 250 Normandy Lane, Walnut Creek, CA 94598 (US). **KINNEY, Gene** [US/US]; 2800 S Ocean Blvd, Unit 14L/M, Boca Raton, FL 33432 (US). **ZAGO, Wagner** [US/US]; 1291 Crestview Drive, San Carlos, CA 94070 (US). **NIJJAR, Tarlochan, S.** [US/US]; 712 Ironbark Court, Orinda, CA 94563 (US).

(74) Agent: **GATTARI, Patrick, G.**; McDonnell Boehnen Hulbert & Berghoff LLP, 300 South Wacker Drive, Chicago, IL 60606 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN,

(54) Title: MULTI-EPITOPE VACCINE FOR THE TREATMENT OF ALZHEIMER'S DISEASE

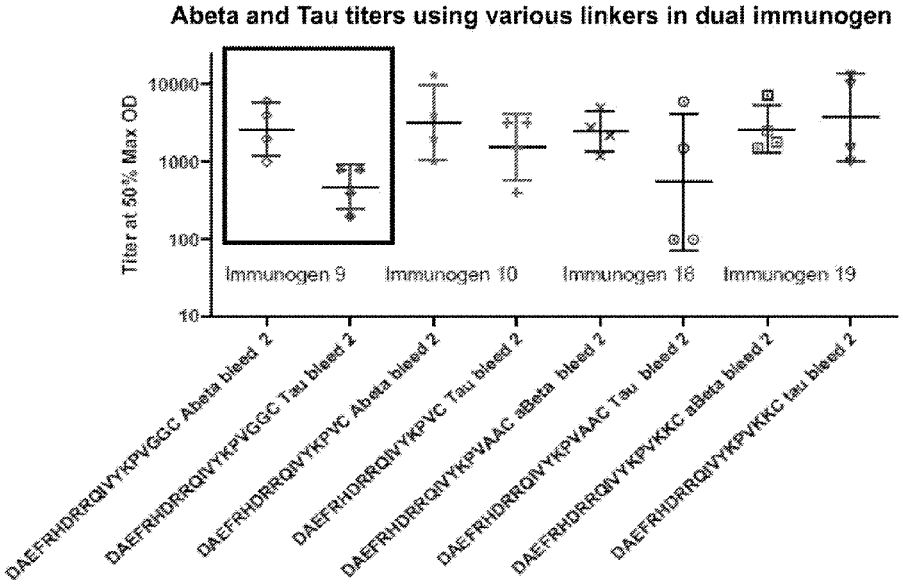


FIG. 5A

(57) Abstract: The disclosure provides peptide compositions and immunotherapy compositions comprising an amyloid-beta (Aβ) peptide and a fau. peptide. The disclosure also provides methods of treating or effecting prophylaxis of Alzheimer's disease or oilier diseases with beta-amyloid deposition in a subject, including methods of clearing deposits, inhibiting or reducing aggregation of Aβ and/or tan, blocking the uptake by neurons, clearing amyloid, and inhibiting propagation of tau seeds in a subject having or at risk of developing Alzheimer's disease or other diseases containing tau and/or amyloid-beta accumulations. The methods include administering to such patients the compositions comprising an amyloid-beta (Aβ) peptide and a tau peptide.

WO 2021/236809 A3

[Continued on next page]

HR, HU, ID, IL, IN, IR, IS, IT, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, WS, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:

— *with international search report (Art. 21(3))*

— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*

— *with sequence listing part of description (Rule 5.2(a))*

(88) Date of publication of the international search report:
30 December 2021 (30.12.2021)

MULTIEPITOPE VACCINE FOR THE TREATMENT OF ALZHEIMER'S DISEASE

RELATED APPLICATIONS

[0001] This application claims the benefit of U.S. Provisional Patent Application No. 63/140,917, filed January 24, 2021, U.S. Provisional Patent Application Serial No. 63/062,903, filed August 7, 2020, and U.S. Provisional Patent Application Serial No. 63/027,150, filed May 19, 2020, each of which is incorporated by reference herein in its entirety.

SEQUENCE LISTING STATEMENT

[0002] A computer readable form of the Sequence Listing is filed with this application by electronic submission and is incorporated into this application by reference in its entirety. The Sequence Listing is contained in the file created on May 19, 2021, having the file name "20-050-WO_Sequence-Listing_ST25.txt" and is 183 kb in size.

FIELD

[0003] The disclosure relates to the technical fields of immunology and medicine, and in particular to the treatment of Alzheimer's disease and other diseases of protein misfolding.

BACKGROUND

[0004] Alzheimer's disease (AD) is a progressive disease resulting in senile dementia. Broadly speaking, the disease falls into two categories: late onset, which occurs in old age (65+ years) and early onset, which develops well before the senile period, *i.e.*, between 35 and 60 years. In both types of disease, the pathology is the same, but the abnormalities tend to be more severe and widespread in cases beginning at an earlier age. The disease is characterized by at least two types of lesions in the brain, neurofibrillary tangles and senile plaques. Neurofibrillary tangles are intracellular deposits of microtubule associated tau protein consisting of two filaments twisted about each other in pairs. Senile plaques (*i.e.*, amyloid plaques) are areas of disorganized neuropil up to 150 μm across with extracellular amyloid deposits at the center which are visible by microscopic analysis of sections of brain tissue. The accumulation of amyloid plaques within the central nervous system is also associated

with Down's syndrome and other cognitive disorders, Cerebral amyloid angiopathy (CAA), and the ocular disease Age-Related Macular Degeneration.

[0005] A principal constituent of the plaques is a peptide termed Aβ or β-amyloid peptide. Aβ peptide is a 4-kDa internal fragment of 38-43 amino acids of a larger transmembrane glycoprotein named amyloid precursor protein (APP). As a result of proteolytic processing of APP by different secretase enzymes, Aβ is primarily found in both a short form, 40 amino acids in length, and a long form, ranging from 42-43 amino acids in length. Part of the hydrophobic transmembrane domain of APP is found at the carboxy end of Aβ, and may account for the ability of Aβ to aggregate into plaques, particularly in the case of the long form. Accumulation of amyloid plaques in the brain eventually leads to neuronal cell death. The cognitive and physical symptoms associated with this type of neural deterioration characterize Alzheimer's disease.

[0006] Another protein reported to occur at increased levels in Alzheimer's patients relative to the general population is tau, the principal constituent of neurofibrillary tangles, which together with amyloid plaques are a hallmark characteristic of Alzheimer's disease. Tau tangles constitute abnormal fibrils measuring 10 nm in diameter occurring in pairs wound in a helical fashion with a regular periodicity of 80 nm. The tau within neurofibrillary tangles is abnormally phosphorylated (hyperphosphorylated) with phosphate groups attached to specific sites on the molecule. Severe involvement of neurofibrillary tangles is seen in the layer II neurons of the entorhinal cortex, the CA1 and subicular regions of the hippocampus, the amygdala, and the deeper layers (layers III, V, and superficial VI) of the neocortex in Alzheimer's disease. Tau pathologies are known to correlate to cognitive decline.

[0007] Accordingly, there exists the need for new therapies and reagents for the prevention or treatment of Alzheimer's disease, in particular, therapies and reagents capable of causing an immune response to the Aβ and Tau present in patients.

SUMMARY

[0008] In some embodiments, disclosure is directed to a polypeptide including a first peptide comprising 3-10 amino acids from residues 1-10 of SEQ ID NO:01

linked to a second peptide including 3-13 amino acids from residues 244-400 of SEQ ID NO:02. For example, the second peptide may be from the microtubule binding region (MTBR) of tau (residues 244-372 of SEQ ID NO:02). The first peptide may be N-terminal to the second peptide or the first peptide may be C-terminal to the second peptide. In addition, the first peptide may include an amino acid sequence of one of SEQ ID NOS: 3 to 38 or SEQ ID NOS:1002 to 1057 and the second peptide may include an amino acid sequence of one of SEQ ID NOS: 39-56, 83-86, or 146-996. For example, the first polypeptide may be DAEFRHD (SEQ ID NO:06), DAEFR (SEQ ID NO:08), or EFRHD (SEQ ID NO:21), and the second polypeptide may be 5-13 amino acids, for example QIVYKPV (SEQ ID NO:39), EIVYKSV (SEQ ID NO:42), EIVYKSP (SEQ ID NO:43), EIVYKPV (SEQ ID NO:44), 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).

[0009] In other embodiments, the first peptide and second peptide may be linked by a cleavable linker, which may be an amino acid sequence. A cleavable peptide linker, if present, can be 1-10 amino acids in length. In some embodiments, the linker comprises between about 1-10 amino acids, about 1-9 amino acids, about 1-8 amino acids, about 1-7 amino acids, about 1-6 amino acids, about 1-5 amino acids, about 1-4 amino acids, about 1-3 amino acids, about 2 amino acids, or one (1) amino acid. In some embodiments, the cleavable peptide linker is 1 amino acid, 2 amino acids, 3 amino acids, 4 amino acids, 5 amino acids, 6 amino acids, 7 amino acids, 8 amino acids, 9 amino acids, or 10 amino acids. For example, the linker may be 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), Ala-Gly-Ala-Gly (SEQ ID NO:81), or Lys-Gly-Lys-Gly (SEQ ID NO:82). In particular embodiments, the polypeptide may be DAEFRHDRRQIVYKPV (SEQ ID NO:57), DAEFRHDRREIVYKSV (SEQ ID NO:58), DAEFRHDRRVKSKIGSTGGC (SEQ ID NO:997), DAEFRHDRRSKIGSTENGGC (SEQ ID NO:998), DAEFRHDRRTENLKHQPGGC (SEQ ID NO:999),

DAEFRHDRRENLKHQPGGGC (SEQ ID NO:1000), or
DAEFRHDRRSKIGSKDNIKHGGC (SEQ ID NO:1001).

[0010] In further embodiments, the polypeptide may include a linker to a carrier at a C-terminal portion of the polypeptide, or at a N-terminal portion of the polypeptide. A linker, if present, can be 1-10 amino acids in length. In some embodiments, the linker comprises between about 1-10 amino acids, about 1-9 amino acids, about 1-8 amino acids, about 1-7 amino acids, about 1-6 amino acids, about 1-5 amino acids, about 1-4 amino acids, about 1-3 amino acids, about 2 amino acids, or one (1) amino acid. In some embodiments, the linker is 1 amino acid, 2 amino acids, 3 amino acids, 4 amino acids, 5 amino acids, 6 amino acids, 7 amino acids, 8 amino acids, 9 amino acids, or 10 amino acids. For example, the linker may include an amino acid sequence of GG, GGG, AA, AAA, KK, KKK, SS and SSS. In addition, the linker to the carrier, if present at the C-terminus, may include a C-terminal cysteine (C). Alternatively, the linker to the carrier, if present at the N-terminus, may include a N-terminal cysteine (C). For example, the polypeptide may include the amino acid sequence of DAEFRHDRRQIVYKPVXXC (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). For example, the polypeptide may include the amino acid sequence of DAEFRHDRREIVYKSVXXC (SEQ ID NO:79), 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), and KGKG (SEQ ID NO:82).

[0011] In other embodiments, the disclosure is directed to an immunotherapy composition including the polypeptides of the disclosure, wherein the polypeptide may be linked to a carrier. The carrier may include 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.

[0012] Still further, embodiments of the disclosure are directed to a pharmaceutical formulation includes the polypeptides or the immunotherapy compositions of the disclosure, and including at least one adjuvant. The adjuvant may

be aluminum hydroxide, aluminum phosphate, aluminum sulfate, 3 De-O-acylated monophosphoryl lipid A (MPL), QS-21, QS-18, QS-17, QS-7, TQL1055, 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. In addition, the formulation may include a liposomal formulation, a diluent, or a multiple antigen presenting system (MAP). The MAP may include 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.

[0013] Still further, embodiments of the disclosure are directed to an immunotherapy composition including 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. The first peptide may include an amino acid sequence of one of SEQ ID NOS: 3 to 38 or SEQ ID NOS:1002 to 1057, and the second peptide may include an amino acid sequence of one of SEQ ID NOS: 39 to 56, SEQ ID NOS:83-86 or SEQ ID NOS:146-996. Each of the first peptide and the second peptide may include a linker to a carrier at a C-terminal portion of the polypeptide, or at a N-terminal portion of the polypeptide. When present, the linker may include an amino acid sequence selected from GG, GGG, AA, AAA, KK, KKK, SS, SSS, GAGA (SEQ ID NO:80), AGAG (SEQ ID NO:81), and KGKG (SEQ ID NO:82), and may include a C-terminal cysteine (C). In some embodiments, where the C-terminal residues in the immunogen are either IVYKPV (SEQ ID NO:194), VYKPV (SEQ ID NO:195), YKPV (SEQ ID NO:196), KPV, or PV the linker is an amino acid linker that does not have a N-terminal glycine (*e.g.*, GG, GAGA (SEQ ID NO:80)). The carrier may include 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.

[0014] In addition, the immunotherapy composition may include at least one pharmaceutically acceptable diluent and/or a multiple antigen presenting system

(MAP). The MAP may include 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.

[0015] The immunotherapy composition may be included in a pharmaceutical composition including the immunotherapy composition and at least one adjuvant such as aluminum hydroxide, aluminum phosphate, aluminum sulfate, 3 De-O-acylated monophosphoryl lipid A (MPL), QS-21, QS-18, QS-17, QS-7, TQL1055, 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.

[0016] Embodiments of the disclosure are also directed to nucleic acid sequences encoding the polypeptides and the immunotherapy compositions of the disclosure. The nucleic acids may be included in a nucleic acid immunotherapy composition including the nucleic acid and at least one adjuvant.

[0017] Still further, embodiments of the disclosure are directed to a methods for treating or effecting prophylaxis of Alzheimer's disease in a subject, and methods for inhibiting or reducing aggregation of at least one of Aβ and tau in a subject having or at risk of developing Alzheimer's disease. The methods include administrating to the subject an immunotherapy composition, a nucleic acids immunotherapy composition, or a pharmaceutical formulation of the disclosure.

[0018] The methods of the disclosure may include repeating the administering at least a second time, at least a third time, at least a fourth time, at least a fifth time, or at least a sixth time, and may include repeating the administering at an interval of about 21 to about 28 days.

[0019] Still further, methods of the disclosure are directed to inducing an immune response in an animal. The methods include administering to the animal a polypeptide, an immunotherapy composition, a pharmaceutical formulation or a nucleic acid immunotherapy composition of the disclosure in a regimen effective to generate an immune response including antibodies that specifically bind to Aβ, tau, or both Aβ and tau. The immune response may include antibodies that specifically bind to the N-terminal region of Aβ and/or the microtubule region of tau.

[0020] In other embodiments, the disclosure is directed to an immunization kit including an immunotherapy composition of the disclosure and may include an adjuvant, wherein the immunotherapy composition may be in a first container and the adjuvant may be a second container.

[0021] Still further, the disclosure is directed to a kit including a nucleic acid immunotherapy composition of the disclosure and may include an adjuvant. The nucleic acid may be in a first container and the adjuvant may be in a second container.

BRIEF DESCRIPTION OF THE FIGURES

[0022] **FIG. 1** shows the results of an experiment comparing the geometric mean titers of Guinea Pig serum for immunogen DAEFRHDRRQIVYKPV (SEQ ID NO:57) on monomeric Aβ amino acids 1-28 (DAEFRHDSGYEVHHQKLFFAEDVGSNKG; SEQ ID NO:67), soluble aggregate species of Aβ (Aβ 42), full length tau, and tau MTBR epitope containing GGGSVQIVYKPVDLS (SEQ ID NO:68) containing an N-terminal biotin.

[0023] **FIG. 2A** shows the results of an experiment comparing the titers of Guinea pig serum for a single peptide immunogen versus dual peptide immunogens of the disclosure on all forms of Aβ and full-length tau protein (DAEFRHD is SEQ ID NO:6; QIVYKPV is SEQ ID NO: 39; DAEFRHDRRQIVYKPV is SEQ ID NO:57).

[0024] **FIG. 2B** shows the results of an experiment comparing the titers of Guinea pig serum for a single peptide immunogen versus dual peptide immunogens of the disclosure on all forms of Aβ and full-length tau protein (DAEFRHD is SEQ ID NO:6; QIVYKPV is SEQ ID NO:39; EIVYKSP is SEQ ID NO:43; DAEFRHDRRQIVYKPV is SEQ ID NO:57).

[0025] **FIG. 3A** shows staining of Aβ and Tau pathology in fresh frozen human AD brain tissue using serum (1:300 dilution) from a Guinea pig vaccinated with Immunogen 9 (DAEFRHDRRQIVYKPVGGC; SEQ ID NO:59).

[0026] **FIG. 3B** shows staining of Aβ and Tau pathology in fresh frozen human AD brain tissue using serum (1:300 dilution) from a Guinea pig vaccinated with Immunogen 9 (DAEFRHDRRQIVYKPVGGC; SEQ ID NO:59).

[0027] **FIG. 3C** shows staining of Aβ and Tau pathology in fresh frozen human AD brain tissue using serum (1:1500 dilution) from a Guinea pig vaccinated with Immunogen 9 (DAEFRHDRRQIVYKPVGGC; SEQ ID NO:59).

[0028] **FIG. 3D** shows lack of staining of Aβ and Tau pathology in fresh frozen human AD brain tissue using serum (1:300 dilution) from an unvaccinated Guinea pig.

[0029] **FIG. 3E** shows lack of staining of Aβ and Tau pathology in fresh frozen human AD brain tissue using serum (1:300 dilution) from an unvaccinated Guinea pig.

[0030] **FIG. 3F** shows lack of staining of Aβ and Tau pathology in fresh frozen human AD brain tissue using serum (1:1500 dilution) from an unvaccinated Guinea pig.

[0031] **FIG. 4A** shows that Guinea pig serum from animals vaccinated with a dual immunogen peptide, DAEFRHDRRQIVYKPVGGC (SEQ ID NO:59; Immunogen 9), inhibited Abeta soluble aggregates binding to primary neurons in a dose-dependent manner.

[0032] **FIG. 4B** shows examples of Ab staining on primary neurons in the presence or absence of Guinea pig serum from animals vaccinated with a dual immunogen peptide, DAEFRHDRRQIVYKPVGGC (SEQ ID NO:59; Immunogen 9).

[0033] **FIG. 5A** shows that mice vaccinated with dual peptide antigens with various linkers produce similar titers to Aβ and Tau.

[0034] **FIG. 5B** shows that mice vaccinated with dual peptide antigens with the Tau sequence EIVYKSP (SEQ ID NO:43) produce titers to Aβ and Tau.

[0035] **FIG. 6A** shows staining of Aβ and Tau pathology in fresh frozen human AD brain tissue using serum (1:1000 dilution) from a mouse vaccinated with Immunogen 19.

[0036] **FIG. 6B** shows staining of Aβ and Tau pathology in fresh frozen human AD brain tissue using serum (1:1000 dilution) from a mouse vaccinated with Immunogen 19.

[0037] **FIG. 6C** shows lack of staining of Aβ and Tau pathology in fresh frozen human AD brain tissue using serum (1:1000 dilution) from an unvaccinated mouse.

[0038] **FIG. 6D** shows staining of Tau pathology in fresh frozen human AD brain tissue using anti-Tau antibody m6H3 (0.1 µg/ml).

[0039] **FIG. 6E** shows comparable staining of Tau pathology in fresh frozen human AD brain tissue using serum (1:1500 dilution) from a Guinea pig vaccinated with Immunogen 9 (DAEFRHDRRQIVYKPVGGC; SEQ ID NO:59).

[0040] **FIGS. 7A and 7B** show titers of dual Aβ-tau immunogen in two injection paradigms. Titers to Aβ1-28, full-length tau and the carrier CRM protein of the two injection schedules ((**FIG. 7A**) showing 0, 4, 12 and 24 weeks; (**FIG. 7B**) showing 0, 8 and 24 weeks) over the experiment are expressed as mean titer +/- SEM.

[0041] **FIG. 8A** shows individual animal titers to Aβ and tau two weeks post each injection for the injection schedule of Fig. 7A, i.e., at weeks 2, 6, 14 and 26.

[0042] **FIG. 8B** shows individual animal titers to Aβ and tau two weeks post each injection for the injection schedule of Fig. 7B, i.e., at weeks 2, 14 and 26.

[0043] **FIG. 9A** shows staining of Aβ and Tau pathology in fresh frozen human AD brain tissue using week 26 serum (1:300 dilution) from cynomolgus monkey #1001 vaccinated with Immunogen 15 (DAEFRHDRRQIVYKPVGGC; SEQ ID NO:59) on a four injection vaccination schedule.

[0044] **FIG. 9B** shows a zoomed view of the rectangle indicating staining of Aβ pathology in **FIG. 9A**.

[0045] **FIG. 9C** shows a shows a zoomed view of the rectangle indicating staining of Tau pathology in **FIG. 9A**.

[0046] **FIG. 10A** shows staining of Aβ pathology in fresh frozen human AD brain tissue using serum (1:300 dilution) from cynomolgus monkey #1003 vaccinated with Immunogen 15 (DAEFRHDRRQIVYKPVGGC; SEQ ID NO:59).

[0047] **FIG. 10B** shows modest staining of Tau pathology in fresh frozen human AD brain tissue using serum (1:300 dilution) from cynomolgus monkey #1003.

[0048] **FIG. 11A** shows staining of Aβ pathology in fresh frozen human AD brain tissue using serum (1:300 dilution) from cynomolgus monkey #1501 vaccinated with Immunogen 15 (DAEFRHDRRQIVYKPVGGC; SEQ ID NO:59).

[0049] **FIG. 11B** shows minimal staining of Tau pathology in fresh frozen human AD brain tissue using serum (1:300 dilution) from cynomolgus monkey #1501.

[0050] **FIG. 12A** shows staining of Aβ pathology in fresh frozen human AD brain tissue using serum (1:300 dilution) from cynomolgus monkey #2501 vaccinated with Immunogen 15 (DAEFRHDRRQIVYKPVGGC; SEQ ID NO:59).

[0051] **FIG. 12B** shows a lack of staining of Tau pathology in fresh frozen human AD brain tissue using serum (1:300 dilution) from cynomolgus monkey #2501.

[0052] **FIG. 13** shows animal titers to Aβ and tau 9 weeks post injection at day 0, at 4 weeks and at 8 weeks for the dual Abeta-tau constructs DAEFRHDRRVKSKIGSTGGC (SEQ ID NO:997); DAEFRHDRRSKIGSTENGGC (SEQ ID NO:998); DAEFRHDRRTENLKHQPGGC (SEQ ID NO:999); DAEFRHDRRENLKHQPGGGC (SEQ ID NO:1000); and DAEFRHDRRSKIGSKDNIKHGGC (SEQ ID NO:1001).

[0053] **FIG. 14** shows blocking of tau binding to Heparin by sera from Aβ-tau constructs DAEFRHDRRVKSKIGSTGGC (SEQ ID NO:997); DAEFRHDRRSKIGSTENGGC (SEQ ID NO:998); DAEFRHDRRTENLKHQPGGC (SEQ ID NO:999); DAEFRHDRRENLKHQPGGGC (SEQ ID NO:1000); and DAEFRHDRRSKIGSKDNIKHGGC (SEQ ID NO:1001).

[0054] **FIG. 15A** shows competition of tau by sera from DAEFRHDRRVKSKIGSTGGC construct (SEQ ID NO:997).

[0055] **FIG. 15B** shows competition of tau by sera from DAEFRHDRRSKIGSTENGGC construct (SEQ ID NO:998).

[0056] **FIG. 15C** shows competition of tau by sera from DAEFRHDRRTENLKHQPGGC construct (SEQ ID NO:999).

[0057] **FIG. 15D** shows competition of tau by sera from DAEFRHDRRENLKHQPGGGC construct (SEQ ID NO:1000).

[0058] **FIG. 15E** shows competition of tau by sera from DAEFRHDRRSKIGSKDNIKHGGC construct (SEQ ID NO:1001).

[0059] **FIG. 15F** shows competition of tau by sera from controls.

[0060] **FIG. 15G** shows competition of tau by sera from DAEFRHDRRSKIGSKDNIKHGGC construct (SEQ ID NO:1001).

[0061] **FIG. 16A** shows Abeta/Tau Dual Vaccine Mouse Serum 2.3_031521 (1:300) Example of staining with DAEFRHDRRVKSKIGSTGGC (SEQ ID NO:997).

[0062] **FIG. 16B** shows Abeta/Tau Dual Vaccine Mouse Serum 3.1_031521 (1:300) Example of staining with DAEFRHDRRSKIGSTENGGC (SEQ ID NO:998).

[0063] **FIG. 16C** shows Abeta/Tau Dual Vaccine Mouse Serum 8.4_031521 (1:300) Example of staining with DAEFRHDRRTENLKHQPGGC (SEQ ID NO:999).

[0064] **FIG. 16D** shows Abeta/Tau Dual Vaccine Mouse Serum 9.2_031521 (1:300) Example of staining with DAEFRHDRRENLKHQPGGGC (SEQ ID NO:1000).

[0065] **FIG. 16E** shows Abeta/Tau Dual Vaccine Mouse Serum 11.1_031521 (1:300) Example of staining with DAEFRHDRRSKIGSKDNIKHGGC (SEQ ID NO: 1001).

DESCRIPTION

[0066] The disclosure provides peptide compositions and immunotherapy compositions comprising an amyloid-beta (Aβ) peptide and a tau peptide. The disclosure also provides methods of treating or effecting prophylaxis of Alzheimer's disease or other diseases with beta-amyloid deposition in a subject, including methods of clearing and preventing formation of deposits, inhibiting or reducing aggregation of Aβ and/or tau, blocking the binding and/or uptake of Aβ and/or tau by neurons, inhibiting transmission of tau species between cells, and inhibiting propagation of pathology between brain regions in a subject having or at risk of developing Alzheimer's disease or other diseases containing tau and/or amyloid-beta accumulations. The methods include administering to such patients the compositions comprising an amyloid-beta (Aβ) peptide and a tau peptide.

[0067] A number of terms are defined below. As used herein, the singular forms "a," "an", and "the" include plural referents unless the context clearly dictates otherwise. For example, the term "a compound" or "at least one compound" can include a plurality of compounds, including mixtures thereof.

[0068] Unless otherwise apparent from the context, the term "about" encompasses insubstantial variations, such as values within a standard margin of error of measurement (*e.g.*, SEM) of a stated value. For example the term "about" as used herein when referring to a measurable value such as a parameter, an amount, a temporal duration, can encompass variations of +/-10% or less, +/-5% or less, or +/-1% or less or less of and from the specified value. Designation of a range of values includes all integers within or defining the range, and all subranges defined by integers within the range. As used herein, statistical significance means $p \leq 0.05$.

[0069] Compositions or methods "comprising" or "including" one or more recited elements may include other elements not specifically recited. For example, a composition that "comprises" or "includes" a polypeptide sequence may contain the sequence alone or in combination with other sequences or ingredients.

[0070] An individual is at increased risk of a disease if the subject has at least one known risk-factor (*e.g.*, age, genetic, biochemical, family history, and situational exposure) placing individuals with that risk factor at a statistically significant greater risk of developing the disease than individuals without the risk factor.

[0071] The term "patient" includes human and other mammalian subjects that receive either prophylactic or therapeutic treatment, including treatment naïve subjects. As used herein, the terms "subject" or "patient" refer to any single subject for which treatment is desired, including other mammalian subjects such as, humans, cattle, dogs, guinea pigs, rabbits, and so on. Also intended to be included as a subject are any subjects involved in clinical research trials not showing any clinical sign of disease, or subjects involved in epidemiological studies, or subjects used as controls.

[0072] The term "disease" refers to any abnormal condition that impairs physiological function. The term is used broadly to encompass any disorder, illness, abnormality, pathology, sickness, condition, or syndrome in which physiological function is impaired, irrespective of the nature of the etiology.

[0073] The term "symptom" refers to a subjective evidence of a disease, such as altered gait, as perceived by the subject. A "sign" refers to objective evidence of a disease as observed by a physician.

[0074] As used herein, the terms "treat" and "treatment" refer to the alleviation or amelioration of one or more symptoms or effects associated with the disease, prevention, inhibition or delay of the onset of one or more symptoms or effects of the disease, lessening of the severity or frequency of one or more symptoms or effects of the disease, and/or increasing or trending toward desired outcomes as described herein.

[0075] The terms "prevention", "prevent", or "preventing" as used herein refer to contacting (for example, administering) the peptide(s) or immunotherapy compositions of the present disclosure with a subject before the onset of a disease, with or without Aβ and/or tau pathology already present (primary and secondary prevention), thereby delaying the onset of clinical symptoms and/or alleviating symptoms of the disease after the onset of the disease, compared to when the subject is not contacted with the peptide or immunotherapy compositions, and does not refer to completely suppressing the onset of the disease. In some cases, prevention may occur for limited time after administration of the peptide or immunotherapy compositions of the present disclosure. In other cases, prevention may occur for the duration of a treatment regimen comprising administering the peptide or immunotherapy compositions of the present disclosure.

[0076] The terms "reduction", "reduce", or "reducing" as used herein refer to decreasing the amount of Aβ and/or tau present in a subject or in tissue of the subject, or suppressing an increase in the amount of Aβ and/or tau present in a subject or in tissue of the subject, which encompasses decreasing or suppressing an increase in (*e.g.*, decreasing the rate of increase) the amount of Aβ and/or tau present, accumulated, aggregated, or deposited in the subject or tissue in the subject. In certain embodiments, the decrease in or suppression of an increase in (*e.g.*, decreasing the rate of increase) the amount of Aβ and/or tau present, accumulated, aggregated, or deposited in the subject refers to an amount of Aβ and/or tau present, accumulated, aggregated, or deposited in the central nervous system (CNS) of the subject. In certain embodiments, the decrease in or suppression of an increase in (*e.g.*, decreasing the rate of increase) the amount of Aβ and/or tau present, accumulated, aggregated, or

deposited in the subject refers to an amount of Aβ and/or tau present, accumulated, aggregated, or deposited in the periphery (*e.g.*, peripheral circulatory system) of the subject. In certain embodiments, the decrease in or suppression of an increase in (*e.g.*, decreasing the rate of increase) the amount of Aβ and/or tau present, accumulated, aggregated, or deposited in the subject refers to an amount of Aβ and/or tau present, accumulated, aggregated, or deposited in the brain of the subject. In some embodiments, the Aβ and/or tau reduced is the pathological form(s) of the Aβ (*e.g.*, extracellular plaque deposits of the β-amyloid peptide (Aβ), neuritic amyloid plaques), and/or tau (*e.g.*, neurofibrillary tangles of tau, dystrophic neurites). In yet other embodiments, pathological indicators of neurodegenerative disease are decreased.

[0077] The terms "epitope" or "antigenic determinant" refers to a site on an antigen to which B and/or T cells respond, or to a site on an antigen to which an antibody binds. Epitopes can be formed both from contiguous amino acids or from noncontiguous amino acids juxtaposed by tertiary folding of a protein. Epitopes formed from contiguous amino acids are typically retained on exposure to denaturing solvents whereas epitopes formed by tertiary folding are typically lost on treatment with denaturing solvents. An epitope typically includes at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, or at least 13 amino acids in a unique spatial conformation. Methods of determining spatial conformation of epitopes include, for example, x-ray crystallography and 2-dimensional nuclear magnetic resonance. *See, e.g.*, Epitope Mapping Protocols in Methods in Molecular Biology, Vol. 66, Glenn E. Morris, Ed. (1996).

[0078] An "immunogenic agent" or "immunogen" or "antigen" is capable of inducing an immunological response against itself or modified/processed versions of itself upon administration to an animal, optionally in conjunction with an adjuvant. The terms "immunogenic agent" or "immunogen" or "antigen" refer to a compound or composition comprising a peptide, polypeptide or protein which is "antigenic" or "immunogenic" when administered in an appropriate amount (an "immunogenically effective amount"), *i.e.*, capable of inducing, eliciting, augmenting or boosting a cellular and/or humoral immune response and of being recognized by the products of that response (T cells, antibodies). An immunogen can be a peptide, or a combination of two or more same or different peptides, that includes at least 3, at least 4, at least 5,

at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, or at least 13 amino acids in a liner or spatial conformation.

[0079] An immunogen may be effective when given alone or in combination, or linked to, or fused to, another substance (which can be administered at one time or over several intervals). An immunogenic agent or immunogen may include an antigenic peptide or polypeptide that is linked to a carrier as described herein.

[0080] A nucleic acid such as DNA or RNA that encodes an antigenic peptide, or polypeptide is referred to as a "DNA [or RNA] immunogen," as the encoded peptide or polypeptide is expressed *in vivo* after administration of the DNA or RNA. The peptide or polypeptide can be recombinantly expressed from a vaccine vector, which can be naked DNA or RNA that comprises the peptide or polypeptide coding sequence operably linked to a promoter, *e.g.*, an expression vector or cassette as described herein.

[0081] The term "adjuvant" refers to a compound that, when administered in conjunction with an antigen, augments the immune response to the antigen, but when administered alone does not generate an immune response to the antigen. Adjuvants can augment an immune response by several mechanisms including lymphocyte recruitment, stimulation of B and/or T cells, and stimulation of macrophages. An adjuvant may be a natural compound, a modified version of or derivative of a natural compound, or a synthetic compound.

[0082] The terms "peptide" and "polypeptide" are used interchangeably herein and refer to a chain of two or more consecutive amino acids. If and when a distinction is made, context makes the meaning clear. For example, if two or more peptides described herein are joined to make a dimeric or multimeric peptide, polypeptide may be used to indicate "poly" or "more than one" peptide.

[0083] The term "pharmaceutically acceptable" means that the carrier, diluent, excipient, adjuvant, or auxiliary is compatible with the other ingredients of a pharmaceutical formulation and not substantially deleterious to the recipient thereof.

[0084] The terms "immunotherapy" or "immune response" refer to the development of a beneficial humoral (antibody mediated) and/or a cellular (mediated by antigen-specific T cells or their secretion products) response directed against an Aβ and/or tau peptide in a recipient. Such a response can be an active response induced

by administration of immunogen (*e.g.* an Aβ and/or tau peptide). A cellular immune response is elicited by the presentation of polypeptide epitopes in association with Class I or Class II MHC molecules to activate antigen-specific $CD4^+$ T helper cells and/or $CD8^+$ cytotoxic T cells. The response may also involve activation of monocytes, macrophages, NK cells, basophils, dendritic cells, astrocytes, microglia cells, eosinophils or other components of innate immunity. The presence of a cell-mediated immunological response can be determined by proliferation assays ($CD4^+$ T cells) or CTL (cytotoxic T lymphocyte) assays. The relative contributions of humoral and cellular responses to the protective or therapeutic effect of an immunogen can be distinguished by separately isolating antibodies and T-cells from an immunized syngeneic animal and measuring protective or therapeutic effect in a second subject.

[0085] Amyloid Beta (Aβ)

[0086] Aβ (also referred to herein as beta amyloid peptide or Abeta) peptide is about a 4-kDa internal fragment of 38-43 amino acids of APP (Aβ39, Aβ40, Aβ41, Aβ42, and Aβ43). Aβ40, for example, consists of residues 672-711 of APP and Aβ42 consists of residues 673-713 of APP. As a result of proteolytic processing of APP by different secretase enzymes *in vivo* or *in situ*, Aβ is found in both a "short form", 40 amino acids in length, and a "long form", ranging from 42-43 amino acids in length. Epitopes or antigenic determinants, as described herein, are located within the N-terminus of the Aβ peptide and include residues within amino acids 1-10 and 12-25 of Aβ, for example from residues 1-3, 1-4, 1-5, 1-6, 1-7, or 3-7, 2-4, 2-5, 2-6, 2-7, or 2-8 of Aβ, residues 3-5, 3-6, 3-7, 3-8, or 3-9 of Aβ, or residues 4-7, 4-8, 4-9, or 4-10 residues 12-24, 12-23, 12-22, 13-25, 13-24, 13-23, 13-22, 14-25, 14-24, 14-23, 14-22, 15-25, 15-24, 15-23, or 15-22 of Aβ. For example, from residues 12-17, 12-18, 12-19, 12-20, 12-21, 13-17, 13-18, 13-19, 13-20, 13-21, 13-22, 14-17, 14-18, 14-19, 14-20, 14-21, 14-22, 14-23, 15-17, 15-18, 15-19, 15-20, 15-21, 15-22, 15-23, or 15-24 of Aβ42. Additional examples of epitopes or antigenic determinants include residues 16-18, 16-19, 16-20, 16-21, 16-22, 16-23, 16-24, 16-25, 17-19, 17-20, 17-21, 17-22, 17-23, 17-24 or 17-25 of Aβ42. Other examples of epitopes or antigenic determinants include residues 18-20, 18-21, 18-22, 18-23, 18-24, 18-25, 19-21, 19-22, 19-23, 19-24, 19-25, 20-22, 20-23, 20-24, 20-25, 21-23, 21-24 or 21-25 of Aβ42.

[0087] Aβ (Abeta) is the principal component of characteristic plaques of Alzheimer's disease. Aβ is generated by processing of a larger protein APP by two

enzymes, termed beta and gamma secretases. Known mutations in APP associated with Alzheimer's disease occur proximate to the site of beta or gamma secretase, or within Aβ. Part of the hydrophobic transmembrane domain of APP is found at the carboxy end of Aβ, and may account for the ability of Aβ to aggregate into plaques, particularly in the case of the long form. Accumulation of amyloid plaques in the brain eventually leads to neuronal cell death. The physical symptoms associated with this type of neural deterioration characterize Alzheimer's disease.

[0088] Tau

[0089] Tau is a protein with a molecular weight of about 50,000 that is normally present in nerve axons or the like, and contributes to microtubular stability. The tau proteins (or τ proteins) are a group of six highly-soluble protein isoforms produced by alternative splicing from the gene MAPT (microtubule-associated protein tau). They have roles primarily in maintaining the stability of microtubules in axons and are abundant in the neurons of the central nervous system (CNS). They are less common elsewhere but are also expressed at very low levels in CNS astrocytes and oligodendrocytes. Pathologies and dementias of the nervous system such as Alzheimer's disease and Parkinson's disease are associated with tau proteins that have become hyperphosphorylated insoluble aggregates called neurofibrillary tangles. Pathogenic tau species causes toxic effects through direct binding to cells and/ or accumulation inside cells and/or initiation of misfolding processes (seeding) and is can be propagated from one cell to another via cell-to-cell transmission. Toxicity could also happen by neurofibrillary tangles (NFTs), which leads to cell death and cognitive decline. Other tauopathies include, for example, progressive supranuclear palsy, corticobasal syndrome, some frontotemporal dementias, and chronic traumatic encephalopathy.

[0090] Aβ/Tau Polypeptides of an Immunogen

[0091] An agent used for active immunization can induce in a patient an immune response and can serve as an immunotherapy. Agents used for active immunization can be, for example, the same types of immunogens used for generating monoclonal antibodies in laboratory animals, and may include 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, or 13 or more contiguous amino acids from a region of Aβ and/or tau peptide.

In each of the embodiments of the peptides described herein, the peptides may comprise, consist, or consist essentially of the recited sequences.

[0092] In some embodiments of the disclosure, an Aβ/tau immunogen can include an Aβ peptide comprising 3-10 amino acids from residues 1-10 or 12-25 of the N-terminal sequence of Aβ (SEQ ID NO:01) linked to a tau peptide comprising 3-10 amino acids from residues 244-400 of the long form of tau (SEQ ID NO:02). For example, the tau peptide may comprise 3-13 amino acids from the microtubule binding region of tau (residues 344-372 of SEQ ID NO:02).

[0093] In some embodiments of the disclosure, the Aβ peptide can include 3-10 amino acids from residues 1-10 or 12-25 of DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA (SEQ ID NO:01). For example, the Aβ peptide is selected from the following:

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),
SGY (SEQ ID NO:38),
VHHQKLVFFA (SEQ ID NO:1002),
VHHQKLVFF (SEQ ID NO:1003),
VHHQKLVF (SEQ ID NO:1004),
VHHQKLV (SEQ ID NO:1005),
VHHQKL (SEQ ID NO:1006),
HHQKLVFFAE (SEQ ID NO:1007),
HHQKLVFFA (SEQ ID NO:1008),
HHQKLVFF (SEQ ID NO:1009),
HHQKLVF (SEQ ID NO:1010),
HHQKLV (SEQ ID NO:1011),
HHQKL (SEQ ID NO:1012),
HQKLVFFAED (SEQ ID NO:1013),
HQKLVFFAE (SEQ ID NO:1014),
HQKLVFFA (SEQ ID NO:1015),
HQKLVFF (SEQ ID NO:1016),
HQKLVF (SEQ ID NO:1017),
HQKLV (SEQ ID NO:1018),
HQKL (SEQ ID NO:1019),
QKLVFFAEDV (SEQ ID NO:1020),

QKLVFFAED (SEQ ID NO:1021),
QKLVFFAE (SEQ ID NO:1022),
QKLVFFA (SEQ ID NO:1023),
QKLVFF (SEQ ID NO:1024),
QKLVF (SEQ ID NO:1025),
QKLV (SEQ ID NO:1026),
QKL (SEQ ID NO:1027),
KLVFFAEDVG (SEQ ID NO:1028),
KLVFFAEDV (SEQ ID NO:1029),
KLVFFAED (SEQ ID NO:1030),
KLVFFAE (SEQ ID NO:1031),
KLVFFA (SEQ ID NO:1032),
KLVFF (SEQ ID NO:1033),
KLVF (SEQ ID NO:1034),
KLV (SEQ ID NO:1035),
LVFFAEDVG (SEQ ID NO:1036),
LVFFAEDV (SEQ ID NO:1037),
LVFFAED (SEQ ID NO:1038),
LVFFAE (SEQ ID NO:1039),
LVFFA (SEQ ID NO:1040),
LVFF (SEQ ID NO:1041),
LVF (SEQ ID NO:1042),
VFFAEDVG (SEQ ID NO:1043),
VFFAEDV (SEQ ID NO:1044),
VFFAED (SEQ ID NO:1045),
VFFAE (SEQ ID NO:1046),
VFFA (SEQ ID NO:1047),
VFF (SEQ ID NO:1048),
FFAEDVG (SEQ ID NO:1049),
FFAEDV (SEQ ID NO:1050),
FFAED (SEQ ID NO:1051),
FFAE (SEQ ID NO:1052),
FFA (SEQ ID NO:1053),
FAEDVG (SEQ ID NO:1054),

FAEDV (SEQ ID NO:1055),
FAED (SEQ ID NO:1056), and
FAE (SEQ ID NO:1057).

[0094] In certain embodiments, the Aβ peptide is DAEFRHD (SEQ ID NO:06), DAEFR (SEQ ID NO:08) or EFRHD (SEQ ID NO:21).

[0095] The tau peptide can correspond to a peptide comprising 3-13 amino acids from residues 244-400 of SEQ ID NO:02. In some embodiments, the fragment is unphosphorylated. In some embodiments, the fragment is phosphorylated. In some embodiments, the tau peptide comprises an amino acid sequence represented by the consensus motif (Q/E)IVYK(S/P) (SEQ ID NO:996). In some embodiments, the tau peptide comprises an amino acid sequence represented by the consensus motif KXXSXXNX(K/H)H (SEQ ID NO: 995) where X is any amino acid. In some embodiments, the tau peptide is selected from SEQ ID NOS: 146-996. In some embodiments, the tau peptide is selected from the following:

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), and
SKIGSLDNIKH (SEQ ID NO:988).

In each of these embodiments, the peptide may comprise, consist, or consist essentially of the recited sequences.

[0096] In some embodiments, the Aβ and tau peptides are linked to form a dual Aβ/Tau polypeptide. The Aβ and tau peptides can be linked by an intra-peptide linker. For example, a polypeptide linker located between the C-terminal of the first peptide and the N terminal of the second peptide. With or without the intra-peptide linker, the Aβ peptide and the tau peptide may be positioned in a dual Aβ/tau polypeptide in any order. For example, the Aβ peptide may be positioned at the N-terminal portion of the dual polypeptide and the tau peptide may be positioned at the C-terminal portion of the dual polypeptide. Or, the tau peptide may be positioned at the N-terminal portion of the dual polypeptide and the Aβ peptide may be positioned at the C-terminal portion of the dual polypeptide side of the tau peptide. Reference to a first peptide or a second peptide herein is not intended to suggest an order of the Aβ or tau peptides in the polypeptide of the immunogens.

[0097] In addition, the C-terminal portion of the Aβ peptide, the tau peptide, or the dual Aβ-tau polypeptide can include a linker for conjugating the peptides or the polypeptide to a carrier. Linkers that couple the peptides or dual polypeptide to the carrier may include, for example, GG, GGG, KK, KKK, AA, AAA, SS, SSS, GAGA (SEQ ID NO:80), AGAG (SEQ ID NO:81), KGKG (SEQ ID NO:82), and the like between the peptides or dual polypeptide and the carrier and may further include a C-terminal or a N-terminal cysteine to provide a short peptide linker (*e.g.*, G-G-C-, K-K-C-, A-A-C-, or S-S-C-). In some embodiments, where the C-terminal residues in the immunogen are either IVYKPV (SEQ ID NO:194), VYKPV (SEQ ID NO:195),

YKPV (SEQ ID NO:196), KPV, or PV the linker is an amino acid linker that does not have a N-terminal glycine (*e.g.*, GG, GAGA (SEQ ID NO:80)). In some embodiments, the linker comprises an amino acid sequence any one of AA, AAA, KK, KKK, SS, SSS, AGAG (SEQ ID NO:81), GG, GGG, GAGA (SEQ ID NO:80), and KGKG (SEQ ID NO:82). In some embodiments, any of the Aβ peptide, the tau peptide, and the dual Aβ/tau polypeptide may include a C-terminal cysteine without the spacer. In some embodiments, any of the Aβ peptide, the tau peptide, and the dual Aβ/tau polypeptide may include a N-terminal cysteine without the spacer.

[0098] When the Aβ and tau polypeptides are linked to form a dual Aβ/tau polypeptide, the linker may be a cleavable linker. As used herein, the term "cleavable linker" refers to any linker between the antigenic peptides that promotes or otherwise renders the Aβ peptide and the tau peptide more susceptible to separation from each other by cleavage (for example, by endopeptidases, proteases, low pH or any other means that may occur within or around the antigen-presenting cell) and, thereby, processing by the antigen-presenting cell, than equivalent peptides lacking such a cleavable linker. In some compositions, the cleavable linker is a protease-sensitive dipeptide or oligopeptide cleavable linker. In certain embodiments, the cleavable linker is sensitive to cleavage by a protease of the trypsin family of proteases. In some compositions, the cleavable linker comprises an amino acid sequence selected from the group consisting of 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), GAGA (SEQ ID NO:80), AGAG (SEQ ID NO:81), and KGKG (SEQ ID NO:82). In some compositions, the cleavable linker is arginine-arginine (Arg-Arg).

[0099] In some embodiments of the disclosure, the dual Aβ/tau polypeptide comprises, consists or consists essentially of an amino acid sequence selected from DAEFRHDRRQIVYKPV (SEQ ID NO:57) or DAEFRHDRREIVYKSV (SEQ ID NO:58), or DAEFRHDRRQIVYKPVXXC (SEQ ID NO:70), wherein XX and the C-terminal cysteine are each independently optional, or DAEFRHDRREIVYKSVXXC (SEQ ID NO:79), 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), and KGKG (SEQ ID NO:82).

[00100] In some embodiments, the dual Aβ/tau polypeptide is as follows:

[first peptide]-[linker 1]-[second peptide]-[linker 2]-[Cys],

wherein, if the [first peptide] is an Aβ peptide then the [second peptide] is a tau peptide, and if the [first peptide] is a tau peptide, then the [second peptide] is an Aβ peptide, each of [linker 1], [linker 2] and [Cys] are optional, and [linker 1] and [linker 2] are the same or different linkers.

[00101] In certain embodiments, the dual Aβ/tau polypeptide is as follows:

[Cys]-[linker 2]-[first peptide]-[linker 1]-[second peptide]

wherein, if the [first peptide] is an Aβ peptide then the [second peptide] is a tau peptide, and if the [first peptide] is a tau peptide, then the [second peptide] is an Aβ peptide, and each of [linker 1], [linker 2] and [Cys] are optional, and [linker 1] and [linker 2] are the same or different linkers.

[00102] Examples of the Aβ peptide include any one SEQ ID NOS 3-38 or SEQ ID NOS:1002-1057.

[00103] Examples of the tau peptide include any one of SEQ ID NOS: 39-56, 83-86, or 146-996.

[00104] **[Linker 1]** is optional, and when present, may be a cleavable linker. A cleavable linker, if present, can be 1-10 amino acids in length. In some embodiments, the linker comprises between about 1-10 amino acids, about 1-9 amino acids, about 1-8 amino acids, about 1-7 amino acids, about 1-6 amino acids, about 1-5 amino acids, about 1-4 amino acids, about 1-3 amino acids, about 2 amino acids, or one (1) amino acid. In some embodiments, the cleavable linker is 1 amino acid, 2 amino acids, 3 amino acids, 4 amino acids, 5 amino acids, 6 amino acids, 7 amino acids, 8 amino acids, 9 amino acids, or 10 amino acids. In some embodiments, the linker may be a cleavable linker having an amino acid sequence selected from the group consisting of 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 (Gly-Ala-Gly-Ala; SEQ ID NO:81), and lysine-glycine-lysine-glycine (Lys-Gly-Lys-Gly; SEQ ID NO:82).

[00105] **[Linker 2]** is optional, and when present is a linker that couples the polypeptide to a carrier. A linker, if present, can be 1-10 amino acids in length. In some embodiments, the linker comprises between about 1-10 amino acids, about 1-9 amino acids, about 1-8 amino acids, about 1-7 amino acids, about 1-6 amino acids, about 1-5 amino acids, about 1-4 amino acids, about 1-3 amino acids, about 2 amino acids, or one (1) amino acid. In some embodiments, the linker is 1 amino acid, 2 amino acids, 3 amino acids, 4 amino acids, 5 amino acids, 6 amino acids, 7 amino acids, 8 amino acids, 9 amino acids, or 10 amino acids. In some embodiments, the amino acid composition of a linker can mimic the composition of linkers found in natural multidomain proteins, where certain amino acids are overrepresented, underrepresented or equi-represented in natural linkers as compared to their abundance in whole protein. For example, threonine (Thr), serine (Ser), proline (Pro), glycine (Gly), aspartic acid (Asp), lysine (Lys), glutamine (Gln), asparagine (Asn), arginine (Arg), phenylalanine (Phe), glutamic acid (Glu) and alanine (Ala) are overrepresented in natural linkers. In contrast, isoleucine (Ile), tyrosine (Tyr), tryptophan (Trp), and cysteine (Cys) are underrepresented. In general, overrepresented amino acids were polar uncharged or charged residues, which constitute approximately 50% of naturally encoded amino acids, and Pro, Thr, and Gln were the most preferable amino acids for natural linkers. In some embodiments, the amino acid composition of a linker can mimic the composition of linkers commonly found in recombinant proteins, which can generally by classified as flexible or rigid linkers. For example, flexible linkers found in recombinant proteins are generally composed of small, non-polar (*e.g.* Gly) or polar (*e.g.* Ser or Thr) amino acids whose small size provides flexibility and allows for mobility of the connecting functional domains. The incorporation of, *e.g.*, Ser or Thr can maintain the stability of the linker in aqueous solutions by forming hydrogen bonds with the water molecules, and therefore can reduce interactions between the linker and the immunogens. In some embodiments, a linker comprises stretches of Gly and Ser residues ("GS" linker). An example of a widely used flexible linker is (Gly-Gly-Ser)n, (Gly-Gly-Gly-Ser)n (SEQ ID NO:1062) or (Gly-Gly-Gly-Gly-Ser)n (SEQ ID NO:1063), where n=1-3. Adjusting the copy number "n" can optimize a linker to achieve sufficient separation of the functional immunogen domains to, *e.g.*, maximize an immunogenic response. Many other flexible linkers have been designed for recombinant fusion proteins that can be used herein. In some embodiments, linkers can be rich in small or

polar amino acids such as Gly and Ser but also contain additional amino acids such as Thr and Ala to maintain flexibility, as well as polar amino acids such as Lys and Glu to improve solubility. *See, e.g.*, Chen, X. *et al.*, "Fusion Protein Linkers: Property, Design and Functionality" *Adv Drug Deliv Rev.*, 15; 65(10): 1357–1369 (203). In certain embodiments, when present, the linker can be an amino acid sequence selected from the group consisting of as GG, GGG, KK, KKK, AA, AAA, SS, SSS, G-A-G-A (SEQ ID NO:80), A-G-A-G (SEQ ID NO:81), and K-G-K-G (SEQ ID NO:82).

[00106] **[Cys]** is optional and can be helpful to conjugate the polypeptide to a carrier. When present, the Cys can be at the C-terminal portion of the polypeptide, or at the N-terminal portion of the polypeptide.

[00107] Examples of the [first peptide]-[linker 1]-[second peptide]-[linker 2]-[Cys] dual Aβ/tau polypeptide of the disclosure include the following:

Table 1

Immunogen Lab ID	Abeta Sequence	Abeta SEQ ID NO.	Endo peptidase linker	Tau Sequence	tau SEQ ID NO.	C-Terminal linker	Cys	Immunogen SEQ ID NO
9	DAEFRHD	06	RR	QIVYKPV	39	GG	C	59
10	DAEFRHD	06	RR	QIVYKPV	39	None	C	60
18	DAEFRHD	06	RR	QIVYKPV	39	AA	C	61
19	DAEFRHD	06	RR	QIVYKPV	39	KK	C	62
20	DAEFRHD	06	RR	EIVYKSP	43	GG	C	63
21	DAEFRHD	06	RR	EIVYKSP	43	AA	C	64
22	DAEFRHD	06	RR	EIVYKSP	43	None	C	65
23	DAEFRHD	06	RR	EIVYKSP	43	KK	C	66
12	DAEFRHD	06	RR	NIKHVP	48	GG	C	78

[00108] **Polypeptide Immunogens**

[00109] The Aβ peptide, the tau peptide and, the dual Aβ/tau polypeptide are immunogens in accordance with the disclosure. In some embodiments, the peptides and the dual Aβ-tau polypeptide can be linked to a suitable carrier to help elicit an immune response. Accordingly, one or more the peptides and dual Aβ-tau polypeptides of the disclosure can be linked to a carrier. For example, each of the Aβ peptide, tau peptide and the Aβ-tau polypeptide may be linked to the carrier with or

without spacer amino acids (*e.g.*, Gly-Gly, Gly-Gly-Gly, Ala-Ala, Ala-Ala-Ala, Lys-Lys, Lys-Lys-Lys, Ser-Ser, Ser-Ser-Ser, Gly-Ala-Gly-Ala (SEQ ID NO:80), Ala-Gly-Ala-Gly (SEQ ID NO:81), or Lys-Gly-Lys-Gly (SEQ ID NO:82)). In certain embodiments, the dual Aβ-tau polypeptide can be linked to a suitable carrier using a C-terminal cysteine to provide a linker between the peptide(s) and the carrier or the dual Aβ/tau polypeptide and the carrier. In certain embodiments, the dual Aβ-tau polypeptide can be linked to a suitable carrier using an N-terminal cysteine to provide a linker between the peptide(s) and the carrier. In some embodiments, where the C-terminal residues in the immunogen are either IVYKPV (SEQ ID NO:194), VYKPV (SEQ ID NO:195), YKPV (SEQ ID NO:196), KPV, or PV the linker is an amino acid linker that does not have a N-terminal glycine (*e.g.*, GG, GAGA (SEQ ID NO:80)).

[00110] Suitable carriers include, but are not limited to serum albumins, keyhole limpet hemocyanin, immunoglobulin molecules, thyroglobulin, ovalbumin, tetanus toxoid, or a toxoid from other pathogenic bacteria, such as diphtheria (*e.g.*, CRM197), *E. coli*, cholera, or *H. pylori*, or an attenuated toxin derivative. T cell epitopes are also suitable carrier molecules. Some conjugates can be formed by linking peptide immunogens of the invention to an immunostimulatory polymer molecule (*e.g.*, tripalmitoyl-S-glycerine cysteine (Pam3Cys), mannan (a mannose polymer), or glucan (a β 1-2 polymer)), cytokines (*e.g.*, IL-1, IL-1 alpha and β peptides, IL-2, γ-INF, IL-10, GM-CSF), and chemokines (*e.g.*, MIP1-α and β, and RANTES). Additional carriers include virus-like particles. In some compositions, immunogenic peptides can also be linked to carriers by chemical crosslinking. Techniques for linking an immunogen to a carrier include the formation of disulfide linkages using N-succinimidyl 3-(2-pyridylthio)propionate (SPDP), and succinimidyl 4-(N-maleimidomethyl)cyclohexane-1-carboxylate (SMCC) (if the peptide lacks a sulfhydryl group, this can be provided by addition of a cysteine residue). These reagents create a disulfide linkage between themselves and peptide cysteine resides on one protein and an amide linkage through the epsilon-amino on a lysine, or other free amino group in other amino acids. In some embodiments, chemical crosslinking can comprise use of SBAP (succinimidyl 3-(bromoacetamido)propionate), which is a short (6.2 angstrom) cross-linker for amine-to-sulfhydryl conjugation via N-hydroxysuccinimide (NHS) ester and bromoacetyl reactive groups. A variety of such disulfide/amide-forming agents are described by Jansen *et al.*, "Immunotoxins:

Hybrid Molecules Combining High Specificity and Potent Cytotoxicity" *Immunological Reviews* 62:185-216 (February 1982). Other bifunctional coupling agents form a thioether rather than a disulfide linkage. Many of these thio-ether-forming agents are commercially available and include reactive esters of 6-maleimidocaproic acid, 2-bromoacetic acid, and 2-iodoacetic acid, 4-(N-maleimido-methyl)cy- clohexane-1-carboxylic acid. The carboxyl groups can be activated by combining them with succinimide or 1-hydroxyl-2-nitro-4-sulfonic acid, sodium salt. Virus-like particles (VLPs), also called pseudovirions or virus-derived particles, represent subunit structures composed of multiple copies of a viral capsid and/or envelope protein capable of self-assembly into VLPs of defined spherical symmetry *in vivo*. (Powilleit, *et al.*, (2007) *PLoS ONE* 2(5):e415.) Alternatively, peptide immunogens can be linked to at least one artificial T-cell epitope capable of binding a large proportion of MHC Class II molecules, such as the pan DR epitope ("PADRE"). Pan DR-binding peptides (PADRE) are described in US 5,736,142, WO 95/07707, and Alexander, *et al*, *Immunity*, 1:751-761 (1994).

[00111] Active immunogens can be presented in multimeric form in which multiple copies of an immunogen (peptide of polypeptide) are presented on a carrier as a single covalent molecule. In some embodiments, the carrier includes various forms of the dual Aβ/tau polypeptide. For instance, the dual Aβ/tau polypeptide of the immunogen can include polypeptides that have the Aβ antigen and the tau antigen in different orders, or may be present with or without an intrapeptide linker and/or a linker to a carrier.

[00112] In some compositions, the immunogenic peptides can also be expressed as fusion proteins with carriers. In certain compositions, the immunogenic peptides can be linked at the amino terminus, the carboxyl terminus, or internally to the carrier. In some compositions, the carrier is CRM197. In some compositions, the carrier is diphtheria toxoid.

[00113] **Nucleic Acids**

[00114] The disclosure further provides nucleic acids encoding any of the amyloid-beta (Aβ) peptides and the tau peptides as disclosed herein. The nucleic acid immunotherapy compositions, as disclosed herein, comprise, consist of, or consist essentially of, a first nucleic acid sequence encoding an amyloid-beta (Aβ) peptide,

and a second nucleic acid sequence encoding a tau peptide as disclosed herein. For example, the Aβ peptide is a sequence that is 3-10 amino acid residues in length and from the first ten N-terminal residues of SEQ ID NO:01, and the tau peptide is a sequence that is 3-13 amino acids in length and from residues 244-400 of SEQ ID NO:02. Accordingly, a nucleic acid encoding any of SEQ ID NOS: 3-38 or SEQ ID NOS:1002-1057 may be combined with a nucleic acid encoding any of SEQ ID NOS: 39-56, 83-86, or 146-996 to provide an immunogen and a component of pharmaceutical composition of the disclosure. Likewise, one or more nucleic acids encoding any of Abeta and tau sequences may include the codons for an RR- N-terminal or -RR C-terminal dipeptide. In certain embodiments, the Aβ and tau peptide sequences may be encoded by the same nucleic acid sequence or by separate nucleic acid sequences. In some embodiments, the nucleic acid sequences may also encode a linker to a carrier and/or a C-terminal cysteine as described herein. In addition, when a single nucleic acid sequence encodes both peptides, the sequence may also encode an intra-peptide linker as described herein. The nucleic acid compositions described herein (pharmaceutical compositions) can be used in methods for treating or effecting prophylaxis and/or prevention of Alzheimer's disease. In another embodiment, the nucleic acid immunotherapy compositions as disclosed herein provide compositions for reducing pathogenic forms of Aβ and/or tau in the subject and/or in the tissue of the subject. In some embodiments, the Aβ and/or tau reduced by the immunotherapy compositions is the pathological form(s) of the Aβ (*e.g.* extracellular plaque deposits of the β-amyloid peptide (Aβ); neuritic amyloid plaques), and/or tau (*e.g.* flame-shaped neurofibrillary tangles of tau; neurofibrillary tangles of tau). In yet other embodiment, pathological indicators of neurodegenerative disease are decreased by the nucleic acid immunotherapy compositions. In another embodiment, the nucleic acid immunotherapy compositions as disclosed herein provide compositions for reducing brain Aβ and brain tau.

[00115] A nucleic acid such as DNA that encodes an immunogen and is used as a vaccine can be referred to as a "DNA immunogen" or "DNA vaccine" as the encoded polypeptides are expressed *in vivo* after administration of the DNA. DNA vaccines are intended to induce antibodies against the proteins of interest they encode in a subject by: integrating DNA encoding the proteins of interest into a vector (a plasmid or virus); administering the vector to the subject; and expressing the proteins

of interest in the subject in which the vector has been administered to stimulate the immune system of the subject. A DNA vaccine remains in the body of the subject for a long time after the administration, and continues to slowly produce the encoded proteins. Thus, excessive immune responses can be avoided. DNA vaccines can also be modified using a genetic engineering techniques. Optionally, such nucleic acids further encode a signal peptide and can be expressed with the signal peptide linked to peptide. Coding sequences of nucleic acids can be operably linked with regulatory sequences to ensure expression of the coding sequences, such as a promoter, enhancer, ribosome binding site, transcription termination signal, and the like. The nucleic acids encoding Aβ and tau can occur in isolated form or can be cloned into one or more vectors. The nucleic acids can be synthesized by, for example, solid state synthesis or PCR of overlapping oligonucleotides. Nucleic acids encoding Aβ and tau peptides and polypeptides with and without linkers or cleavable linkers and with our without protein based carriers can be joined as one contiguous nucleic acid, *e.g.*, within an expression vector.

[00116] DNA is more stable than RNA, but involves some potential safety risks such as induction of anti-DNA antibodies, thus in some embodiments, the nucleic acid can be RNA. RNA nucleic acid that encodes an immunogen and is used as a vaccine can be referred to as a "RNA immunogen" or "RNA vaccine" or "mRNA vaccine" as the encoded polypeptides are expressed *in vivo* after administration of the RNA. Ribonucleic acid (RNA) vaccines can safely direct a subject's cellular machinery to produce one or more polypeptide(s) of interest. In some embodiments, a RNA vaccine can be a non-replicating mRNA (messenger-RNA) or a virally derived, self-amplifying RNA. mRNA-based vaccines encode the antigens of interest and contain 5′ and 3′ untranslated regions (UTRs), whereas self-amplifying RNAs encode not only the antigens, but also the viral replication machinery that enables intracellular RNA amplification and abundant protein expression. *In vitro* transcribed mRNA can be produced from a linear DNA template using a T7, a T3 or an Sp6 phage RNA polymerase. The resulting product can contain an open reading frame that encodes the peptides of interest as disclosed herein, flanking 5′- and 3′-UTR sequences, a 5′ cap and a poly(A) tail. In some embodiments, a RNA vaccine can comprise trans-amplifying RNA (for example, *see* Beissert *et al., Molecular Therapy* January 2020 28(1):119-128). In certain embodiments, RNA vaccines encode an Aβ peptide and a

tau peptide as disclosed herein, and are capable of expressing the Aβ and a tau peptides, in particular if transferred into a cell such as an immature antigen presenting cell. RNA may also contain sequences which encode other polypeptide sequences such as immune stimulating elements. In some embodiments, the RNA of a RNA vaccine can be modified RNA. The term "modified" in the context of the RNA can include any modification of RNA which is not naturally present in RNA. For example, modified RNA can refer to RNA with a 5'-cap; however, RNA may comprise further modifications. A 5'-cap can be modified to possess the ability to stabilize RNA when attached thereto. In certain embodiments, a further modification may be an extension or truncation of the naturally occurring poly(A) tail or an alteration of the 5'- or 3'-untranslated regions (UTR). In some embodiments, the RNA *e.g.* or mRNA vaccine is formulated in an effective amount to produce an antigen specific immune response in a subject. For example, the RNA vaccine formulation is administered to a subject in order to stimulate the humoral and/or cellular immune system of the subject against the Aβ and tau antigens, and thus may further comprise one or more adjuvant(s), diluents, carriers, and/or excipients, and is applied to the subject in any suitable route in order to elicit a protective and/or therapeutic immune reaction against the Aβ and tau antigens.

[00117] Basic texts disclosing general methods of molecular biology, all of which are incorporated by reference, include: Sambrook, J *et al.*, Molecular Cloning: A Laboratory Manual, 2nd Edition, Cold Spring Harbor Press, Cold Spring Harbor, N.Y., 1989; Ausubel, F M *et al.* Current Protocols in Molecular Biology, Vol. 2, Wiley-Interscience, New York, (current edition); Kriegler, Gene Transfer and Expression: A Laboratory Manual (1990); Glover, D M, ed, DNA Cloning: A Practical Approach, vol. I & II, IRL Press, 1985; Albers, B. *et al.*, Molecular Biology of the Cell, 2nd Ed., Garland Publishing, Inc., New York, N.Y. (1989); Watson, J D *et al.*, Recombinant DNA, 2nd Ed., Scientific American Books, New York, 1992; and Old, R W *et al.*, Principles of Gene Manipulation: An Introduction to Genetic Engineering, 2nd Ed., University of California Press, Berkeley, Calif. (1981).

[00118] Techniques for the manipulation of nucleic acids, such as, *e.g.*, generating mutations in sequences, sub-cloning, labeling probes, sequencing, hybridization and the like are well described in the scientific and patent literature. See, *e.g.*, Sambrook, ed., MOLECULAR CLONING: A LABORATORY MANUAL

(2ND ED.), Vols. 1-3, Cold Spring Harbor Laboratory, (1989); CURRENT PROTOCOLS IN MOLECULAR BIOLOGY, Ausubel, ed. John Wiley & Sons, Inc., New York (1997); LABORATORY TECHNIQUES IN BIOCHEMISTRY AND MOLECULAR BIOLOGY: HYBRIDIZATION WITH NUCLEIC ACID PROBES, Part I. Tijssen, ed. Elsevier, N.Y. (1993).

[00119] Nucleic acids, vectors, capsids, polypeptides, and the like can be analyzed and quantified by any of a number of general means well known to those of skill in the art. These include, *e.g.*, analytical biochemical methods such as NMR, spectrophotometry, radiography, electrophoresis, capillary electrophoresis, high performance liquid chromatography (HPLC), thin layer chromatography (TLC), and hyperdiffusion chromatography, various immunological methods, *e.g.* fluid or gel precipitin reactions, immunodiffusion, immuno-electrophoresis, radioimmunoassays (RIAs), enzyme-linked immunosorbent assays (ELISAs), immunofluorescence assays, Southern analysis, Northern analysis, dot-blot analysis, gel electrophoresis (*e.g.*, SDS-PAGE), RT-PCR, quantitative PCR, other nucleic acid or target or signal amplification methods, radiolabeling, scintillation counting, and affinity chromatography.

[00120] **Pharmaceutical Compositions**

[00121] Each of the peptides and immunogens described herein can be presented in a pharmaceutical composition that is administered with pharmaceutically acceptable adjuvants and pharmaceutically acceptable excipients. The adjuvant increases the titer of induced antibodies and/or the binding affinity of induced antibodies relative to the situation if the peptide were used alone. A variety of adjuvants can be used in combination with an immunogen of the disclosure to elicit an immune response. Some adjuvants augment the intrinsic response to an immunogen without causing conformational changes in the immunogen that affect the qualitative form of the response. An adjuvant may be a natural compound, a modified version of or derivative of a natural compound, or a synthetic compound.

[00122] Some adjuvants include aluminum salts, such as aluminum hydroxide and aluminum phosphate, 3 De-O-acylated monophosphoryl lipid A (MPL™) (*see* GB 2220211 (RIBI ImmunoChem Research Inc., Hamilton, Montana, now part of

Corixa). As used herein, MPL refers to natural and synthetic versions of MPL. Examples of synthetic versions include PHAD®, 3D-PHAD® and 3D(6A)-PHAD® (Avanti Polar Lipids, Alabaster, Alabama).

[00123] QS-21 is a triterpene glycoside or saponin isolated from the bark of the Quillaja saponaria Molina tree found in South America (*see* Kensil *et al.*, in Vaccine Design: The Subunit and Adjuvant Approach (eds. Powell & Newman, Plenum Press, NY, 1995)) QS-21 products include Stimulon® (Antigenics, Inc., New York, NY; now Agenus, Inc. Lexington, MA) and QS-21 Vaccine Adjuvant (Desert King, San Diego, CA). QS-21 has been disclosed, characterized, and evaluated in US 5,057,540, and US 8,034,348, the disclosures of which are herein incorporated by reference. Additionally, QS-21 has been evaluated in numerous clinical trials in various dosages. See, NCT00960531 (clinicaltrials.gov/ct2/show/study/NCT00960531), Hüll *et al.*, *Curr Alzheimer Res.* 2017 Jul; 14(7): 696–708 (evaluated 50 mcg of QS-21 in with various doses of vaccine ACC-001); Gilman *et al.*, "Clinical effects of Abeta immunization (AN1792) in patients with AD in an interrupted trial" *Neurology*. 2005 May 10; 64(9):1553-62; Wald *et al.*, "Safety and immunogenicity of long HSV-2 peptides complexed with rhHsc70 in HSV-2 seropositive persons" Vaccine 2011; 29(47):8520–8529; and Cunningham *et al.*, "Efficacy of the Herpes Zoster Subunit Vaccine in Adults 70 Years of Age or Older." *NEJM*. 2016 Sep 15; 375(11):1019-32. QS-21 is used in FDA approved vaccines including SHINGRIX. SHINGRIX contains 50 mcg of QS-21. In certain embodiments, the amount of QS-21 is from about 10 μg to about 500 μg.

[00124] TQL1055 is an analogue of QS-21 (Adjuvance Technologies, Lincoln, NE). The semi-synthetic TQL1055 has been characterized in comparison to QS-21 as having high purity, increased stability, decreased local tolerability, decreased systemic tolerability. TQL1055 has been disclosed, characterized, and evaluated in US20180327436 A1, WO2018191598 A1, WO2018200656 A1, and WO2019079160 A1, the disclosures of which are herein incorporated by reference. US20180327436 A1 teaches that 2.5 fold more TQ1055 was superior to 20 μg QS-21 but there was not an improvement over 50 μg TQ1055. However, unlike QS-21 there was no increase in either weight loss or hemolysis of RBC as the TQL1055 dose increased. WO2018200656 A1 teaches that with an optimal amount of TQ1055, one can lower

the amount of antigen and achieve superior titers. In certain embodiments, the amount of TQL1055 is from about 10 μg to about 500 μg.

[00125] Other adjuvants are oil in water emulsions (such as squalene or peanut oil), optionally in combination with immune stimulants, such as monophosphoryl lipid A (*see* Stoute *et al.*, *N. Engl. J. Med.* 336, 86-91 (1997)), pluronic polymers, and killed mycobacteria. Ribi adjuvants are oil-in-water emulsions. Ribi contains a metabolizable oil (squalene) emulsified with saline containing Tween 80. Ribi also contains refined mycobacterial products which act as immunostimulants and bacterial monophosphoryl lipid A. Other adjuvants can be CpG oligonucleotides (*see* WO 98/40100), cytokines (*e.g.*, IL-1, IL-1 alpha and β peptides, IL-2, γ-INF, IL-10, GM-CSF), chemokines (*e.g.*, MIP1-α and β, and RANTES), saponins, RNA, and/or TLR agonists (for example, TLR4 agonists such as MPL and synthetic MPL molecules), aminoalkyl glucosaminide phosphate and other TLR agonists. Adjuvants can be administered as a component of a therapeutic composition with an active agent or can be administered separately, before, concurrently with, or after administration of the therapeutic agent.

[00126] In various embodiments of the disclosure, the adjuvant is QS-21 (Stimulon™). In some compositions, the adjuvant is MPL. In certain embodiments, the amount of MPL is from about 10 μg to about 500 μg. In some compositions, the adjuvant is TQL1055. In certain embodiments, the amount of TQL1055 is from about 10 μg to about 500 μg. In some compositions, the adjuvant is QS21. In certain embodiments, the amount of QS21 is from about 10 μg to about 500 μg. In some compositions, the adjuvant is a combination of MPL and QS-21. In some compositions, the adjuvant is a combination of MPL and TQL1055. In some compositions, the adjuvant can be in a liposomal formulation.

[00127] In addition, some embodiments of the disclosure can comprise a multiple antigen presenting system (MAP). Multiple antigen-presenting peptide vaccine systems have been developed to avoid the adverse effects associated with conventional vaccines (*i.e.*, live-attenuated, killed or inactivated pathogens), carrier proteins and cytotoxic adjuvants. Two main approaches have been used to develop multiple antigen presenting peptide vaccine systems: (1) the addition of functional components, *e.g.*, T-cell epitopes, cell-penetrating peptides, and lipophilic moieties; and (2) synthetic approaches using size-defined nanomaterials, *e.g.*, self-assembling

peptides, non-peptidic dendrimers, and gold nanoparticles, as antigen-displaying platforms. Use of a multiple antigenic peptide (MAP) system can improve the sometimes poor immunogenicity of subunit peptide vaccines. In a MAP system, multiple copies of antigenic peptides are simultaneously bound to the a- and ε-amino groups of a non-immunogenic Lys-based dendritic scaffold, helping to confer stability from degradation, thus enhancing molecular recognition by immune cells, and induction of stronger immune responses compared with small antigenic peptides alone. In some compositions, 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.

[00128] Pharmaceutical compositions for parenteral administration are preferably sterile and substantially isotonic and manufactured under GMP conditions. Pharmaceutical compositions can be provided in unit dosage form (*i.e.*, the dosage for a single administration). Pharmaceutical compositions can be formulated using one or more physiologically acceptable carriers, diluents, excipients or auxiliaries. The formulation depends on the route of administration chosen. For injection, the peptides of the disclosure can be formulated in aqueous solutions, preferably in physiologically compatible buffers such as Hank's solution, Ringer's solution, or physiological saline or acetate buffer (to reduce discomfort at the site of injection). The solution can contain formulatory agents such as suspending, stabilizing and/or dispersing agents. Alternatively, peptide compositions can be in lyophilized form for constitution with a suitable vehicle, *e.g.*, sterile pyrogen-free water, before use.

[00129] Peptides (and optionally a carrier fused to the peptide(s)) can also be administered in the form of a nucleic acid encoding the peptide(s) and expressed *in situ* in a subject. A nucleic acid segment encoding an immunogen is typically linked to regulatory elements, such as a promoter and enhancer that allow expression of the DNA segment in the intended target cells of a subject. For expression in blood cells, as is desirable for induction of an immune response, promoter and enhancer elements from, for example, light or heavy chain immunoglobulin genes or the CMV major intermediate early promoter and enhancer are suitable to direct expression. The linked regulatory elements and coding sequences are often cloned into a vector.

[00130] DNA and RNA can be delivered in naked form (*i.e.*, without colloidal or encapsulating materials). Alternatively a number of viral vector systems can be used including retroviral systems (see, *e.g.*, Boris-Lawrie and Teumin, *Cur. Opin. Genet. Develop.* 3(1):102-109 (1993)); adenoviral vectors (see, *e.g.*, Bett *et al*, *J. Virol.* 67(10);5911-21 (1993)); adeno-associated virus vectors (see, *e.g.*, Zhou *et al.*, *J. Exp. Med.* 179(6):1867-75 (1994)), viral vectors from the pox family including vaccinia virus and the avian pox viruses, viral vectors from the alpha virus genus such as those derived from Sindbis and Semliki Forest Viruses (*see*, *e.g.*, Dubensky *et al.*, *J. Virol.* 70(1):508-519 (1996)), Venezuelan equine encephalitis virus (*see* US 5,643,576) and rhabdoviruses, such as vesicular stomatitis virus (*see* WO 96/34625) and papillomaviruses (WO 94/12629; Ohe *et al.*, *Human Gene Therapy* 6(3):325-333 (1995); and Xiao & Brandsma, *Nucleic Acids. Res.* 24(13):2620-2622 (1996)).

[00131] DNA and RNA encoding an immunogen, or a vector containing the same, can be packaged into liposomes, nanoparticles or lipoproteins complexes. Suitable other polymers, include, for example, protamine liposomes, polysaccharide particles, cationic nanoemulsion, cationic polymer, cationic polymer liposome, cationic lipid nanoparticles, cationic lipid, cholesterol nanoparticles, cationic lipid-cholesterol, PEG nanoparticle, or dendrimer nanoparticles. Additional suitable lipids and related analogs are described by US 5,208,036, US 5,264,618, US 5,279,833, and US 5,283,185, each of which are herein incorporated by reference in their entirety. Vectors and DNA encoding an immunogen can also be adsorbed to or associated with particulate carriers, examples of which include polymethyl methacrylate polymers and polylactides and poly(lactide-co-glycolides), (*see*, *e.g.*, McGee *et al.*, *J. Micro Encap.* Mar-Apr 1997; 14(2):197-210).

[00132] Pharmaceutically acceptable carrier compositions can also include additives, including, but not limited to, water, pharmaceutically acceptable organic solvents, collagen, polyvinyl alcohol, polyvinylpyrrolidone, carboxyvinyl polymers, carboxymethylcellulose sodium, sodium polyacrylate, sodium alginate, water-soluble dextran, carboxymethyl starch sodium, pectin, methylcellulose, ethylcellulose, xanthan gum, gum arabic, casein, agar, polyethylene glycol, diglycerine, glycerine, propylene glycol, petrolatum, paraffin, stearyl alcohol, stearic acid, human serum albumin, mannitol, sorbitol, lactose, and surfactants acceptable as pharmaceutical additives.

[00133] Subjects Amenable to Treatment

[00134] The presence of Aβ plaques and/or neurofibrillary tangles has been found in several diseases including Alzheimer's disease, Down's syndrome, mild cognitive impairment, cerebral amyloid angiopathy, primary age-related tauopathy, postencephalitic parkinsonism, posttraumatic dementia or dementia pugilistica, Pick's disease, type C Niemann-Pick disease, supranuclear palsy, frontotemporal dementia, frontotemporal lobar degeneration, argyrophilic grain disease, globular glial tauopathy, amyotrophic lateral sclerosis/parkinsonism dementia complex of Guam, corticobasal degeneration (CBD), dementia with Lewy bodies, Lewy body variant of Alzheimer's disease (LBVAD), chronic traumatic encephalopathy (CTE), globular glial tauopathy (GGT), Parkinson's disease, progressive supranuclear palsy (PSP), dry age-related macular degeneration (AMD), and inclusion-body myositis.

[00135] The compositions and methods of the disclosure can be used in treatment or prophylaxis of any of these diseases. Because of the widespread association between neurological diseases and Aβ and/or tau, the compositions and methods of the disclosure can be used in treatment or prophylaxis of any subject showing elevated levels of Aβ and/or tau (*e.g.*, in the CSF) compared with a mean value in individuals without neurological disease. The compositions and methods of the disclosure can also be used in treatment or prophylaxis of neurological disease in individuals having a mutation in Aβ and/or tau associated with neurological disease. The methods are particularly suitable for treatment or prophylaxis of Alzheimer's disease.

[00136] Subjects amenable to treatment include individuals at risk of disease but not showing symptoms, as well as patients presently showing symptoms, including treatment naïve subjects that have not been previous treated for disease. Subjects at risk of disease include those in an aging population, asymptomatic subjects with Aβ and/or tau pathologies and having a known genetic risk of disease. Such individuals include those having relatives who have experienced this disease, and those whose risk is determined by analysis of genetic or biochemical markers. Genetic markers of risk include mutations in Aβ and/or tau, as well as mutations in other genes associated with neurological disease. For example, the ApoE4 allele in heterozygous and even more so in homozygous form is associated with risk of Alzheimer's disease (AD). Other markers of risk of Alzheimer's disease include

mutations in the APP gene, particularly mutations at position 717 and positions 670 and 671 referred to as the Hardy and Swedish mutations respectively, mutations in the presenilin genes, PS1 and PS2, a family history of AD, hypercholesterolemia or atherosclerosis. Individuals presently suffering from Alzheimer's disease can be recognized by PET imaging, from characteristic dementia, as well as the presence of risk factors described above. In addition, a number of diagnostic tests are available for identifying individuals who have AD. These include measurement of CSF or blood tau or phospho-tau and Aβ42 levels. Elevated tau or phospho-tau and decreased Aβ42 levels signify the presence of AD. Some mutations associated with Parkinson's disease, for example, Ala30Pro or Ala53Thr, or mutations in other genes associated with Parkinson's disease such as leucine-rich repeat kinase (LRRK2 or PARK8). Subjects can also be diagnosed with any of the neurological diseases mentioned above by the criteria of the DSM IV TR.

[00137] In asymptomatic subjects, treatment can begin at any age (*e.g.*, 10, 20, 30, or more). Usually, however, it is not necessary to begin treatment until a subject reaches 20, 30, 40, 50, 60, 70, 80, or 90 years of age. Treatment typically entails multiple dosages over a period of time. Treatment can be monitored by assaying antibody levels over time. If the response falls, a booster dosage is indicated. In the case of potential Down's syndrome patients, treatment can begin antenatally by administering therapeutic agent to the mother or shortly after birth.

[00138] **Methods of Treatments and Uses**

[00139] The disclosure provides methods of inhibiting or reducing aggregation of Abeta and/or tau in a subject having or at risk of developing a neurodegenerative disease (*e.g.*, Alzheimer's disease). The methods include administering to the subject the compositions as disclosed herein. A therapeutically effective amount is a dosage that, when given for an effective period of time, achieves the desired immunological or clinical effect. Dosage regimens may be adjusted to provide the optimum therapeutic response. For example, several divided doses may be administered at set intervals (*e.g.*, weekly, monthly) or the dose may be proportionally reduced as indicated by the exigencies of the therapeutic situation.

[00140] In prophylactic applications, the compositions described herein can be administered to a subject susceptible to, or otherwise at risk of a disease (*e.g.*, Alzheimer's disease) in a regimen (dose, frequency and route of administration) effective to reduce the risk, lessen the severity, or delay the onset of at least one sign or symptom of the disease. In particular, the regimen is effective to inhibit or delay Aβ plaque formation and/or inhibit or delay tau or phospho-tau and paired filaments formed from it in the brain, and/or inhibit or delay its toxic effects and/or inhibit/or delay development of behavioral deficits. In therapeutic applications, the compositions described herein are administered to a subject suspected of, or a patient already suffering from a disease (*e.g.*, Alzheimer's disease) in a regimen (dose, frequency and route of administration) effective to ameliorate or at least inhibit further deterioration of at least one sign or symptom of the disease. In particular, the regimen is preferably effective to reduce or at least inhibit further increase of levels of Aβ plaques and/or tau, phosphor-tau, or paired filaments formed from it, associated toxicities and/or behavioral deficits.

[00141] A regimen is considered therapeutically or prophylactically effective if an individual treated achieves an outcome more favorable than the mean outcome in a control population of comparable subjects not treated by methods of the invention, or if a more favorable outcome is demonstrated in treated subjects versus control subjects in a controlled clinical trial (*e.g.*, a phase II, phase II/III or phase III trial) at the $p < 0.05$ or 0.01 or even 0.001 level.

[00142] Effective doses of vary depending on many different factors, such as means of administration, target site, physiological state of the patient, whether the patient is an ApoE carrier, whether the patient is human or an animal, other medications administered, and whether treatment is prophylactic or therapeutic.

[00143] In some embodiments, the effective amount is a total dose of 25 μg to 1000 μg, or 50 μg to 1000 μg. In some embodiments, the effective amount is a total dose of 100 μg. In some embodiments, the effective amount is a dose of 25 μg administered to the subject a total of two times. In some embodiments, the effective amount is a dose of 100 μg administered to the subject a total of two times. In some embodiments, the effective amount is a dose of 400 μg administered to the subject a total of two times. In some embodiments, the effective amount is a dose of 500 μg administered to the subject a total of two times. In some embodiments, a RNA (*e.g.*,

mRNA) vaccine is administered to a subject by intradermal, intramuscular injection, or by intranasal administration.

[00144] In some embodiments, the amount of an agent for active immunotherapy varies from 1 to 1,000 micrograms (μg), or from 0.1-500 μg, or from 10 to 500 μg, or from 50 to 250 μg per patient and can be from 1-100 or 1-10 μg per injection for human administration. The timing of injections can vary significantly from once a day, to once a week, to once a month, to once a year, to once a decade. A typical regimen consists of an immunization followed by booster injections at time intervals, such as 6 week intervals or two months. Another regimen consists of an immunization followed by one or more booster injections 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12 months later. Another regimen entails an injection every two months for life. Alternatively, booster injections can be on an irregular basis as indicated by monitoring of immune response. The frequency of administration may be once or more as long as the side effects are within a clinically acceptable range.

[00145] In some embodiments, the compositions or methods as disclosed herein comprise administering to a subject a nucleic acid vaccine comprising one or more DNA or RNA polynucleotides having an open reading frame encoding a first peptide and a second peptide wherein a dosage of between 10 μg/kg and 400 μg /kg of the nucleic acid vaccine is administered to the subject. In some embodiments the dosage of the RNA polynucleotide is 1-5 μg, 5-10 μg, 10-15 μg, 15-20 μg, 10-25 μg, 20-25 μg, 20-50 μg, 30-50 μg, 40-50 μg, 40-60 μg, 60-80 μg, 60-100 μg, 50-100 μg, 80-120 μg, 40-120 μg, 40-150 μg, 50-150 μg, 50-200 μg, 80-200 μg, 100-200 μg, 120-250 μg, 150-250 μg, 180-280 μg, 200-300 μg, 50-300 μg, 80-300 μg, 100-300 μg, 40-300 μg, 50-350 μg, 100-350 μg, 200-350 μg, 300-350 μg, 320-400 μg, 40-380 μg, 40-100 μg, 100-400 μg, 200-400 μg, or 300-400 μg per dose. In some embodiments, the nucleic acid is administered to the subject by intradermal or intramuscular injection. In some embodiments, the nucleic acid is administered to the subject on day zero. In some embodiments, a second dose of the nucleic acid is administered to the subject on day seven, or fourteen, or twenty one.

[00146] The compositions described herein are preferably administered via a peripheral route (*i.e.*, one in which the administered composition results in a robust immune response and/or the induced antibody population crosses the blood brain barrier to reach an intended site in the brain, spinal cord, or eye). For peripheral

diseases, the induced antibodies leave the vasculature to reach the intended peripheral organs. Routes of administration include oral, subcutaneous, intranasal, intradermal, or intramuscular. Some routes for active immunization are subcutaneous and intramuscular. Intramuscular administration and subcutaneous administration can be made at a single site or multiple sites. Intramuscular injection is most typically performed in the arm or leg muscles. In some methods, agents are injected directly into a particular tissue where deposits have accumulated.

[00147] The number of dosages administered can be adjusted to result in a more robust immune response (for example, higher titers). For acute disorders or acute exacerbations of a chronic disorder, between 1 and 10 doses are often sufficient. Sometimes a single bolus dose, optionally in divided form, is sufficient for an acute disorder or acute exacerbation of a chronic disorder. For chronic disorders, a vaccine/immunotherapy as disclosed herein can be administered at regular intervals, *e.g.*, weekly, fortnightly, monthly, quarterly, every six months for at least 1, 5 or 10 years, or the life of the patient.

[00148] An effective amount of a DNA or RNA encoded immunogen can be between about 1 nanogram and about 1 gram per kilogram of body weight of the recipient, or about between about 0.1 μg/kg and about 10 mg/kg, or about between about 1 μg/kg and about 1 mg/kg. Dosage forms suitable for internal administration preferably contain (for the latter dose range) from about 0.1 μg to 100 μg of active ingredient per unit. The active ingredient may vary from 0.5 to 95% by weight based on the total weight of the composition. Alternatively, an effective dose of dendritic cells loaded with the antigen is between about 10^4 and 10^8 cells. Those skilled in the art of immunotherapy will be able to adjust these doses without undue experimentation.

[00149] The nucleic acid compositions may be administered in a convenient manner, *e.g.*, injection by a convenient and effective route. Routes can include, but are not limited to, intradermal "gene gun" delivery or intramuscular injection. The modified dendritic cells are administered by subcutaneous, intravenous or intramuscular routes. Other possible routes include oral administration, intrathecal, inhalation, transdermal application, or rectal administration.

[00150] Depending on the route of administration, the composition may be coated in a material to protect the compound from the action of enzymes, acids and other natural conditions which may inactivate the compound. Thus, it may be necessary to coat the composition with, or co-administer the composition with, a material to prevent its inactivation. For example, an enzyme inhibitors of nucleases or proteases (*e.g.*, pancreatic trypsin inhibitor, diisopropylfluorophosphate and trasylol) or in an appropriate carrier such as liposomes (including water-in-oil-in-water emulsions) as well as conventional liposomes (Strejan *et al.*, *J. Neuroimmunol* 7(1):27-41, 1984).

[00151] The immunotherapeutic compositions disclosed herein may also be used in combination with other treatments for diseases associated with the accumulation of Aβ or tau, for example, anti-Aβ antibodies such as antibodies that specifically bind to any of the Aβ epitopes disclosed herein. For example, aducanumab or any of the antibodies disclosed in, for example, U.S. Patent Publication No. 20100202968 and U.S. Patent No. 8,906,367, and/or anti-tau antibodies such as antibodies that specifically bind to any of the tau epitopes disclosed herein, ABBV-8E12, gosuranemab, zagotenemab, RG-6100, BIIB076 or any of the antibodies disclosed in WO2014/165271, US 10,501,531, WO2017/191559, WO2017/191560, WO2017/191561, US 20190330314, US 20190330316, and WO2018/204546. In some combination therapy methods, the patient receives passive immunotherapy prior to the active immunotherapy methods disclosed herein. In other methods, the patient receives passive and active immunotherapy during the same period of treatment. Alternatively, patients may receive active immunotherapy prior to passive immunotherapy. Combinations may also include small molecule therapies and non-immunogenic therapies such as RAZADYNE® (galantamine), EXELON® (rivastigmine), and ARICEPT® (donepezil) and other compositions that improve the function of nerve cells in the brain.

[00152] The compositions of the disclosure may be used in the manufacture of medicaments for the treatment regimens described herein.

[00153] **Treatment Regimens**

[00154] Desired outcomes of the methods of treatment as disclosed herein vary according to the disease and patient profile and are determinable to those skilled in the

art. Desired outcomes include an improvement in the patient's health status. Generally, desired outcomes include measurable indices such as reduction or clearance of pathologic amyloid fibrils, decreased or inhibited amyloid aggregation and/or deposition of amyloid fibrils, and increased immune response to pathologic and/or aggregated amyloid fibrils. Desired outcomes also include amelioration of amyloid disease-specific symptoms. As used herein, relative terms such as "improve," "increase," or "reduce" indicate values relative to a control, such as a measurement in the same individual prior to initiation of treatment described herein, or a measurement in a control individual or group. A control individual is an individual afflicted with the same amyloid disease as the individual being treated, who is about the same age as the individual being treated (to ensure that the stages of the disease in the treated individual and the control individual are comparable), but who has not received treatment using the disclosed immunotherapy/vaccine formulations. Alternatively, a control individual is a healthy individual, who is about the same age as the individual being treated. Changes or improvements in response to therapy are generally statistically significant and described by a p-value less than or equal to 0.1, less than 0.05, less than 0.01, less than 0.005, or less than 0.001 may be regarded as significant.

[00155] Effective doses of the compositions as disclosed herein, for the treatment of a subject vary depending upon many different factors, including means of administration, target site, physiological state of the patient, whether the patient is human or an animal, other medications administered, if any, and whether treatment is prophylactic or therapeutic. Treatment dosages can be titrated to optimize safety and efficacy. The amount of immunogen can also depend on whether adjuvant is also administered, with higher dosages being required in the absence of adjuvant. The amount of an immunogen for administration sometimes varies from 1-500 μg per patient and more usually from 5-500 μg per injection for human administration. Occasionally, a higher dose of 1-2 mg per dosage is used. Typically, about 10, 20, 50 or 100 μg is used for each human dosage. The timing of dosages can vary significantly from once a day, to once a year, to once a decade. On any given day that a dosage of immunogen is given, the dosage is greater than 1 μg/patient and usually greater than 10 μg/patient if adjuvant is also administered, and greater than 10 μg/patient and usually greater than 100 μg/patient in the absence of adjuvant. A

typical regimen consists of an immunization followed by booster dosage(s) at 6-week intervals. Another regimen consists of an immunization followed by booster dosage(s) 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11,or 12 months later. Another regimen entails dosage(s) every two months for life. Alternatively, booster dosage(s) can be on an irregular basis as indicated by monitoring of immune response.

[00156] When administered in combination with a second treatment for Alzheimer's disease, such as, Razadyne® (galantamine), Exelon® (rivastigmine), and Aricept® (donepezil), the second treatment can be administered according the product label or as necessary in view of the treatment with the compositions of the disclosure.

[00157] **Kits**

[00158] The disclosure further provides kits (*e.g.*, containers) comprising the compositions disclosed herein and related materials, such as instructions for use (*e.g.*, package insert). The instructions for use may contain, for example, instructions for administration of the compositions and optionally one or more additional agents. The containers of peptide and/or nucleic acid compositions may be unit doses, bulk packages (*e.g.*, multi-dose packages), or sub-unit doses.

[00159] Package insert refers to instructions customarily included in commercial packages of therapeutic products that contain information about the indications, usage, dosage, administration, contraindications and/or warnings concerning the use of such therapeutic products. Kits can also include a second container comprising a pharmaceutically acceptable buffer, such as bacteriostatic water for injection (BWFI), phosphate-buffered saline, Ringer's solution and dextrose solution. It can also include other materials desirable from a commercial and user standpoint, including other buffers, diluents, filters, needles, and syringes.

[00160] **Uses**

[00161] Each of the peptides, polypeptides, immunogens, and pharmaceutical compositions described herein may be for use in treating one or more of the diseases as described herein. In addition, each of the peptides, polypeptides, immunogens, and pharmaceutical compositions described herein may be for use in methods for treating one or more of the diseases as described herein. Each of the peptides, polypeptides, immunogens, and pharmaceutical compositions described herein may be used in a

method for manufacturing a medicament for treating or use in treating one or more of the diseases as described herein.

[00162] The following are provided for exemplification purposes only and are not intended to limit the scope of the invention described in broad terms above.

[00163] All U.S. and international patent applications identified herein are incorporated by reference in their entirety.

Examples

[00164] **Example 1: Immunization of Guinea Pigs**

[00165] Guinea pigs were injected intramuscularly with 50 µg of a test immunogen, 25 µg QS21 in 200 µl of Addavax on day 0, 21, 49 and 77. Bleeds were done 7 days post immunization. The peptides tested included DAEFRHD (SEQ ID NO:06), QIVYKPV (SEQ ID NO:39), and DAEFRHDRRQIVYKPV (SEQ ID NO:57). The specific immunogens were DAEFRHDC (SEQ ID NO:71), QIVYKPVGGC (SEQ ID NO:72), and DAEFRHDRRQIVYKPVGGC (SEQ ID NO:59). The peptides were coupled through the C-terminal cysteine to CRM-197 with a maleimide linkage.

[00166] Female Guinea Pigs were at least 5 weeks old at the start of the study having an approximate body weight of 350-500g. Appropriate animal housing and research procedures for animal husbandry and care were conducted in an accredited facility in accordance with the guidelines of the U.S. Department of Agriculture's (USDA) and the Assessment and Accreditation of Laboratory Animal Care (AAALAC) International.

[00167] The immunogen concentration was 0.5 mg/ml. Prior to each administration of the test immunogen, approximately a 3 cm^2 area on each hind limb was shaved and wiped with ethanol for visualization of the injection site. Each animal received a test immunogen dose of 200 microliters (0.25 micrograms/microliter) divided into two separate sites each of 100 microliter per injection (*i.e.*, animals received 50 µg of immunogen in 100 µl PBS + 25 µg of QS21 in 100 µl MF59). A 25G-27G needle was inserted intramuscularly into the hind limb, approximately 0.25 - 0.5 cm deep, and injected at 100 microliters per site. Injection sites were rotated

each administration between four separate sites per hind limb and separated by at least 2 cm.

[00168] Example 2: Measurement of Antibody Titers

[00169] Whole blood samples were collected into clot activator tubes via jugular vein at 250-350 microliters per collection at weeks 1, 4, and 8. The maximum volume of whole blood was collected into clot activator tubes via cardiac puncture at termination on week 12. All blood samples were allowed to clot at room temperature for greater than 30 minutes, centrifuged at ambient temperature (approximately 20-25°C) at 3,000 RPM for 10-15 minutes, and serum supernatant was transferred individually into clean cryovials. Serum supernatant was stored frozen at -80 °C (± 12 °C).

[00170] Titer Guinea pig bleed on soluble Aβ aggregates

[00171] 2.5 µg/ml of a soluble aggregate Aβ prep (HFIP film of Aβ 42 was resuspended and incubated overnight with shaking, then spun to remove insoluble aggregate) was coated on to the plate at 100 µl per well in PBS and incubated overnight at room temperature. Plates were blocked for 1 hour with 1% BSA in PBS. Plates were aspirated and to row A, 200 µl of 0.1% BSA in PBS Tween was added to 1-4. In 1 neg. GP serum was added at 1/100 while 2-4 contained 1/100 test serum. Rows B-H contained 100 µl of 0.1% BSA in PBS Tween. Rows were serially diluted ½ down the plate giving dilution of 1/100 to 1/12800. Wells were incubated 2 hours at room temperature, then were washed and a 1/5000 dilution of anti Guinea Pig IgG HRP in 0.1% BSA in PBS Tween was prepared and then 100 µl added to the washed well. This incubated for 1 hour and was washed. OPD substrate was prepared using Thermo-Fisher OPD tablets at 1 tablet per 10 mls. Thermo fisher substrate buffer was added at 1/10 and each well had 100 µl added and incubated for 15 minutes. 50 µl of 2N H_2SO_4 was added to stop the reaction and plates were read on a molecular devices spectromax at 490 nM. Titer defined as the dilution giving 50% maximum OD and was extrapolated if it fell between dilutions

[00172] Titer Guinea Pig bleeds on Tau

[00173] 2 µg/ml recombinant WT Tau 4R2N was coated on to the plate using 100 µl per well in PBS and incubated overnight at room temperature. Plates were blocked for 1 hour with 1% BSA in PBS. Plates were aspirated and to row A 200 µl

of 0.1% BSA in PBS Tween was added. In column 1 neg. GP serum was added at 1/100 while the rest of the row contained 1/100 test serums. Rows were serially diluted ½ down the plate giving dilution of 1/100 to 1/12800. Wells incubated 2 hours at room temperature then were washed and a 1/5000 dilution of anti-Guinea Pig IgG HRP in 0.1% BSA in PBS Tween was prepared and then 100 µl added to the washed well. This incubated for 1 hour and was washed. OPD substrate was prepared using Thermo-Fisher OPD tablets at 1 tablet per 10 mls. Thermo fisher substrate buffer was added at 1/10 and each well had 100 µl added and was incubated for 15 minutes. 50 µl of 2N H_2SO_4 was added to stop the reaction and plates were read on a molecular devices spectromax at 490 nM. Titer was defined as the dilution giving 50% maximum OD and was extrapolated if it fell between dilutions.

[00174] Titer Guinea Pig Bleed on Aβ 1-28 or Aβ 1-15

[00175] Aβ 1-15 and Aβ 1-28 were both used at different parts of the study. Both of these will not form aggregates. 2 µg/ml Aβ monomers were coated at coated on to the plate 100 µl per well in PBS and incubated overnight at room temperature. Plates were blocked for 1 hour with 1% BSA in PBS. Plates were aspirated and to row A 200 µl of 0.1% BSA in PBS Tween was added. In column 1 neg. GP serum was added at 1/100 while the rest of the row contained 1/100 test serums. Rows were serially diluted ½ down the plate giving dilution of 1/100 to 1/12800. Wells incubated 2 hours at room temperature then were washed and a 1/5000 dilution of anti Guinea Pig IgG HRP in 0.1% BSA in PBS Tween was prepared and then 100 µl added to the washed well. This incubated for 1 hour and was washed. OPD substrate was prepared using Thermo-Fisher OPD tablets at 1 tablet per 10 mls. Thermo fisher substrate buffer was added at 1/10 and each well had 100 µl added and was incubated for 15 minutes. 50 µl of 2N H_2SO_4 was added to stop the reaction and plates were read on a molecular devices spectromax at 490 nM. Titer was defined as the dilution giving 50% maximum OD and was extrapolated if it fell between dilutions.

[00176] Titering the tau against a peptide containing its epitope

[00177] Thermofisher neutavidin plates were rehydrated with 0.05%Tween in TBS and aspirated. Peptide GGGSVQIVYKPVDLS (SEQ ID NO:68) containing a biotin was made up in a 1/500 dilution in 0.1% BSA in PBS tween. Adding 100 µl per well for 1 hour and then washed. To row A of the plate 200 µl of 0.1% BSA in

PBS Tween was added. In column 1 neg. GP serum was added at 1/100 while the rest of the rows contained 1/100 test serums. Rows were serially diluted ½ down the plate giving dilution of 1/100 to 1/12800. Wells incubated 2 hours at room temperature then were washed and a 1/5000 dilution of anti Guinea Pig IgG HRP in 0.1% BSA in PBS Tween was prepared and then 100 µl added to the washed well. This incubated for 1 hour and was washed. OPD substrate was prepared using Thermo-Fisher OPD tablets at 1 tablet per 10 mls. Thermo fisher substrate buffer was added at 1/10 and each well had 100 µl added and was incubated for 15 minutes. 50 µl of 2N H_2SO_4 was added to stop the reaction and plates were read on a molecular devices spectromax at 490 nM. Titer defined as the dilution giving 50% maximum OD and was extrapolated if it fell between dilutions.

[00178] FIG. 1 shows the results comparing the geometric mean titers of Guinea Pig serum for immunogen DAEFRHDRRQIVYKPV (SEQ ID NO:57) titered on monomeric Aβ 1-28 , soluble aggregates of Aβ, full length tau, and tau MTBR epitope containing GGGSVQIVYKPVDLS (SEQ ID NO:68).

[00179] FIG. 2 shows the results for a single peptide immunogen Aβ and tau peptides (DAEFRHD (SEQ ID NO:06) and QIVYKPV (SEQ ID NO:39)) versus dual peptide immunogen DAEFRHDRRQIVYKPV (SEQ ID NO:57) on Aβ 1-28 and full-length tau.

[00180] Example 3: Staining of Alzheimer's brain tissue with sera from Guinea pigs immunized with a vaccine as disclosed herein.

[00181] Autopsy blocks of fresh frozen human brain tissue (~ 0.5 g) were embedded in optimal cutting temperature compound (OCT compound) and cut using a cryostat to generate 10 µm sections. The sections were placed into a solution of glucose oxidase and beta D-glucose, in the presence of sodium azide, to block endogenous peroxidase. Once tissue sections were prepared, the staining with the specified Guinea pig sera from Guinea pigs immunized with a vaccine as disclosed herein was carried out at two dilutions (1:300 and 1:1500), using a rabbit anti-guinea pig secondary antibody and a DAKO DAB Detection Kit as per the manufacturer's instructions. The staining was processed using an automated Leica Bond Stainer. The results indicate that sera from Guinea pigs immunized with a vaccine as disclosed

herein comprises antibodies specific to Aβ and tau in human brain tissue of Alzheimer's patients (*see* FIG. 3A-3F).

[00182] Example 4: Serum from vaccinated animals blocks soluble Aβ aggregates from binding to neurons.

[00183] E18 primary rat hippocampal neurons were cultured as described previously (Zago, *et al.* "Neutralization of Soluble, Synaptotoxic Amyloid β Species by Antibodies Is Epitope Specific," *J Neurosci.* 2012 Feb 22; 32(8): 2696–2702). Soluble Aβ aggregate was pre-incubated with or without guinea pig vaccine serum on culture DIV14-21 to block soluble Aβ aggregate from neuritic binding. Guinea pig serum was isolated from animals vaccinated with dual immunogen peptide: DAEFRHDRRQIVYKPVGGC (SEQ ID NO:59; Immunogen 9). Fresh unlabeled, biotinylated or (9:1) soluble Aβ was prepared one day prior and incubated overnight at 4˚C. Each diluted serum sample (1:1000, 1:300, and 1:100) and soluble Aβ solution was prepared at 2x the final concentration in one-half of final treatment volume using NeuroBasal-no phenol red (NB-NPR) medium. This was combined with one-half final volume of 2x soluble Aβ and with one-half final volume of 2x diluted guinea pig vaccine serum to make up a 1x final concentration in total final treatment volume, which was mixed well and then pre-incubated for 30 minutes at 37˚C. E18 neurons were rinsed with NB-NPR at 150µL/well before adding binding treatment. Guinea pig serum from vaccinated animals/Aβ treatment was added to E18 neurons at 60µL/well, and then incubated for 30 minutes at 37˚C under normal incubator conditions (5% CO_2; 9% O_2). Cells were rinsed twice using 150µL/well of NB-NPR, and then fixed in 4% paraformaldehyde in 1x DPBS for 20 minutes. Cells were permeabilized using 0.1 TX-100 for 5 minutes, and blocked using 10% normal goat serum (NGS) for 1 hour at room temperature (RT). Cells were incubated with MAP2 & NeuN primary antibodies in 100µL/well, 1x DPBS containing 1% BSA + 1% NGS overnight at 4˚C. The next day, cells were rinsed twice in 150µL/well 1x DPBS for 5 minutes each wash. Secondary antibodies were added for 1 hour at RT in 100µL/well 1x DPBS + 1% BSA + 1% NGS. High-content imaging (HCI) analysis was performed to quantify soluble aggregate Aβ neuritic binding using Operetta HCI CLS instrument (Perkin Elmer; modified Neurite Outgrowth algorithm: 40x H_2O objective; 40 fields per well; (n=3) per condition; data shown as mean (+/-) SD); MAP2 & NeuN (Abcam) neuronal markers used to each trace neurite tree and count

cell body number per optical field; Neuritic Aβ souble aggregate spots detected using streptavidin-488 or polyclonal Aβ antibody (Thermo; Millipore); and data reported as Aβ soluble aggregate spots/neuron (or as Integrated Intensity)).

[00184] Approximately 80-150 neurons were observed per well for each condition tested. The results demonstrate that Guinea pig serum from animals vaccinated with a dual immunogen peptide, DAEFRHDRRQIVYKPVGGC (SEQ ID NO:59; Immunogen 9), inhibited Abeta binding to neurons in a dose dependent manner (*see* Figure 4).

[00185] **Example 5: Mice vaccinated with dual peptide antigens produce titers to Aβ and Tau.**

[00186] Swiss Webster Female mice were injected on day 0, 14 and 28 with 25 µg of a dual peptide immunogen (Table 2) and 25 µg QS21(Desert King) in PBS total 200 µl/injection. Each mouse received 200 µl subcutaneously. Mice were bled on day 21 and 35.

Table 2.

Immunogen	Dual peptide immunogen sequence (SEQ ID NO.)
9	DAEFRHDRRQIVYKPVGGC (SEQ ID NO:59)
10	DAEFRHDRRQIVYKPVC (SEQ ID NO:60)
18	DAEFRHDRRQIVYKPVAAC (SEQ ID NO:61)
19	DAEFRHDRRQIVYKPVKKC (SEQ ID NO:62)
20	DAEFRHDRREIVYKSPGGC (SEQ ID NO:63)
21	DAEFRHDRREIVYKSPAAC (SEQ ID NO:64)
22	DAEFRHDRREIVYKSPC (SEQ ID NO:65)
23	DAEFRHDRREIVYKSPKKC (SEQ ID NO:66)

[00187] The immunogens containing Tau peptide EIVYKSP (SEQ ID No:43); see Figure 5B) showed greater variability overall in tau titers (with the exception of immunogen 23) than those with the tau MTBR sequence QIVYKPV (SEQ ID NO:39); therefore the base microtubule binding region (MTBR) peptide containing DAEFRHDRRQIVYKPV (SEQ ID NO:57) was also tested (Figure 5A). Titers of three immunogens with different linkers (no linker, AA and KK) compared to the GGC linker are shown in Figure 5.

[00188] Titers observed from the second bleed are set forth in Tables 3 and 4:

Table 3

Titer Against Abeta 1-28 (at 50% Max OD)						
Immunogen number	mouse #				geometric mean	geometric mean SD factor
	1	2	3	4		
9	4000	2000	6000	1000	2632.15	2.20
10	13000	2000	4000	1000	3193.44	2.98
18	2000	2800	1200	5000	2407.6	1.80
19	7200	2500	1500	1800	2640.34	2.02
20	4000	2000	6000	1000	2470	1.96
21	13000	2000	4000	1000	1665	2.71
22	300	7000	2000	7000	2329	4.43
23	350	3400	4000	7000	2403	3.74

Table 4

Titer Against Tau (at 50% Max OD)						
Immunogen number	mouse #				geometric mean	geometric mean SD factor
	1	2	3	4		
9	400	800	200	800	475.7	1.94
10	400	3200	3200	1500	1574.4	2.67
18	1500	100	6000	100	547.7	7.72
19	10000	1000	13000	1500	3738.9	3.68
20	300	3200	No titer	1000	313	12.07
21	1500	100	6000	100	278.3	7.75
22	100	4000	No titer	13000	477.5	27.33
23	300	3000	1300	500	874.8	2.78

[00189] Titers observed in guinea pigs immunized with Immunogen 9 DAEFRHDRRQIVYKPVGGC (SEQ ID NO:59) are set forth in Table 5 below.

Table 5

Guinea Pig	Titer Against Abeta 1-28	Titer Against Abeta soluble aggregate	Titer Against Tau	Titer Against bio-GGSQIVYKPVDLS (SEQ ID NO:73)
1	3100	1500	1600	1000
2	3200	4000	6400	6400
3	3300	2000	3200	4000

[00190] Example 6: Serum from vaccinated animals stains Aβ plaques and Tau pathologies in human brain tissue.

[00191] Fresh frozen human brain tissues from autopsied Alzheimer's disease donors or non-diseased controls was embedded in OCT, and cut in a cryostat to generate 10 µm frozen sections. The tissue sections were incubated in a solution of glucose oxidase and beta D-glucose, in the presence of sodium azide, to block endogenous peroxidase. The staining with sera from vaccinated mice. Mice were vaccinated with the following dual antigen peptides: DAEFRHDRRQIVYKPVGGC (SEQ ID NO:59, Immunogen 9); DAEFRHDRRQIVYKPVC (SEQ ID NO:60, Immunogen 10); DAEFRHDRRQIVYKPVAAC (SEQ ID NO:61, Immunogen 18); and DAEFRHDRRQIVYKPVKKC (SEQ ID NO:62, Immunogen 19) or control mice. Staining was then carried out at 1:1000 dilution, in an automated Leica Bond Rx Stainer (Leica Biosystems). Antibody binding was detected using the Bond Polymer Refine Detection Kit (DS9800, Leica Biosystems), which is based on an anti-mouse polymer detection, DAB visualization and hematoxylin nuclear counter-staining. After cover-slipping, the stained tissue slides were digitally imaged with a Hamamatsu NanoZoomer 2.0HT slide scanner (Hamamatsu Corporation) with an NDP.scan, 2.5.85 software. The digitized images were viewed and analyzed using the NDP.view, 2.7.43.0 software.

[00192] Results demonstrate Aβ plaques and tau neurofibrillary tangles were identified based on their typical histopathological characteristics. Such pathologies were absent from tissues incubated with control mouse serum. Also, non-diseased tissue had no such pathological staining after incubation with the sera from vaccinated mice. Figures 6A-E and Table 6 summarize the results of Aβ and Tau staining using mouse sera from animals vaccinated with dual antigen peptides (1:1000 dilution of sera used to stain human brain tissue from AD patients).

Table 6

Serum ID	Aβ staining	Tau pathology	Background
9-1	+		Clear
9-2	+		Dark
9-3	+++++		Clear

9-4	++		Clear
10-1	+++++		OK
10-2	+++		Clear
10-3	++++	*	OK
10-4	++++	*	Dark
18-1	++		Dark
18-3	+		Clear
19-1	+++++	+++	OK
19-2	++	*	OK
19-3	+	++	Dark
19-4	++		OK

9: DAEFRHDRRQIVYKPVGGC (SEQ ID NO:59)
10: DAEFRHDRRQIVYKPVC (SEQ ID NO:60)
18: DAEFRHDRRQIVYKPVAAC (SEQ ID NO:61)
19: DAEFRHDRRQIVYKPVKKC (SEQ ID NO:62)
* possible tau pathology, too weak to clearly identify staining as tau

[00193] Example 7: Immunization and Determination of Titers in Cynomolgus monkeys.

[00194] The study described in this example was designed to assess the development of titers to Aβ and tau in cynomolgus monkeys using the dual antigen peptide DAEFRHDRRQIVYKPVGGC (SEQ ID NO:59). We also assessed two injection schedules and persistence of titers.

[00195] Immunizations

[00196] Several dual Aβ-tau linear immunogens with a dendritic cell cleavage site were screened in mice for balanced titer on Aβ and tau proteins (*see* Example 5, above). A subset of immunogens were further evaluated in guinea-pig (*see* Examples 1-5, above) and cynomolgus monkey (this example). Two groups of four monkeys were immunized intramuscularly with 50 µg of immunogen (SEQ ID NO:59; DAEFRHDRRQIVYKPVGGC) coupled to CRM197 carrier protein, and 50 µg of the adjuvant QS21. Group 1 was injected on week 0, 4, 12 and 24 with bleeds taken every 2 weeks through week 38. Group 2 was injected at week 0, 8, 24 with bleeds taken every 2 weeks through week 38. Serum titer levels were determined against Aβ and full-length tau. Fresh frozen human AD or control brain sections were stained with sera from immunized and control animals. The activity of the guinea-pig

immune sera was also assessed on soluble Aβ oligomer binding in primary rat hippocampal neurons.

[00197] Titer Protocol

[00198] Measurement of antibody titer to Aβ 1-28 in cynomolgus monkey

[00199] Cynomolgus monkey bleeds were titered by enzyme-linked immunosorbent assay (ELISA). Plates were coated overnight at 2 µg/mL with Aβ 1-28 (SEQ ID NO:67) in phosphate-buffered saline (PBS) and then blocked 1 hour with 1% bovine serum albumin (BSA) in PBS. Pre-bleed cynomolgus monkey was used as a negative control while known positive anti-serum from previous mouse studies was used as a positive control at the same dilutions of test serum. Bleeds were diluted in PBS / 0.1% BSA / 0/1% Tween 20 (PBS/BSA/T) starting at 1/100 and serially diluted 1:2 down the plate. Plates were washed with TBS / Tween 20 and goat anti–monkey immunoglobulin G (IgG) (heavy + light chains) horseradish peroxidase (HRP) (IgG [H+L] HRP; Invitrogen) was added and incubated 1 hour at room temperature. Plates were washed in TBS/Tween 20, and antibody binding was detected with o-phenylenediamine dihydrochloride (OPD) substrate (Thermo Fisher Scientific, Waltham, MA) following manufacturer's instructions. Plates were read at 490 nM on a Molecular Devices Spectromax. Titer was defined as the dilution giving 50% Maximum OD or 4X background (defined in graphs and tables) extrapolation was used if it fell in between dilutions.

[00200] Measurement of antibody titer to tau in cynomolgus monkey

[00201] Cynomolgus monkey bleeds were titered by enzyme-linked immunosorbent assay (ELISA) against full-length recombinant tau (Proteos, Kalamazoo, MI; SEQ ID NO:02). Plates were coated overnight at 2 µg/mL tau in phosphate-buffered saline (PBS) and then blocked 1 hour with 1% bovine serum albumin (BSA) in PBS. Pre-bleed guinea pig serum was used as a negative control while known positive anti-serum from previous mouse studies was used as a positive control at the same dilutions of test serum. Bleeds were diluted in PBS/0.1% BSA/ 0/1% Tween 20 (PBS/BSA/T) starting at 1/100 and serially diluted 1:2 down the plate. Plates were washed with TBS/Tween 20 and goat anti–monkey immunoglobulin G (IgG) (heavy + light chains) horseradish peroxidase (HRP) (IgG [H+L] HRP; Invitrogen) was added and incubated 1 hour at room temperature. Plates

were washed in TBS/Tween 20, and antibody binding was detected with o-phenylenediamine dihydrochloride (OPD) substrate (Thermo Fisher Scientific, Waltham, MA) following manufacturer's instructions. Plates were read at 490 nM on a Molecular Devices Spectromax. Titer was defined as the dilution giving 50% Maximum OD or 4X background (defined in graphs and tables) extrapolation was used if it fell in between dilutions.

[00202] Titer Cynomolgus monkey bleeds on the carrier protein CRM197

[00203] Cynomolgus monkey bleeds were titered by enzyme-linked immunosorbent assay (ELISA) against CRM197 (FinaBio, Maryland) carrier protein. Plates were coated overnight at 2 µg/mL tau in phosphate-buffered saline (PBS) and then blocked 1 hour with 1% bovine serum albumin (BSA) in PBS. Pre-bleed guinea pig serum was used as a negative control while known positive anti-serum from previous mouse studies was used as a positive control at the same dilutions of test serum. Bleeds were diluted in PBS/0.1% BSA/ 0/1% Tween 20 (PBS/BSA/T) starting at 1/100 and serially diluted 1:2 down the plate. Plates were washed with TBS/Tween 20 and goat anti–monkey immunoglobulin G (IgG) (heavy + light chains) horseradish peroxidase (HRP) (IgG [H+L] HRP; Invitrogen) was added and incubated 1 hour at room temperature. Plates were washed in TBS/Tween 20, and antibody binding was detected with o-phenylenediamine dihydrochloride (OPD) substrate (Thermo Fisher Scientific, Waltham, MA) following manufacturer's instructions. Plates were read at 490 nM on a Molecular Devices Spectromax. Titer was defined as the dilution giving 50% Maximum OD or 4X background (defined in graphs and tables) extrapolation was used if it fell in between dilutions.

[00204] Results

[00205] Titers levels were similar for Aβ and tau. Monkeys subject to the group 1 vaccination schedule had titers with a greater area under the curve than those of group 2 but did not show a significant improvement in maximum titer under these conditions (FIG. 7A, FIG. 7B). Overall titer levels were lower than the guinea pig study described above. This change may be attributable to a change of adjuvant from QS21 in ADDVAX in the Guinea pig to QS21 in phosphate buffered saline (PBS) in cynomolgus monkeys to match approved vaccines. Persistence of titer was modest for both four injection and three injection vaccination schedules (FIG. 8A, FIG. 8B).

These results demonstrate that these immunogens can generate a balanced immune response to Aβ and tau in primates. Optimization of dosing schedule and/or formulation may improve titer levels and persistence.

[00206] Example 8: Immunohistochemistry on AD and Control Brain Sections

[00207] Sera from immunized monkeys were evaluated for the ability to bind pathological Aβ plaques and tau tangles in human brain tissue from subjects with AD. Binding both Aβ plaques and tau tangles is expected reduce plaque burden and reduce tau transmission which in turn should reduce the signs and symptoms of AD.

[00208] Autopsy blocks of fresh frozen human brain tissue were embedded in optimal cutting temperature compound (OCT compound) and cut using a cryostat to generate 10 micron sections. The sections were placed into a solution of glucose oxidase and beta D-glucose, in the presence of sodium azide, to block endogenous peroxidase. Once tissue sections were prepared, the staining with the specified cynomolgus immune sera was carried out at two dilutions (1:300 in 5% goat serum with 0.25% Triton for 1 hour at RT). Binding was detected with a mouse anti-monkey IgG secondary antibody purified unlabeled (Mybiosource 3mg/mL) for 1 hour at RT, and a goat anti-mouse IgG secondary antibody (Jackson, 1:200) for 1 hour at RT, avidin-biotin complex (ABC; Vector PK-4000) and a DAKO DAB Detection Kit according to manufacturer instructions. The staining was processed using an automated Leica Bond Stainer.

[00209] Table 7 shows a summary of the staining in the cynomolgus monkey study. All animal except 1002 had positive staining for Aβ. Only animal 1001 had strong tau staining (FIG. 9A – FIG. 9C), with 1003 (FIG. 10A – FIG. 10B) and 1501 (FIG. 11A – FIG. 11B) demonstrating modest staining. Animal 2501, for example, did not demonstrate significant tau staining (FIG. 12A – FIG. 12B). There did not appear to be a correlation with tau staining and tau titers as evidenced by animal 1001, which did not have a strong tau titer but stained tau strongly.

Table 7

Animal Number	Aβ Staining	Tau Staining	Aβ Titer	Tau Titer

1001	+	++	800	150
1002	-	-	25	25
1003	+++	+	15000	6000
1501	+++	+/-	8000	3200
2001	+++	-	9000	350
2003	++	-	200	1500
2102	+++	-	8000	800
2501	+++	-	8000	1600

[00210] Immune sera bound avidly to Aβ plaques and tau tangles in human AD brain sections at concentrations expected to be achieved in CNS under in vivo conditions. Monkeys with the strongest titers at week 26 stained Aβ, and one monkey with low to moderate tau titers stained both Aβ and tau.

[00211] These results demonstrate that the serum antibody binding of the cynomolgus monkey antibody response to be balanced and bind to pathological Aβ plaques and tau tangles.

[00212] Example 9: Serum Blocking of Soluble Aβ Aggregates from Binding to Neurons and T-Cell Activity

[00213] Primary hippocampal neurons isolated from E18 rat were cultured as described above. Fresh unlabeled, biotinylated or (9:1) soluble Aβ was prepared one day prior to assay and incubated overnight at 4˚C. Neurons were rinsed with NB-NPR at 150µL/well before adding Aβ/serum treatment. An IgG cut of cynomolgus monkey bleeds from vaccinated animals was added to E18 neurons at 60µL/well, and then incubated for 30 minutes at 37˚C under normal incubator conditions (5% CO2; 9% O2). Cells were rinsed twice using 150µL/well of NB-NPR, and then fixed in 4% paraformaldehyde in 1x DPBS for 20 minutes. Cells were permeabilized using 0.1 TX-100 for 5 minutes, and blocked using 10% normal goat serum (NGS; Thermofisher) for 1 hour at room temperature (RT). Cells were incubated with MAP2 & NeuN primary antibodies in 100µL/well, in 1x DPBS containing 1% BSA + 1% NGS overnight at 4˚C.

[00214] The next day, cells were rinsed twice in 150µL/well 1x DPBS for 5 minutes each wash. Secondary antibodies were added for 1 hour at RT in 100µL/well

1x DPBS + 1% BSA + 1% NGS. Aβ soluble aggregate spots were detected using streptavidin-488 or polyclonal Aβ antibody (Thermofisher; Millipore); High-content imaging (HCI) analysis was performed to quantify soluble aggregate Aβ neuritic binding using Operetta HCI CLS instrument (Perkin Elmer; modified Neurite Outgrowth algorithm: 40x H2O objective; 40 fields per well; (n=3) per condition; data shown as mean (+/-) SD); MAP2 & NeuN (Abcam) neuronal markers were used to each trace neurite tree and count cell body number per optical field; Neuritic data were reported as Aβ soluble aggregate spots/neuron (or as Integrated Intensity)). Approximately 80-150 neurons were observed per well for each condition tested (Zago, et al., 2012).

[00215] T-cell reactivity was also investigated. Immune sera inhibited the binding of soluble Aβ aggregates to hippocampal neurons. Immunogens did not elicit cytotoxic T-cell responses to Aβ or tau.

[00216] Example 10: Animals vaccinated with dual peptide antigens produce titers to Aβ and Tau.

[00217] The study described in this example was designed to assess dual Aβ and tau antigen peptides in mice. The dual Aβ-tau constructs in this example effectively demonstrated: high titers for both antigens; blocking of tau binding to heparin; and staining/binding to Aβ and tau peptides in brain tissue from human Alzheimer's patients. Furthermore, titers against tau for an engineered tau immunogen (Dual #11) were comparable, and in some cases, better than other tau immunogens despite including a non-native tau sequence. This demonstrates that engineered immunogens are useful in vaccine constructs.

Table 8

Dual Construct ID #	Abeta Sequence	Abeta SEQ ID NO.	Endo peptidase linker	Tau Sequence	tau SEQ ID NO.	C-Terminal linker	Cys
2	DAEFRHD	06	RR	VKSKIGST	801	GG	C
3	DAEFRHD	06	RR	SKIGSTEN	817	GG	C
8	DAEFRHD	06	RR	TENLKHQP	695	GG	C
9	DAEFRHD	06	RR	ENLKHQPG	689	GG	C
11	DAEFRHD	06	RR	SKIGSKDNIKH	986	GG	C

Table 9

Dual Construct ID #	Sequence	SEQ ID NO:
2	DAEFRHDRRVKSKIGSTGGC	997
3	DAEFRHDRRSKIGSTENGGC	998
8	DAEFRHDRRTENLKHQPGGC	999
9	DAEFRHDRRENLKHQPGGGC	1000
11	DAEFRHDRRSKIGSKDNIKHGGC	1001

[00218] **Conjugation**-Peptides were made by Biopeptide (San Diego, CA) CRM-bromoacetate was received from Fina Biosolutions (Rockville, MD) peptides were coupled to CRM following the below protocol.

[00219] 1M Tris HCL pH 8.0, MilliQ DI Water and 50 mM Borate, 100 mM NaCl, 5 mM EDTA pH 8.5 were sterile filtered and degassed. 1 mg of each peptide was dissolved in 0.2 mls of degassed water, then 0.1 mls degassed Tris_HCL was added. This was followed by 0.2 mls of the stock CRM-Bromoacetate (1 mg total), finally 0.5 mls of the Borate buffer was added. This incubated 24 hours at 4 degrees C on a nutator to provide mixing. Samples were desalted into PBS and 5 µl was run on a 10% Tris gel to confirm conjugation.

[00220] **Injection of animals**: Four (4) female Swiss webster mice were used in each group. Immunogen preparation was 25 µg Immunogen, 25 µg QS21 and 150 µl of 0.02% Tween 80/ PBS per injection. Each mouse received 200 µl subcutaneously. Mice were injected at day 0, at 4 weeks from day 0, and at 8 weeks from day 0, with bleeds taken for titer at 5 weeks from day 0 and animals sacrificed and terminal bleed collected at 9 weeks from day 0 (*see* Figure 13).

[00221] **Titer Assay:** Mouse serum was titered by enzyme-linked immunosorbent assay (ELISA). Plates were coated overnight at 2 µg/mL with either Abeta 1-28 (Anaspec, San Jose,CA), or recombinant tau (Proteos, Kalamazoo, MI in phosphate-buffered saline (PBS), and then blocked 1 hour with 1% bovine serum albumin (BSA) in PBS. Normal mouse serum was used as a negative control while known positive anti-serum from previous mouse studies was used as a positive control at the same dilutions as test serum. Bleeds were diluted in PBS/0.1% BSA/ 0.1% Tween 20 (PBS/BSA/T) starting at 1/100 and serially diluted 1:2 down the plate.

Plates were washed with TBS/Tween 20 and goat anti–mouse immunoglobulin G (IgG) (heavy + light chains) horseradish peroxidase (HRP) (ThermoFisher) 1/5000 was added and incubated 1 hour at room temperature. Plates were washed in TBS/Tween 20, and antibody binding was detected with o-phenylenediamine dihydrochloride (OPD) substrate (Thermo Fisher Scientific, Waltham, MA) following manufacturer's instructions. Plates were read at 490 nM on a Molecular Devices Spectromax. Titer was defined as the dilution giving 4X background (defined in graphs and tables); extrapolation was used if it fell in between dilutions.

[00222] MTBR Binding

[00223] Certain antibodies that bind to MTBR can bind to more than one MTBR region due to the homology of the various MTBR regions. Antiserum is titered on four MTBR regions using peptides of MTBR 1-4 purchased from Anaspec (San Jose, CA)

MTBR peptide 1 QTAPVPMPDLKNVKSKIGSTENLKHQPGGGK

(SEQ ID NO:1058)

MTBR peptide 2 VQIINKKLDLSNVQSKCGSKDNIKHVPGGGS

(SEQ ID NO:1059)

MTBR peptide 3 VQIVYKPVDLSKVTSKCGSLGNIHHKPGGGQ

(SEQ ID NO:1060)

MTBR peptide 4 VEVKSEKLDFKDRVQSKIGSLDNITHVPGGGN

(SEQ ID NO:1061)

[00224] Mouse serum is titered by enzyme-linked immunosorbent assay (ELISA). Plates are coated overnight at 2 µg/mL with each the various MTBR peptides in phosphate-buffered saline (PBS) and then blocked 1 hour with 1% bovine serum albumin (BSA) in PBS. Normal mouse serum is used as a negative control. Bleeds are diluted in PBS/0.1% BSA/ 0.1% Tween 20 (PBS/BSA/T) starting at 1/100 and serially diluted 1:2 down the plate. Plates are washed with TBS/Tween 20 and goat anti–mouse immunoglobulin G (IgG) (heavy + light chains) horseradish peroxidase (HRP) (ThermoFisher) 1/5000 is added and incubated 1 hour at room temperature. Plates are washed in TBS/Tween 20, and antibody binding is detected

with o-phenylenediamine dihydrochloride (OPD) substrate (Thermo Fisher Scientific, Waltham, MA) following manufacturer's instructions. Plates are read at 490 nM on a Molecular Devices Spectromax. Titer is defined as the dilution giving 4X background (defined in graphs and tables); extrapolation is used if it falls in between dilutions.

[00225] Blocking of tau binding to Heparin

[00226] As a potential surrogate marker for the ability of the serum to block uptake of tau into cells an ELISA measuring the blocking of tau binding to Heparin plates was developed. Recombinant tau was biotinylated in-house. Heparin coated plates (Bioworld, Dublin, OH) were blocked with 2% BSA/PBS for 1 hour. In a separate deep well polypropylene 96 well plate (ThermoFisher) Serum was diluted from 1/25-1/3200 in 2% BSA/PBS, 60 µl total, to this 60 µl 200 ng/ml biotinylated tau in 2%BSA/PBS was added for a final concentration of serum 1/50-1/6400 and tau at 100 ng/ml. The mixture of serum and tau incubated for 2 hours then 100 µl/well was transferred to the blocked heparin plates and incubated 1 hour. Plates were washed in 0.1% Tween 20/TBS and goat anti–mouse immunoglobulin G (IgG) (heavy + light chains) horseradish peroxidase (HRP) (ThermoFisher) 1/5000 was added and incubated 1 hour at room temperature. Plates were washed in TBS/Tween 20 and 100 µl ThermoFisher TMB added and incubated 8 minutes stopped H2SO4 and read at 450.

[00227] IHC binding of Serum

[00228] Autopsy blocks of fresh frozen human brain tissue were embedded in optimal cutting temperature compound (OCT compound) and cut using a cryostat to generate 10 µm sections. The sections were placed into a solution of glucose oxidase and beta D-glucose, in the presence of sodium azide, to block endogenous peroxidase. Once tissue sections were prepared, the staining with the specified mouse immune sera was carried out at 1:500 in 5% goat serum with 0.25% triton for 1 hour at RT. To image the binding to plagues and tangles, Biotin-SP-Conjugated Goat anti mouse IgG from Jackson (Lot # 115-065-166) at 1:200 dilution were incubated with the sections. DAKO DAB Detection Kit as per the manufacturer's instructions. The staining was processed using an automated Leica Bond Stainer. The results indicate

that sera from Guinea pigs immunized with a vaccine as disclosed herein comprises antibodies specific to Abeta and tau in human brain tissue of Alzheimer's patients

[00229] Serum blocking of Abeta binding to neurons

[00230] E18 primary rat hippocampal neurons are cultured as described previously (Zago, *et al.* "Neutralization of Soluble, Synaptotoxic Amyloid β Species by Antibodies Is Epitope Specific," *J Neurosci.* 2012 Feb 22; 32(8): 2696--2702). Soluble Aβ aggregate is pre-incubated with or without vaccine serum on culture DIV14-21 to block soluble Aβ aggregate from neuritic binding. Fresh unlabeled, biotinylated or (9:1) soluble Aβ is prepared one day prior and incubated overnight at 4˚C. Each diluted serum sample and soluble Aβ solution is prepared at 2x the final concentration in one-half of final treatment volume using NeuroBasal-no phenol red (NB-NPR) medium. This is combined with one-half final volume of 2x soluble Aβ and with one-half final volume of 2x diluted vaccine serum to make up a 1x final concentration in total final treatment volume, which is mixed well and then pre-incubated for 30 minutes at 37˚C. E18 neurons are rinsed with NB-NPR at 150 µL/well before adding binding treatment. Serum from vaccinated animals/Aβ treatment to is added to E18 neurons at 60µL/well, and then incubated for 30 minutes at 37˚C under normal incubator conditions (5% CO_2; 9% O_2). Cells are rinsed twice using 150 µL/well of NB-NPR, and then fixed in 4% paraformaldehyde in 1x DPBS for 20 minutes. Cells are permeabilized using 0.1 TX-100 for 5 minutes, and blocked using 10% normal goat serum (NGS) for 1 hour at room temperature (RT). Cells are incubated with MAP2 & NeuN primary antibodies in 100µL/well, 1x DPBS containing 1% BSA + 1% NGS overnight at 4˚C. The next day, cells are rinsed twice in 150 µL/well 1x DPBS for 5 minutes each wash. Secondary antibodies are added for 1 hour at RT in 100µL/well 1x DPBS + 1% BSA + 1% NGS. High-content imaging (HCI) analysis is performed to quantify soluble aggregate Aβ neuritic binding using Operetta HCI CLS instrument (Perkin Elmer; modified Neurite Outgrowth algorithm: 40x H_2O objective; 40 fields per well; (n=3) per condition; data shown as mean (+/-) SD); MAP2 & NeuN (Abcam) neuronal markers is used to each trace neurite tree and count cell body number per optical field; Neuritic Aβ souble aggregate spots detected using streptavidin-488 or polyclonal Aβ antibody (Thermo; Millipore); and data reported as Aβ soluble aggregate spots/neuron (or as Integrated

Intensity)). Approximately 80-150 neurons are observed per well for each condition tested.

[00231] Results

[00232] Data for Abeta and tau titers and staining is summarized in Table 10 and Table 11.

Table 10

	Animal	Titer Abeta	Titer Tau	50% blocking tau binding	IHC Abeta	IHC Tau
Dual Construct 2	2.1	35,000	35,000	1:300	++++	+
	2.2	21,000	75,000	1:225	++++	+
	2.3	12,000	21,000	1:550	+++	+++++
	2.4	20,000	7,000	1:200	++	+++++
Dual Construct 3	3.1	22,000	12,000	1:275	+++	++++
	3.2	20,000	2,000	1:200	~	++++
	3.3	7,000	40,000	1:125	++++	++
	3.4	1,000	25,000	1:200	+	++++
Dual Construct 8	8.1	15,000	100,000	1:275	++ (or +½)	++++½
	8.2	7,000	6,800	1:675	++ (or +½)	+++
	8.3	60,000	10,000	1:200	+++	-
	8.4	30,000	20,000	1:200	++++	++++
Dual Construct 9	9.1	150,000	50,000	1:525	+	++++½
	9.2	30,000	21,000	1:325	++	++++
	9.3	13,000	30,000	1:325	+++	++++
	9.4	72,000	30,000	1:625	+++	+++
Dual Construct 11	11.1	30,000	6,000	1:375	++++	++½
	11.2	10,000	40,000	1:875	~	++++
	11.3	11,000	20,000	1:325	++++½	++
	11.4	10,000	10,000	1:275	++++	+

Table 11

Dual Abeta/Tau Mouse Sera	A-beta	Tau		Notes
		Cell bodies	Neurites	
2.1	++++	+	+	
2.2	++++	++	+	Presence of nuclear staining

2.3	+++	+++++	+++	
2.4	++	+++++	++++	
3.1	+++	++++	+++++	
3.2	-	++++	+++++	
3.3	++++	++	+++	Strong nuclear staining
3.4	+	++++	++	
8.1	++	++++	++++	
8.2	++	+++	+++	
8.3	+++	-	-	
8.4	++++	++++	+++++	
9.1	+	++++	++++	
9.2	++	++++	+++	
9.3	+++	++++	++++	
9.4	+++	+++	++++	
11.1	++++	++	+++	
11.2	+	++++	+	
11.3	+++++	++	-	
11.4	++++	+	-	Some nuclear staining

[00233] **Titers**

[00234] As seen in Figure 13 and Tables 10-13, all groups most animals produced high and balanced Abeta and tau titers, though some had a less variable titer response.

Table 12

Titers for the dual Abeta/tau constructs.

	Abeta					**tau**			
Dual Construct 2	Mouse 1	Mouse 2	Mouse 3	Mouse 4		Mouse 1	Mouse 2	Mouse 3	Mouse 4
Bleed 1	30000	25000	25000	12000		150	5000	3000	4000
Bleed 2	35000	21000	12000	20000		35000	75000	21000	7000
Dual Construct 3	Mouse 1	Mouse 2	Mouse 3	Mouse 4		Mouse 1	Mouse 2	Mouse 3	Mouse 4
Bleed 1	6400	800	15000	100		4000	6400	5000	2000
Bleed 2	22000	22000	7000	1000		12000	2000	40000	2500
Dual	Mouse 1	Mouse	Mouse	Mouse		Mouse	Mouse	Mouse	Mouse

Construct 8		2	3	4		1	2	3	4
Bleed 1	1500	2000	20000	18000		10000	25000	200	8000
Bleed 2	15000	7000	60000	30000		100000	6800	1000	20000
Dual Construct 9	Mouse 1	Mouse 2	Mouse 3	Mouse 4		Mouse 1	Mouse 2	Mouse 3	Mouse 4
Bleed 1	2000	12000	13000	6400		800	6000	7000	2000
Bleed 2	150000	30000	13000	72000		5000	21000	30000	30000
Dual Construct 11	Mouse 1	Mouse 2	Mouse 3	Mouse 4		Mouse 1	Mouse 2	Mouse 3	Mouse 4
Bleed 1	6000	2000	5000	7000		6400	7000	2500	4000
	30000	10000	11000	10000		6000	40000	20000	10000

Table 13

Remaining tau bound after serum incubation

dilution	DAEFRHDRRVKSKIGSTGGC (SEQ ID NO:997)			
	Mouse 1	Mouse 2	Mouse 3	Mouse 4
50	19.57	29.12	16.66	12.70
100	28.93	38.25	26.51	25.21
200	41.16	53.48	29.64	46.53
400	59.88	89.43	43.15	81.31
800	95.14	139.21	65.00	134.97
dilution	DAEFRHDRRENLKHQPGGGC (SEQ ID NO:1000)			
	Mouse 1	Mouse 2	Mouse 3	Mouse 4
50	16.44	21.90	24.26	15.35
100	22.07	47.55	39.93	19.39
200	37.10	44.06	48.36	43.65
400	58.32	86.61	86.41	51.98
800	93.54	98.76	115.50	86.00
dilution	DAEFRHDRRSKIGSTENGGC (SEQ ID NO:998)			
	Mouse 1	Mouse 2	Mouse 3	Mouse 4
50	16.84	27.29	28.01	28.56
100	25.18	39.02	53.18	42.60
200	55.66	73.61	93.32	75.38
400	92.87	120.00	131.15	125.27
800	110.16	132.77	130.90	135.93
dilution	DAEFRHDRRSKIGSKDNIKHGGC (SEQ ID NO:1001)			
	Mouse 1	Mouse 2	Mouse 3	Mouse 4

50	15.25	13.15	14.73	17.81
100	19.45	11.20	26.64	37.79
200	37.65	14.59	56.17	54.57
400	74.17	39.69	78.69	91.10
800	90.35	62.16	96.30	109.00
dilution	DAEFRHDRRTENLKHQPGGC (SEQ ID NO:999)			
	Mouse 1	Mouse 2	Mouse 3	Mouse 4
50	20.01	12.36	35.04	42.63
100	37.62	28.44	44.45	47.62
200	54.86	47.97	66.72	61.84
400	114.93	48.51	91.94	87.67
800	110.60	81.25	100.01	97.15
dilution	Negative Control			
	Mouse 1	Mouse 2	Mouse 3	Mouse 4
50	83.35	71.98	84.30	83.96
100	114.78	94.03	103.43	98.98
200	104.03	100.60	97.80	96.83
400	86.73	111.16	95.31	91.72
800	96.20	110.05	99.38	94.45

[00235] Blocking of Tau binding to heparin

[00236] All constructs showed the ability to block the binding of tau to heparin, in particular, construct DAEFRHDRRVKSKIGSTGGC (SEQ ID NO:997) and construct DAEFRHDRRENLKHQPGGGC (SEQ ID NO:1000) showing the most robust blocking. *See* Figure 15, Table 10 and Table 11.

[00237] IHC on Alzheimer Brain

[00238] Most animals had staining of pathological Abeta and tau, *see* Figure 16.

[00239] Example 11: Immunogens

[00240] Immunogens were selected for evaluation in vaccine peptide constructs. Constructs comprise Aβ immunogens and tau immunogens. Some immunogens comprise a tau peptide comprising 3-10 amino acids from tau. Other immunogens comprise an engineered tau immunogen.

[00241] Engineered Tau Immunogens

[00242] Certain immunogenic peptides were designed and selected to (i) raise antibodies that bind within the within microtubule binding repeats (MTBRs) of human Tau protein, (ii) be less likely to generate an unwanted T cell-mediated autoimmune response, and (iii) be less likely to raise antibodies that would cross-react with other human proteins.

[00243] First, sequence analysis and 3D modeling of Tau MTBRs was conducted to identify amino acid residues that may be important for raising antibodies that bind MTBR. The results of these analyses were used to design synthetic Tau immunogenic peptides with conserved residues and shuffled interspersed residues. Resulting engineered synthetic peptides are listed in Table 14.

Table 14

Engineered Tau immunogenic peptides

Engineered tau immunogenic peptides sequence	**SEQ ID NO:**
SKIGSTENLKH	978
SKIGSTENIKH	979
SKIGSKDNLKH	980
SKIGSKENIKH	981
SKIGSLENLKH	982
SKIGSLENIKH	983
SKIGSTDNLKH	984
SKIGSTDNIKH	985
SKIGSKDNIKH	986
SKIGSLDNLKH	987
SKIGSLDNIKH	988
SKIGSTGNLKH	989
SKIGSTGNIKH	990
SKIGSKGNLKH	991
SKIGSKGNIKH	992
SKIGSLGNLKH	993
SKIGSLGNIKH	994

[00244] Next, to assess the potential of an unwanted T cell-mediated autoimmune response, the engineered peptides were subjected to *in silico* analysis to predict MHC II binding using the IEDB (Immune Epitope Database) from National Institute of Allergy and Infectious Diseases/La Jolla Immunology Institute. MHC class II binding is considered a good indicator of a sequence containing a T-cell epitope. A panel of alleles were used for MHC II binding prediction. Engineered

peptides with a predicted half maximal inhibitory concentration (IC50) above a specified cutoff were considered to have a low probability of MHC II binding and were selected for further analysis.

[00245] Finally, the engineered peptides with low predicted MHC II binding were evaluated to predict if the anti-Tau MTBR antibodies that would be raised by the peptides could have unwanted cross-reactivity with other human proteins. Sequences of the engineered peptides were subjected to bioinformatic analysis against a non-redundant human proteome database to determine homology with human proteins. Engineered peptide sequences with low homology to secreted or cell-surface proteins were selected as top candidates to be used as antigens. Top candidate engineered Tau immunogenic peptides are listed in Table 15.

Table 15

Top candidate engineered Tau immunogenic peptides.

Engineered tau immunogenic peptides sequence	**SEQ ID NO:**
SKIGSTDNIKH	985
SKIGSKDNIKH	986
SKIGSLDNIKH	988

[00246] The dual Aβ-tau constructs comprising an engineered tau immunogen (*e.g.*, Dual #11) demonstrated results that were comparable, and in some cases, better than other tau immunogens despite including a non-native tau sequence. Figure 13shows high titers for both Abeta and tau antigens, including an engineered tau sequence. Figure 14 shows blocking of tau binding to heparin. Figure 15G shows resulting tau antibody binding to MTBR region peptides. Figure 16 E shows staining/binding to Aβ and tau peptides in brain tissue from human Alzheimer's patients. This demonstrates that engineered immunogens are useful in vaccine constructs

[00247] **Conclusion**

[00248] Dual immunogen Aβ-tau vaccine constructs were developed and it was shown that these constructs raised balanced titers to Aβ and tau in mice, guinea-pigs, and cynomolgus monkeys. The antibodies were immunoreactive with both Aβ plaques and neurofibrillary tau tangles in human AD brain sections and blocked the binding of soluble Aβ aggregates (oligomers) to neurons without eliciting T-cell

responses for Aβ or tau. These results support the development of a single-agent, dual-immunogen vaccine with the ability to target the pathogenic forms of Aβ and tau. These results support the development of a dual Aβ-tau vaccine with the ability to target pathogenic Aβ and tau for the prevention and/or treatment of AD.

[00249] Although various specific embodiments of the present invention have been described herein, it is to be understood that the invention is not limited to those precise embodiments and that various changes or modifications can be affected therein by one skilled in the art without departing from the scope and spirit of the invention.

[00250] In each of the embodiments of the peptide described herein, the peptide may comprise, consist, or consist essentially of the recited sequences. Thus, incorporated in this disclosure (*see* Table 16) are the following sequences that can be part of the compositions comprising an amyloid-beta (Aβ) peptide and a tau peptide as disclosed herein.

Table 16. SEQUENCES

SEQ ID NO:01 – Abeta 1-42
DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA

SEQ ID NO:02 - TAU (UNIPROTKB - P10636 (*Homo sapiens*)
>P10636-8 (Isoform Tau-F)

```
        10         20         30         40         50
MAEPPQEFEV MEDHAGTYGL GDRKDQGGYT MHQDQEGDTD AGLKESPLQT
        60         70         80         90        100
PTEDGSEEPG SETSDAKSTP TAEDVTAPLV DEGAPGKQAA AQPHTEIPEG
       110        120        130        140        150
TTAEEAGIGD TPSLEDEAAG HVTQARMVSK SKDGTGSDDK KAKGADGKTK
       160        170        180        190        200
IATPRGAAPP GQKGQANATR IPAKTPPAPK TPPSSGEPPK SGDRSGYSSP
       210        220        230        240        250
GSPGTPGSRS RTPSLPTPPT REPKKVAVVR TPPKSPSSAK SRLQTAPVPM
       260        270        280        290        300
PDLKNVKSKI GSTENLKHQP GGGKVQIINK KLDLSNVQSK CGSKDNIKHV
       310        320        330        340        350
PGGGSVQIVY KPVDLSKVTS KCGSLGNIHH KPGGGQVEVK SEKLDFKDRV
       360        370        380        390        400
QSKIGSLDNI THVPGGGNKK IETHKLTFRE NAKAKTDHGA EIVYKSPVVS
       410        420        430        440
GDTSPRHLSN VSSTGSIDMV DSPQLATLAD EVSASLAKQG L
```

A-beta immunogens:

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)
SGY (SEQ ID NO:38)
VHHQKLVFFA (SEQ ID NO:1002)
VHHQKLVFF (SEQ ID NO:1003)
VHHQKLVF (SEQ ID NO:1004)
VHHQKLV (SEQ ID NO:1005)
VHHQKL (SEQ ID NO:1006)
HHQKLVFFAE (SEQ ID NO:1007)
HHQKLVFFA (SEQ ID NO:1008)
HHQKLVFF (SEQ ID NO:1009)
HHQKLVF (SEQ ID NO:1010)
HHQKLV (SEQ ID NO:1011)
HHQKL (SEQ ID NO:1012)
HQKLVFFAED (SEQ ID NO:1013)
HQKLVFFAE (SEQ ID NO:1014)
HQKLVFFA (SEQ ID NO:1015)
HQKLVFF (SEQ ID NO:1016)
HQKLVF (SEQ ID NO:1017)
HQKLV (SEQ ID NO:1018)
HQKL (SEQ ID NO:1019)
QKLVFFAEDV (SEQ ID NO:1020)

QKLVFFAED (SEQ ID NO:1021)
QKLVFFAE (SEQ ID NO:1022)
QKLVFFA (SEQ ID NO:1023)
QKLVFF (SEQ ID NO:1024)
QKLVF (SEQ ID NO:1025)
QKLV (SEQ ID NO:1026)
QKL (SEQ ID NO:1027)
KLVFFAEDVG (SEQ ID NO:1028)
KLVFFAEDV (SEQ ID NO:1029)
KLVFFAED (SEQ ID NO:1030)
KLVFFAE (SEQ ID NO:1031)
KLVFFA (SEQ ID NO:1032)
KLVFF (SEQ ID NO:1033)
KLVF (SEQ ID NO:1034)
KLV (SEQ ID NO:1035)
LVFFAEDVG (SEQ ID NO:1036)
LVFFAEDV (SEQ ID NO:1037)
LVFFAED (SEQ ID NO:1038)
LVFFAE (SEQ ID NO:1039)
LVFFA (SEQ ID NO:1040)
LVFF (SEQ ID NO:1041)
LVF (SEQ ID NO:1042)
VFFAEDVG (SEQ ID NO:1043)
VFFAEDV (SEQ ID NO:1044)
VFFAED (SEQ ID NO:1045)
VFFAE (SEQ ID NO:1046)
VFFA (SEQ ID NO:1047)
VFF (SEQ ID NO:1048)
FFAEDVG (SEQ ID NO:1049)
FFAEDV (SEQ ID NO:1050)
FFAED (SEQ ID NO:1051)
FFAE (SEQ ID NO:1052)
FFA (SEQ ID NO:1053)
FAEDVG (SEQ ID NO:1054)
FAEDV (SEQ ID NO:1055)
FAED (SEQ ID NO:1056)
FAE (SEQ ID NO:1057)

Tau immunogens:

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)
VQIINK (SEQ ID NO:146)
VQIINKK (SEQ ID NO:147)
VQIINKKL (SEQ ID NO:148)
QIINK (SEQ ID NO:149)
QIINKK (SEQ ID NO:150)
QIINKKL (SEQ ID NO:151)
EAAGHVTQC (SEQ ID NO:152)
EAAGHVTQAR (SEQ ID NO:153)
AAGHVTQAC (SEQ ID NO:154)
AGHVTQARC (SEQ ID NO:155)
AGHVTQAR (SEQ ID NO:156)
GYTMHQD (SEQ ID NO:157)
QGGYTMHC (SEQ ID NO:158)
QGGYTMHQD (SEQ ID NO:159)
GGYTMHQC (SEQ ID NO:160)
VPGGGSVQIV (SEQ ID NO:161)
PGGGSVQIV (SEQ ID NO:162)
GGGSVQIV (SEQ ID NO:163)
GGSVQIV (SEQ ID NO:164)
GSVQIV (SEQ ID NO:165)
SVQIV (SEQ ID NO:166)
VQIV (SEQ ID NO:167)
QIV (SEQ ID NO:168)
PGGGSVQIVY (SEQ ID NO:169)
GGGSVQIVY (SEQ ID NO:170)
GGSVQIVY (SEQ ID NO:171)
GSVQIVY (SEQ ID NO:172)
SVQIVY (SEQ ID NO:173)
VQIVY (SEQ ID NO:174)
QIVY (SEQ ID NO:175)
IVY (SEQ ID NO:176)
GGGSVQIVYK (SEQ ID NO:177)
GGSVQIVYK (SEQ ID NO:178)
GSVQIVYK (SEQ ID NO:179)
SVQIVYK (SEQ ID NO:180)
VQIVYK (SEQ ID NO:181)
QIVYK (SEQ ID NO:182)
VYK (SEQ ID NO:183)
GGSVQIVYKP (SEQ ID NO:184)
GSVQIVYKP (SEQ ID NO:185)
SVQIVYKP (SEQ ID NO:186)

VQIVYKP (SEQ ID NO:187)
IVYKP (SEQ ID NO:188)
VYKP (SEQ ID NO:189)
YKP (SEQ ID NO:190)
GSVQIVYKPV (SEQ ID NO:191)
SVQIVYKPV (SEQ ID NO:192)
VQIVYKPV (SEQ ID NO:193)
IVYKPV (SEQ ID NO:194)
VYKPV (SEQ ID NO:195)
YKPV (SEQ ID NO:196)
KPV (SEQ ID NO:197)
SVQIVYKPVD (SEQ ID NO:198)
VQIVYKPVD (SEQ ID NO:199)
QIVYKPVD (SEQ ID NO:200)
IVYKPVD (SEQ ID NO:201)
VYKPVD (SEQ ID NO:203)
YKPVD (SEQ ID NO:204)
KPVD (SEQ ID NO:205)
PVD (SEQ ID NO:206)
VQIVYKPVDL (SEQ ID NO:207)
QIVYKPVDL (SEQ ID NO:208)
IVYKPVDL (SEQ ID NO:209)
VYKPVDL (SEQ ID NO:210)
YKPVDL (SEQ ID NO:211)
KPVDL (SEQ ID NO:212)
PVDL (SEQ ID NO:213)
VDL (SEQ ID NO:214)
QIVYKPVDLS (SEQ ID NO:215)
IVYKPVDLS (SEQ ID NO:216)
VYKPVDLS (SEQ ID NO:217)
YKPVDLS (SEQ ID NO:218)
KPVDLS (SEQ ID NO:219)
PVDLS (SEQ ID NO:220)
VDLS (SEQ ID NO:221)
DLS (SEQ ID NO:222)
IVYKPVDLSK (SEQ ID NO:223)
VYKPVDLSK (SEQ ID NO:224)
YKPVDLSK (SEQ ID NO:225)
KPVDLSK (SEQ ID NO:226)
PVDLSK (SEQ ID NO:227)
VDLSK (SEQ ID NO:228)
DLSK (SEQ ID NO:229)
LSK (SEQ ID NO:230)
VYKPVDLSKV (SEQ ID NO:231)
YKPVDLSKV (SEQ ID NO:232)
KPVDLSKV (SEQ ID NO:233)
PVDLSKV (SEQ ID NO:234)
VDLSKV (SEQ ID NO:235)
DLSKV (SEQ ID NO:236)
LSKV (SEQ ID NO:237)
SKV (SEQ ID NO:238)

YKPVDLSKVT (SEQ ID NO:239)
KPVDLSKVT (SEQ ID NO:240)
PVDLSKVT (SEQ ID NO:241)
VDLSKVT (SEQ ID NO:242)
AKTDHGAEIV (SEQ ID NO:243)
KTDHGAEIV (SEQ ID NO:244)
TDHGAEIV (SEQ ID NO:245)
DHGAEIV (SEQ ID NO:246)
HGAEIV (SEQ ID NO:247)
GAEIV (SEQ ID NO:248)
AEIV (SEQ ID NO:249)
EIV (SEQ ID NO:250)
KTDHGAEIVY (SEQ ID NO:251)
TDHGAEIVY (SEQ ID NO:252)
DHGAEIVY (SEQ ID NO:253)
HGAEIVY (SEQ ID NO:254)
GAEIVY (SEQ ID NO:255)
AEIVY (SEQ ID NO:256)
EIVY (SEQ ID NO:257)
IVY (SEQ ID NO:258)
TDHGAEIVYK (SEQ ID NO:259)
DHGAEIVYK (SEQ ID NO:260)
HGAEIVYK (SEQ ID NO:261)
GAEIVYK (SEQ ID NO:262)
AEIVYK (SEQ ID NO:263)
EIVYK (SEQ ID NO:264)
IVYK (SEQ ID NO:265)
DHGAEIVYKS (SEQ ID NO:266)
HGAEIVYKS (SEQ ID NO:267)
GAEIVYKS (SEQ ID NO:268)
AEIVYKS (SEQ ID NO:269)
EIVYKS (SEQ ID NO:270)
IVYKS (SEQ ID NO:271)
VYKS (SEQ ID NO:272)
YKS (SEQ ID NO:273)
HGAEIVYKSP (SEQ ID NO:274)
GAEIVYKSP (SEQ ID NO:275)
AEIVYKSP (SEQ ID NO:276)
EIVYKSP (SEQ ID NO:277)
IVYKSP (SEQ ID NO:278)
VYKSP (SEQ ID NO:279)
YKSP (SEQ ID NO:280)
KSP (SEQ ID NO:281)
GAEIVYKSPV (SEQ ID NO:282)
AEIVYKSPV (SEQ ID NO:283)
EIVYKSPV (SEQ ID NO:284)
IVYKSPV (SEQ ID NO:285)
VYKSPV (SEQ ID NO:286)
YKSPV (SEQ ID NO:287)
KSPV (SEQ ID NO:288)
SPV (SEQ ID NO:289)

AEIVYKSPVV (SEQ ID NO:290)
EIVYKSPVV (SEQ ID NO:291)
IVYKSPVV (SEQ ID NO:292)
VYKSPVV (SEQ ID NO:293)
YKSPVV (SEQ ID NO:294)
KSPVV (SEQ ID NO:295)
SPVV (SEQ ID NO:296)
PVV (SEQ ID NO:297)
EIVYKSPVVS (SEQ ID NO:298)
IVYKSPVVS (SEQ ID NO:299)
VYKSPVVS (SEQ ID NO:300)
YKSPVVS (SEQ ID NO:301)
KSPVVS (SEQ ID NO:302)
SPVVS (SEQ ID NO:303)
PVVS (SEQ ID NO:304)
VVS (SEQ ID NO:305)
IVYKSPVVSG (SEQ ID NO:306)
VYKSPVVSG (SEQ ID NO:307)
YKSPVVSG (SEQ ID NO:308)
KSPVVSG (SEQ ID NO:309)
SPVVSG (SEQ ID NO:310)
PVVSG (SEQ ID NO:311)
VVSG (SEQ ID NO:312)
VSG (SEQ ID NO:313)
VYKSPVVSGD (SEQ ID NO:314)
YKSPVVSGD (SEQ ID NO:315)
KSPVVSGD (SEQ ID NO:316)
SPVVSGD (SEQ ID NO:317)
PVVSGD (SEQ ID NO:318)
VVSGD (SEQ ID NO:319)
VSGD (SEQ ID NO:320)
SGD (SEQ ID NO:321)
YKSPVVSGDT (SEQ ID NO:322)
KSPVVSGDT (SEQ ID NO:323)
SPVVSGDT (SEQ ID NO:324)
PVVSGDT (SEQ ID NO:325)
VVSGDT (SEQ ID NO:326)
VSGDT (SEQ ID NO:327)
SGDT (SEQ ID NO:328)
GDT (SEQ ID NO:329)
KSPVVSGDTS (SEQ ID NO:330)
SPVVSGDTS (SEQ ID NO:331)
PVVSGDTS (SEQ ID NO:332)
VVSGDTS (SEQ ID NO:333)
VSGDTS (SEQ ID NO:334)
SGDTS (SEQ ID NO:335)
GDTS (SEQ ID NO:336)
DTS (SEQ ID NO:337)
SPVVSGDTSP (SEQ ID NO:338)
PVVSGDTSP (SEQ ID NO:339)
VVSGDTSP (SEQ ID NO:340)

VSGDTSP (SEQ ID NO:341)
SGDTSP (SEQ ID NO:342)
GDTSP (SEQ ID NO:343)
DTSP (SEQ ID NO:344)
TSP (SEQ ID NO:345)
PVVSGDTSPR (SEQ ID NO:346)
VVSGDTSPR (SEQ ID NO:347)
VSGDTSPR (SEQ ID NO:348)
SGDTSPR (SEQ ID NO:349)
GDTSPR (SEQ ID NO:350)
DTSPR (SEQ ID NO:351)
TSPR (SEQ ID NO:352)
SPR (SEQ ID NO:353)
HQPGGGKVQI (SEQ ID NO:354)
QPGGGKVQI (SEQ ID NO:355)
PGGGKVQI (SEQ ID NO:356)
GGGKVQI (SEQ ID NO:357)
GGKVQI (SEQ ID NO:358)
GKVQI (SEQ ID NO:359)
KVQI (SEQ ID NO:360)
VQI (SEQ ID NO:361)
QPGGGKVQII (SEQ ID NO:362)
PGGGKVQII (SEQ ID NO:363)
GGGKVQII (SEQ ID NO:365)
GGKVQII (SEQ ID NO:366)
GKVQII (SEQ ID NO:367)
KVQII (SEQ ID NO:368)
VQII (SEQ ID NO:369)
QII (SEQ ID NO:370)
PGGGKVQIIN (SEQ ID NO:371)
GGGKVQIIN (SEQ ID NO:372)
GGKVQIIN (SEQ ID NO:373)
GKVQIIN (SEQ ID NO:374)
KVQIIN (SEQ ID NO:375)
VQIIN (SEQ ID NO:376)
QIIN (SEQ ID NO:377)
IIN (SEQ ID NO:378)
GGGKVQIINK (SEQ ID NO:379)
GGKVQIINK (SEQ ID NO:380)
GKVQIINK (SEQ ID NO:381)
KVQIINK (SEQ ID NO:382)
IINK (SEQ ID NO:383)
INK (SEQ ID NO:384)
GGKVQIINKK (SEQ ID NO:385)
GKVQIINKK (SEQ ID NO:386)
KVQIINKK (SEQ ID NO:387)
IINKK (SEQ ID NO:388)
INKK (SEQ ID NO:389)
NKK (SEQ ID NO:390)
GKVQIINKKL (SEQ ID NO:391)
KVQIINKKL (SEQ ID NO:392)

IINKKL (SEQ ID NO:393)
INKKL (SEQ ID NO:394)
NKKL (SEQ ID NO:395)
KKL (SEQ ID NO:396)
KVQIINKKLD (SEQ ID NO:397)
VQIINKKLD (SEQ ID NO:398)
QIINKKLD (SEQ ID NO:399)
IINKKLD (SEQ ID NO:400)
INKKLD (SEQ ID NO:401)
NKKLD (SEQ ID NO:402)
KKLD (SEQ ID NO:403)
KLD (SEQ ID NO:404)
VQIINKKLDL (SEQ ID NO:405)
QIINKKLDL (SEQ ID NO:406)
IINKKLDL (SEQ ID NO:407)
INKKLDL (SEQ ID NO:408)
NKKLDL (SEQ ID NO:409)
KKLDL (SEQ ID NO:410)
KLDL (SEQ ID NO:411)
LDL (SEQ ID NO:412)
QIINKKLDLS (SEQ ID NO:413)
IINKKLDLS (SEQ ID NO:414)
INKKLDLS (SEQ ID NO:415)
NKKLDLS (SEQ ID NO:416)
KKLDLS (SEQ ID NO:417)
KLDLS (SEQ ID NO:418)
LDLS (SEQ ID NO:419)
IINKKLDLSN (SEQ ID NO:420)
INKKLDLSN (SEQ ID NO:421)
NKKLDLSN (SEQ ID NO:422)
KKLDLSN (SEQ ID NO:423)
KLDLSN (SEQ ID NO:424)
LDLSN (SEQ ID NO:425)
DLSN (SEQ ID NO:426)
LSN (SEQ ID NO:427)
INKKLDLSNV (SEQ ID NO:428)
NKKLDLSNV (SEQ ID NO:429)
KKLDLSNV (SEQ ID NO:430)
KLDLSNV (SEQ ID NO:431)
LDLSNV (SEQ ID NO:432)
DLSNV (SEQ ID NO:433)
LSNV (SEQ ID NO:434)
SNV (SEQ ID NO:435)
NKKLDLSNVQ (SEQ ID NO:436)
KKLDLSNVQ (SEQ ID NO:437)
KLDLSNVQ (SEQ ID NO:438)
LDLSNVQ (SEQ ID NO:439)
DLSNVQ (SEQ ID NO:440)
LSNVQ (SEQ ID NO:441)
SNVQ (SEQ ID NO:442)
NVQ (SEQ ID NO:443)

KKLDLSNVQS (SEQ ID NO:444)
KLDLSNVQS (SEQ ID NO:445)
LDLSNVQS (SEQ ID NO:446)
DLSNVQS (SEQ ID NO:447)
LSNVQS (SEQ ID NO:448)
SNVQS (SEQ ID NO:449)
NVQS (SEQ ID NO:450)
VQS (SEQ ID NO:451)
SKCGSKDNIK (SEQ ID NO:452)
KCGSKDNIK (SEQ ID NO:453)
CGSKDNIK (SEQ ID NO:454)
GSKDNIK (SEQ ID NO:455)
SKDNIK (SEQ ID NO:456)
KDNIK (SEQ ID NO:457)
DNIK (SEQ ID NO:458)
NIK (SEQ ID NO:459)
KCGSKDNIKH (SEQ ID NO:460)
CGSKDNIKH (SEQ ID NO:461)
GSKDNIKH (SEQ ID NO:462)
SKDNIKH (SEQ ID NO:463)
KDNIKH (SEQ ID NO:464)
DNIKH (SEQ ID NO:465)
NIKH (SEQ ID NO:466)
IKH (SEQ ID NO:467)
CGSKDNIKHV (SEQ ID NO:468)
GSKDNIKHV (SEQ ID NO:469)
SKDNIKHV (SEQ ID NO:470)
KDNIKHV (SEQ ID NO:471)
DNIKHV (SEQ ID NO:472)
NIKHV (SEQ ID NO:473)
IKHV (SEQ ID NO:474)
KHV (SEQ ID NO:475)
GSKDNIKHVP (SEQ ID NO:476)
SKDNIKHVP (SEQ ID NO:477)
KDNIKHVP (SEQ ID NO:478)
DNIKHVP (SEQ ID NO:479)
IKHVP (SEQ ID NO:480)
KHVP (SEQ ID NO:481)
HVP (SEQ ID NO:482)
SKDNIKHVPG (SEQ ID NO:483)
KDNIKHVPG (SEQ ID NO:484)
DNIKHVPG (SEQ ID NO:485)
NIKHVPG (SEQ ID NO:486)
IKHVPG (SEQ ID NO:487)
KHVPG (SEQ ID NO:488)
HVPG (SEQ ID NO:489)
VPG (SEQ ID NO:490)
KDNIKHVPGG (SEQ ID NO:491)
DNIKHVPGG (SEQ ID NO:492)
NIKHVPGG (SEQ ID NO:493)
IKHVPGG (SEQ ID NO:494)

KHVPGG (SEQ ID NO:495)
VPGG (SEQ ID NO:496)
PGG (SEQ ID NO:497)
DNIKHVPGGG (SEQ ID NO:498)
NIKHVPGGG (SEQ ID NO:499)
IKHVPGGG (SEQ ID NO:500)
VPGGG (SEQ ID NO:501)
PGGG (SEQ ID NO:502)
GGG (SEQ ID NO:503)
NIKHVPGGGS (SEQ ID NO:504)
IKHVPGGGS (SEQ ID NO:505)
KHVPGGGS (SEQ ID NO:506)
HVPGGGS (SEQ ID NO:507)
VPGGGS (SEQ ID NO:508)
PGGGS (SEQ ID NO:509)
GGGS (SEQ ID NO:510)
GGS (SEQ ID NO:511)
IKHVPGGGSV (SEQ ID NO:512)
KHVPGGGSV (SEQ ID NO:513)
HVPGGGSV (SEQ ID NO:514)
VPGGGSV (SEQ ID NO:515)
PGGGSV (SEQ ID NO:516)
GGGSV (SEQ ID NO:517)
GGSV (SEQ ID NO:518)
GSV (SEQ ID NO:519)
KHVPGGGSVQ (SEQ ID NO:520)
HVPGGGSVQ (SEQ ID NO:521)
VPGGGSVQ (SEQ ID NO:522)
PGGGSVQ (SEQ ID NO:523)
GGGSVQ (SEQ ID NO:524)
GGSVQ (SEQ ID NO:525)
GSVQ (SEQ ID NO:526)
SVQ (SEQ ID NO:527)
HVPGGGSVQI (SEQ ID NO:528)
VPGGGSVQI (SEQ ID NO:529)
PGGGSVQI (SEQ ID NO:530)
GGGSVQI (SEQ ID NO:531)
GGSVQI (SEQ ID NO:532)
GSVQI (SEQ ID NO:533)
SVQI (SEQ ID NO:534)
GGSVQIVYKS (SEQ ID NO:535)
GSVQIVYKS (SEQ ID NO:536)
SVQIVYKS (SEQ ID NO:537)
VQIVYKS (SEQ ID NO:538)
QIVYKS (SEQ ID NO:539)
IVYKS (SEQ ID NO:540)
VYKS (SEQ ID NO:541)
YKS (SEQ ID NO:542)
GSVQIVYKSV (SEQ ID NO:543)
SVQIVYKSV (SEQ ID NO:544)
VQIVYKSV (SEQ ID NO:545)

QIVYKSV (SEQ ID NO:546)
IVYKSV (SEQ ID NO:547)
VYKSV (SEQ ID NO:548)
YKSV (SEQ ID NO:549)
SVQIVYKSVD (SEQ ID NO:550)
VQIVYKSVD (SEQ ID NO:551)
QIVYKSVD (SEQ ID NO:552)
IVYKSVD (SEQ ID NO:553)
VYKSVD (SEQ ID NO:554)
YKSVD (SEQ ID NO:555)
KSVD (SEQ ID NO:556)
SVD (SEQ ID NO:557)
VQIVYKSVDL (SEQ ID NO:558)
QIVYKSVDL (SEQ ID NO:559)
IVYKSVDL (SEQ ID NO:560)
VYKSVDL (SEQ ID NO:561)
YKSVDL (SEQ ID NO:562)
KSVDL (SEQ ID NO:563)
SVDL (SEQ ID NO:564)
QIVYKSVDLS (SEQ ID NO:565)
IVYKSVDLS (SEQ ID NO:566)
VYKSVDLS (SEQ ID NO:567)
YKSVDLS (SEQ ID NO:568)
KSVDLS (SEQ ID NO:569)
SVDLS (SEQ ID NO:570)
IVYKSVDLSK (SEQ ID NO:571)
VYKSVDLSK (SEQ ID NO:572)
YKSVDLSK (SEQ ID NO:573)
KSVDLSK (SEQ ID NO:574)
SVDLSK (SEQ ID NO:364)
VYKSVDLSKV (SEQ ID NO:575)
YKSVDLSKV (SEQ ID NO:576)
KSVDLSKV (SEQ ID NO:577)
SVDLSKV (SEQ ID NO:578)
YKSVDLSKVT (SEQ ID NO:579)
KSVDLSKVT (SEQ ID NO:580)
SVDLSKVT (SEQ ID NO:581)
DLSKVT (SEQ ID NO:582)
LSKVT (SEQ ID NO:583)
SKVT (SEQ ID NO:584)
KVT (SEQ ID NO:585)
HGAEIVYKSV (SEQ ID NO:586)
GAEIVYKSV (SEQ ID NO:587)
AEIVYKSV (SEQ ID NO:588)
GAEIVYKSVV (SEQ ID NO:589)
AEIVYKSVV (SEQ ID NO:590)
EIVYKSVV (SEQ ID NO:591)
IVYKSVV (SEQ ID NO:592)
VYKSVV (SEQ ID NO:593)
YKSVV (SEQ ID NO:594)
KSVV (SEQ ID NO:595)

SVV (SEQ ID NO:596)
AEIVYKSVVS (SEQ ID NO:597)
EIVYKSVVS (SEQ ID NO:598)
IVYKSVVS (SEQ ID NO:599)
VYKSVVS (SEQ ID NO:600)
YKSVVS (SEQ ID NO:601)
KSVVS (SEQ ID NO:602)
SVVS (SEQ ID NO:603)
EIVYKSVVSG (SEQ ID NO:604)
IVYKSVVSG (SEQ ID NO:605)
VYKSVVSG (SEQ ID NO:606)
YKSVVSG (SEQ ID NO:607)
KSVVSG (SEQ ID NO:608)
SVVSG (SEQ ID NO:609)
VVSG (SEQ ID NO:610)
VSG (SEQ ID NO:611)
IVYKSVVSGD (SEQ ID NO:612)
VYKSVVSGD (SEQ ID NO:613)
YKSVVSGD (SEQ ID NO:614)
KSVVSGD (SEQ ID NO:615)
SVVSGD (SEQ ID NO:616)
VVSGD (SEQ ID NO:617)
VYKSVVSGDT (SEQ ID NO:618)
YKSVVSGDT (SEQ ID NO:619)
KSVVSGDT (SEQ ID NO:620)
SVVSGDT (SEQ ID NO:621)
YKSVVSGDTS (SEQ ID NO:622)
KSVVSGDTS (SEQ ID NO:623)
SVVSGDTS (SEQ ID NO:624)
YKSVVSGDTS (SEQ ID NO:625)
KSVVSGDTS (SEQ ID NO:626)
SVVSGDTS (SEQ ID NO:627)
VVSGDTS (SEQ ID NO:628)
KSVVSGDTSP (SEQ ID NO:629)
SVVSGDTSP (SEQ ID NO:630)
SVVSGDTSPR (SEQ ID NO:631)
DHGAEIVYKP (SEQ ID NO:632)
HGAEIVYKP (SEQ ID NO:633)
GAEIVYKP (SEQ ID NO:634)
AEIVYKP (SEQ ID NO:635)
HGAEIVYKPV (SEQ ID NO:636)
GAEIVYKPV (SEQ ID NO:637)
AEIVYKPV (SEQ ID NO:638)
GAEIVYKPVV (SEQ ID NO:639)
AEIVYKPVV (SEQ ID NO:640)
EIVYKPVV (SEQ ID NO:641)
IVYKPVV (SEQ ID NO:642)
VYKPVV (SEQ ID NO:643)
YKPVV (SEQ ID NO:644)
KPVV (SEQ ID NO:645)
AEIVYKPVVS (SEQ ID NO:646)

EIVYKPVVS (SEQ ID NO:647)
IVYKPVVS (SEQ ID NO:648)
VYKPVVS (SEQ ID NO:649)
YKPVVS (SEQ ID NO:650)
KPVVS (SEQ ID NO:651)
EIVYKPVVSG (SEQ ID NO:652)
IVYKPVVSG (SEQ ID NO:653)
VYKPVVSG (SEQ ID NO:654)
YKPVVSG (SEQ ID NO:655)
KPVVSG (SEQ ID NO:656)
IVYKPVVSGD (SEQ ID NO:657)
VYKPVVSGD (SEQ ID NO:658)
YKPVVSGD (SEQ ID NO:659)
KPVVSGD (SEQ ID NO:660)
VYKPVVSGDT (SEQ ID NO:661)
YKPVVSGDT (SEQ ID NO:662)
KPVVSGDT (SEQ ID NO:663)
YKPVVSGDTS (SEQ ID NO:664)
KPVVSGDTS (SEQ ID NO:665)
PVVSGDTS (SEQ ID NO:666)
VVSGDTS (SEQ ID NO:667)
KPVVSGDTSP (SEQ ID NO:668)
CNIK (SEQ ID NO:669)
CNIKH (SEQ ID NO:670)
CNIKHV (SEQ ID NO:671)
CNIKHVPGG (SEQ ID NO:672)
CNIKHVPGGG (SEQ ID NO:673)
CNIKHVPGGGS (SEQ ID NO:674)
ENLKHQPGGG (SEQ ID NO:675)
NLKHQPGGG (SEQ ID NO:676)
LKHQPGGG (SEQ ID NO:677)
KHQPGGG (SEQ ID NO:678)
HQPGGG (SEQ ID NO:679)
QPGGG (SEQ ID NO:680)
TENLKHQPGG (SEQ ID NO:681)
ENLKHQPGG (SEQ ID NO:682)
NLKHQPGG (SEQ ID NO:683)
LKHQPGG (SEQ ID NO:684)
KHQPGG (SEQ ID NO:685)
HQPGG (SEQ ID NO:686)
QPGG (SEQ ID NO:687)
TENLKHQPG (SEQ ID NO:688)
ENLKHQPG (SEQ ID NO:689)
NLKHQPG (SEQ ID NO:690)
LKHQPG (SEQ ID NO:691)
KHQPG (SEQ ID NO:692)
HQPG (SEQ ID NO:693)
QPG (SEQ ID NO:694)
TENLKHQP (SEQ ID NO:695)
ENLKHQP (SEQ ID NO:696)
NLKHQP (SEQ ID NO:697)

LKHQP (SEQ ID NO:698)
KHQP (SEQ ID NO:699)
HQP (SEQ ID NO:700)
TENLKHQ (SEQ ID NO:701)
ENLKHQ (SEQ ID NO:702)
NLKHQ (SEQ ID NO:703)
LKHQ (SEQ ID NO:704)
KHQ (SEQ ID NO:705)
TENLKH (SEQ ID NO:706)
ENLKH (SEQ ID NO:707)
NLKH (SEQ ID NO:708)
LKH (SEQ ID NO:709)
TENLK (SEQ ID NO:710)
ENLK (SEQ ID NO:711)
NLK (SEQ ID NO:712)
TENL (SEQ ID NO:713)
ENL (SEQ ID NO:714)
TEN (SEQ ID NO:715)
KDNIKHVPGGG (SEQ ID NO:716)
KDNI (SEQ ID NO:717)
KDN (SEQ ID NO:718)
IKHVGGG (SEQ ID NO:719)
IKHVGG (SEQ ID NO:720)
IKHVG (SEQ ID NO:721)
KHVGGG (SEQ ID NO:722)
KHVGG (SEQ ID NO:723)
KHVG (SEQ ID NO:724)
LGNIHHKPGGG (SEQ ID NO:725)
GNIHHKPGGG (SEQ ID NO:726)
NIHHKPGGG (SEQ ID NO:727)
IHHKPGGG (SEQ ID NO:728)
HHKPGGG (SEQ ID NO:729)
KPGGG (SEQ ID NO:730)
LGNIHHKPGG (SEQ ID NO:731)
GNIHHKPGG (SEQ ID NO:732)
NIHHKPGG (SEQ ID NO:733)
IHHKPGG (SEQ ID NO:734)
HHKPGG (SEQ ID NO:735)
KPGG (SEQ ID NO:736)
LGNIHHKPG (SEQ ID NO:737)
GNIHHKPG (SEQ ID NO:738)
NIHHKPG (SEQ ID NO:739)
IHHKPG (SEQ ID NO:740)
HHKPG (SEQ ID NO:741)
HKPG (SEQ ID NO:742)
KPG (SEQ ID NO:743)
LGNIHHKP (SEQ ID NO:744)
GNIHHKP (SEQ ID NO:745)
NIHHKP (SEQ ID NO:746)
IHHKP (SEQ ID NO:747)
HHKP (SEQ ID NO:748)

HKP (SEQ ID NO:749)
LGNIHHK (SEQ ID NO:750)
GNIHHK (SEQ ID NO:751)
NIHHK (SEQ ID NO:752)
IHHK (SEQ ID NO:753)
HHK (SEQ ID NO:754)
LGNIHH (SEQ ID NO:755)
GNIHH (SEQ ID NO:756)
NIHH (SEQ ID NO:757)
IHH (SEQ ID NO:758)
LGNIH (SEQ ID NO:759)
GNIH (SEQ ID NO:760)
NIH (SEQ ID NO:761)
LGNI (SEQ ID NO:762)
GNI (SEQ ID NO:763)
LGN (SEQ ID NO:764)
LDNITHVPGGG (SEQ ID NO:765)
DNITHVPGGG (SEQ ID NO:766)
NITHVPGGG (SEQ ID NO:767)
ITHVPGGG (SEQ ID NO:768)
THVPGGG (SEQ ID NO:769)
LDNITHVPGG (SEQ ID NO:770)
DNITHVPGG (SEQ ID NO:771)
NITHVPGG (SEQ ID NO:772)
ITHVPGG (SEQ ID NO:773)
THVPGG (SEQ ID NO:774)
LDNITHVPG (SEQ ID NO:775)
DNITHVPG (SEQ ID NO:776)
NITHVPG (SEQ ID NO:777)
ITHVPG (SEQ ID NO:778)
THVPG (SEQ ID NO:779)
LDNITHVP (SEQ ID NO:780)
DNITHVP (SEQ ID NO:781)
NITHVP (SEQ ID NO:782)
ITHVP (SEQ ID NO:783)
THVP (SEQ ID NO:784)
LDNITHV (SEQ ID NO:785)
DNITHV (SEQ ID NO:786)
NITHV (SEQ ID NO:787)
ITHV (SEQ ID NO:788)
THV (SEQ ID NO:789)
LDNITH (SEQ ID NO:790)
DNITH (SEQ ID NO:791)
NITH (SEQ ID NO:792)
ITH (SEQ ID NO:793)
LDNIT (SEQ ID NO:794)
DNIT (SEQ ID NO:795)
NIT (SEQ ID NO:796)
LDNI (SEQ ID NO:797)
LDN (SEQ ID NO:798)
KNVKSKIGST (SEQ ID NO:799)

NVKSKIGST (SEQ ID NO:800)
VKSKIGST (SEQ ID NO:801)
KSKIGST (SEQ ID NO:802)
SKIGST (SEQ ID NO:803)
KIGST (SEQ ID NO:804)
IGST (SEQ ID NO:805)
GST (SEQ ID NO:806)
NVKSKIGSTE (SEQ ID NO:807)
VKSKIGSTE (SEQ ID NO:808)
KSKIGSTE (SEQ ID NO:809)
SKIGSTE (SEQ ID NO:810)
KIGSTE (SEQ ID NO:811)
IGSTE (SEQ ID NO:812)
GSTE (SEQ ID NO:813)
STE (SEQ ID NO:814)
VKSKIGSTEN (SEQ ID NO:815)
KSKIGSTEN (SEQ ID NO:816)
SKIGSTEN (SEQ ID NO:817)
KIGSTEN (SEQ ID NO:818)
IGSTEN (SEQ ID NO:819)
GSTEN (SEQ ID NO:820)
STEN (SEQ ID NO:821)
KSKIGSTENL (SEQ ID NO:822)
SKIGSTENL (SEQ ID NO:823)
KIGSTENL (SEQ ID NO:824)
IGSTENL (SEQ ID NO:825)
GSTENL (SEQ ID NO:826)
STENL (SEQ ID NO:827)
SKIGSTENLK (SEQ ID NO:828)
KIGSTENLK (SEQ ID NO:829)
IGSTENLK (SEQ ID NO:830)
GSTENLK (SEQ ID NO:831)
STENLK (SEQ ID NO:832)
KIGSTENLKH (SEQ ID NO:833)
IGSTENLKH (SEQ ID NO:834)
GSTENLKH (SEQ ID NO:835)
STENLKH (SEQ ID NO:836)
IGSTENLKHQ (SEQ ID NO:837)
GSTENLKHQ (SEQ ID NO:838)
STENLKHQ (SEQ ID NO:839)
GSTENLKHQP (SEQ ID NO:840)
STENLKHQP (SEQ ID NO:841)
STENLKHQPG (SEQ ID NO:842)
SNVQSKCGSK (SEQ ID NO:843)
NVQSKCGSK (SEQ ID NO:844)
VQSKCGSK (SEQ ID NO:845)
QSKCGSK (SEQ ID NO:846)
SKCGSK (SEQ ID NO:847)
KCGSK (SEQ ID NO:848)
CGSK (SEQ ID NO:849)
GSK (SEQ ID NO:850)

NVQSKCGSKD (SEQ ID NO:851)
VQSKCGSKD (SEQ ID NO:852)
QSKCGSKD (SEQ ID NO:853)
SKCGSKD (SEQ ID NO:854)
KCGSKD (SEQ ID NO:855)
CGSKD (SEQ ID NO:856)
GSKD (SEQ ID NO:857)
SKD (SEQ ID NO:858)
VQSKCGSKDN (SEQ ID NO:859)
QSKCGSKDN (SEQ ID NO:860)
SKCGSKDN (SEQ ID NO:861)
KCGSKDN (SEQ ID NO:862)
CGSKDN (SEQ ID NO:863)
GSKDN (SEQ ID NO:864)
SKDN (SEQ ID NO:865)
QSKCGSKDNI (SEQ ID NO:866)
SKCGSKDNI (SEQ ID NO:867)
KCGSKDNI (SEQ ID NO:868)
CGSKDNI (SEQ ID NO:869)
GSKDNI (SEQ ID NO:870)
SKDNI (SEQ ID NO:871)

SKVTSKCGSL (SEQ ID NO:872)
KVTSKCGSL (SEQ ID NO:873)
VTSKCGSL (SEQ ID NO:874)
TSKCGSL (SEQ ID NO:875)
SKCGSL (SEQ ID NO:876)
KCGSL (SEQ ID NO:877)
CGSL (SEQ ID NO:878)
GSL (SEQ ID NO:879)
KVTSKCGSLG (SEQ ID NO:880)
VTSKCGSLG (SEQ ID NO:881)
TSKCGSLG (SEQ ID NO:882)
SKCGSLG (SEQ ID NO:883)
KCGSLG (SEQ ID NO:884)
CGSLG (SEQ ID NO:885)
GSLG (SEQ ID NO:886)
SLG (SEQ ID NO:887)
VTSKCGSLGN (SEQ ID NO:888)
TSKCGSLGN (SEQ ID NO:889)
SKCGSLGN (SEQ ID NO:890)
KCGSLGN (SEQ ID NO:891)
CGSLGN (SEQ ID NO:892)
GSLGN (SEQ ID NO:893)
SLGN (SEQ ID NO:894)
TSKCGSLGNI (SEQ ID NO:895)
SKCGSLGNI (SEQ ID NO:896)
KCGSLGNI (SEQ ID NO:897)
CGSLGNI (SEQ ID NO:898)
GSLGNI (SEQ ID NO:899)
SLGNI (SEQ ID NO:900)

SKCGSLGNIH (SEQ ID NO:901)
KCGSLGNIH (SEQ ID NO:902)
CGSLGNIH (SEQ ID NO:903)
GSLGNIH (SEQ ID NO:904)
SLGNIH (SEQ ID NO:905)
KCGSLGNIHH (SEQ ID NO:906)
CGSLGNIHH (SEQ ID NO:907)
GSLGNIHH (SEQ ID NO:908)
SLGNIHH (SEQ ID NO:909)
CGSLGNIHHK (SEQ ID NO:910)
GSLGNIHHK (SEQ ID NO:911)
SLGNIHHK (SEQ ID NO:912)
GSLGNIHHKP (SEQ ID NO:913)
SLGNIHHKP (SEQ ID NO:914)
SLGNIHHKPG (SEQ ID NO:915)
DRVQSKIGSL (SEQ ID NO:916)
RVQSKIGSL (SEQ ID NO:917)
VQSKIGSL (SEQ ID NO:918)
QSKIGSL (SEQ ID NO:919)
SKIGSL (SEQ ID NO:920)
KIGSL (SEQ ID NO:921)
IGSL (SEQ ID NO:922)
RVQSKIGSLD (SEQ ID NO:923)
VQSKIGSLD (SEQ ID NO:924)
QSKIGSLD (SEQ ID NO:925)
SKIGSLD (SEQ ID NO:926)
KIGSLD (SEQ ID NO:927)
IGSLD (SEQ ID NO:928)
GSLD (SEQ ID NO:929)
SLD (SEQ ID NO:930)
VQSKIGSLDN (SEQ ID NO:931)
QSKIGSLDN (SEQ ID NO:932)
SKIGSLDN (SEQ ID NO:933)
KIGSLDN (SEQ ID NO:934)
IGSLDN (SEQ ID NO:935)
GSLDN (SEQ ID NO:936)
SLDN (SEQ ID NO:937)
QSKIGSLDNI (SEQ ID NO:938)
SKIGSLDNI (SEQ ID NO:939)
KIGSLDNI (SEQ ID NO:940)
IGSLDNI (SEQ ID NO:941)
GSLDNI (SEQ ID NO:942)
SKIGSLDNIT (SEQ ID NO:943)
KIGSLDNIT (SEQ ID NO:944)
IGSLDNIT (SEQ ID NO:945)
GSLDNIT (SEQ ID NO:946)
SLDNIT (SEQ ID NO:947)
KIGSLDNITH (SEQ ID NO:948)
IGSLDNITH (SEQ ID NO:949)
GSLDNITH (SEQ ID NO:950)
SLDNITH (SEQ ID NO:951)

IGSLDNITHV (SEQ ID NO:952)
GSLDNITHV (SEQ ID NO:953)
SLDNITHV (SEQ ID NO:954)
GSLDNITHVP (SEQ ID NO:955)
SLDNITHVP (SEQ ID NO:956)
SLDNITHVPG (SEQ ID NO:957)
PDLKNVKS (SEQ ID NO:958)
DLKNVKSK (SEQ ID NO:959)
LKNVKSKI (SEQ ID NO:960)
KNVKSKIG (SEQ ID NO:961)
NVKSKIGS (SEQ ID NO:962)
DLSNVQSK (SEQ ID NO:963)
LSNVQSKC (SEQ ID NO:964)
SNVQSKCG (SEQ ID NO:965)
NVQSKCGS (SEQ ID NO:966)
VDLSKVTS (SEQ ID NO:967)
DLSKVTSK (SEQ ID NO:968)
LSKVTSKC (SEQ ID NO:969)
SKVTSKCG (SEQ ID NO:970)
KVTSKCGS (SEQ ID NO:971)
LDFKDRVQ (SEQ ID NO:972)
DFKDRVQS (SEQ ID NO:973)
FKDRVQSK (SEQ ID NO:974)
KDRVQSKI (SEQ ID NO:975)
DRVQSKIG (SEQ ID NO:976)
RVQSKIGS (SEQ ID NO:977)
SKIGSTENLKH (SEQ ID NO:978)
SKIGSTENIKH (SEQ ID NO:979)
SKIGSKDNLKH (SEQ ID NO:980)
SKIGSKENIKH (SEQ ID NO:981)
SKIGSLENLKH (SEQ ID NO:982)
SKIGSLENIKH (SEQ ID NO:983)
SKIGSTDNLKH (SEQ ID NO:984)
SKIGSTDNIKH (SEQ ID NO:985)
SKIGSKDNIKH (SEQ ID NO:986)
SKIGSLDNLKH (SEQ ID NO:987)
SKIGSLDNIKH (SEQ ID NO:988)
SKIGSTGNLKH (SEQ ID NO:989)
SKIGSTGNIKH (SEQ ID NO:990)
SKIGSKGNLKH (SEQ ID NO:991)
SKIGSKGNIKH (SEQ ID NO:992)
SKIGSLGNLKH (SEQ ID NO:993)
SKIGSLGNIKH (SEQ ID NO:994)

Lys Xaa_1 Xaa_2 Ser Xaa_3 Xaa_4 Asn Xaa_5 Xaa_6 His (SEQ ID NO:995), wherein
Xaa_1 is I or C;
Xaa_2 is G;
Xaa_3 is T, K or L;
Xaa_4 is E, D or G;
Xaa_5 is L or I;

Xaa_6 is K, H or T.

(Q/E)IVYK(S/P) (SEQ ID NO: 996)

DAEFRHDRRQIVYKPV (SEQ ID NO:57)
DAEFRHDRREIVYKSV (SEQ ID NO:58)
DAEFRHDRRQIVYKPVGGC (SEQ ID NO:59)
DAEFRHDRRQIVYKPVC (SEQ ID NO:60)
DAEFRHDRRQIVYKPVAAC (SEQ ID NO:61)
DAEFRHDRRQIVYKPVKKC (SEQ ID NO:62)
DAEFRHDRREIVYKSPGGC (SEQ ID NO:63)
DAEFRHDRREIVYKSPAAC (SEQ ID NO:64)
DAEFRHDRREIVYKSPC (SEQ ID NO:65)
DAEFRHDRREIVYKSPKKC (SEQ ID NO:66)
DAEFRHDSGYEVHHQKLFFAEDVGSNKG (SEQ ID NO:67)
GGGSVQIVYKPVDLS (SEQ ID NO:68)

Arg-Val-Arg-Arg (RVRR; SEQ ID NO:69)
Gly-Ala-Gly-Ala (GAGA; SEQ ID NO:80)
Ala-Gly-Ala-Gly (AGAG; SEQ ID NO:81)
Lys-Gly-Lys-Gly (KGKG; SEQ ID NO:82)

DAEFRHDRRQIVYKPVXXC (SEQ ID NO:70)
If present, XX can be GG or AA or KK or SS.

DAEFRHDRREIVYKSVXXC (SEQ ID NO:79)
If present, XX can be GG or AA or KK or SS.

DAEFRHDC (SEQ ID NO:71)
QIVYKPVGGC (SEQ ID NO:72)
GGSQIVYKPVDLS (SEQ ID NO:73)
DAEFRHDRREIVYKSVGGC (SEQ ID NO:74)
DAEFRHDRREIVYKSVAAC (SEQ ID NO:75)
DAEFRHDRREIVYKSVC (SEQ ID NO:76)
DAEFRHDRREIVYKSVKKC (SEQ ID NO:77)
DAEFRHDRRNIKHVPGGC (SEQ ID NO:78)
DAEFRHDRRVKSKIGSTGGC (SEQ ID NO:997)
DAEFRHDRRSKIGSTENGGC (SEQ ID NO:998)
DAEFRHDRRTENLKHQPGGC (SEQ ID NO:999)
DAEFRHDRRENLKHQPGGGC (SEQ ID NO:1000)
DAEFRHDRRSKIGSKDNIKHGGC (SEQ ID NO:1001)

MTBR peptide 1 QTAPVPMPDLKNVKSKIGSTENLKHQPGGGK
(SEQ ID NO:1058)

MTBR peptide 2 VQIINKKLDLSNVQSKCGSKDNIKHVPGGGS
(SEQ ID NO:1059)

MTBR peptide 3 VQIVYKPVDLSKVTSKCGSLGNIHHKPGGGQ
(SEQ ID NO:1060)

MTBR peptide 4 VEVKSEKLDFKDRVQSKIGSLDNITHVPGGGN (SEQ ID NO:1061)

GGGS (SEQ ID NO:1062)
GGGGS (SEQ ID NO:1063)

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).

13. The polypeptide of any of claims 1 to 11, wherein the first peptide is DAEFR (SEQ ID NO:08).

14. The polypeptide of any of claims 1 to 11, wherein the first peptide is EFRHD (SEQ ID NO:21).

15. The polypeptide of any of claims 1 to 11, wherein the second peptide comprises 5-10 amino acids.

16. The polypeptide of any of claims 1 to 11, wherein the second peptide comprises the amino acid sequence QIVYKPV (SEQ ID NO:39).

17. The polypeptide of any of claims 1 to 11, wherein the second peptide comprises the amino acid sequence EIVYKSP (SEQ ID NO:43).

18. The polypeptide of any of claims 1 to 11, wherein the second peptide comprises the amino acid sequence NIKHVP (SEQ ID NO:48).

19. The polypeptide of any of claims 1 to 11, wherein the second peptide comprises the amino acid sequence VKSKIGST (SEQ ID NO:801).

20. The polypeptide of any of claims 1 to 11, wherein the second peptide comprises the amino acid sequence SKIGSTEN (SEQ ID NO:817).

21. The polypeptide of any of claims 1 to 11, wherein the second peptide comprises the amino acid sequence TENLKHQP (SEQ ID NO:803).

22. The polypeptide of any of claims 1 to 11, wherein the second peptide comprises the amino acid sequence ENLKHQPG (SEQ ID NO:689).

23. The polypeptide of any of claims 1 to 11, wherein the second peptide comprises the amino acid sequence SKIGSTDNIKH (SEQ ID NO:985).

24. The polypeptide of any of claims 1 to 11, wherein the second peptide comprises the amino acid sequence SKIGSKDNIKH (SEQ ID NO:986).

25. The polypeptide of any of claims 1 to 11, wherein the second peptide comprises the amino acid sequence SKIGSLDNIKH (SEQ ID NO:988).

26. The polypeptide of claim 1, comprising an amino acid sequence of DAEFRHDRRQIVYKPV (SEQ ID NO:57).

27. The polypeptide of claim 1, comprising an amino acid sequence of DAEFRHDRREIVYKSV (SEQ ID NO:58).

28. The polypeptide of claim 1, comprising an amino acid sequence of DAEFRHDRRQIVYKPVGGC (SEQ ID NO:59).

29. The polypeptide of claim 1, comprising an amino acid sequence of DAEFRHDRRQIVYKPVC (SEQ ID NO:60).

30. The polypeptide of claim 1, comprising an amino acid sequence of DAEFRHDRRQIVYKPVAAC (SEQ ID NO:61).

31. The polypeptide of claim 1, comprising an amino acid sequence of DAEFRHDRRQIVYKPVKKC (SEQ ID NO:62).

32. The polypeptide of claim 1, comprising an amino acid sequence of DAEFRHDRREIVYKSPGGC (SEQ ID NO:63).

33. The polypeptide of claim 1, comprising an amino acid sequence of DAEFRHDRREIVYKSPAAC (SEQ ID NO:64).

34. The polypeptide of claim 1, comprising an amino acid sequence of DAEFRHDRREIVYKSPC (SEQ ID NO:65).

35. The polypeptide of claim 1, comprising an amino acid sequence of DAEFRHDRREIVYKSPKKC (SEQ ID NO:66).

36. The polypeptide of claim 1, comprising an amino acid sequence of DAEFRHDRRNIKHVPGGC (SEQ ID NO:78).

37. The polypeptide of claim 1, comprising an amino acid sequence of DAEFRHDRRVKSKIGSTGGC (SEQ ID NO:997).

38. The polypeptide of claim 1, comprising an amino acid sequence of DAEFRHDRRSKIGSTENGGC (SEQ ID NO:998).

39. The polypeptide of claim 1, comprising an amino acid sequence of DAEFRHDRRTENLKHQPGGC (SEQ ID NO:999).

40. The polypeptide of claim 1, comprising an amino acid sequence of DAEFRHDRRENLKHQPGGGC (SEQ ID NO:1000).

41. The polypeptide of claim 1, comprising an amino acid sequence of DAEFRHDRRSKIGSKDNIKHGGC (SEQ ID NO:1001).

42. The polypeptide of claim 1, comprising the amino acid sequence of DAEFRHDRRQIVYKPVXXC (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).

43. An immunotherapy composition, comprising the polypeptide of any of claims 1 to 42, wherein the polypeptide is linked to a carrier.

44. The immunotherapy composition of claim 22, 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.

45. The immunotherapy composition of claim 23, wherein the carrier is CRM197.

46. The immunotherapy composition of claim 23, wherein the carrier is diphtheria toxoid.

47. A pharmaceutical formulation comprising (a) the polypeptide of any one of claims 1 to 42 or the immunotherapy composition of any of claims 43 to 46 and (b) at least one adjuvant.

48. The pharmaceutical formulation of claim 47, 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.

49. The pharmaceutical formulation of claim 48, wherein the adjuvant is QS-21 or TQL1055.

50. The pharmaceutical formulation of claim 48, wherein the adjuvant is MPL.

51. The pharmaceutical formulation of claim 48, wherein the adjuvant is a combination of MPL and QS-21 or a combination of MPL and TQL1055.

52. The pharmaceutical formulation of any of claims 47 to 51, wherein the adjuvant comprises a liposomal formulation.

53. The pharmaceutical formulation of any of claims 47 to 52, wherein the composition comprises at least one pharmaceutically acceptable diluent.

54. The pharmaceutical formulation of any of claims 47 to 53, comprising a multiple antigen presenting system (MAP).

55. The pharmaceutical formulation of claim 54, 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.

56. 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.

57. The immunotherapy composition of claim 56, 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.

58. The immunotherapy composition of any one of claims 56 to 57, 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.

59. The immunotherapy composition of claim 58, 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).

60. The immunotherapy composition of claim 59, wherein the linker to the carrier may optionally comprise a C-terminal cysteine (C).

61. The immunotherapy composition of any one of claims 59 to 60, 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.

62. The immunotherapy composition of claim 61, wherein the carrier is CRM197.

63. The immunotherapy composition of claim 61, wherein the carrier is diphtheria toxoid.

64. The immunotherapy composition of any one of claims 56 to 63, further comprising at least one pharmaceutically acceptable diluent.

65. The immunotherapy composition of any one of claims 56 to 64, further comprising a multiple antigen presenting system (MAP).

66. The immunotherapy composition of claim 65, 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.

67. A pharmaceutical composition comprising the immunotherapy composition of any of claims 56 to 66 and at least one adjuvant.

68. The pharmaceutical composition of claim 67, 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.

69. The pharmaceutical composition of claim 68, wherein the adjuvant is QS-21 or TQL1055.

70. The pharmaceutical composition of claim 68, wherein the adjuvant is MPL.

71. The pharmaceutical composition of claim 68, wherein the adjuvant is a combination of MPL and QS-21 or a combination of MPL and TQL1055.

72. A nucleic acid comprising a nucleic acid sequence encoding a polypeptide of any one of claims 1 to 42 of the immunotherapy composition of claims 56 to 60.

73. A nucleic acid immunotherapy composition comprising the nucleic acid of claim 72 and at least one adjuvant.

74. A method of treating or effecting prophylaxis of Alzheimer's disease in a subject, comprising administrating to the subject the immunotherapy composition of any of claims 43 to 46 and 56 to 66 or the pharmaceutical formulations of any of claims 47 to 55 and 67 to 71.

75. A method of inhibiting or reducing aggregation of at least one of Aβ and tau in a subject having or at risk of developing Alzheimer's disease, comprising, administering to the subject the immunotherapy composition of any of claims 43 to 46 and 56 to 66 or the pharmaceutical formulations of any of claims 47 to 55 and 67 to 71.

76. A method of treating or effecting prophylaxis of Alzheimer's disease in a subject, comprising administrating to the subject the nucleic acid immunotherapy composition of claim 73.

77. A method of inhibiting or reducing aggregation of at least one of Aβ and tau in a subject having or at risk of developing Alzheimer's disease, comprising administering to the subject the nucleic acid immunotherapy composition of claim 73.

78. The method of any of claims 74 to 77, further comprising repeating the administering at least a second time, at least a third time, at least a fourth time, at least a fifth time, or at least a sixth time.

79. The method of claim 78, further comprising repeating the administering at an interval of about 21 to about 28 days.

80. A method of inducing an immune response in an animal, comprising administering to the animal any one of the polypeptide of claims 1 to 42, the immunotherapy composition of claims 43 to 46 and 56 to 66, the pharmaceutical formulations of claims 47 to 55 and 67 to 71 or the nucleic acid immunotherapy composition of claim 73 in a regimen effective to generate an immune response comprising antibodies that specifically bind to Aβ, tau, or both Aβ and tau.

81. The method of claim 80, wherein the immune response comprises antibodies that specifically bind to Aβ and antibodies that specifically bind to tau.

82. The method of any of claims 80 to 81, wherein the inducing the immune response comprises antibodies that specifically bind to the N-terminal region of Aβ and/or the microtubule region of tau.

83. An immunization kit comprising the immunotherapy composition of any of claims 43 to 46 and 56 to 66.

84. The kit of claim 83, further comprising an adjuvant.

85. The kit of claim 84, wherein the immunotherapy composition is in a first container and the adjuvant is in a second container.

86. A kit comprising the nucleic acid immunotherapy composition of claim 73.

87. The kit of claim 86, further comprising an adjuvant.

88. The kit of claim 87, wherein the nucleic acid is in a first container and the adjuvant is in a second container.

FIG. 1

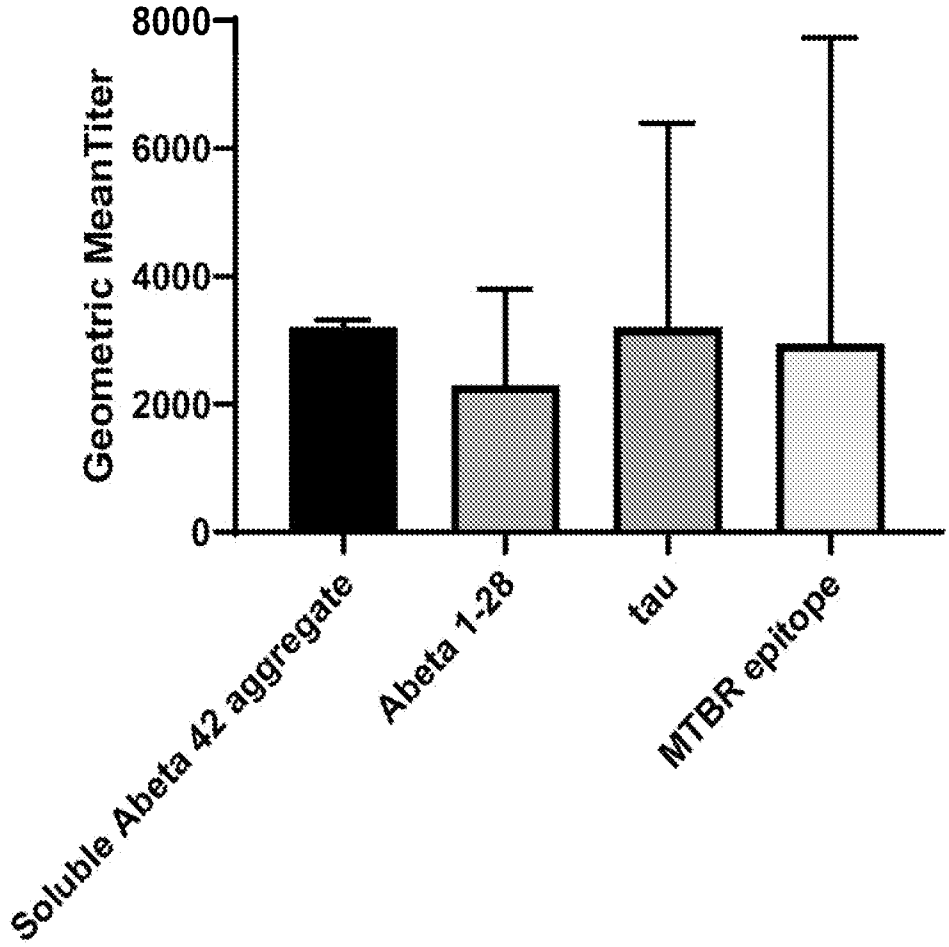

8000
6000
4000
2000
0
Geometric MeanTiter
Soluble Abeta 42 aggregate
Abeta 1-28
tau
MTBR epitope

FIG. 2A

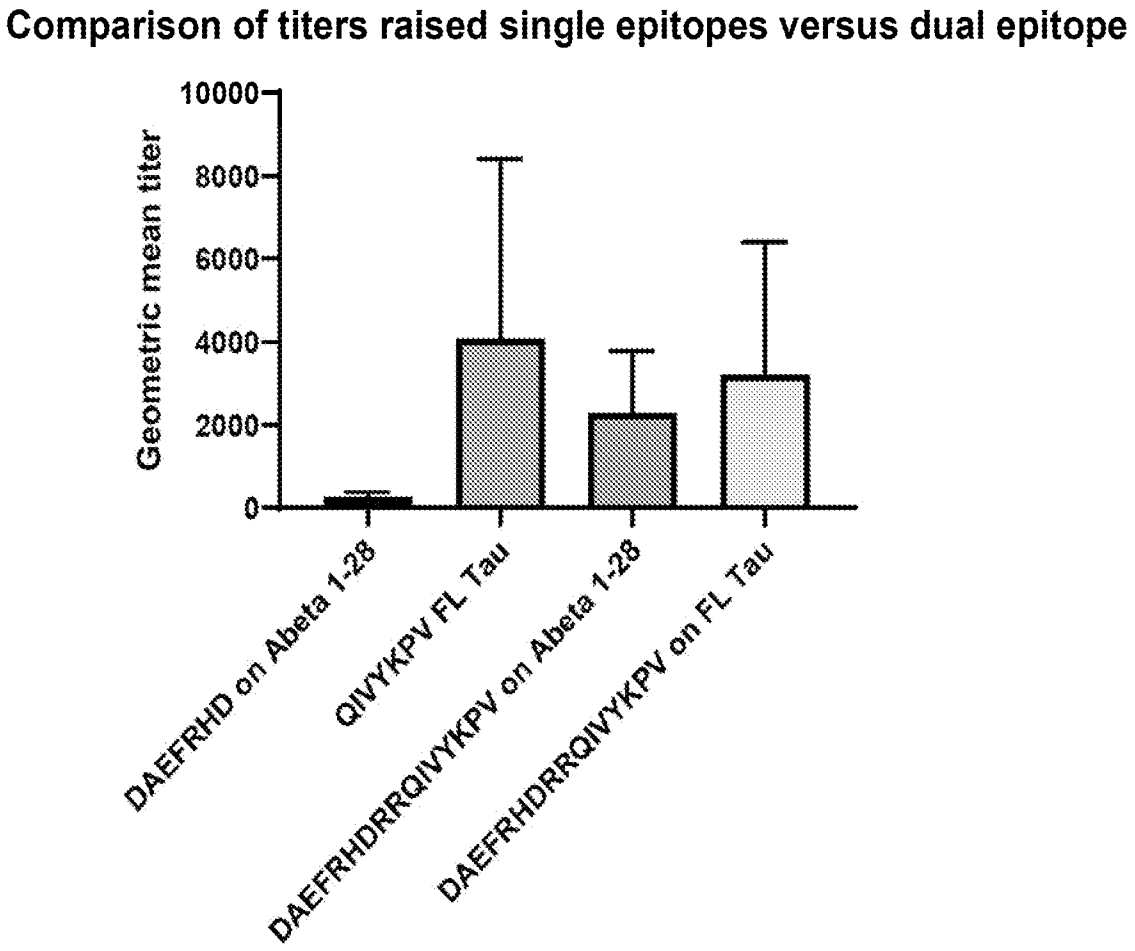

Comparison of titers raised single epitopes versus dual epitope
Geometric mean titer
10000
8000
6000
4000
2000
0
DAEFRHD on Abeta 1-28
QIVYKPV FL Tau
DAEFRHDRRQIVYKPV on Abeta 1-28
DAEFRHDRRQIVYKPV on FL Tau

FIG. 2B

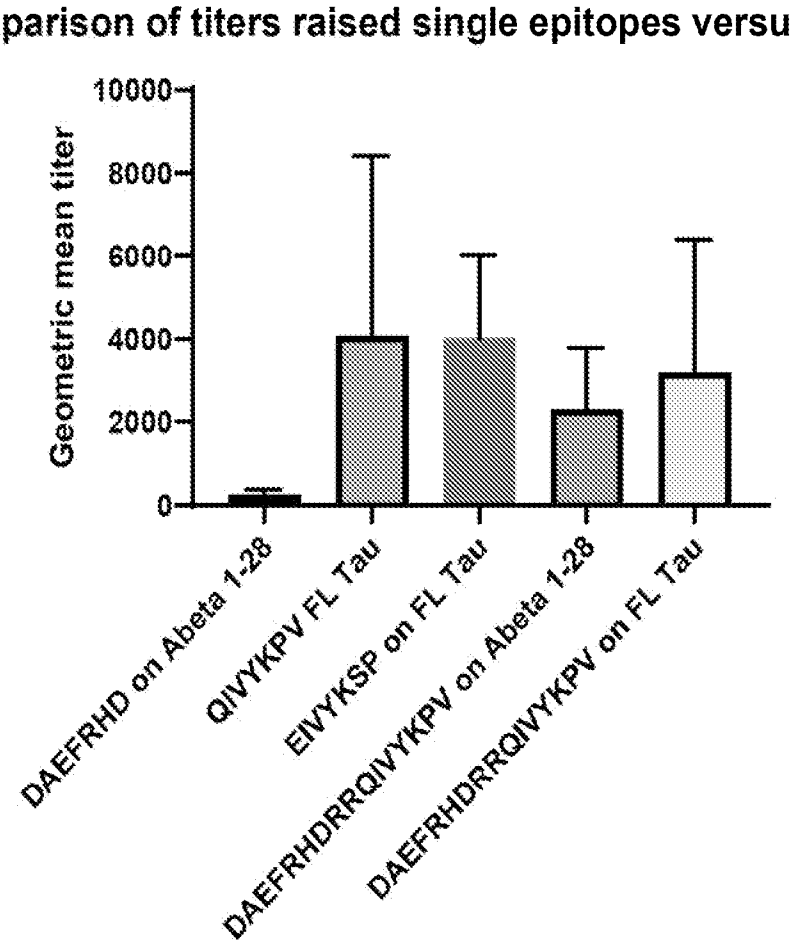
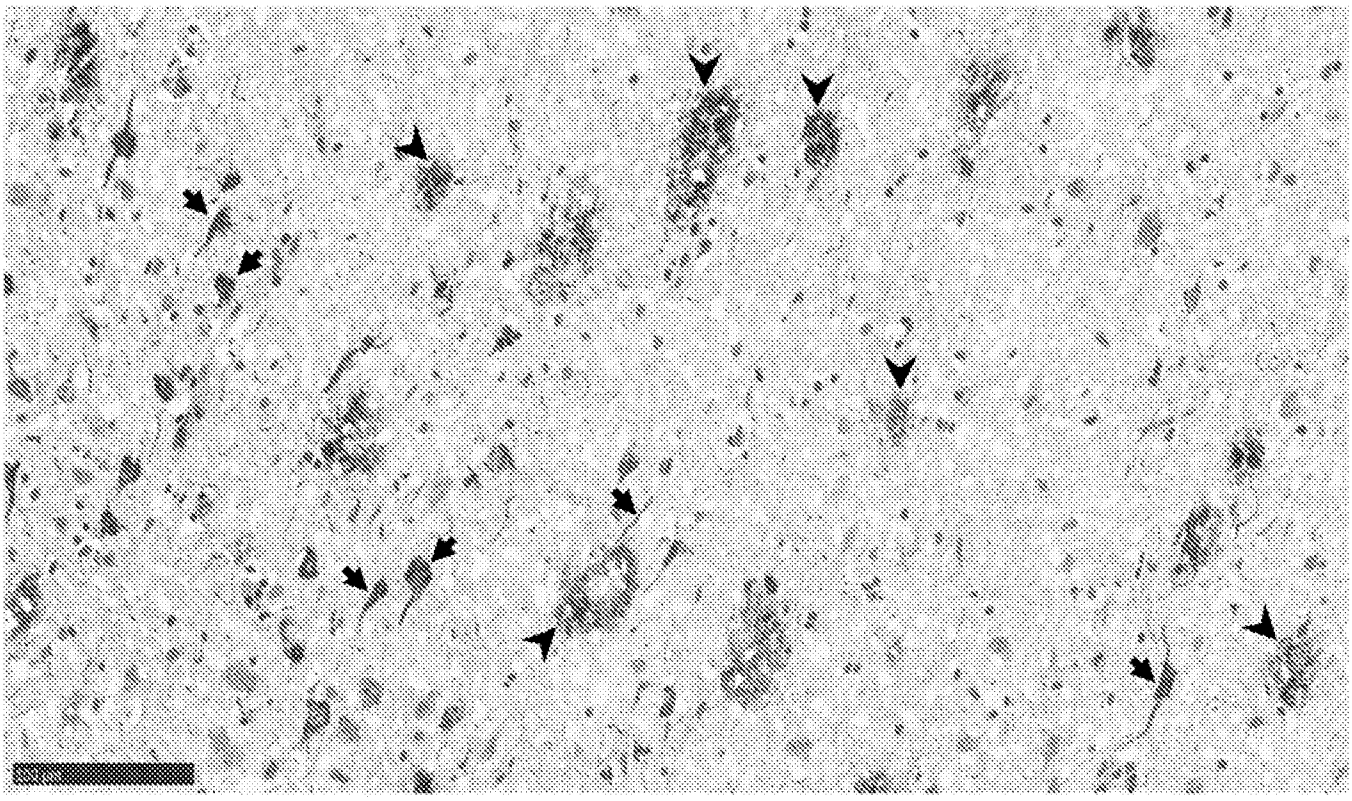

Comparison of titers raised single epitopes versus dual epitope
Geometric mean titer
10000
8000
6000
4000
2000
0
DAEFRHD on Abeta 1-28
QIVYKPV FL Tau
EIVYKSP on FL Tau
DAEFRHDRRQIVYKPV on Abeta 1-28
DAEFRHDRRQIVYKPV on FL Tau

FIG. 3A

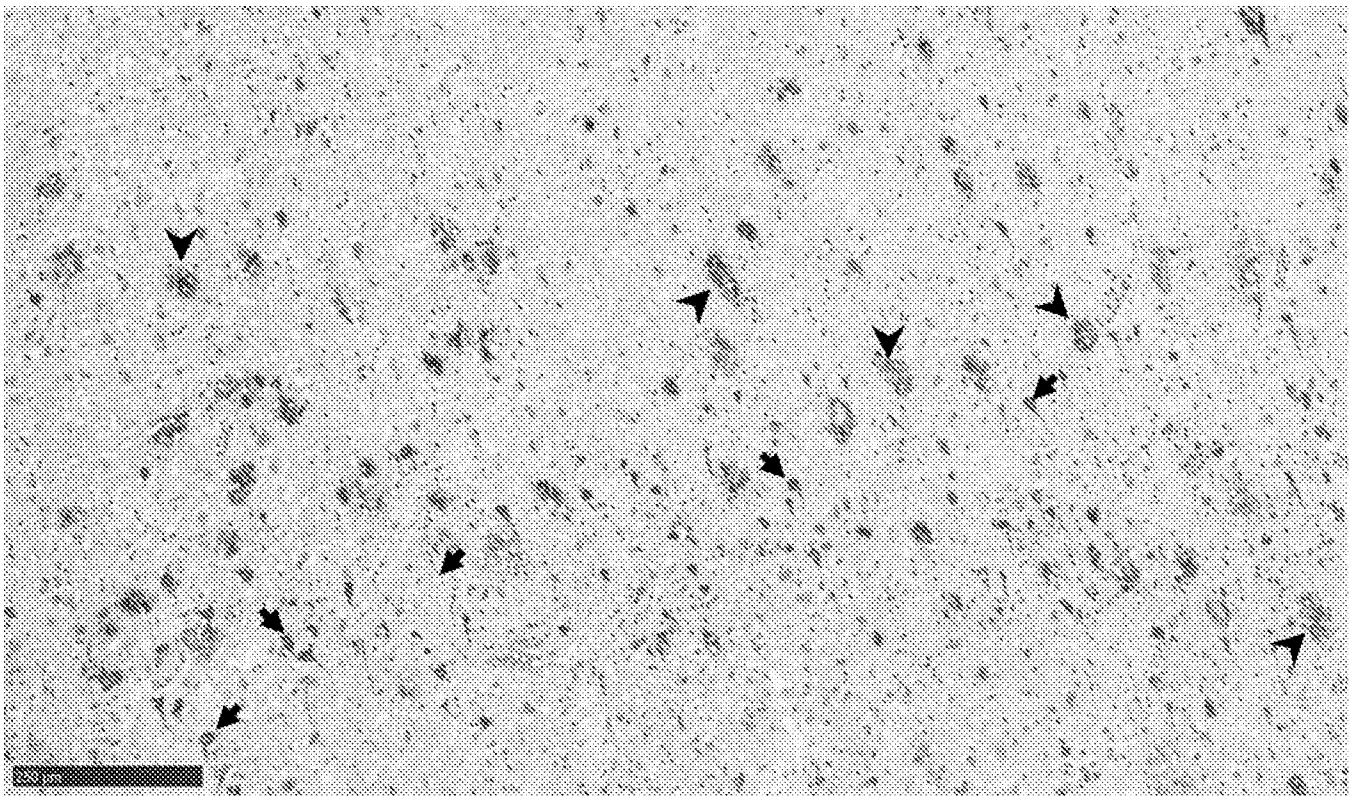
Brain AD 04-33 - Vaccine Serum 2 – Dilution 1-300



Arrows: tau pathology
Arrowheads: A-beta pathology
Vaccine Serum 2: serum from vaccinated Guinea pig number 2
Immunogen 9 DAEFRHDRRQIVYKPVGGC

FIG. 3B

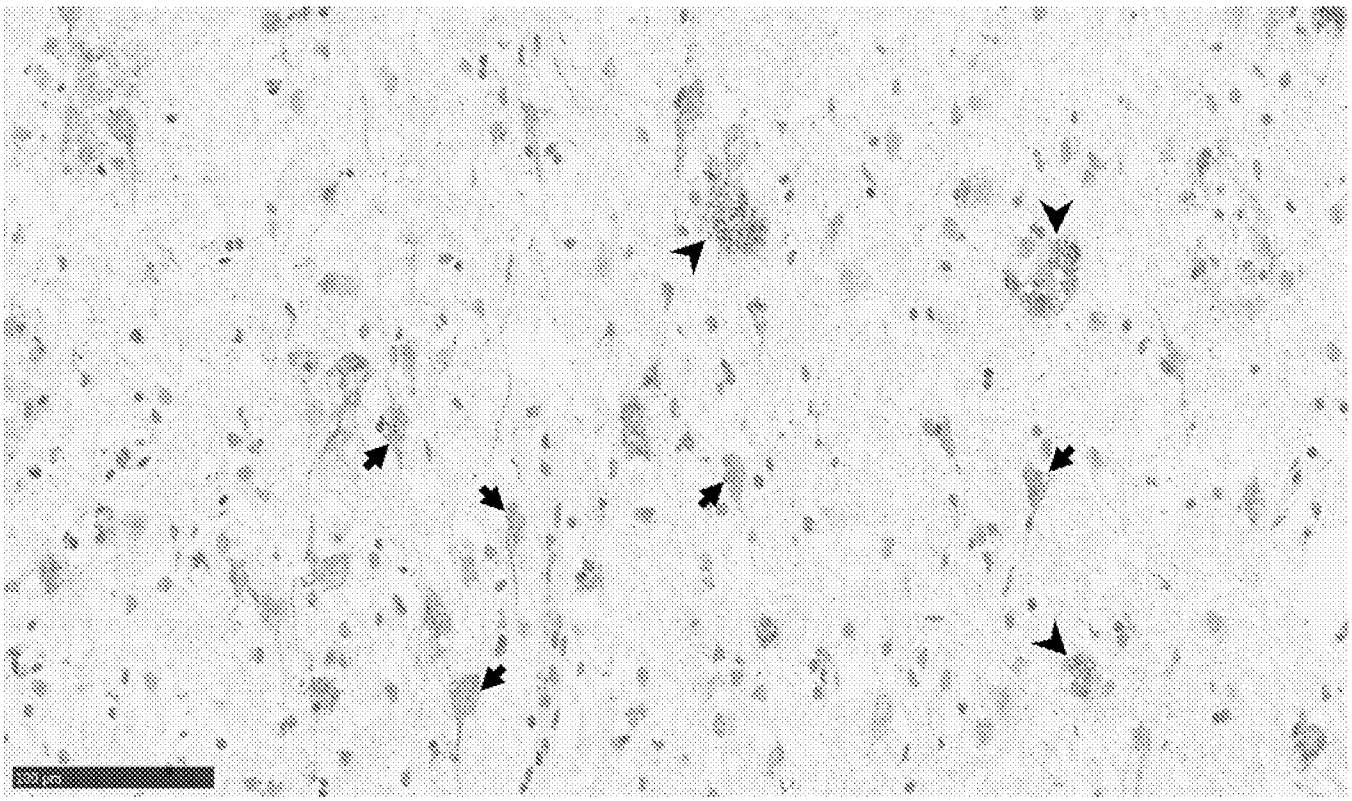
Brain AD 04-33 - Vaccine Serum 2 – Dilution 1-300



Arrows: tau pathology
Arrowheads: A-beta pathology
Vaccine Serum 2: serum from vaccinated Guinea pig number 2
Immunogen 9 DAEFRHDRRQIVYKPVGGC

FIG. 3C

Brain AD 04-33 - Vaccine Serum 2 – Dilution 1-1500



Arrows: tau pathology
Arrowheads: A-beta pathology
Vaccine Serum 2: serum from vaccinated Guinea pig number 2

FIG. 3D

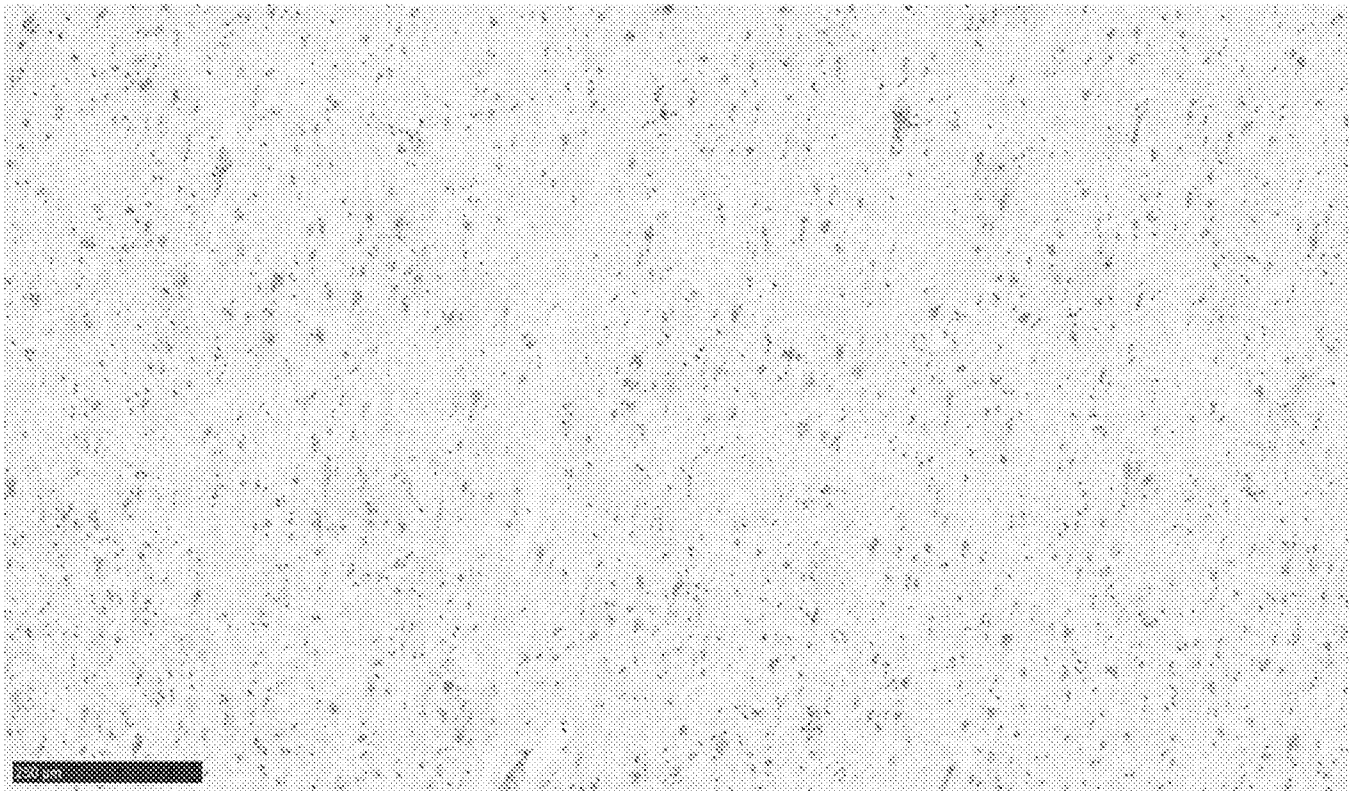


FIG. 3E

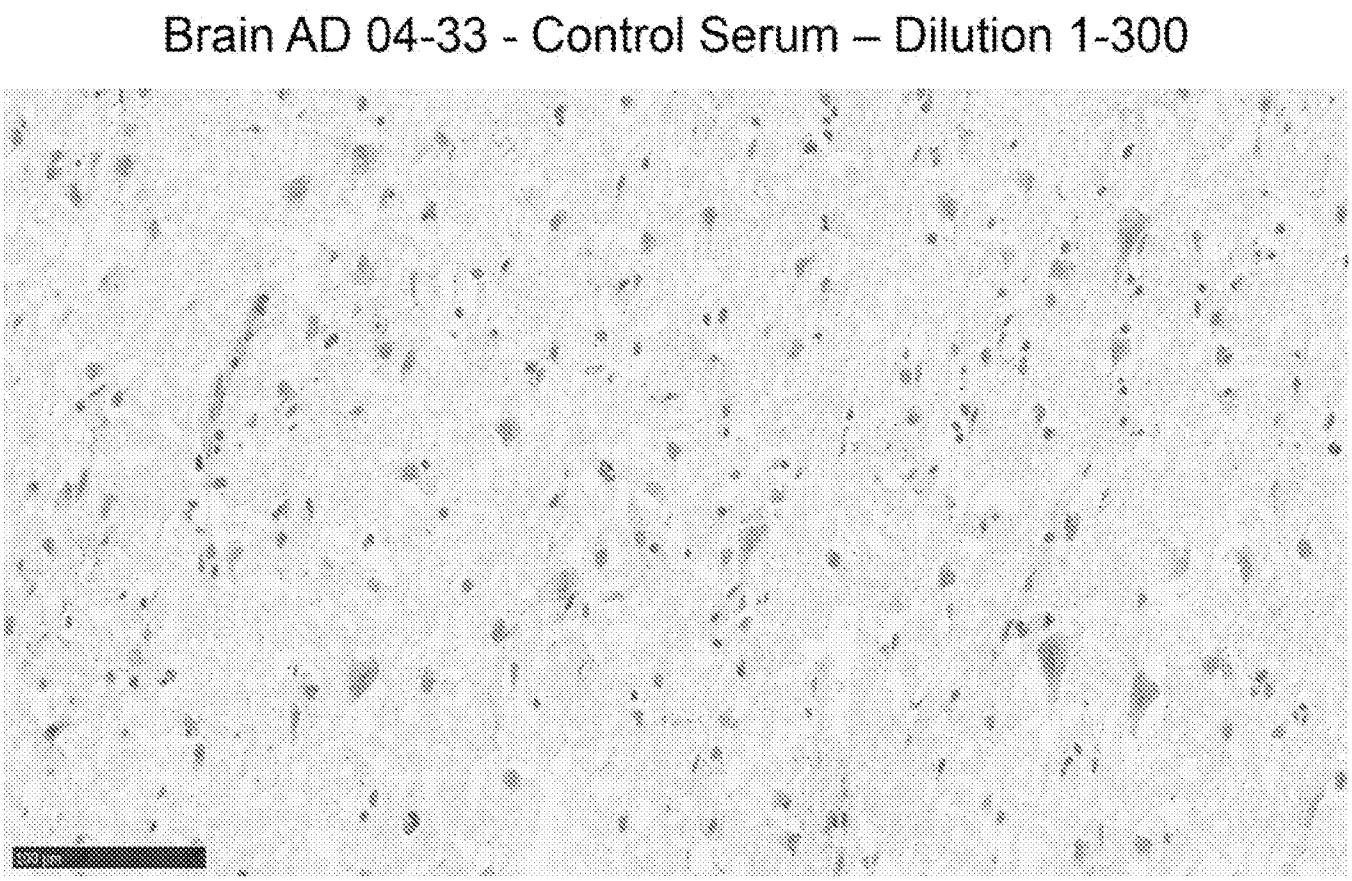


FIG. 3F

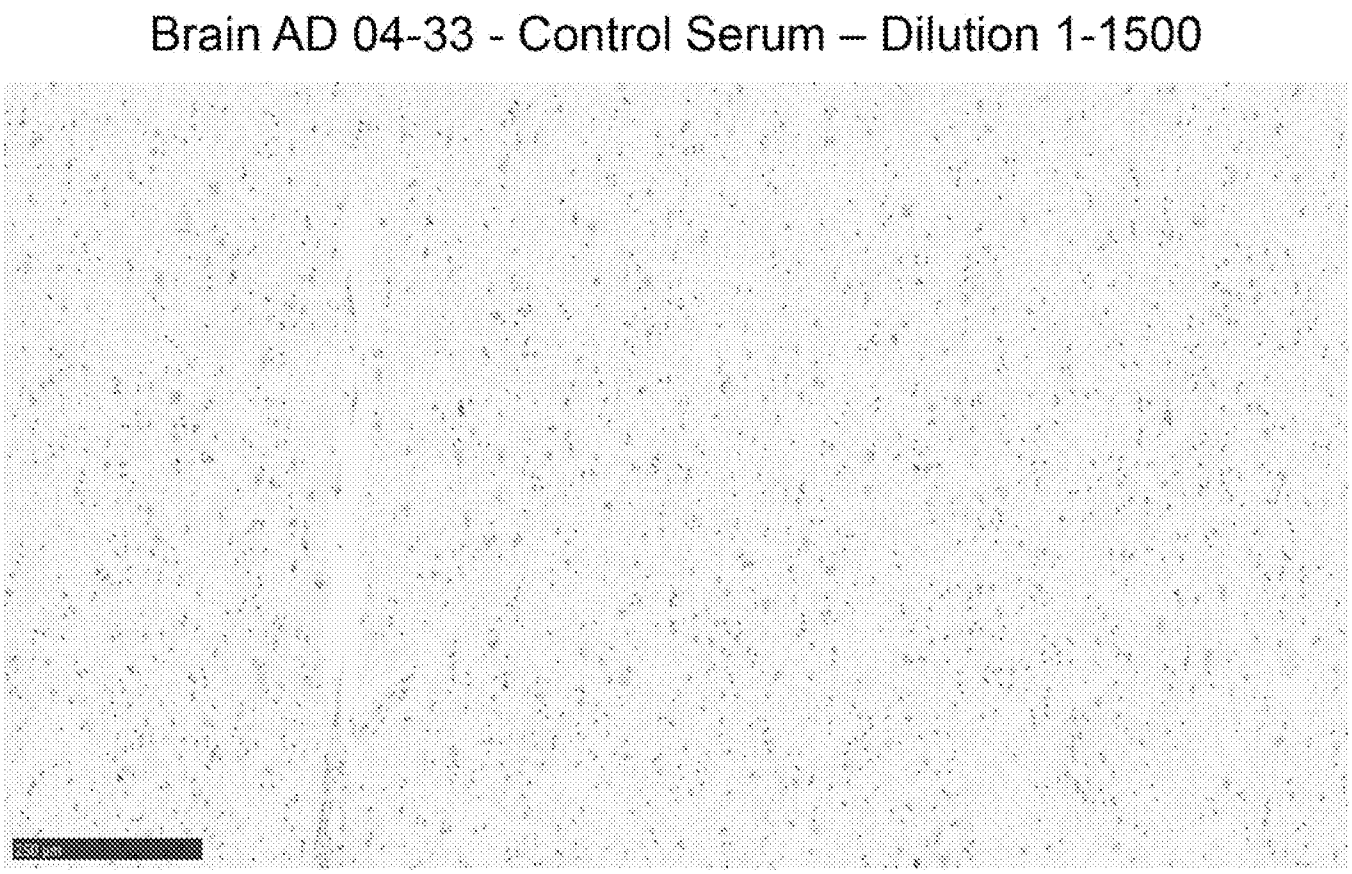


FIG. 4A

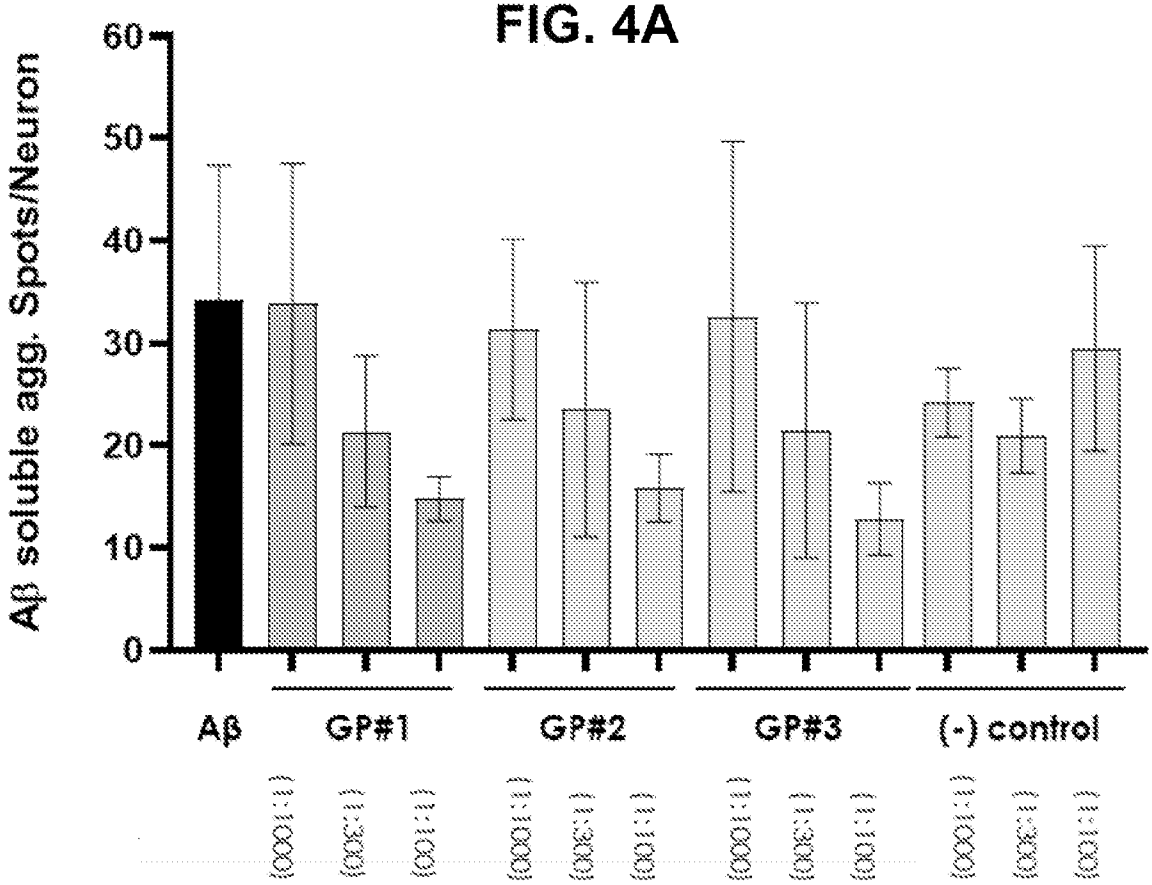

Aβ soluble agg. Spots/Neuron
60
50
40
30
20
10
0
Aβ
GP#1
GP#2
GP#3
(-) control
(1:1000)
(1:300)
(1:100)
(1:1000)
(1:300)
(1:100)
(1:1000)
(1:300)
(1:100)
(1:1000)
(1:300)
(1:100)

FIG. 4B

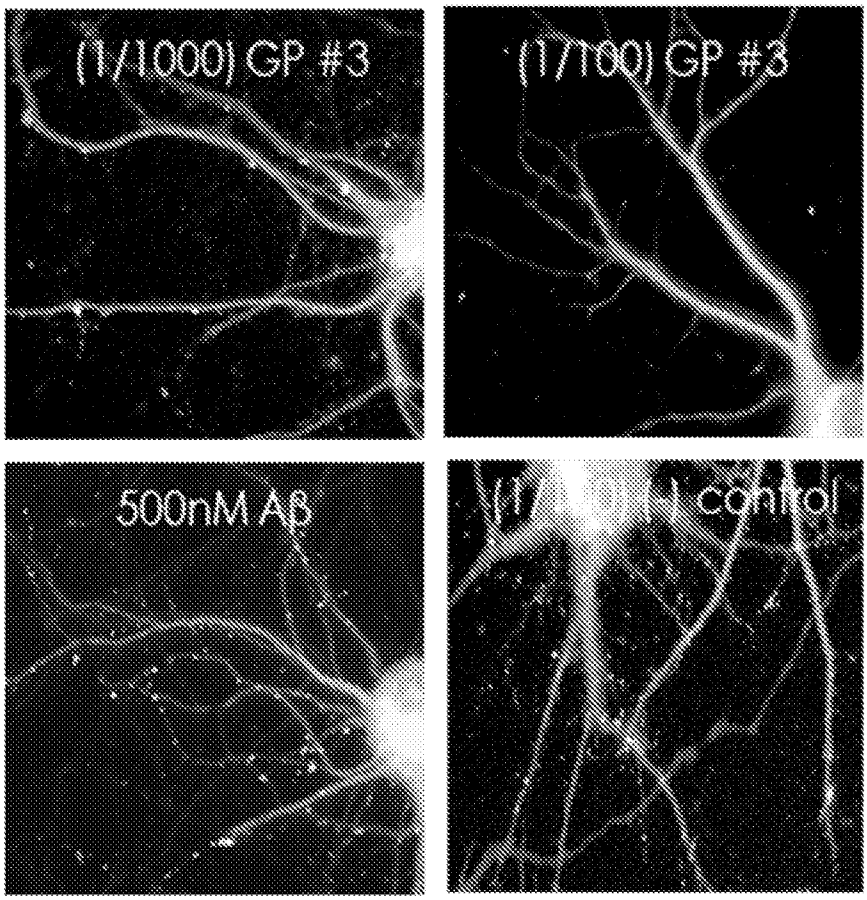

(1/1000) GP #3
(1/100) GP #3
500nM Aβ

FIG. 5A

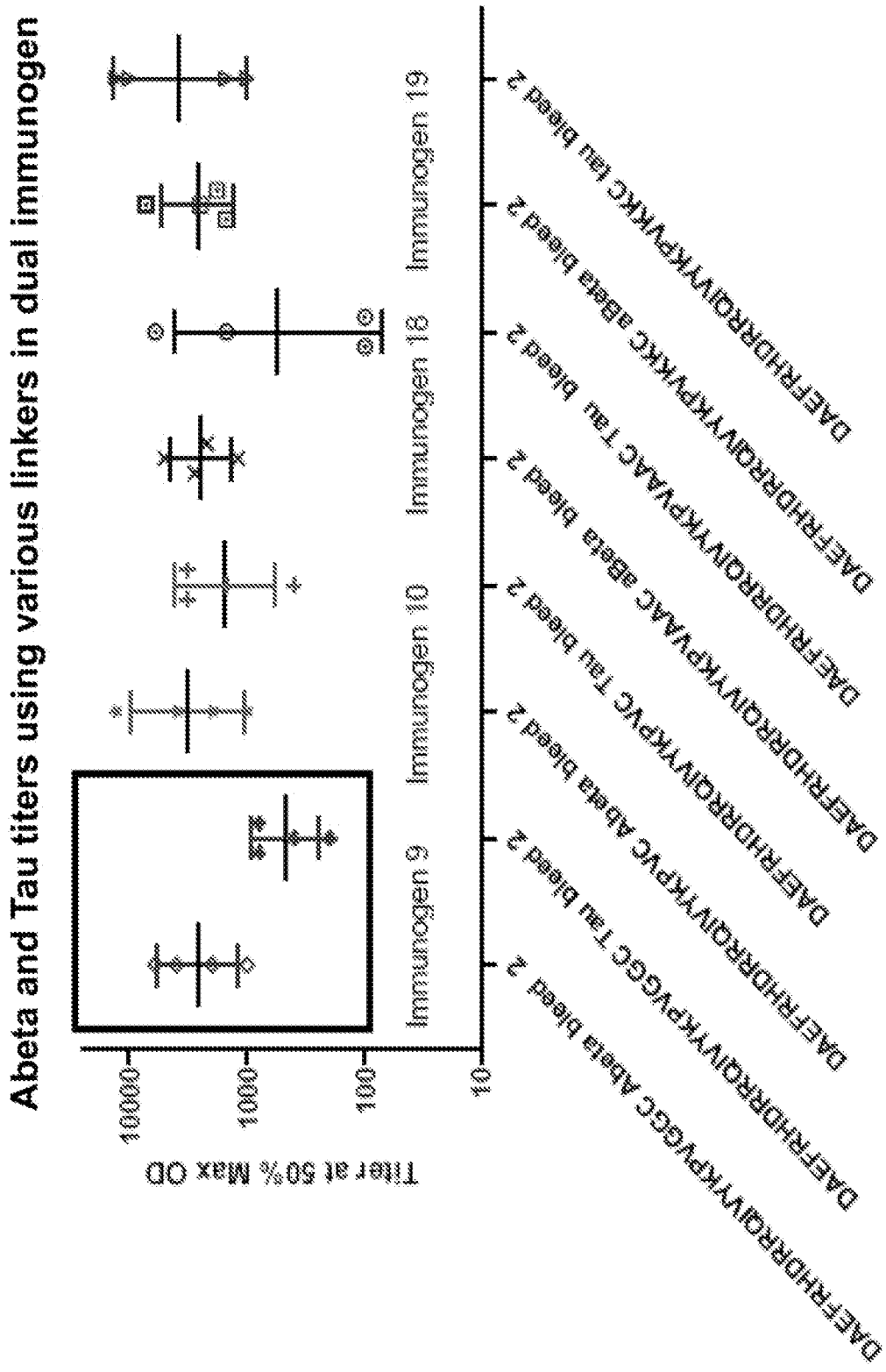

Abeta and Tau titers using various linkers in dual immunogen
Titer at 50% Max OD
10000
1000
100
10
Immunogen 9
Immunogen 10
Immunogen 18
Immunogen 19
DAEFRHDRRQIVKPVGGC Abeta bleed 2
DAEFRHDRRQIVKPVGGC Tau bleed 2
DAEFRHDRRQIVKPVKC Abeta bleed 2
DAEFRHDRRQIVKPVKC Tau bleed 2
DAEFRHDRRQIVKPVAAC Abeta bleed 2
DAEFRHDRRQIVKPVAAC Tau bleed 2
DAEFRHDRRQIVKPVKKC abeta bleed 2
DAEFRHDRRQIVKPVKKC tau bleed 2

FIG. 5B

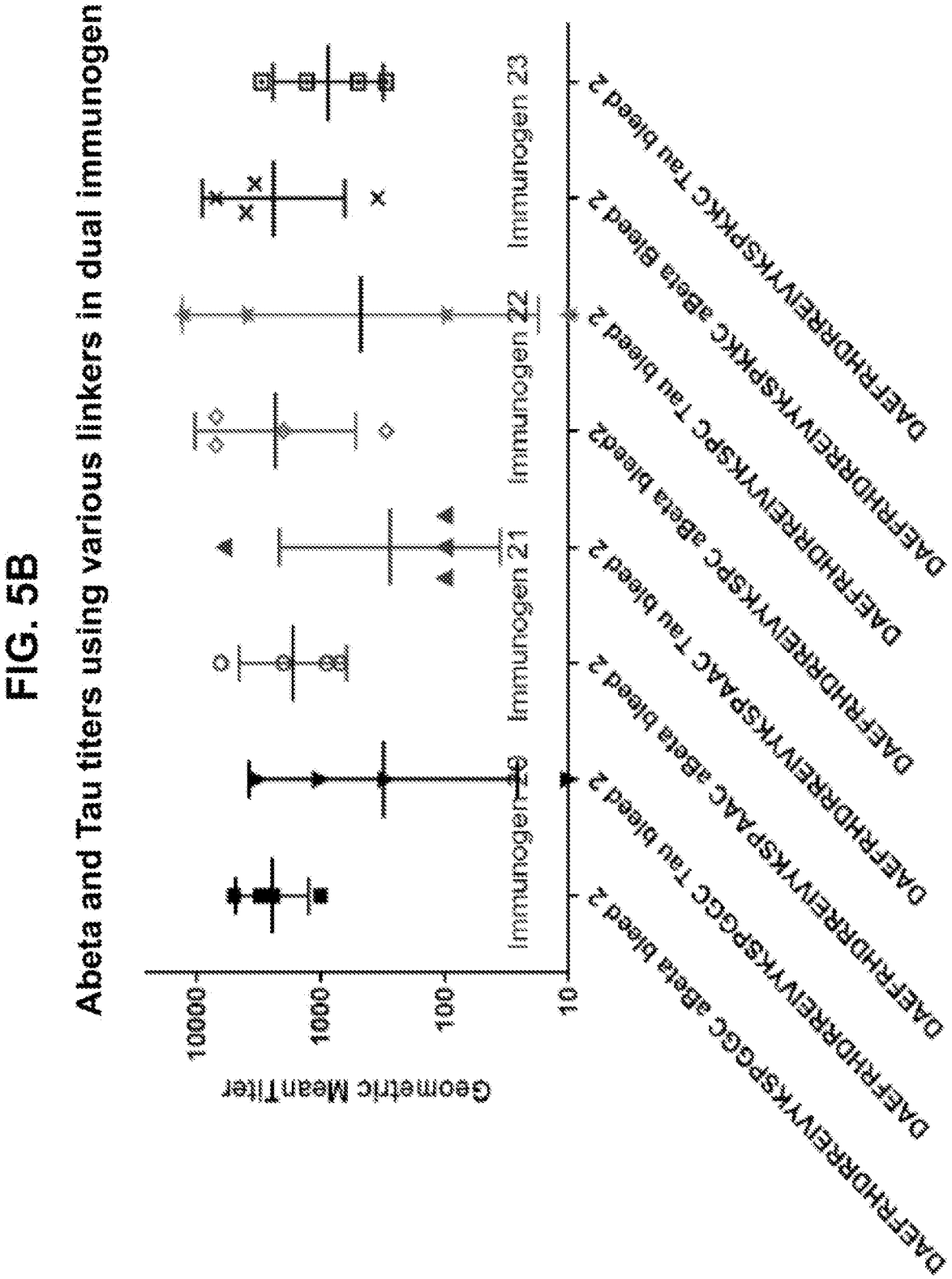

Abeta and Tau titers using various linkers in dual immunogen
Geometric Mean Titer
10000
1000
100
10
Immunogen 20
Immunogen 21
Immunogen 22
Immunogen 23
DAEFRHDREEIVKSPGGC abeta bleed 2
DAEFRHDREEIVKSPAAC Tau bleed 2
DAEFRHDREEIVKSPAAC abeta bleed 2
DAEFRHDREEIVKSPC abeta bleed2
DAEFRHDREEIVKSPC Tau bleed 2
DAEFRHDREEIVKSPKKC abeta Bleed 2
DAEFRHDREEIVKSPKKC Tau bleed 2

FIG. 6A

Immunogen 19 Mouse 1 – 1:1000 dilution

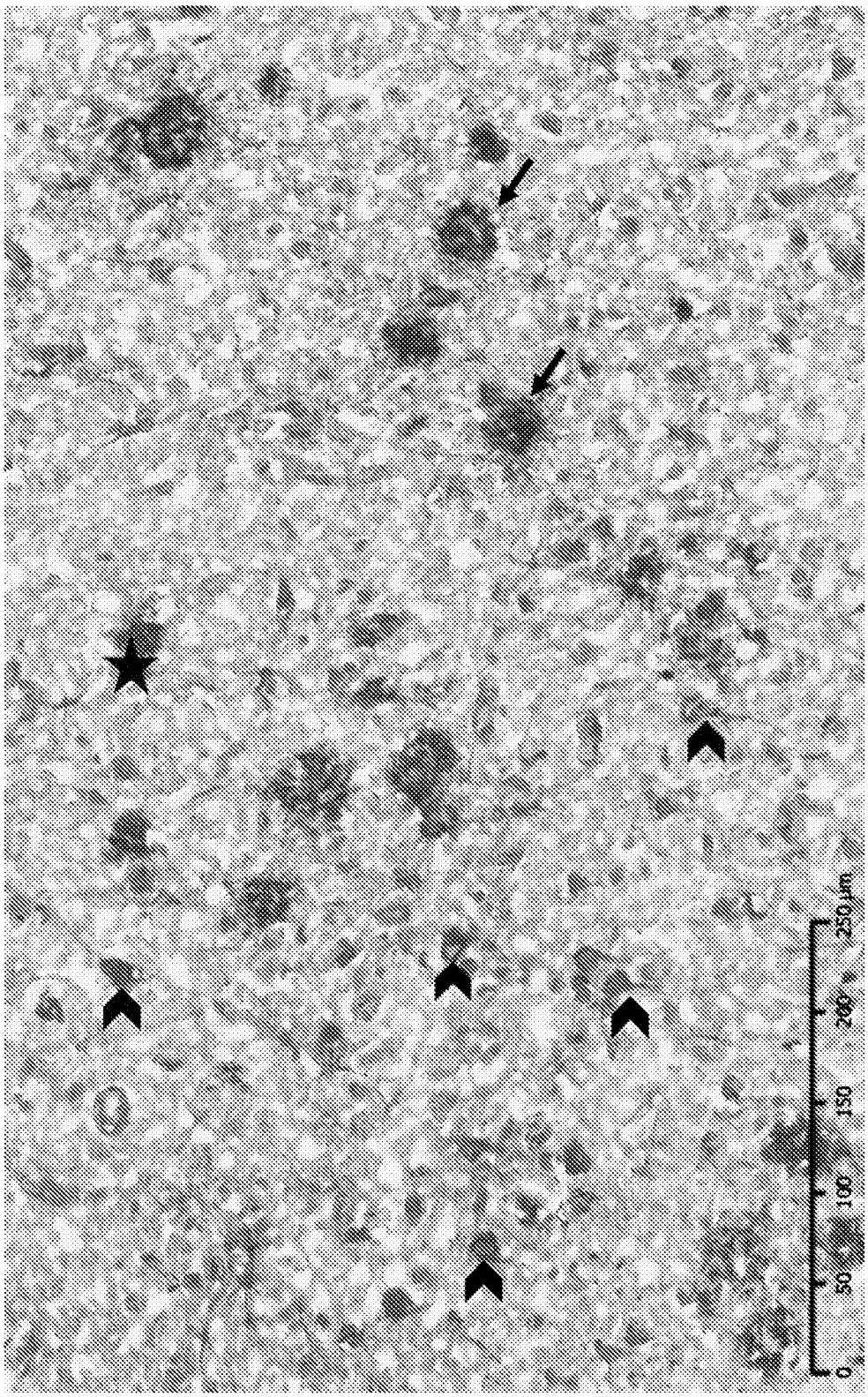


FIG. 6B

Immunogen 19 Mouse 3 – 1:1000 dilution

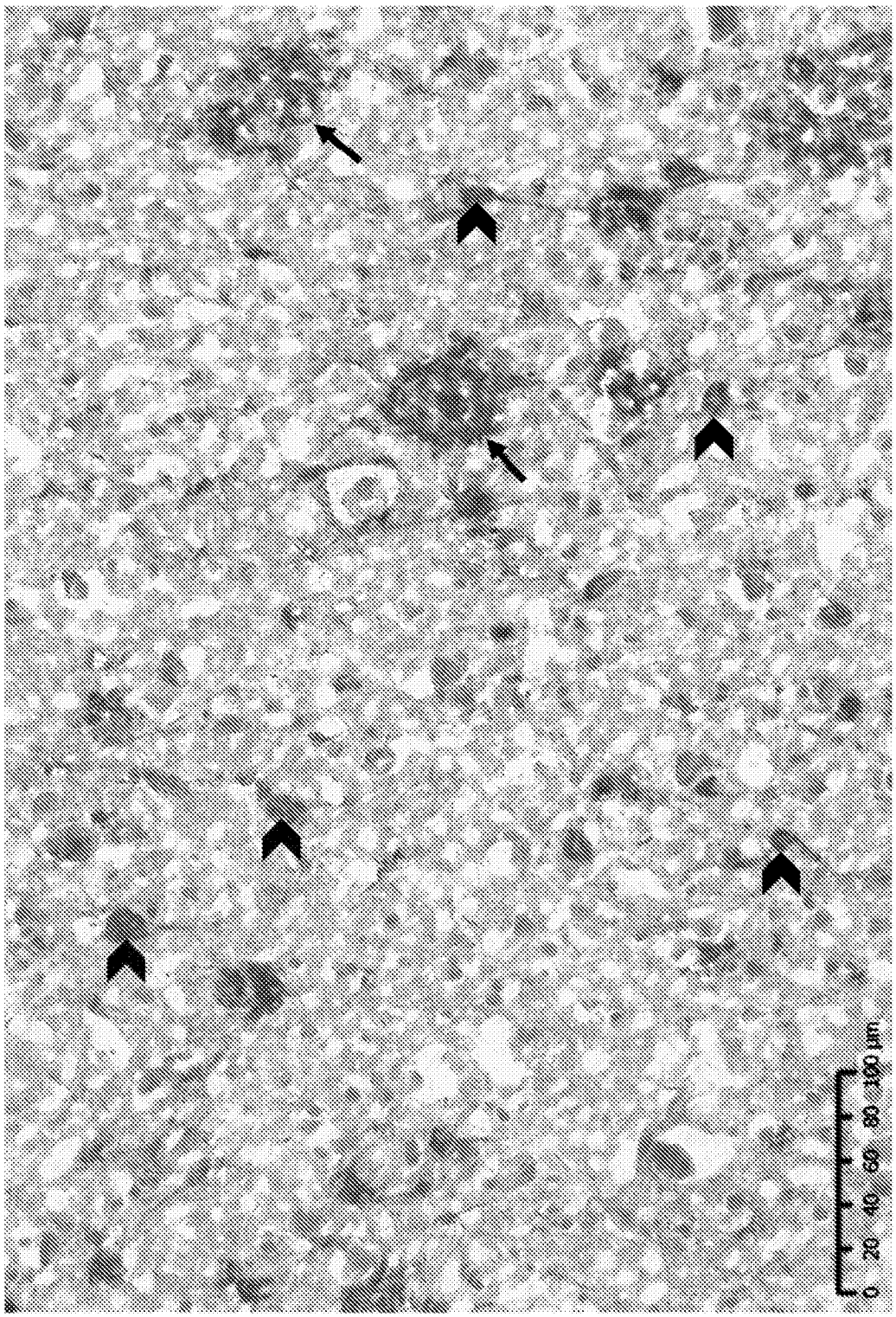
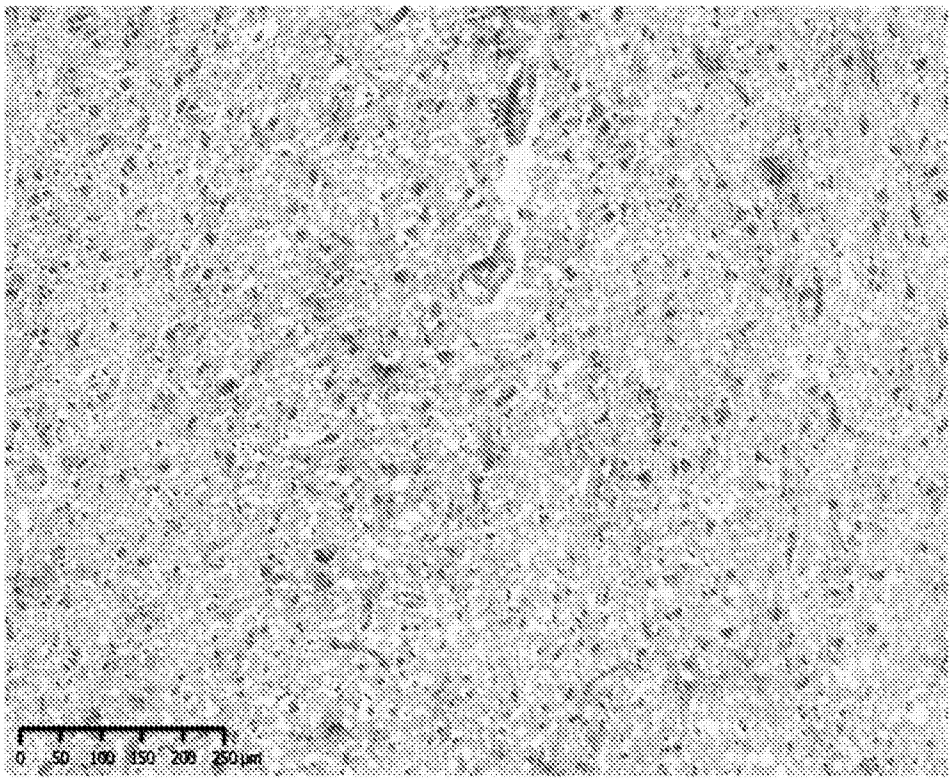


FIG. 6C

Negative Control - mouse serum – 1:1000 dilution



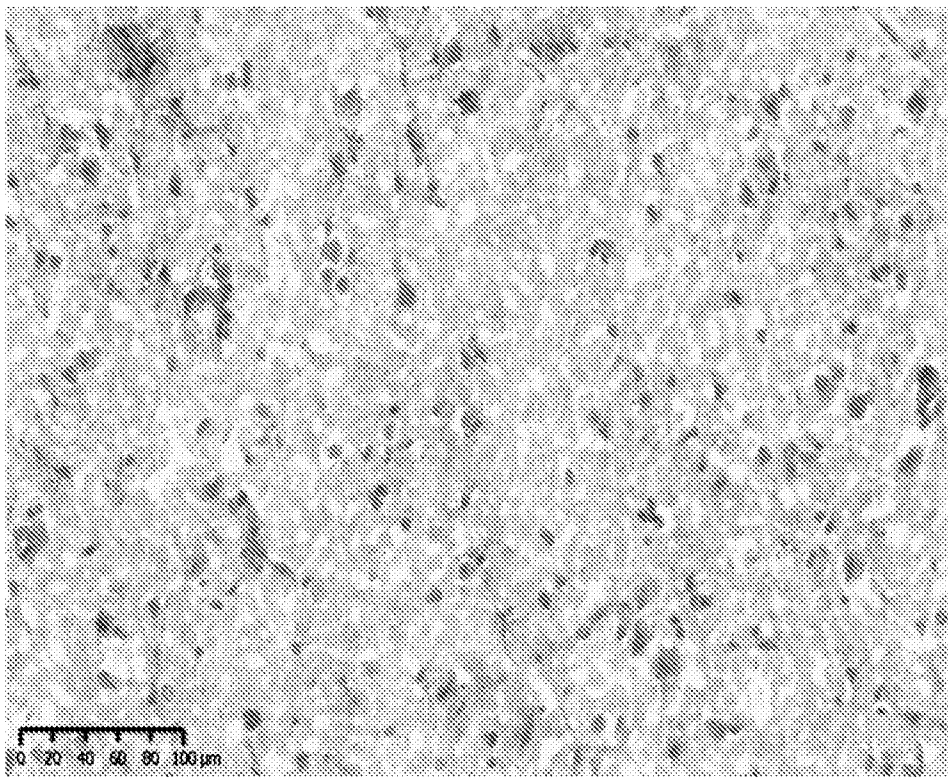


FIG. 6D

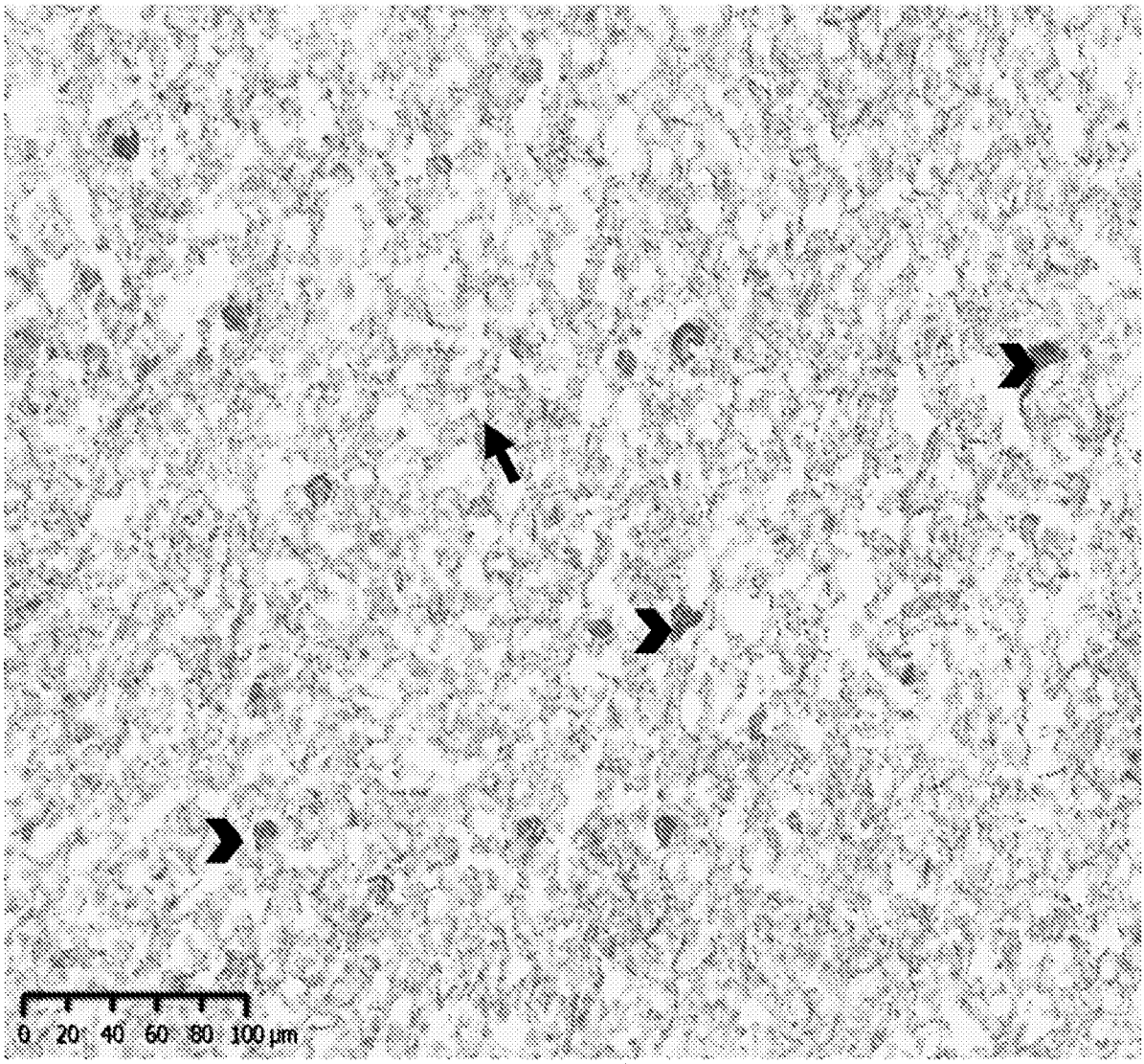
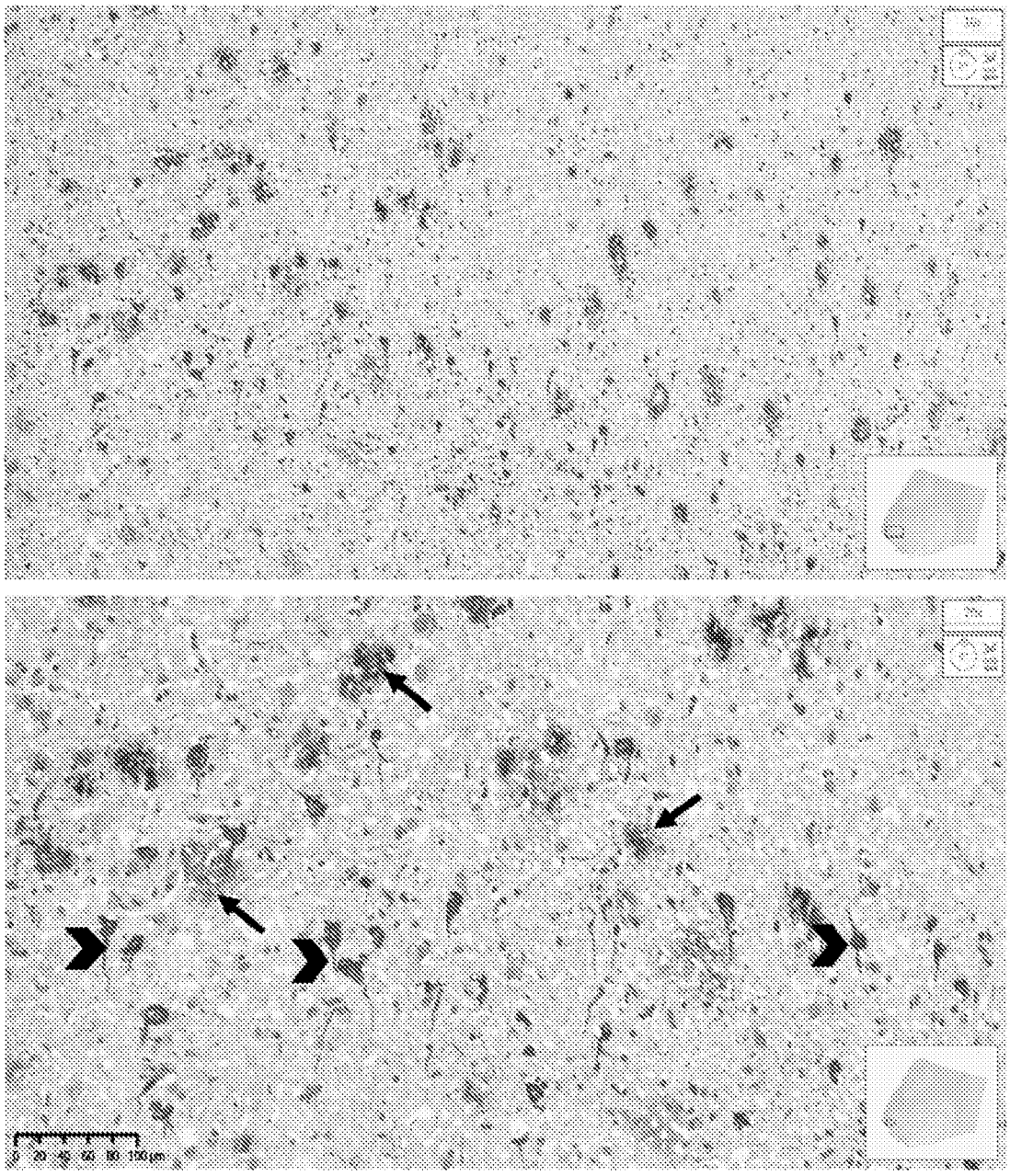

Positive Tau control - m6H3 Ab – 0.1 ug/ml
0 20 40 60 80 100 µm
Tau pathology

FIG. 6E

REFERENCE: Guinea pig serum Immunogen 9
Vaccine GP # 2 – 1:300 dilution



A-beta →
Tau ❯

FIG. 7A

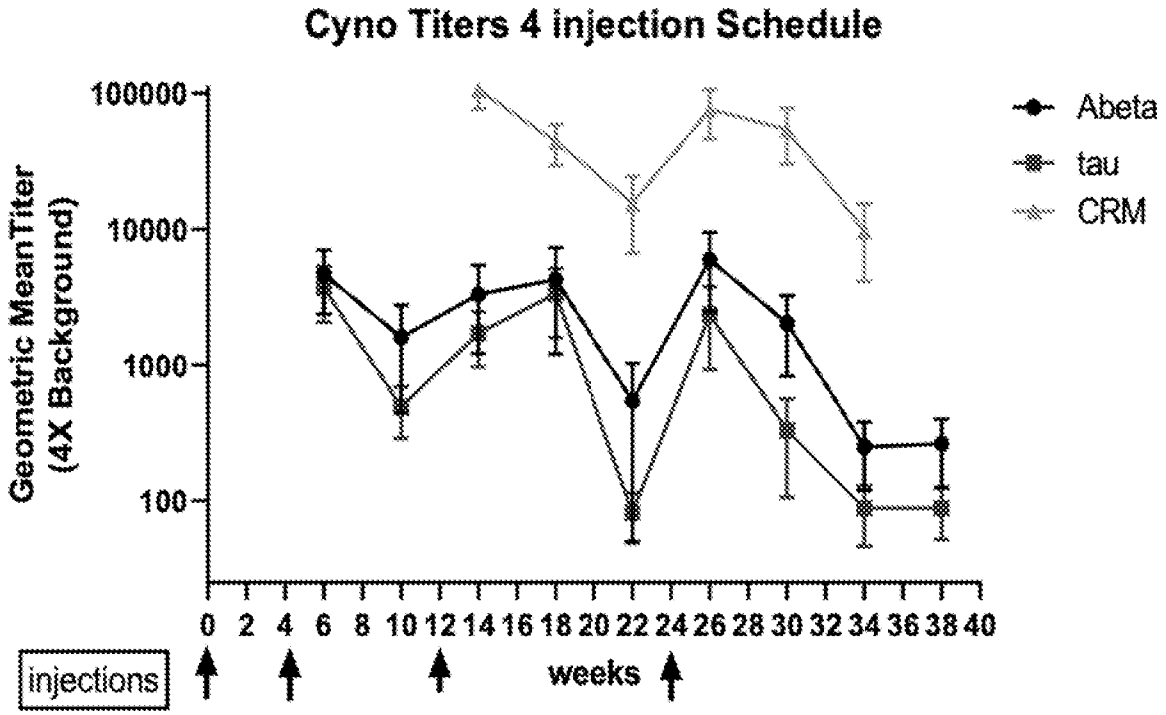

Cyno Titers 4 injection Schedule
Geometric MeanTiter (4X Background)
100000
10000
1000
100
0 2 4 6 8 10 12 14 16 18 20 22 24 26 28 30 32 34 36 38 40
weeks
injections
Abeta
tau
CRM

FIG. 7B

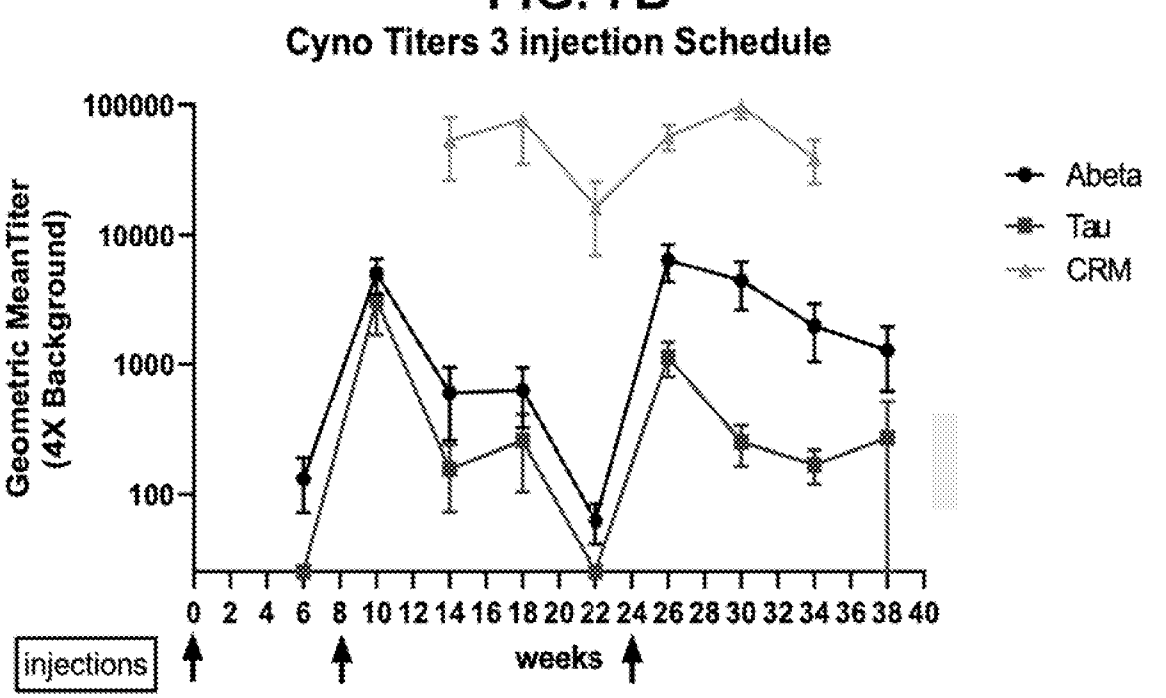

Cyno Titers 3 injection Schedule
Geometric MeanTiter (4X Background)
100000
10000
1000
100
0 2 4 6 8 10 12 14 16 18 20 22 24 26 28 30 32 34 36 38 40
weeks
injections
Abeta
Tau
CRM

FIG. 8A

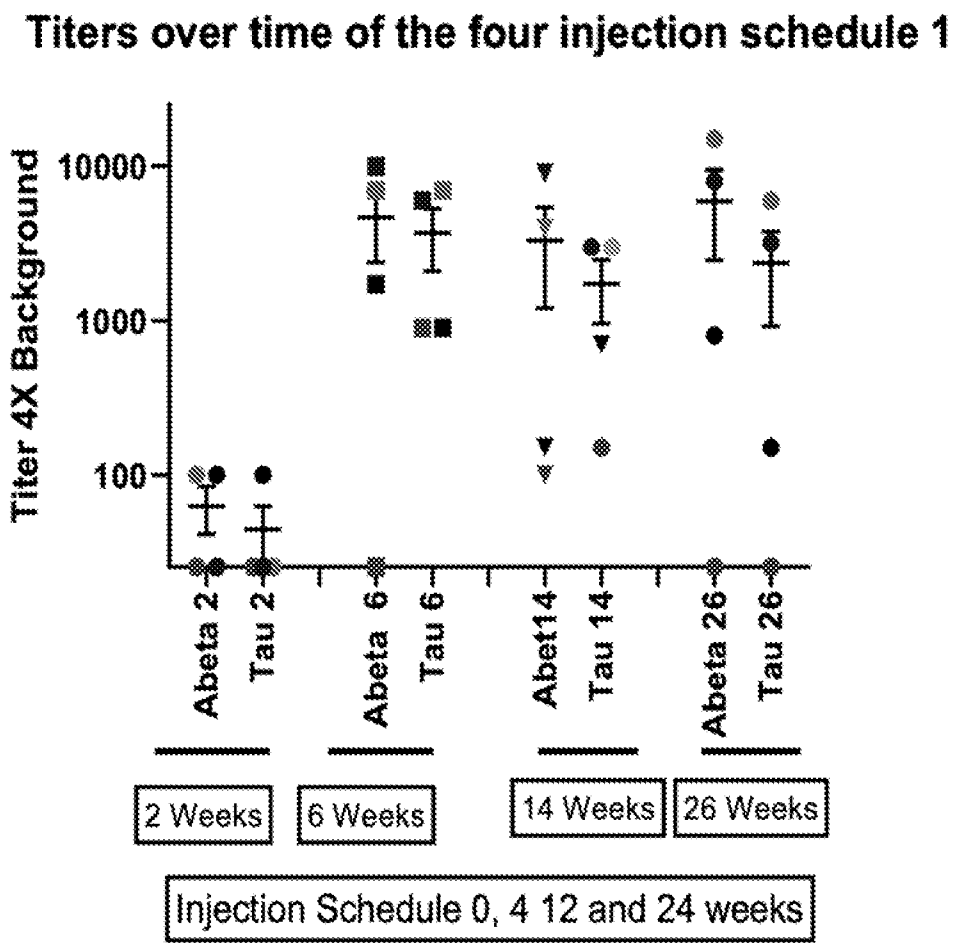

Titers over time of the four injection schedule 1
Titer 4X Background
10000
1000
100
Abeta 2
Tau 2
Abeta 6
Tau 6
Abet14
Tau 14
Abeta 26
Tau 26
2 Weeks
6 Weeks
14 Weeks
26 Weeks
Injection Schedule 0, 4 12 and 24 weeks

FIG. 8B

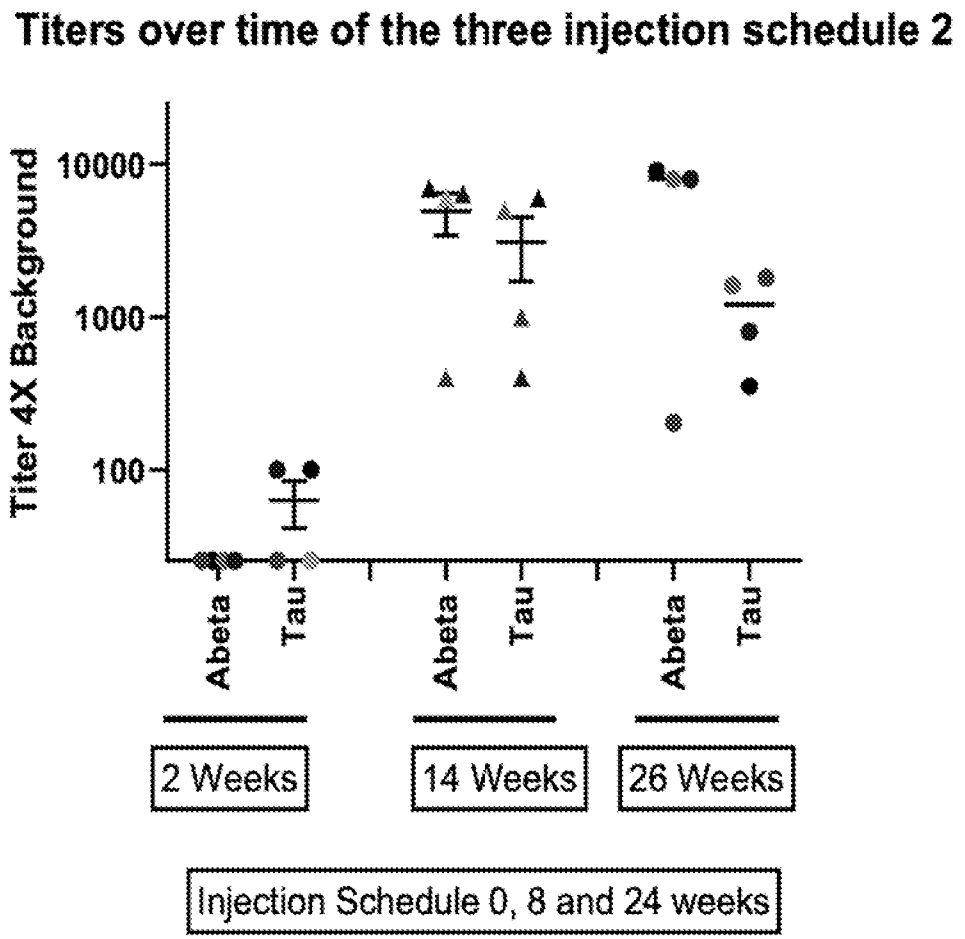

Titers over time of the three injection schedule 2
Titer 4X Background
10000
1000
100
Abeta
Tau
Abeta
Tau
Abeta
Tau
2 Weeks
14 Weeks
26 Weeks
Injection Schedule 0, 8 and 24 weeks

FIG. 9A

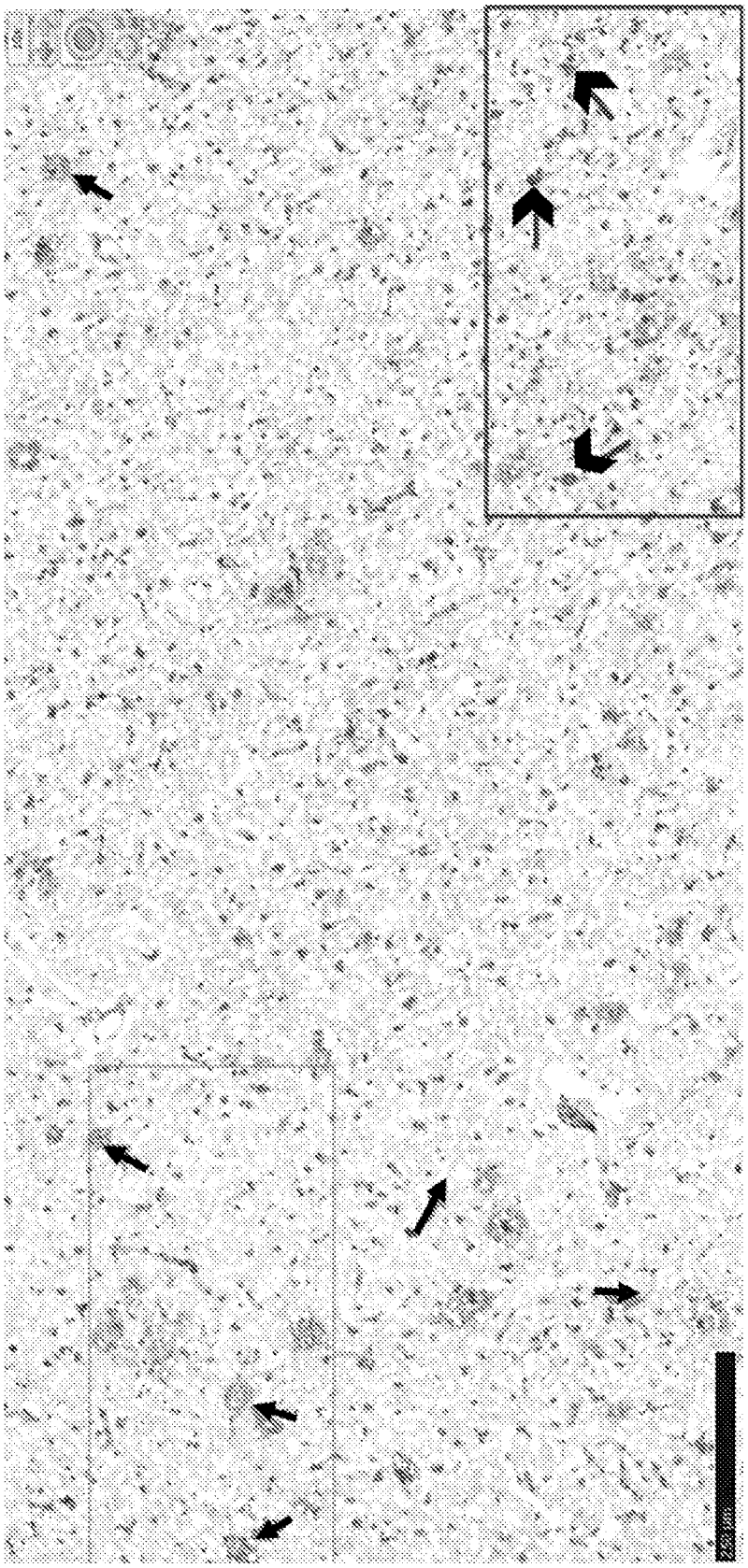


FIG. 9B

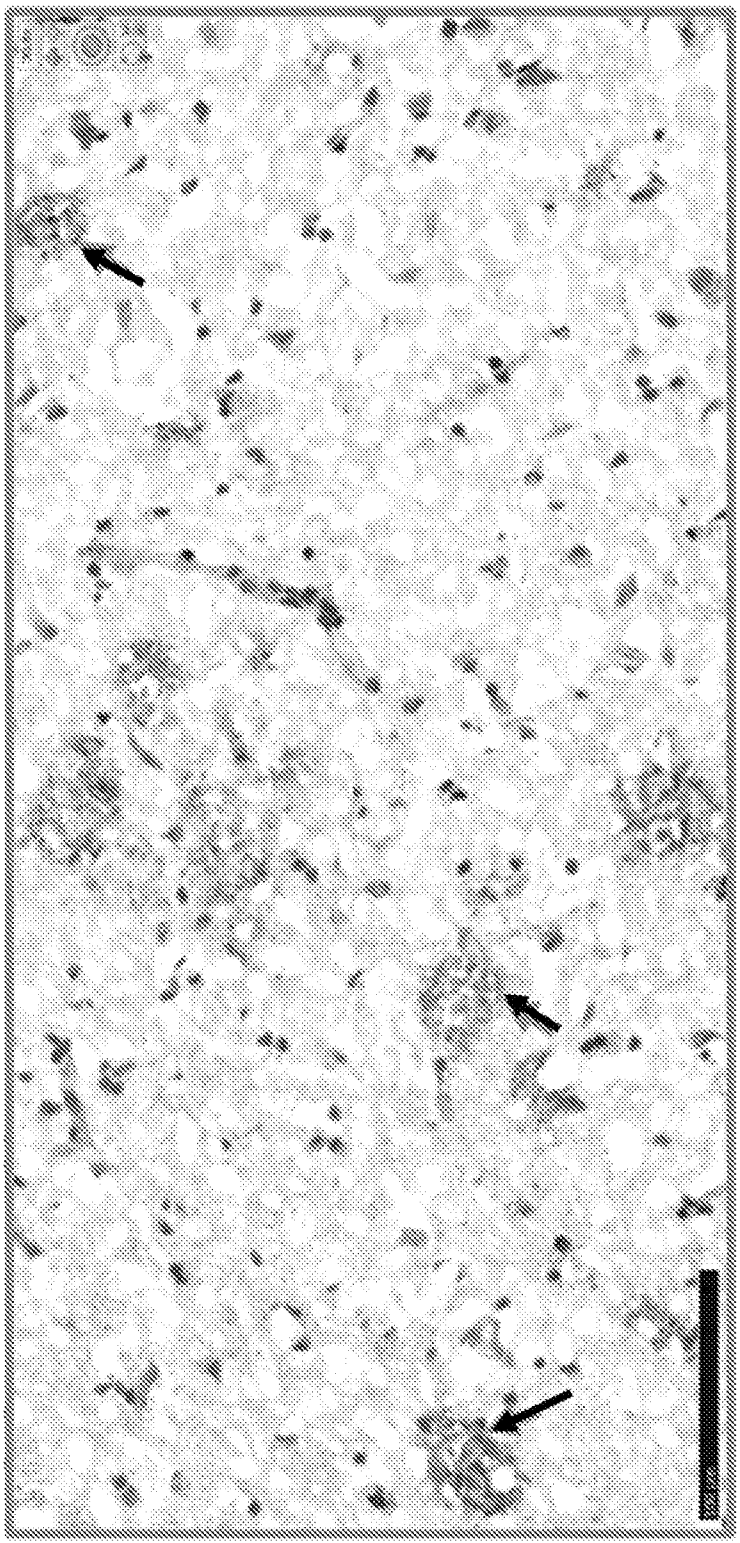


FIG. 9C

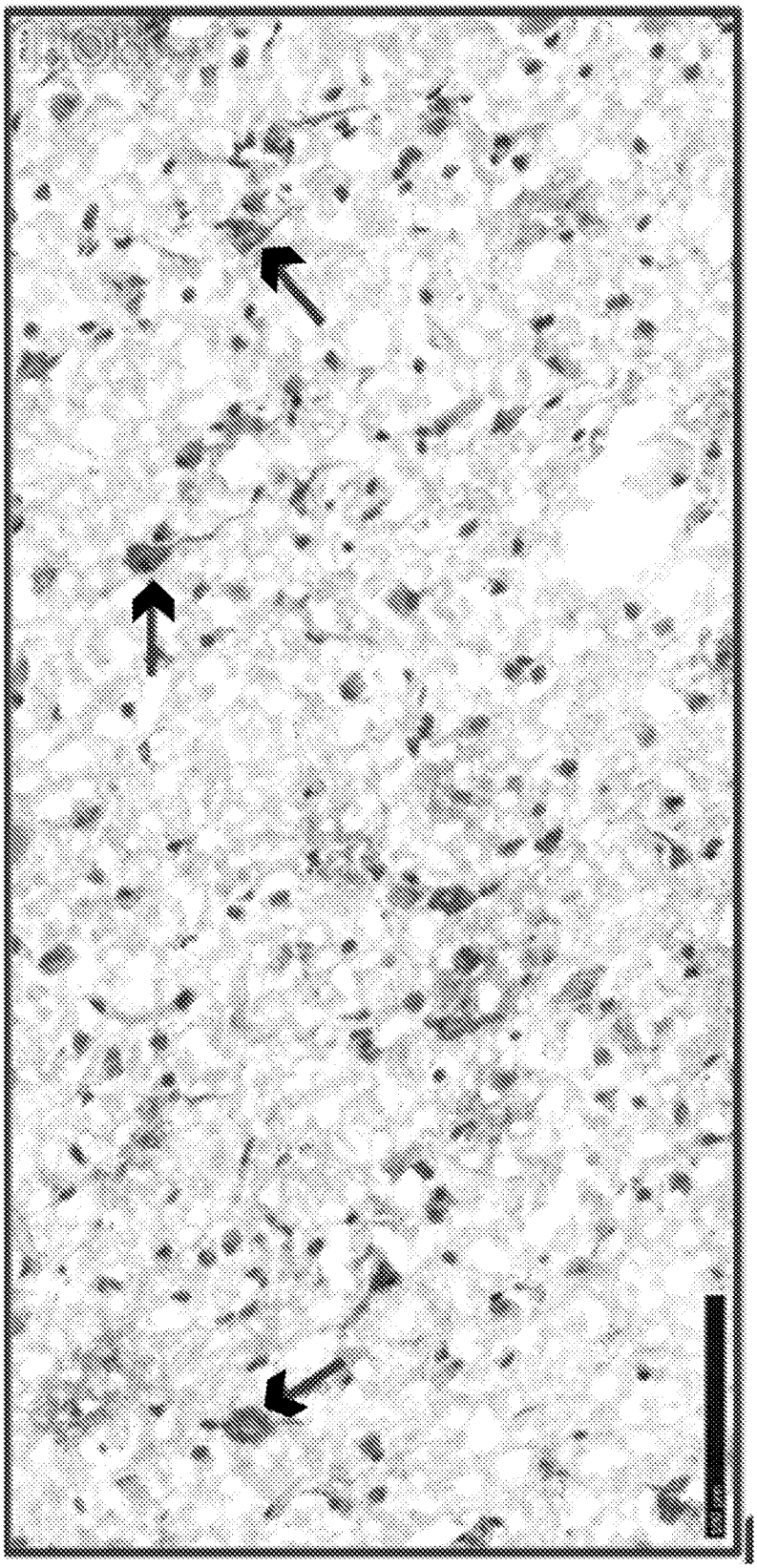


FIG. 10A

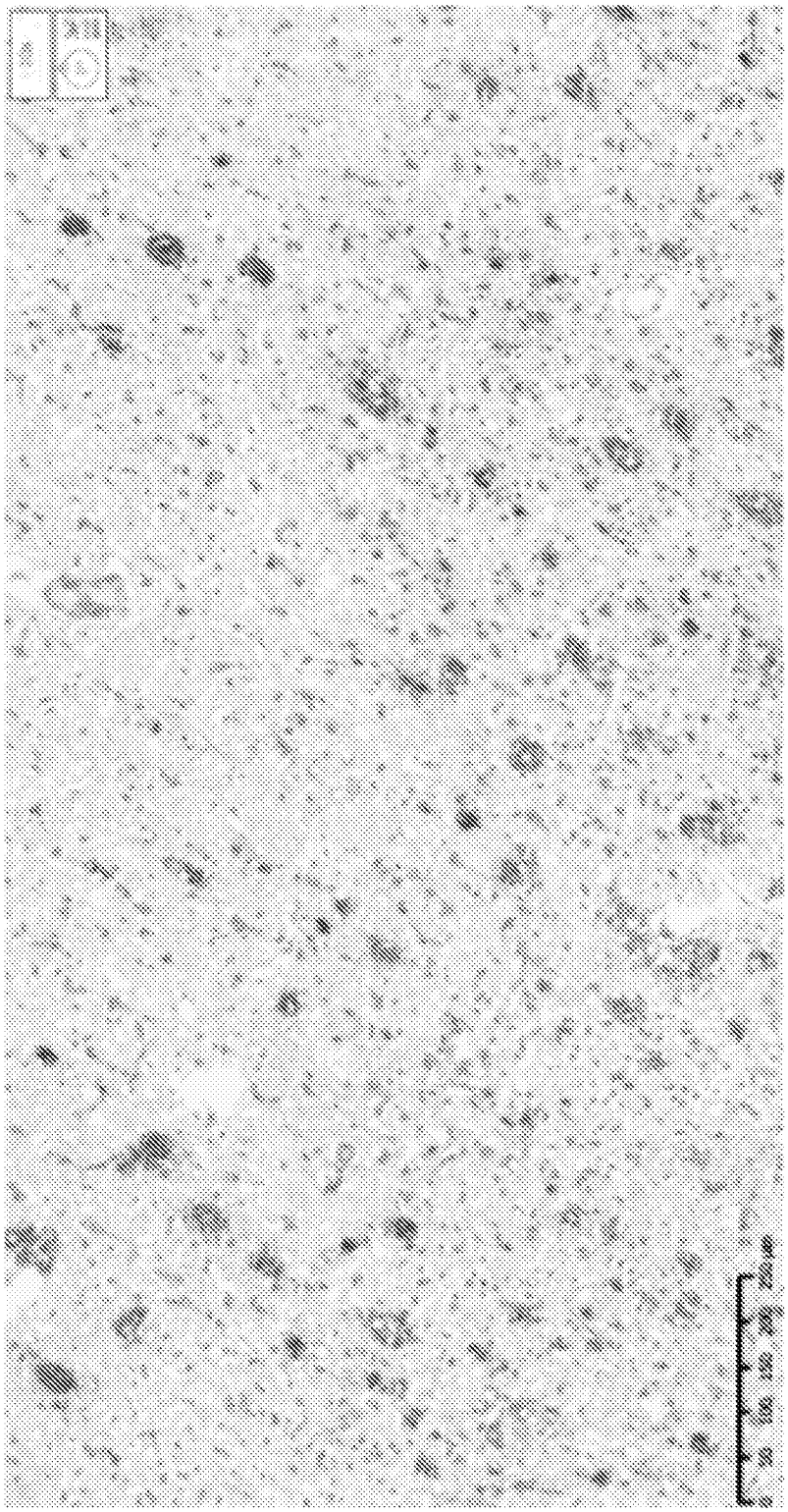


FIG. 10B

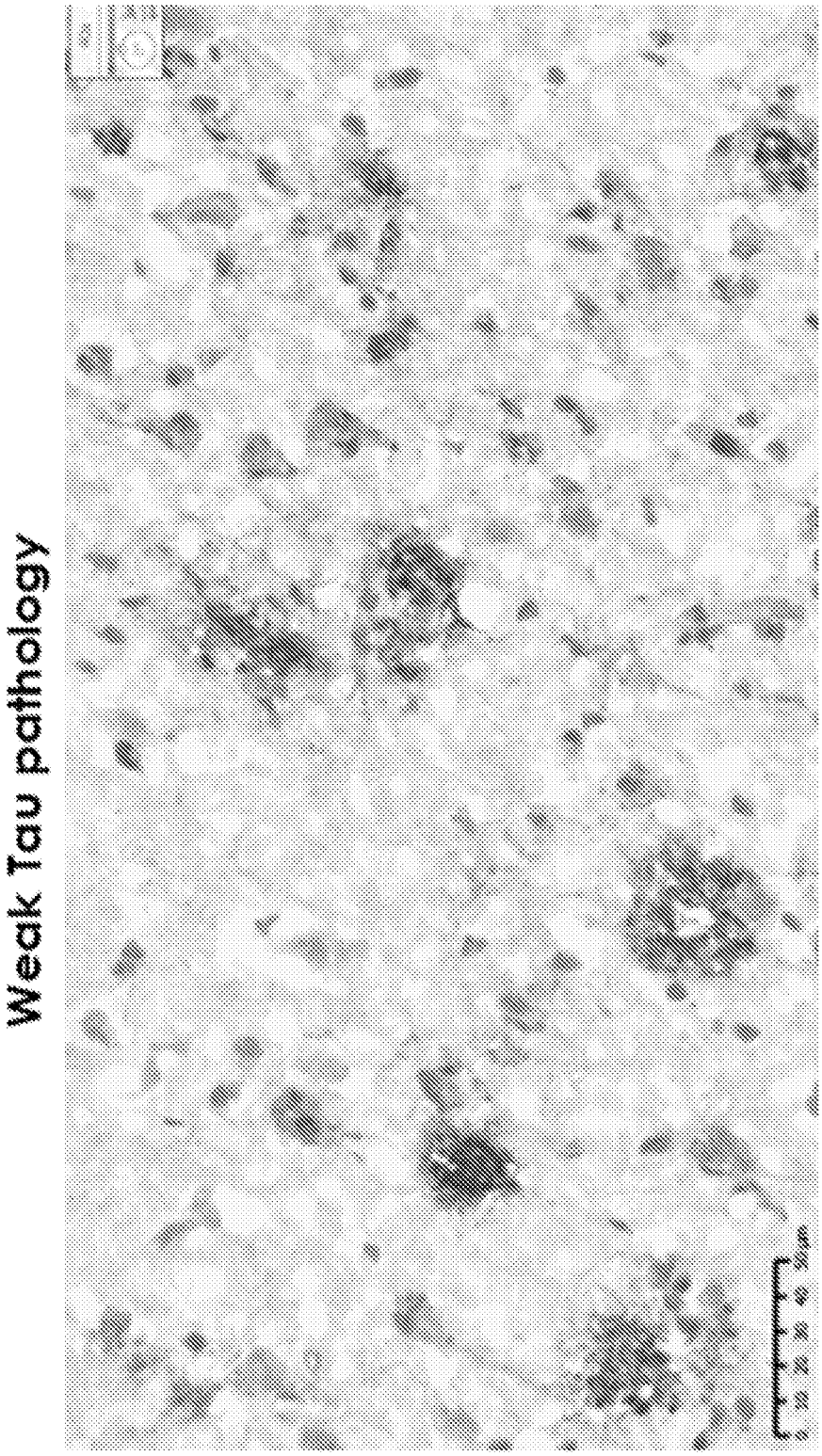


FIG. 11A

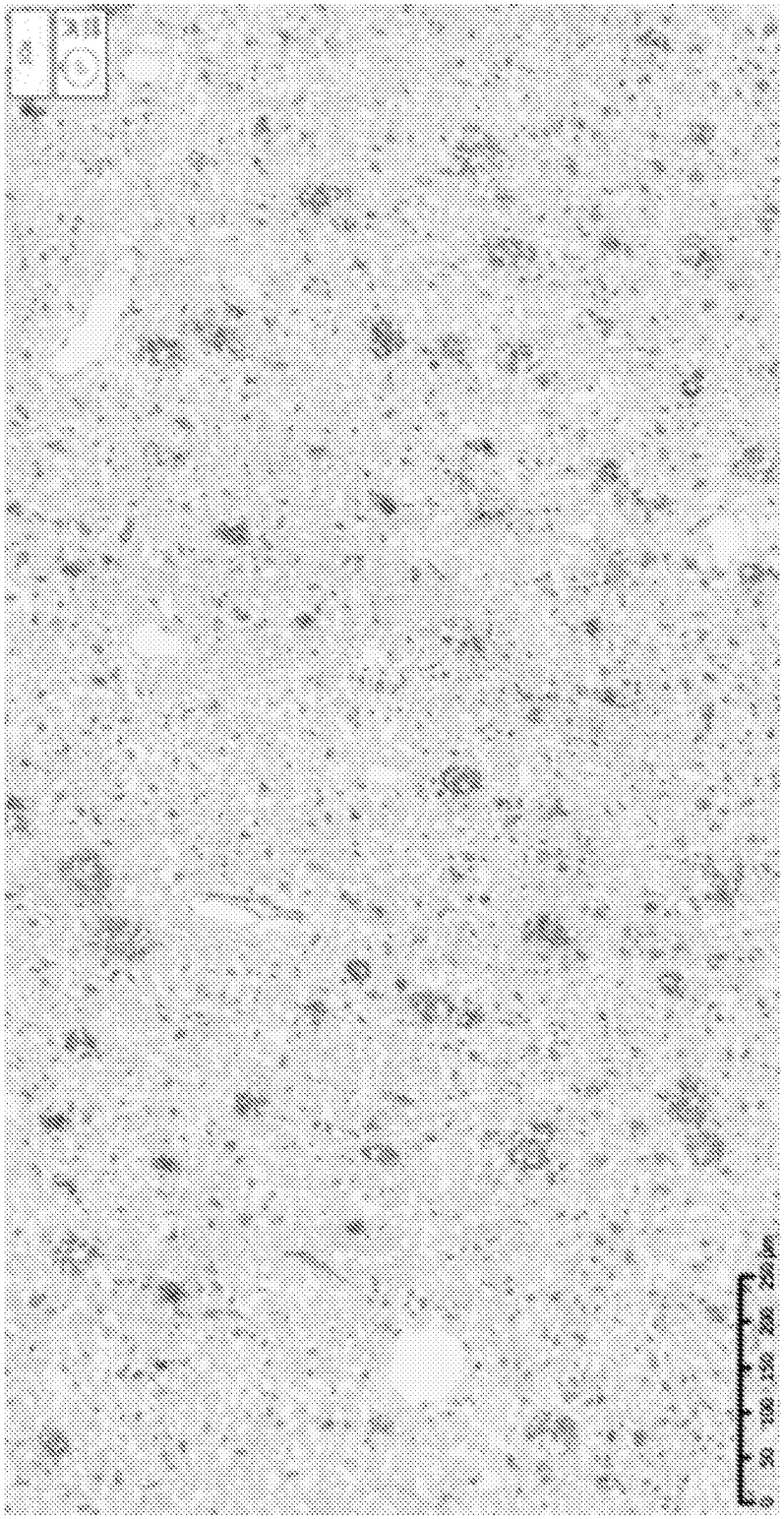


FIG. 11B

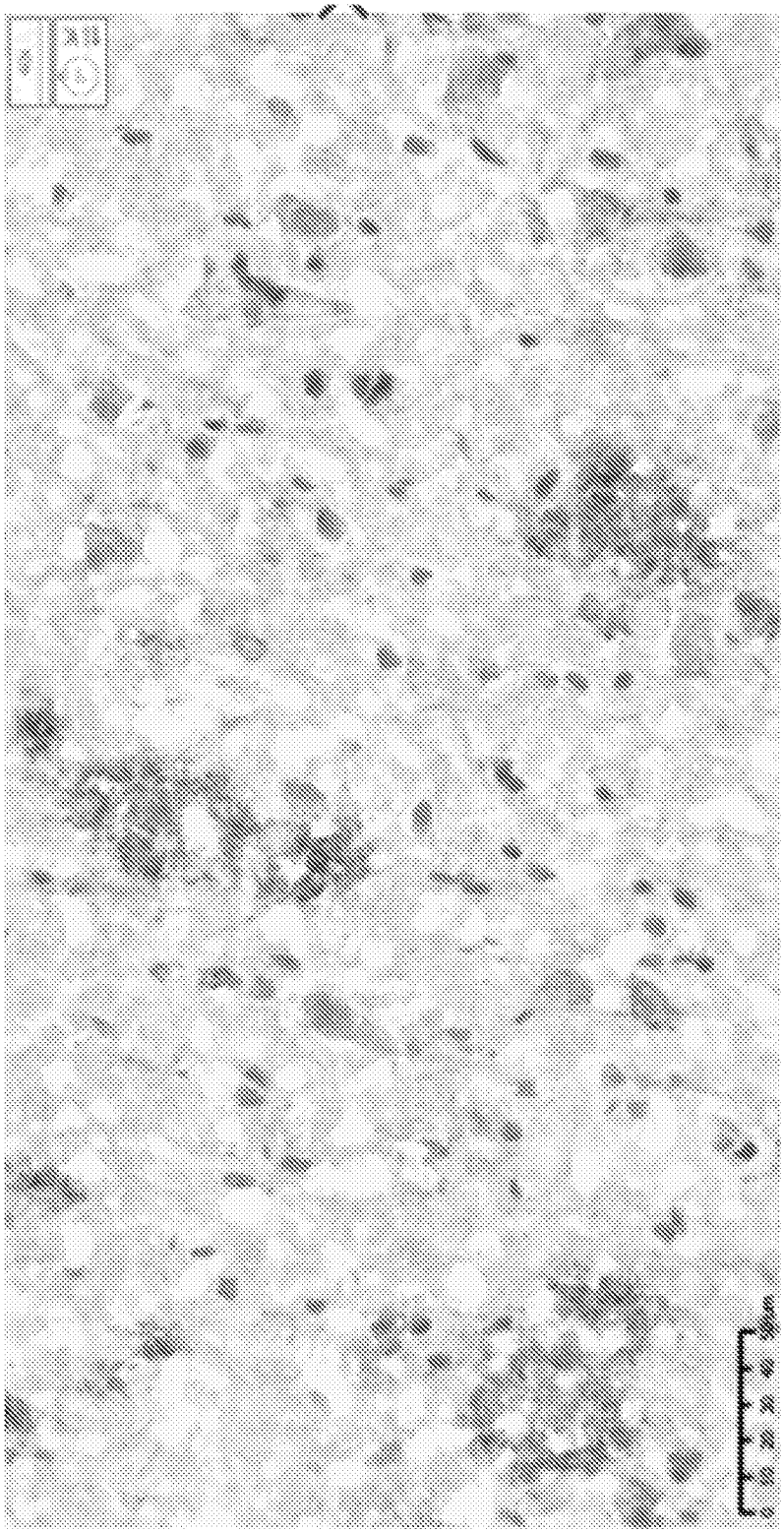


FIG. 12A

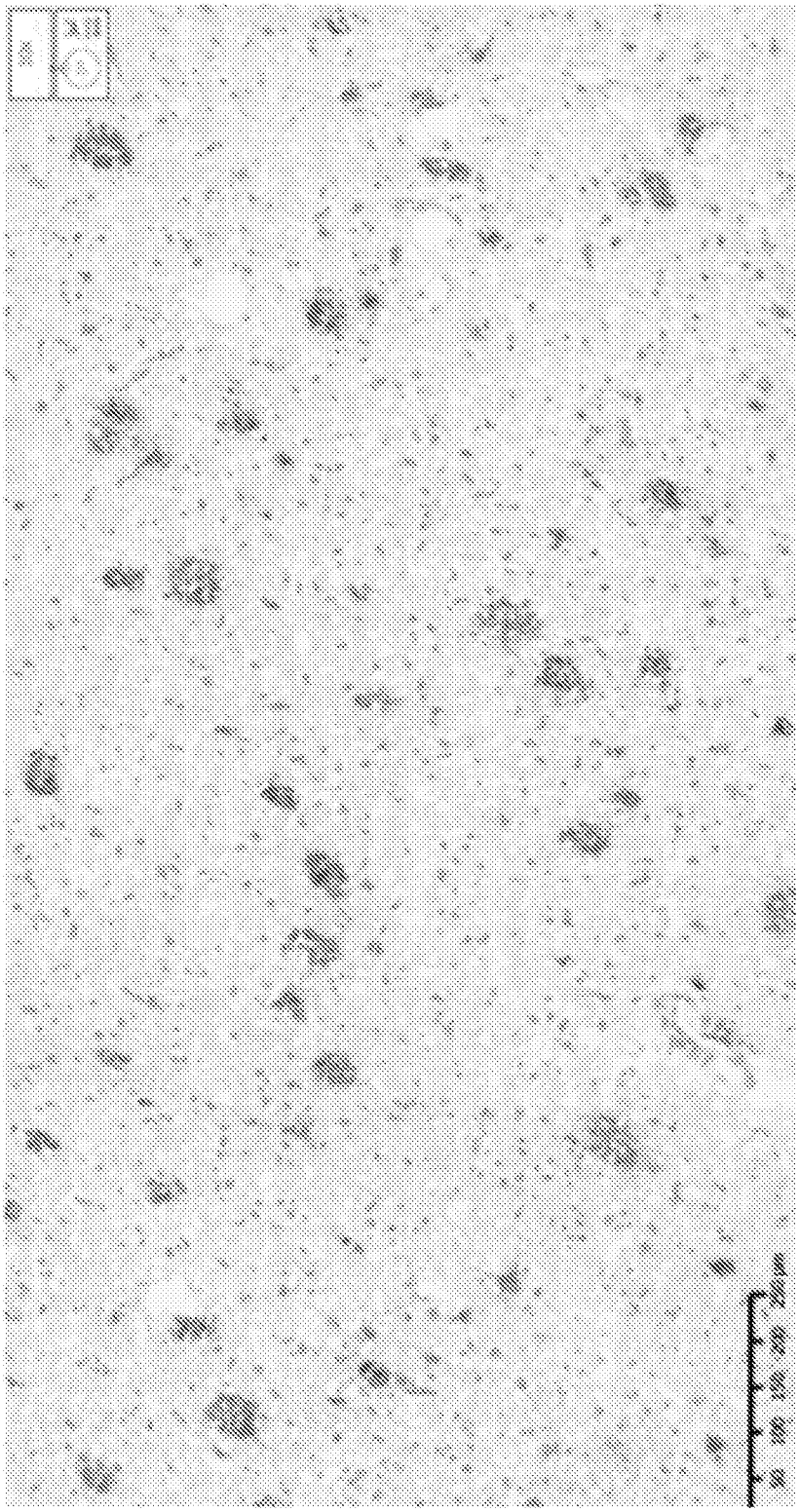


FIG. 12B

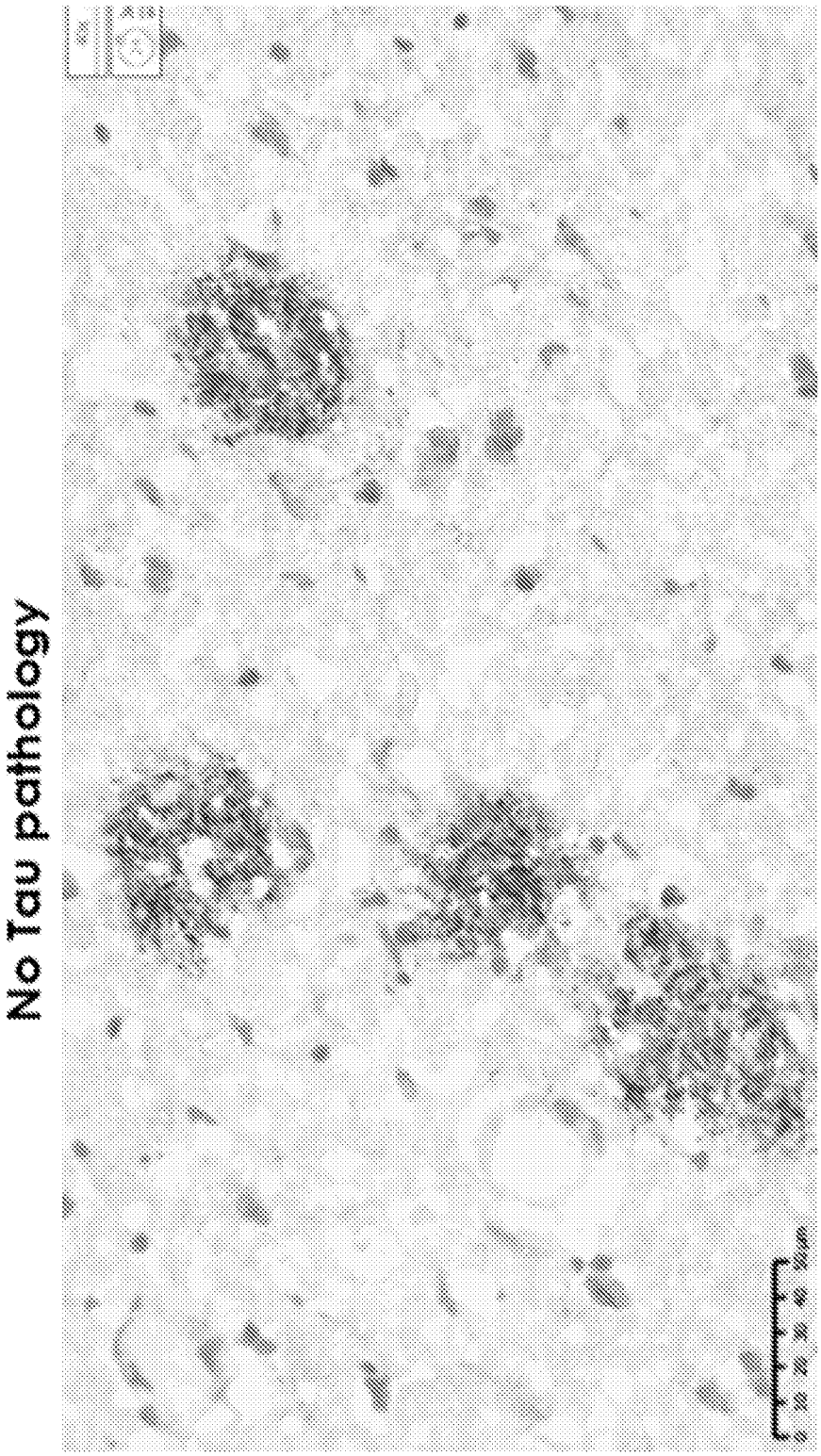


FIG. 13

Final bleed of dual Abeta-Tau constructs

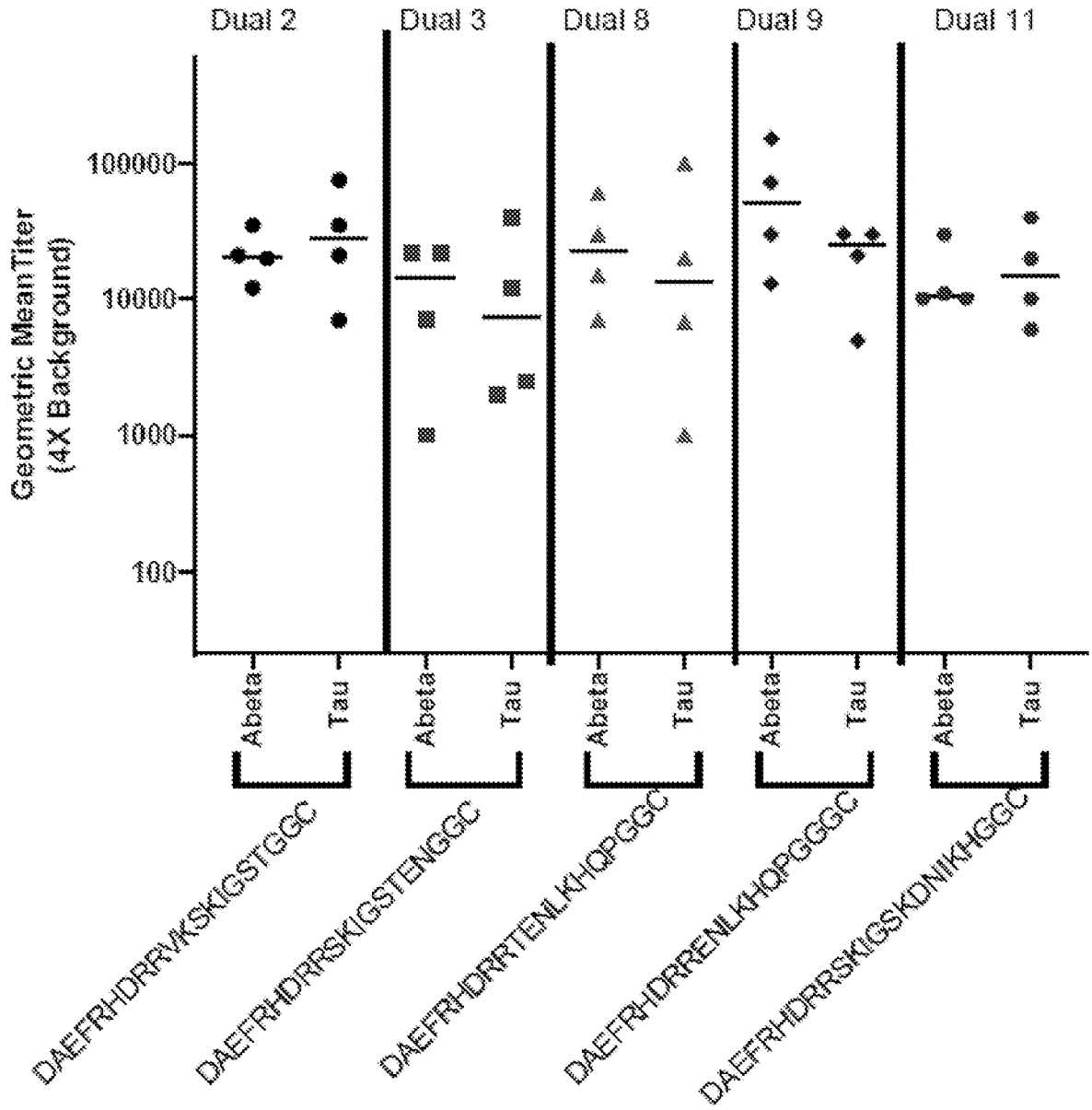


FIG. 14

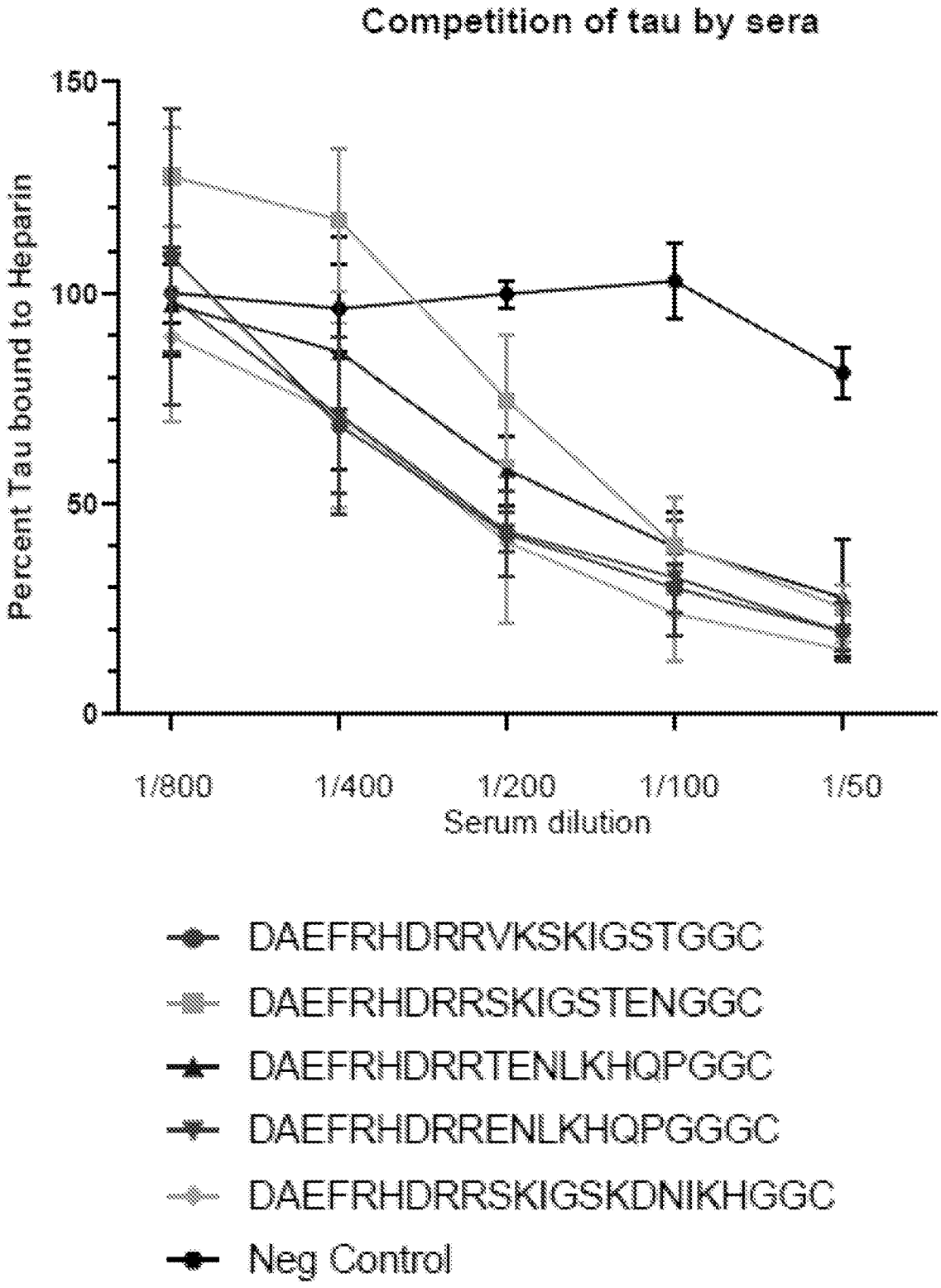

Competition of tau by sera
Percent Tau bound to Heparin
150
100
50
0
1/800
1/400
1/200
1/100
1/50
Serum dilution
DAEFRHDRRVKSKIGSTGGC
DAEFRHDRRSKIGSTENGGC
DAEFRHDRRTENLKHQPGGC
DAEFRHDRRENLKHQPGGGC
DAEFRHDRRSKIGSKDNIKHGGC
Neg Control

FIG. 15A

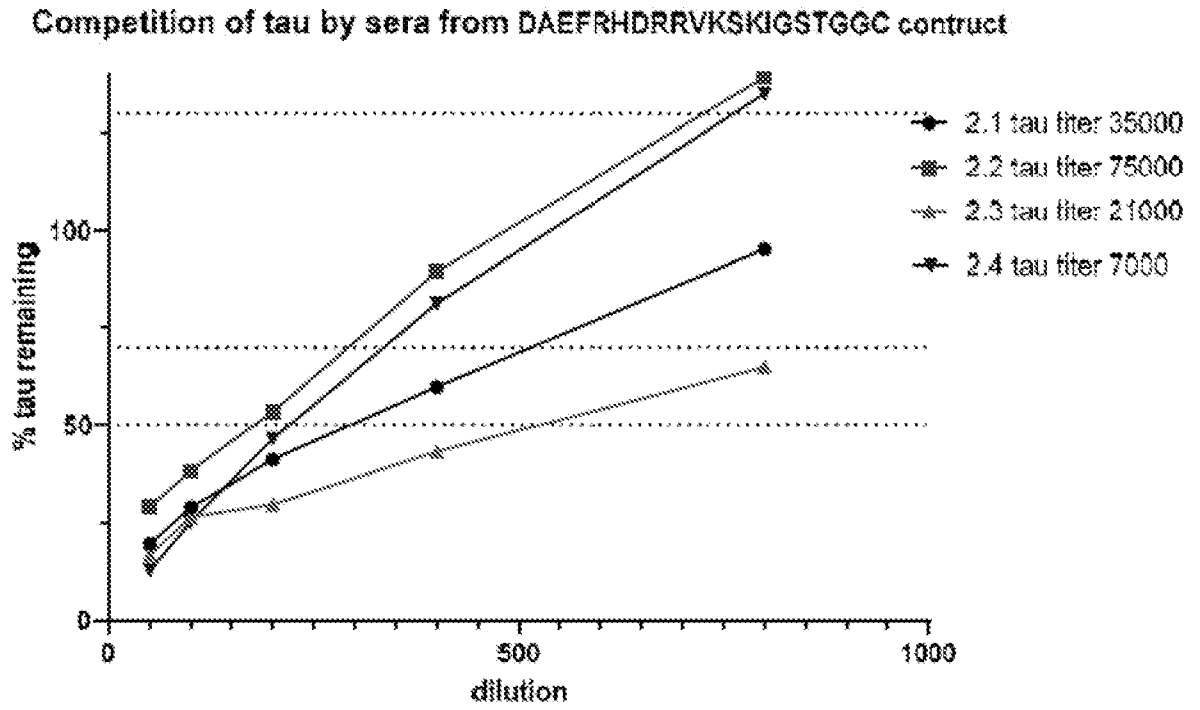


FIG. 15B

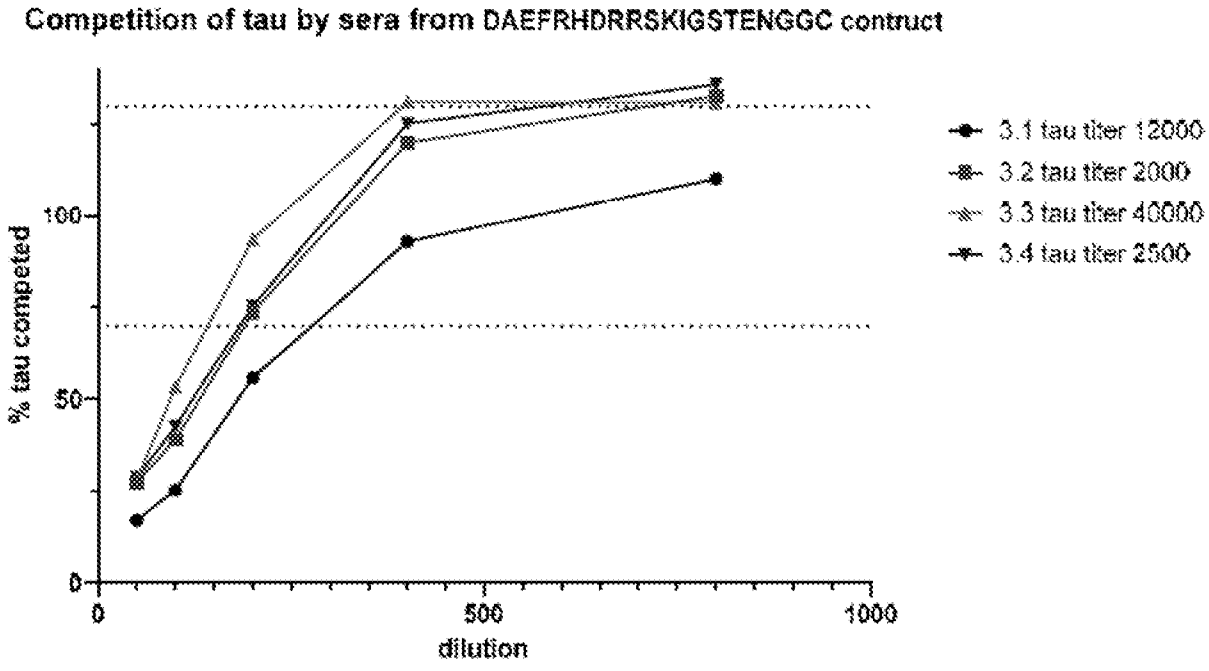


FIG. 15C

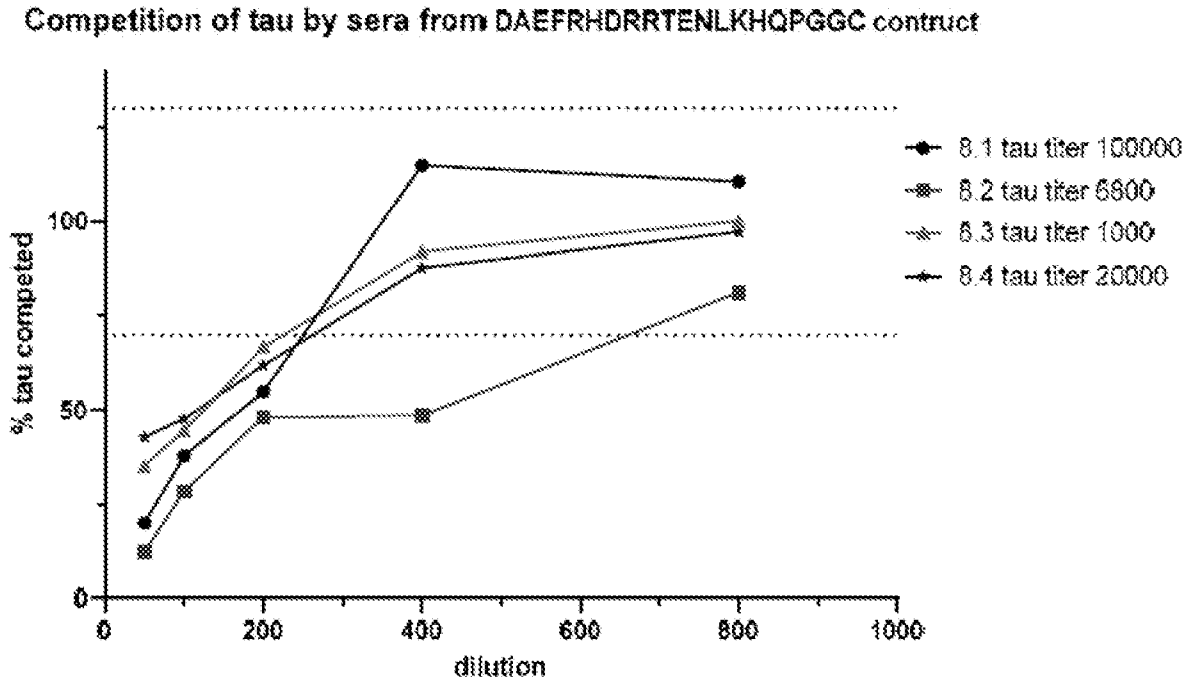


FIG. 15D

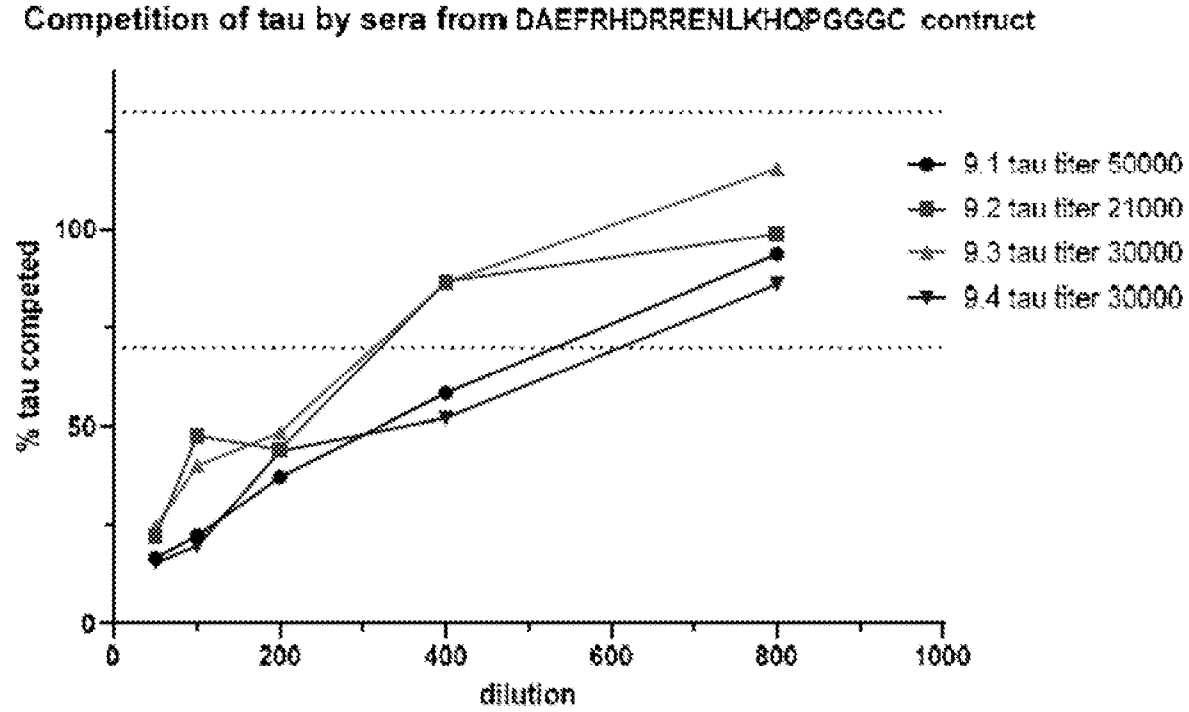


FIG. 15E

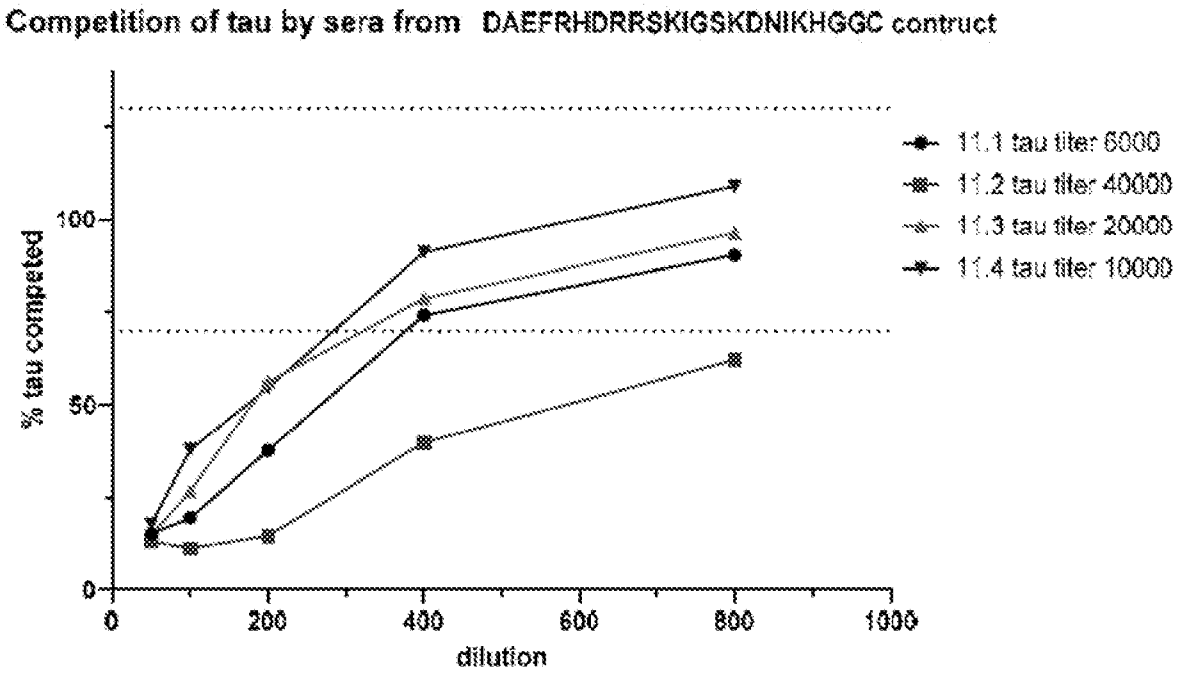


FIG. 15F

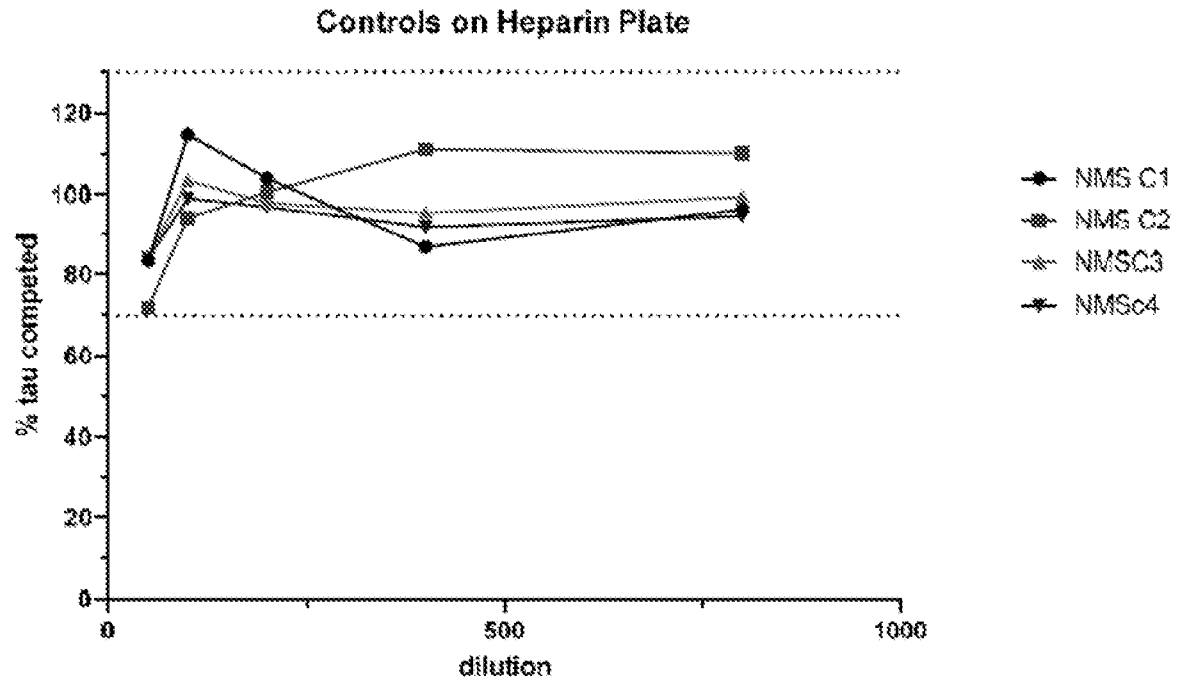


FIG. 15G

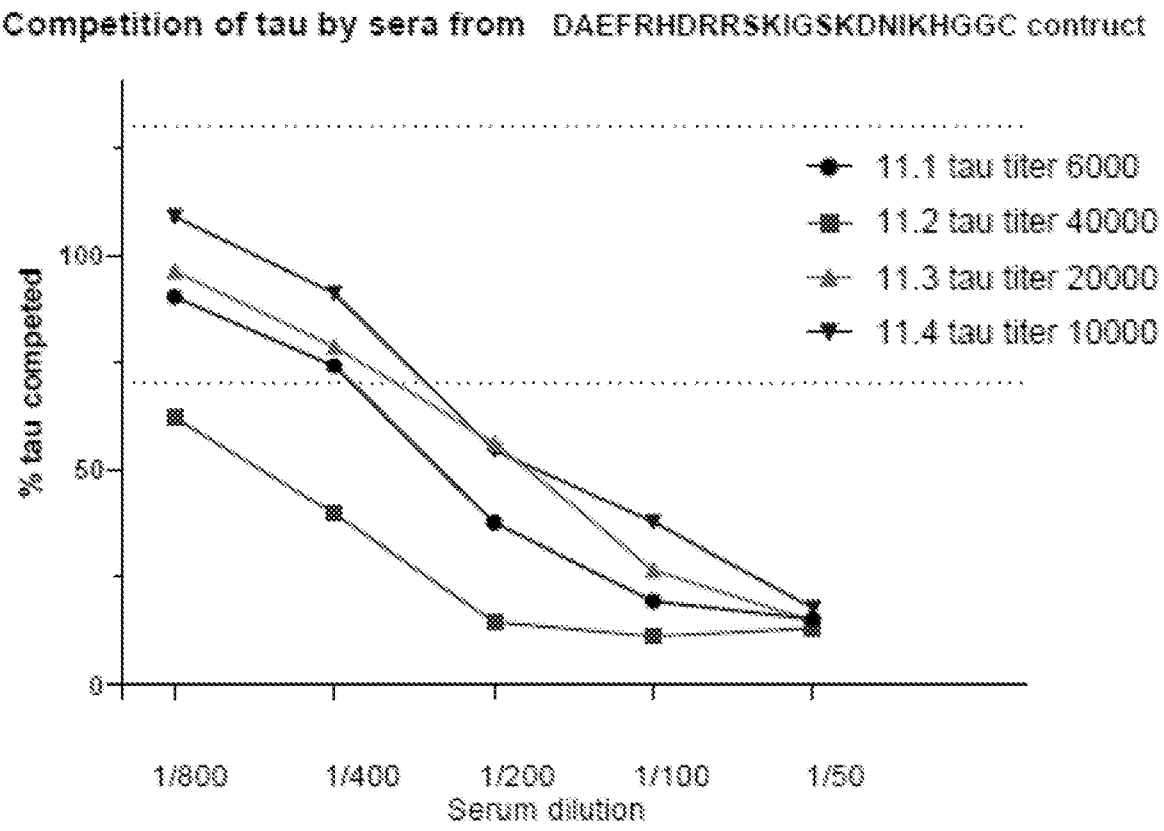

Competition of tau by sera from DAEFRHDRRSKIGSKDNIKHGGC contruct
11.1 tau titer 6000
11.2 tau titer 40000
11.3 tau titer 20000
11.4 tau titer 10000
% tau competed
100
50
0
1/800
1/400
1/200
1/100
1/50
Serum dilution

FIG. 16A

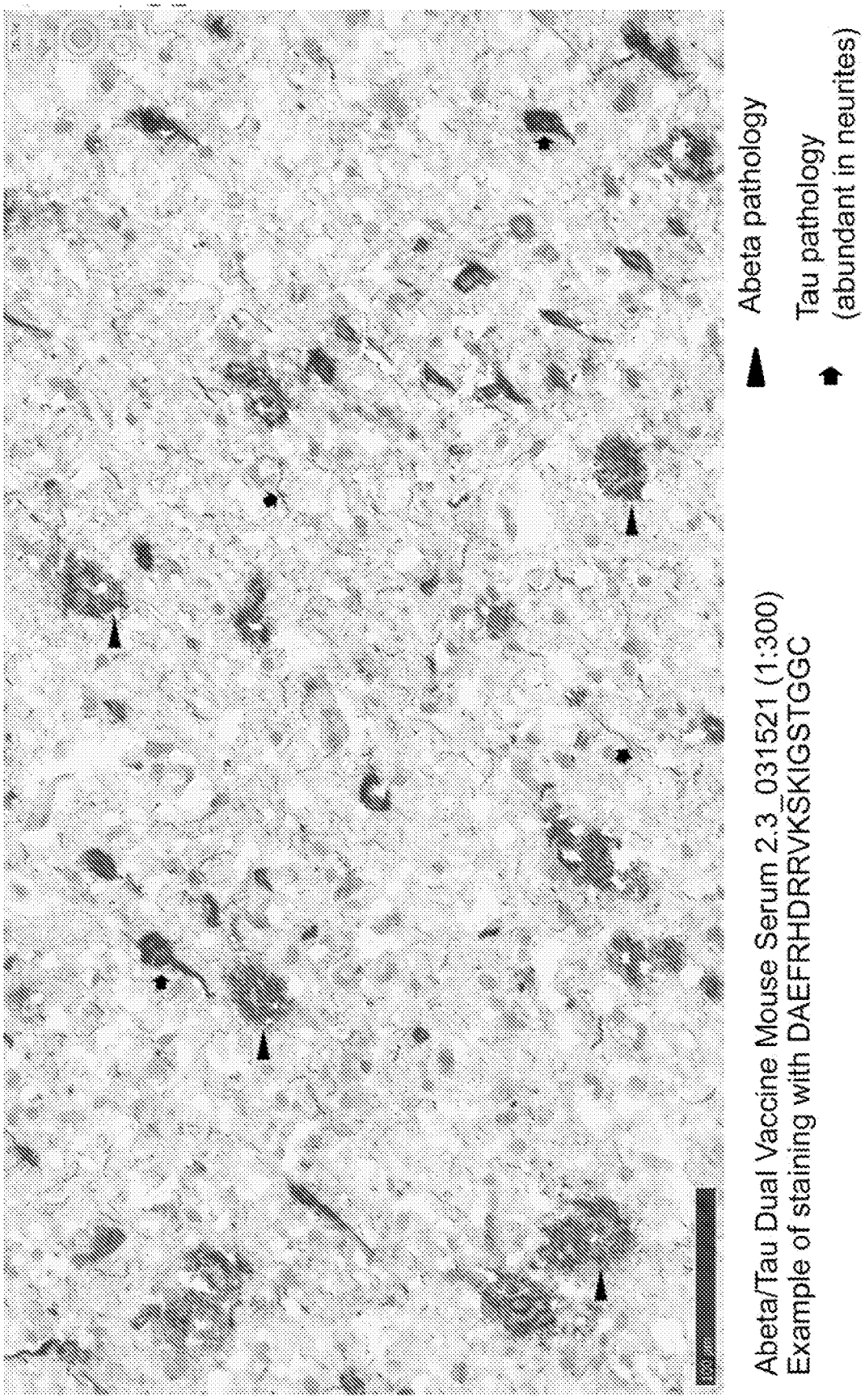

Abeta pathology
Tau pathology
(abundant in neurites)
Abeta/Tau Dual Vaccine Mouse Serum 2.3_031521 (1:300)
Example of staining with DAEFRHDRRVKSKIGSTGGC

FIG. 16B

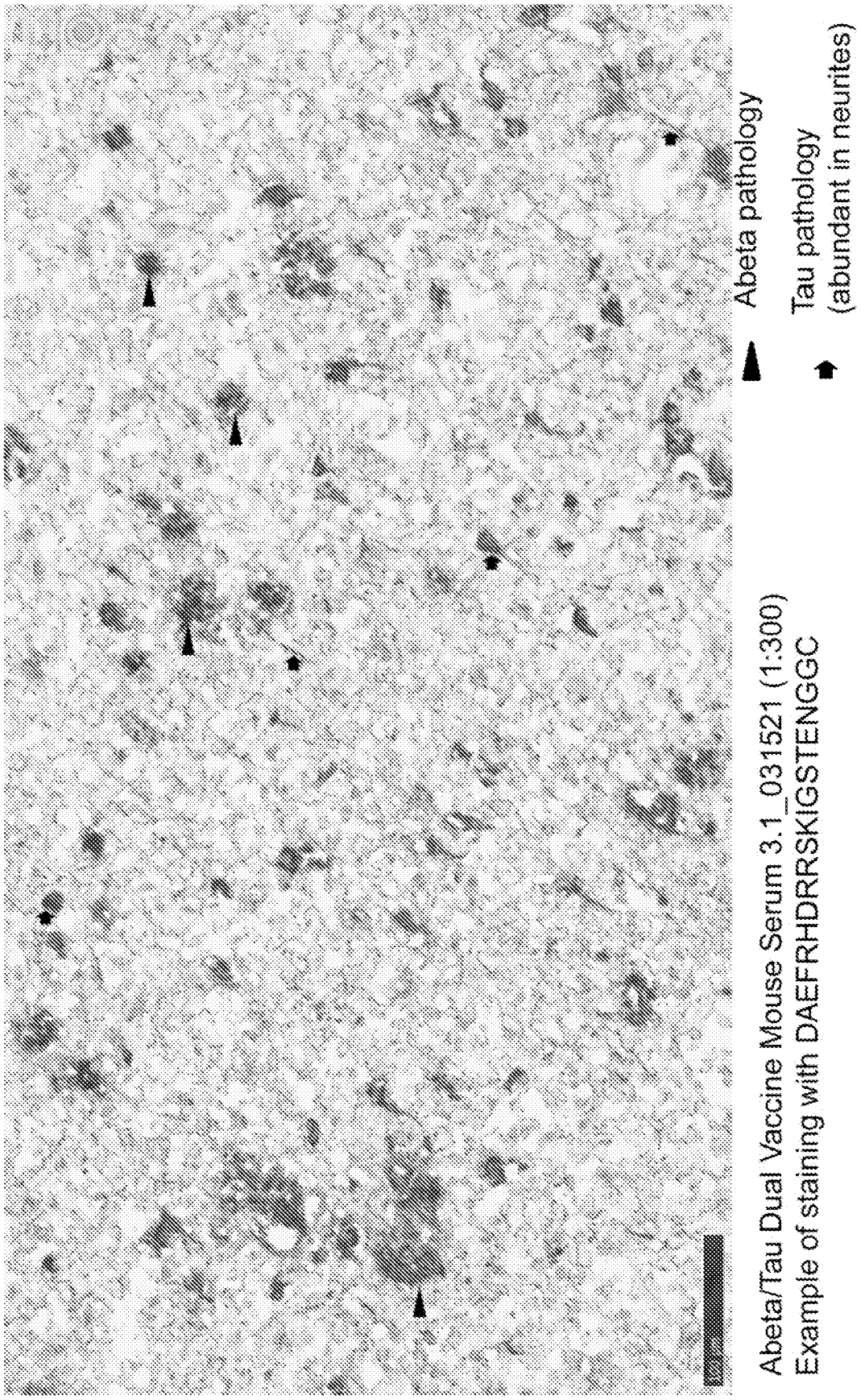

Abeta pathology
Tau pathology
(abundant in neurites)
Abeta/Tau Dual Vaccine Mouse Serum 3.1_031521 (1:300)
Example of staining with DAEFRHDRRSKIGSTENGGC

FIG. 16C

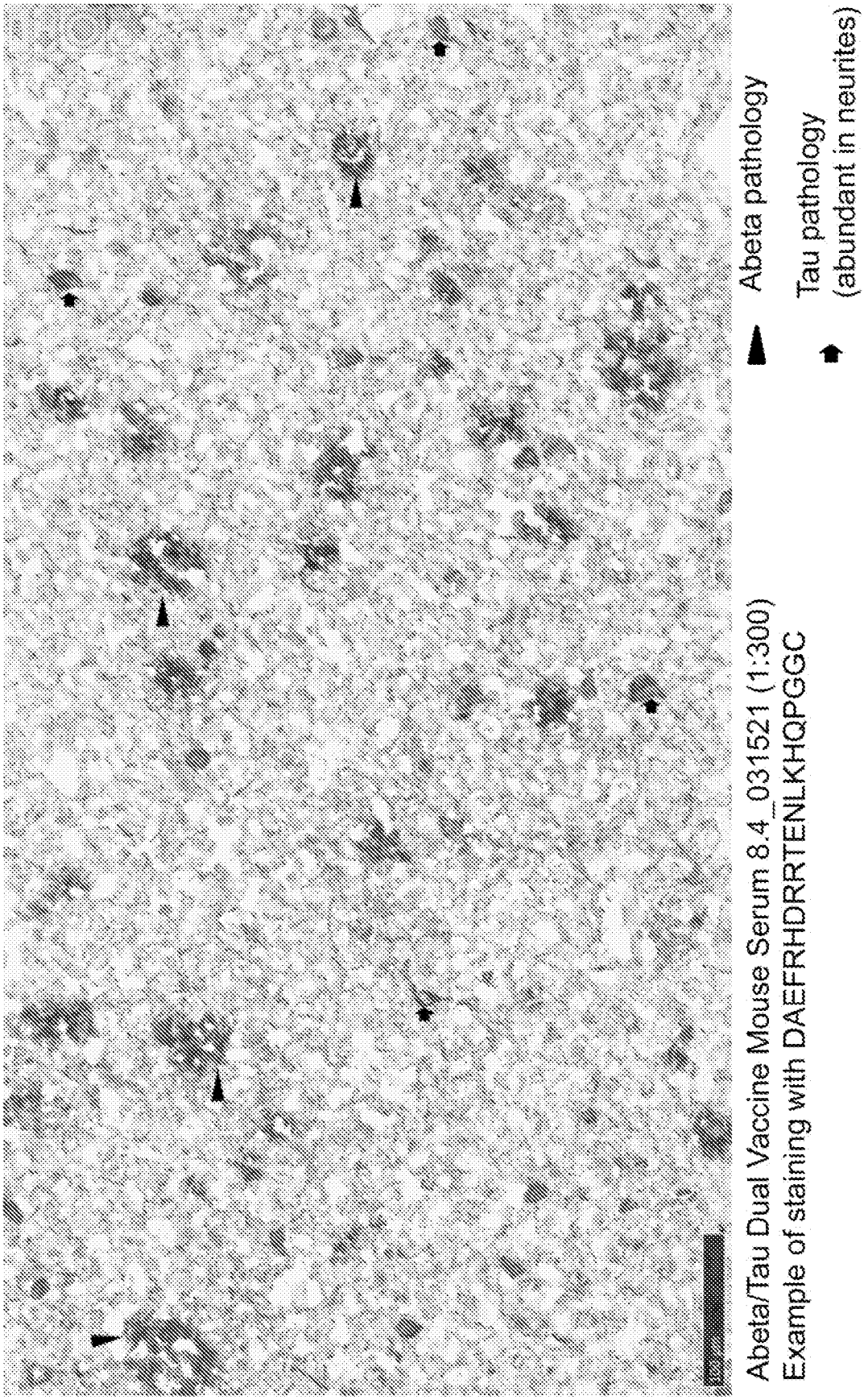

Abeta pathology
Tau pathology
(abundant in neurites)
Abeta/Tau Dual Vaccine Mouse Serum 8.4_031521 (1:300)
Example of staining with DAEFRHDRRTENLKHQPGGC

FIG. 16D

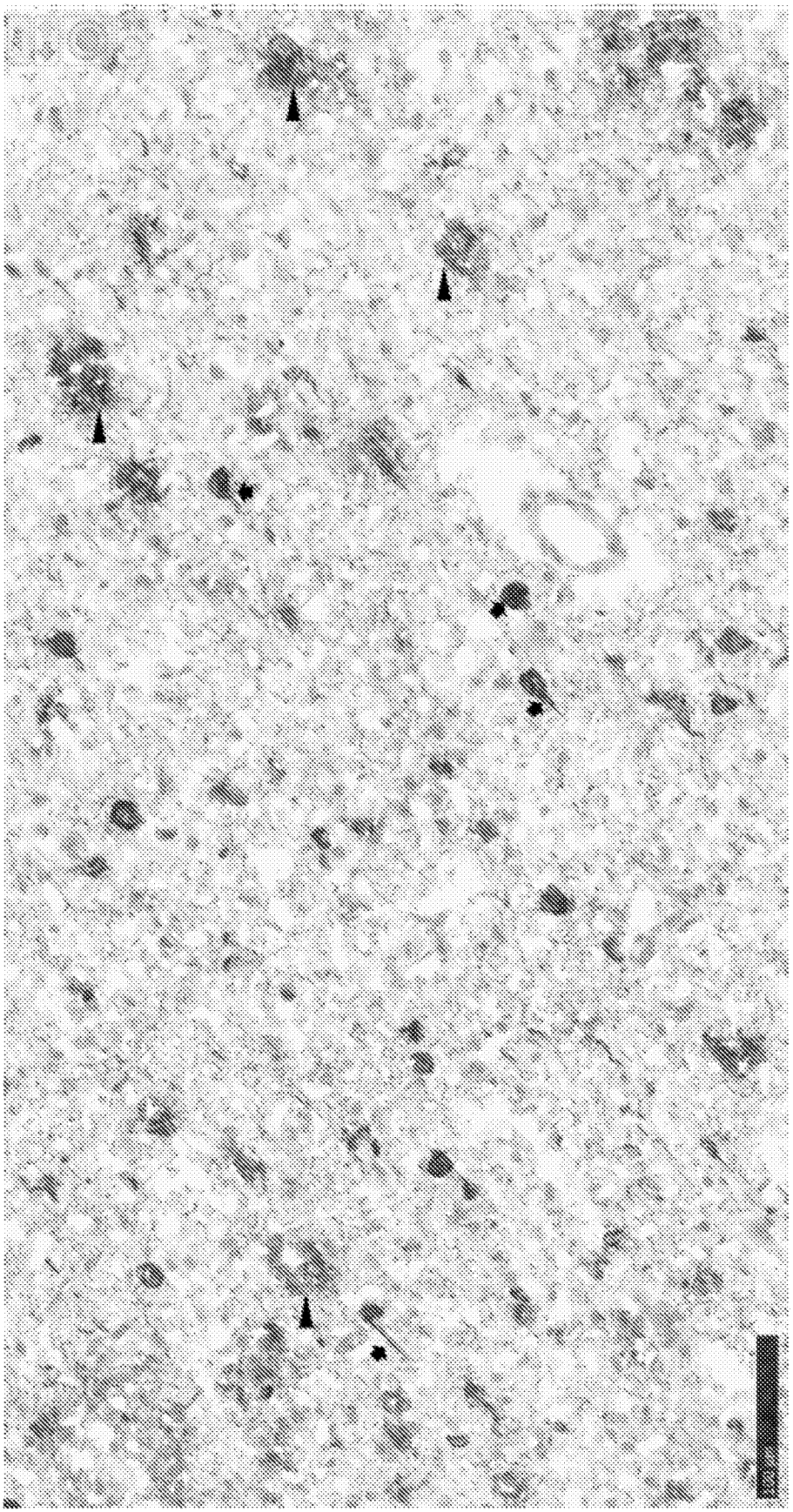
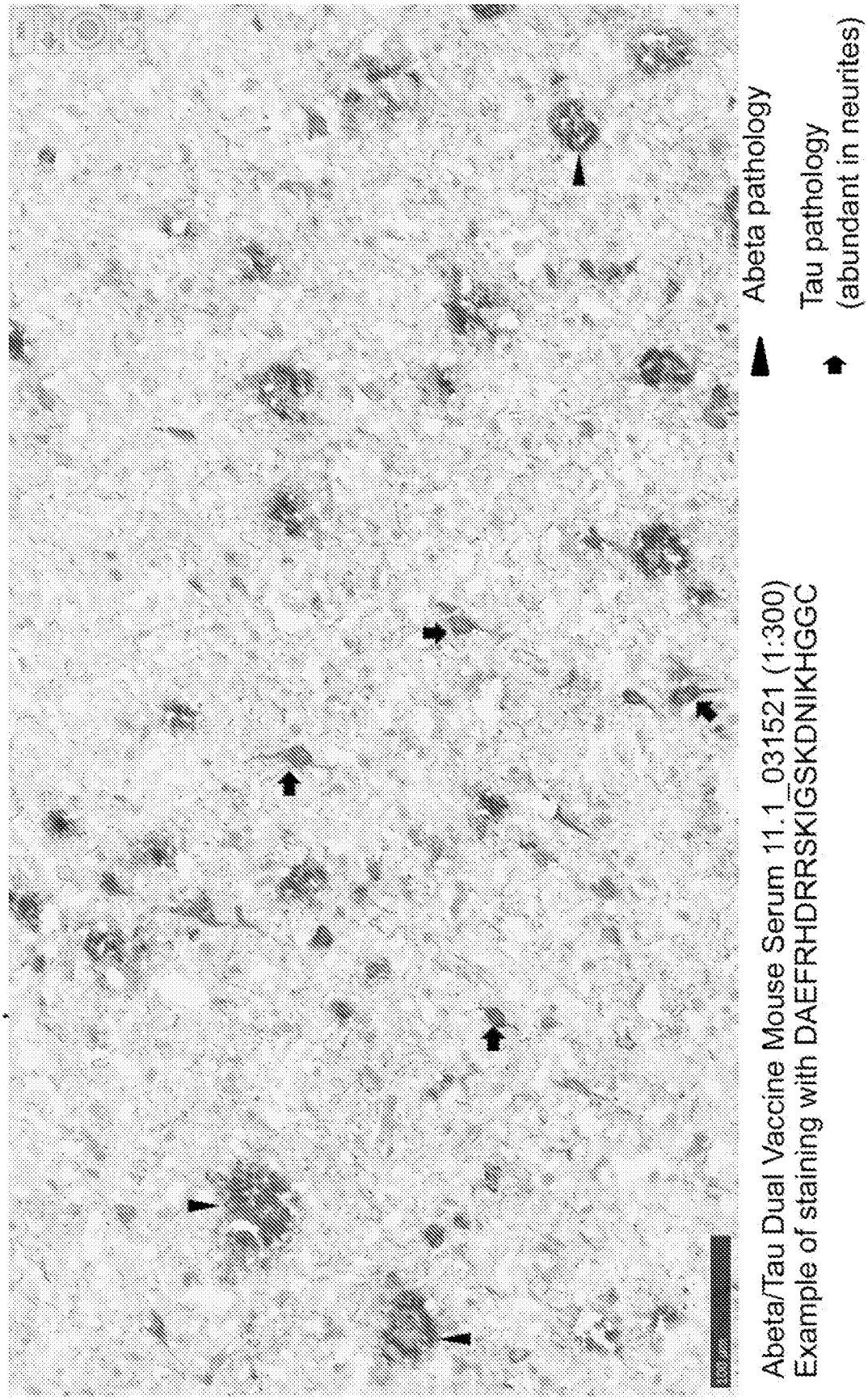

Abeta pathology
Tau pathology
(abundant in neurites)
Abeta/Tau Dual Vaccine Mouse Serum 9.2_031521 (1:300)
Example of staining with DAEFRHDRRENLKHQPGGGC

FIG. 16E


Abeta pathology
Tau pathology
(abundant in neurites)
Abeta/Tau Dual Vaccine Mouse Serum 11.1_031521 (1:300)
Example of staining with DAEFRHDRRSKIGSKDNIKHGGC

SEQUENCE LISTING

<110> Othair Biosciences Limited

<120> MULTIEPITOPE VACCINE FOR THE TREATMENT

<130> 20-050-WO (763-WO)

<150> US 63/140,917
<151> 2021-01-24

<150> US 63/062,903
<151> 2020-08-07

<150> US 63/027,150
<151> 2020-05-19

<160> 1063

<170> PatentIn version 3.5

<210> 1
<211> 42
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1

Asp Ala Glu Phe Arg His Asp Ser Gly Tyr Glu Val His His Gln Lys
1 5 10 15

Leu Val Phe Phe Ala Glu Asp Val Gly Ser Asn Lys Gly Ala Ile Ile
20 25 30

Gly Leu Met Val Gly Gly Val Val Ile Ala
35 40

<210> 2
<211> 441
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 2

Met Ala Glu Pro Arg Gln Glu Phe Glu Val Met Glu Asp His Ala Gly

```
1               5                   10                  15

Thr Tyr Gly Leu Gly Asp Arg Lys Asp Gln Gly Gly Tyr Thr Met His
            20                  25                  30

Gln Asp Gln Glu Gly Asp Thr Asp Ala Gly Leu Lys Glu Ser Pro Leu
        35                  40                  45

Gln Thr Pro Thr Glu Asp Gly Ser Glu Glu Pro Gly Ser Glu Thr Ser
    50                  55                  60

Asp Ala Lys Ser Thr Pro Thr Ala Glu Asp Val Thr Ala Pro Leu Val
65                  70                  75                  80

Asp Glu Gly Ala Pro Gly Lys Gln Ala Ala Ala Gln Pro His Thr Glu
                85                  90                  95

Ile Pro Glu Gly Thr Thr Ala Glu Glu Ala Gly Ile Gly Asp Thr Pro
            100                 105                 110

Ser Leu Glu Asp Glu Ala Ala Gly His Val Thr Gln Ala Arg Met Val
        115                 120                 125

Ser Lys Ser Lys Asp Gly Thr Gly Ser Asp Asp Lys Lys Ala Lys Gly
    130                 135                 140

Ala Asp Gly Lys Thr Lys Ile Ala Thr Pro Arg Gly Ala Ala Pro Pro
145                 150                 155                 160

Gly Gln Lys Gly Gln Ala Asn Ala Thr Arg Ile Pro Ala Lys Thr Pro
                165                 170                 175

Pro Ala Pro Lys Thr Pro Pro Ser Ser Gly Glu Pro Pro Lys Ser Gly
            180                 185                 190

Asp Arg Ser Gly Tyr Ser Ser Pro Gly Ser Pro Gly Thr Pro Gly Ser
        195                 200                 205

Arg Ser Arg Thr Pro Ser Leu Pro Thr Pro Pro Thr Arg Glu Pro Lys
    210                 215                 220
```

```
Lys Val Ala Val Val Arg Thr Pro Pro Lys Ser Pro Ser Ser Ala Lys
225                 230                 235                 240


Ser Arg Leu Gln Thr Ala Pro Val Pro Met Pro Asp Leu Lys Asn Val
                245                 250                 255


Lys Ser Lys Ile Gly Ser Thr Glu Asn Leu Lys His Gln Pro Gly Gly
            260                 265                 270


Gly Lys Val Gln Ile Ile Asn Lys Lys Leu Asp Leu Ser Asn Val Gln
        275                 280                 285


Ser Lys Cys Gly Ser Lys Asp Asn Ile Lys His Val Pro Gly Gly Gly
    290                 295                 300


Ser Val Gln Ile Val Tyr Lys Pro Val Asp Leu Ser Lys Val Thr Ser
305                 310                 315                 320


Lys Cys Gly Ser Leu Gly Asn Ile His His Lys Pro Gly Gly Gly Gln
                325                 330                 335


Val Glu Val Lys Ser Glu Lys Leu Asp Phe Lys Asp Arg Val Gln Ser
            340                 345                 350


Lys Ile Gly Ser Leu Asp Asn Ile Thr His Val Pro Gly Gly Gly Asn
        355                 360                 365


Lys Lys Ile Glu Thr His Lys Leu Thr Phe Arg Glu Asn Ala Lys Ala
    370                 375                 380


Lys Thr Asp His Gly Ala Glu Ile Val Tyr Lys Ser Pro Val Val Ser
385                 390                 395                 400


Gly Asp Thr Ser Pro Arg His Leu Ser Asn Val Ser Ser Thr Gly Ser
                405                 410                 415


Ile Asp Met Val Asp Ser Pro Gln Leu Ala Thr Leu Ala Asp Glu Val
            420                 425                 430


Ser Ala Ser Leu Ala Lys Gln Gly Leu
```

435 440

<210> 3
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 3

Asp Ala Glu Phe Arg His Asp Ser Gly Tyr
1 5 10

<210> 4
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 4

Asp Ala Glu Phe Arg His Asp Ser Gly
1 5

<210> 5
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 5

Asp Ala Glu Phe Arg His Asp Ser
1 5

<210> 6
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 6

Asp Ala Glu Phe Arg His Asp
1 5

<210> 7
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 7

Asp Ala Glu Phe Arg His
1 5

<210> 8
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 8

Asp Ala Glu Phe Arg
1 5

<210> 9
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 9

Asp Ala Glu Phe
1

<210> 10
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 10

Asp Ala Glu
1

<210> 11
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 11

Ala Glu Phe Arg His Asp Ser Gly Tyr
1 5

<210> 12
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 12

Ala Glu Phe Arg His Asp Ser Gly
1 5

<210> 13
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 13

Ala Glu Phe Arg His Asp Ser
1 5

<210> 14
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 14

Ala Glu Phe Arg His Asp
1   5

<210> 15
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 15

Ala Glu Phe Arg His
1   5

<210> 16
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 16

Ala Glu Phe Arg
1

<210> 17
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 17

Ala Glu Phe
1

<210> 18
<211> 8
<212> PRT

<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 18

Glu Phe Arg His Asp Ser Gly Tyr
1 5

<210> 19
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 19

Glu Phe Arg His Asp Ser Gly
1 5

<210> 20
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 20

Glu Phe Arg His Asp Ser
1 5

<210> 21
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 21

Glu Phe Arg His Asp
1 5

<210> 22

<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 22

Glu Phe Arg His
1

<210> 23
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 23

Glu Phe Arg
1

<210> 24
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 24

Phe Arg His Asp Ser Gly Tyr
1 5

<210> 25
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 25

Phe Arg His Asp Ser Gly
1 5

<210> 26
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 26

Phe Arg His Asp Ser
1   5

<210> 27
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 27

Phe Arg His Asp
1

<210> 28
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 28

Phe Arg His
1

<210> 29
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 29

Arg His Asp Ser Gly Tyr

1 5

<210> 30
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 30

Arg His Asp Ser Gly
1 5

<210> 31
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 31

Arg His Asp Ser
1

<210> 32
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 32

Arg His Asp
1

<210> 33
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 33

His Asp Ser Gly Tyr
1   5

<210> 34
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 34

His Asp Ser Gly
1

<210> 35
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 35

His Asp Ser
1

<210> 36
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 36

Asp Ser Gly Tyr
1

<210> 37
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 37

Asp Ser Gly
1

<210> 38
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 38

Ser Gly Tyr
1

<210> 39
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 39

Gln Ile Val Tyr Lys Pro Val
1 5

<210> 40
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 40

Gln Ile Val Tyr Lys Pro
1 5

<210> 41
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 41

Gln Ile Val Tyr Lys Ser Val
1   5

<210> 42
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 42

Glu Ile Val Tyr Lys Ser Val
1   5

<210> 43
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 43

Glu Ile Val Tyr Lys Ser Pro
1   5

<210> 44
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 44

Glu Ile Val Tyr Lys Pro Val
1   5

<210> 45
<211> 7
<212> PRT

<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 45

Ile Val Tyr Lys Ser Pro Val
1 5

<210> 46
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 46

Ile Val Tyr Lys
1

<210> 47
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 47

Cys Asn Ile Lys His Val Pro
1 5

<210> 48
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 48

Asn Ile Lys His Val Pro
1 5

<210> 49

<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 49

His Val Pro Gly Gly Gly
1   5

<210> 50
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 50

His Val Pro Gly Gly
1   5

<210> 51
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 51

His Lys Pro Gly Gly Gly
1   5

<210> 52
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 52

His Lys Pro Gly Gly
1   5

<210> 53
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 53

Lys His Val Pro Gly Gly Gly
1   5

<210> 54
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 54

Lys His Val Pro Gly Gly
1   5

<210> 55
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 55

His Gln Pro Gly Gly Gly
1   5

<210> 56
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 56

His Gln Pro Gly Gly

1 5

<210> 57
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 57

Asp Ala Glu Phe Arg His Asp Arg Arg Gln Ile Val Tyr Lys Pro Val
1 5 10 15

<210> 58
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 58

Asp Ala Glu Phe Arg His Asp Arg Arg Glu Ile Val Tyr Lys Ser Val
1 5 10 15

<210> 59
<211> 19
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 59

Asp Ala Glu Phe Arg His Asp Arg Arg Gln Ile Val Tyr Lys Pro Val
1 5 10 15

Gly Gly Cys

<210> 60
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 60

Asp Ala Glu Phe Arg His Asp Arg Arg Gln Ile Val Tyr Lys Pro Val
1   5   10   15

Cys

<210> 61
<211> 19
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 61

Asp Ala Glu Phe Arg His Asp Arg Arg Gln Ile Val Tyr Lys Pro Val
1   5   10   15

Ala Ala Cys

<210> 62
<211> 19
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 62

Asp Ala Glu Phe Arg His Asp Arg Arg Gln Ile Val Tyr Lys Pro Val
1   5   10   15

Lys Lys Cys

<210> 63
<211> 19
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 63

Asp Ala Glu Phe Arg His Asp Arg Arg Glu Ile Val Tyr Lys Ser Pro
1   5   10   15

Gly Gly Cys

<210> 64
<211> 19
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 64

Asp Ala Glu Phe Arg His Asp Arg Arg Glu Ile Val Tyr Lys Ser Pro
1   5   10   15

Ala Ala Cys

<210> 65
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 65

Asp Ala Glu Phe Arg His Asp Arg Arg Glu Ile Val Tyr Lys Ser Pro
1   5   10   15

Cys

<210> 66
<211> 19
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 66

Asp Ala Glu Phe Arg His Asp Arg Arg Glu Ile Val Tyr Lys Ser Pro
1   5   10   15

Lys Lys Cys

<210> 67
<211> 28
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 67

Asp Ala Glu Phe Arg His Asp Ser Gly Tyr Glu Val His His Gln Lys
1   5   10   15

Leu Phe Phe Ala Glu Asp Val Gly Ser Asn Lys Gly
            20   25

<210> 68
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 68

Gly Gly Gly Ser Val Gln Ile Val Tyr Lys Pro Val Asp Leu Ser
1   5   10   15

<210> 69
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 69

Arg Val Arg Arg
1

<210> 70
<211> 19
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<220>
<221> MISC_FEATURE
<222> (17)..(18)
<223> Xaa Xaa can be GG or AA or KK or SS

<400> 70

Asp Ala Glu Phe Arg His Asp Arg Arg Gln Ile Val Tyr Lys Pro Val
1 5 10 15

Xaa Xaa Cys

<210> 71
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 71

Asp Ala Glu Phe Arg His Asp Cys
1 5

<210> 72
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 72

Gln Ile Val Tyr Lys Pro Val Gly Gly Cys

1 5 10

<210> 73
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 73

Gly Gly Ser Gln Ile Val Tyr Lys Pro Val Asp Leu Ser
1 5 10

<210> 74
<211> 19
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 74

Asp Ala Glu Phe Arg His Asp Arg Arg Glu Ile Val Tyr Lys Ser Val
1 5 10 15

Gly Gly Cys

<210> 75
<211> 19
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 75

Asp Ala Glu Phe Arg His Asp Arg Arg Glu Ile Val Tyr Lys Ser Val
1 5 10 15

Ala Ala Cys

<210> 76

<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 76

Asp Ala Glu Phe Arg His Asp Arg Arg Glu Ile Val Tyr Lys Ser Val
1 5 10 15

Cys

<210> 77
<211> 19
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 77

Asp Ala Glu Phe Arg His Asp Arg Arg Glu Ile Val Tyr Lys Ser Val
1 5 10 15

Lys Lys Cys

<210> 78
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 78

Asp Ala Glu Phe Arg His Asp Arg Arg Asn Ile Lys His Val Pro Gly
1 5 10 15

Gly Cys

<210> 79

<211> 19
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<220>
<221> MISC_FEATURE
<222> (17)..(18)
<223> Xaa Xaa can be GG or AA or KK or SS

<400> 79

Asp Ala Glu Phe Arg His Asp Arg Arg Glu Ile Val Tyr Lys Ser Val
1 5 10 15

Xaa Xaa Cys

<210> 80
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 80

Gly Ala Gly Ala
1

<210> 81
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 81

Ala Gly Ala Gly
1

<210> 82
<211> 4
<212> PRT

<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 82

Lys Gly Lys Gly
1

<210> 83
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 83

Gln Ile Val Tyr Lys Ser
1 5

<210> 84
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 84

Glu Ile Val Tyr Lys Ser
1 5

<210> 85
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 85

Glu Ile Val Tyr Lys Pro
1 5

<210> 86

<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 86

Cys Asn Ile Lys His Val Pro Gly
1 5

<210> 87

<400> 87
000

<210> 88

<400> 88
000

<210> 89

<400> 89
000

<210> 90

<400> 90
000

<210> 91

<400> 91
000

<210> 92

<400> 92
000

<210> 93

<400> 93
000

<210> 94

<400> 94
000

<210> 95

<400> 95
000

<210> 96

<400> 96
000

<210> 97

<400> 97
000

<210> 98

<400> 98
000

<210> 99

<400> 99
000

<210> 100

<400> 100
000

<210> 101

<400> 101
000

<210> 102

<400> 102
000

<210> 103

<400> 103
000

<210> 104

<400> 104
000

<210> 105

<400> 105
000

<210> 106

<400> 106
000

<210> 107

<400> 107
000

<210> 108

<400> 108
000

<210> 109

<400> 109
000

<210> 110

<400> 110
000

<210> 111

<400> 111
000

<210> 112

<400> 112
000

<210> 113

<400> 113
000

<210> 114

<400> 114
000

<210> 115

<400> 115
000

<210> 116

<400> 116
000

<210> 117

<400> 117
000

<210> 118

<400> 118
000

<210> 119

<400> 119
000

<210> 120

<400> 120
000

<210> 121

<400> 121
000

<210> 122

<400> 122
000

<210> 123

<400> 123
000

<210> 124

<400> 124
000

<210> 125

<400> 125
000

<210> 126

<400> 126
000

<210> 127

<400> 127

000

<210> 128

<400> 128
000

<210> 129

<400> 129
000

<210> 130

<400> 130
000

<210> 131

<400> 131
000

<210> 132

<400> 132
000

<210> 133

<400> 133
000

<210> 134

<400> 134
000

<210> 135

<400> 135
000

<210> 136

<400> 136
000

<210> 137

<400> 137
000

<210> 138

<400> 138
000

<210> 139

<400> 139
000

<210> 140

<400> 140
000

<210> 141

<400> 141
000

<210> 142

<400> 142
000

<210> 143

<400> 143
000

<210> 144

<400> 144
000

<210> 145

<400> 145
000

<210> 146
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 146

Val Gln Ile Ile Asn Lys
1 5

<210> 147
<211> 7

<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 147

Val Gln Ile Ile Asn Lys Lys
1   5

<210> 148
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 148

Val Gln Ile Ile Asn Lys Lys Leu
1   5

<210> 149
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 149

Gln Ile Ile Asn Lys
1   5

<210> 150
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 150

Gln Ile Ile Asn Lys Lys
1   5

<210> 151
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 151

Gln Ile Ile Asn Lys Lys Leu
1 5

<210> 152
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 152

Glu Ala Ala Gly His Val Thr Gln Cys
1 5

<210> 153
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 153

Glu Ala Ala Gly His Val Thr Gln Ala Arg
1 5 10

<210> 154
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 154

Ala Ala Gly His Val Thr Gln Ala Cys
1 5

<210> 155
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 155

Ala Gly His Val Thr Gln Ala Arg Cys
1 5

<210> 156
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 156

Ala Gly His Val Thr Gln Ala Arg
1 5

<210> 157
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 157

Gly Tyr Thr Met His Gln Asp
1 5

<210> 158
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 158

Gln Gly Gly Tyr Thr Met His Cys
1 5

<210> 159
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 159

Gln Gly Gly Tyr Thr Met His Gln Asp
1 5

<210> 160
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 160

Gly Gly Tyr Thr Met His Gln Cys
1 5

<210> 161
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 161

Val Pro Gly Gly Gly Ser Val Gln Ile Val
1 5 10

<210> 162
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 162

Pro Gly Gly Gly Ser Val Gln Ile Val
1 5

<210> 163
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 163

Gly Gly Gly Ser Val Gln Ile Val
1 5

<210> 164
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 164

Gly Gly Ser Val Gln Ile Val
1 5

<210> 165
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 165

Gly Ser Val Gln Ile Val
1 5

<210> 166
<211> 5
<212> PRT
<213> Artificial Sequence

<220>

<223> Synthetic peptide

<400> 166

Ser Val Gln Ile Val
1   5

<210> 167
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 167

Val Gln Ile Val
1

<210> 168
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 168

Gln Ile Val
1

<210> 169
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 169

Pro Gly Gly Gly Ser Val Gln Ile Val Tyr
1   5   10

<210> 170
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 170

Gly Gly Gly Ser Val Gln Ile Val Tyr
1   5

<210> 171
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 171

Gly Gly Ser Val Gln Ile Val Tyr
1   5

<210> 172
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 172

Gly Ser Val Gln Ile Val Tyr
1   5

<210> 173
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 173

Ser Val Gln Ile Val Tyr
1   5

<210> 174
<211> 5

<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 174

Val Gln Ile Val Tyr
1 5

<210> 175
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 175

Gln Ile Val Tyr
1

<210> 176
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 176

Ile Val Tyr
1

<210> 177
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 177

Gly Gly Gly Ser Val Gln Ile Val Tyr Lys
1 5 10

<210> 178
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 178

Gly Gly Ser Val Gln Ile Val Tyr Lys
1 5

<210> 179
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 179

Gly Ser Val Gln Ile Val Tyr Lys
1 5

<210> 180
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 180

Ser Val Gln Ile Val Tyr Lys
1 5

<210> 181
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 181

Val Gln Ile Val Tyr Lys
1 5

<210> 182
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 182

Gln Ile Val Tyr Lys
1   5

<210> 183
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 183

Val Tyr Lys
1

<210> 184
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 184

Gly Gly Ser Val Gln Ile Val Tyr Lys Pro
1   5   10

<210> 185
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 185

Gly Ser Val Gln Ile Val Tyr Lys Pro
1   5

<210> 186
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 186

Ser Val Gln Ile Val Tyr Lys Pro
1   5

<210> 187
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 187

Val Gln Ile Val Tyr Lys Pro
1   5

<210> 188
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 188

Ile Val Tyr Lys Pro
1   5

<210> 189
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 189

Val Tyr Lys Pro
1

<210> 190
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 190

Tyr Lys Pro
1

<210> 191
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 191

Gly Ser Val Gln Ile Val Tyr Lys Pro Val
1 5 10

<210> 192
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 192

Ser Val Gln Ile Val Tyr Lys Pro Val
1 5

<210> 193
<211> 8
<212> PRT
<213> Artificial Sequence

<220>

<223> Synthetic peptide

<400> 193

Val Gln Ile Val Tyr Lys Pro Val
1   5

<210> 194
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 194

Ile Val Tyr Lys Pro Val
1   5

<210> 195
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 195

Val Tyr Lys Pro Val
1   5

<210> 196
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 196

Tyr Lys Pro Val
1

<210> 197
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 197

Lys Pro Val
1

<210> 198
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 198

Ser Val Gln Ile Val Tyr Lys Pro Val Asp
1   5   10

<210> 199
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 199

Val Gln Ile Val Tyr Lys Pro Val Asp
1   5

<210> 200
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 200

Gln Ile Val Tyr Lys Pro Val Asp
1   5

<210> 201
<211> 7

<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 201

Ile Val Tyr Lys Pro Val Asp
1   5

<210> 202

<400> 202
000

<210> 203
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 203

Val Tyr Lys Pro Val Asp
1   5

<210> 204
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 204

Tyr Lys Pro Val Asp
1   5

<210> 205
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 205

Lys Pro Val Asp
1

<210> 206
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 206

Pro Val Asp
1

<210> 207
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 207

Val Gln Ile Val Tyr Lys Pro Val Asp Leu
1   5   10

<210> 208
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 208

Gln Ile Val Tyr Lys Pro Val Asp Leu
1   5

<210> 209
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 209

Ile Val Tyr Lys Pro Val Asp Leu
1 5

<210> 210
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 210

Val Tyr Lys Pro Val Asp Leu
1 5

<210> 211
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 211

Tyr Lys Pro Val Asp Leu
1 5

<210> 212
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 212

Lys Pro Val Asp Leu
1 5

<210> 213
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 213

Pro Val Asp Leu
1

<210> 214
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 214

Val Asp Leu
1

<210> 215
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 215

Gln Ile Val Tyr Lys Pro Val Asp Leu Ser
1   5   10

<210> 216
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 216

Ile Val Tyr Lys Pro Val Asp Leu Ser
1   5

<210> 217
<211> 8
<212> PRT

<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 217

Val Tyr Lys Pro Val Asp Leu Ser
1   5

<210> 218
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 218

Tyr Lys Pro Val Asp Leu Ser
1   5

<210> 219
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 219

Lys Pro Val Asp Leu Ser
1   5

<210> 220
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 220

Pro Val Asp Leu Ser
1   5

<210> 221

<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 221

Val Asp Leu Ser
1

<210> 222
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 222

Asp Leu Ser
1

<210> 223
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 223

Ile Val Tyr Lys Pro Val Asp Leu Ser Lys
1   5   10

<210> 224
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 224

Val Tyr Lys Pro Val Asp Leu Ser Lys
1   5

<210> 225
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 225

Tyr Lys Pro Val Asp Leu Ser Lys
1   5

<210> 226
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 226

Lys Pro Val Asp Leu Ser Lys
1   5

<210> 227
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 227

Pro Val Asp Leu Ser Lys
1   5

<210> 228
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 228

Val Asp Leu Ser Lys

1 5

<210> 229
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 229

Asp Leu Ser Lys
1

<210> 230
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 230

Leu Ser Lys
1

<210> 231
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 231

Val Tyr Lys Pro Val Asp Leu Ser Lys Val
1 5 10

<210> 232
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 232

Tyr Lys Pro Val Asp Leu Ser Lys Val
1   5

<210> 233
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 233

Lys Pro Val Asp Leu Ser Lys Val
1   5

<210> 234
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 234

Pro Val Asp Leu Ser Lys Val
1   5

<210> 235
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 235

Val Asp Leu Ser Lys Val
1   5

<210> 236
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 236

Asp Leu Ser Lys Val
1 5

<210> 237
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 237

Leu Ser Lys Val
1

<210> 238
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 238

Ser Lys Val
1

<210> 239
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 239

Tyr Lys Pro Val Asp Leu Ser Lys Val Thr
1 5 10

<210> 240
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 240

Lys Pro Val Asp Leu Ser Lys Val Thr
1   5

<210> 241
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 241

Pro Val Asp Leu Ser Lys Val Thr
1   5

<210> 242
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 242

Val Asp Leu Ser Lys Val Thr
1   5

<210> 243
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 243

Ala Lys Thr Asp His Gly Ala Glu Ile Val
1   5   10

<210> 244
<211> 9
<212> PRT

<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 244

Lys Thr Asp His Gly Ala Glu Ile Val
1 5

<210> 245
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 245

Thr Asp His Gly Ala Glu Ile Val
1 5

<210> 246
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 246

Asp His Gly Ala Glu Ile Val
1 5

<210> 247
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 247

His Gly Ala Glu Ile Val
1 5

<210> 248

<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 248

Gly Ala Glu Ile Val
1 5

<210> 249
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 249

Ala Glu Ile Val
1

<210> 250
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 250

Glu Ile Val
1

<210> 251
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 251

Lys Thr Asp His Gly Ala Glu Ile Val Tyr
1 5 10

<210> 252
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 252

Thr Asp His Gly Ala Glu Ile Val Tyr
1   5

<210> 253
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 253

Asp His Gly Ala Glu Ile Val Tyr
1   5

<210> 254
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 254

His Gly Ala Glu Ile Val Tyr
1   5

<210> 255
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 255

Gly Ala Glu Ile Val Tyr

1 5

<210> 256
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 256

Ala Glu Ile Val Tyr
1 5

<210> 257
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 257

Glu Ile Val Tyr
1

<210> 258
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 258

Ile Val Tyr
1

<210> 259
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 259

Thr Asp His Gly Ala Glu Ile Val Tyr Lys
1   5   10

<210> 260
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 260

Asp His Gly Ala Glu Ile Val Tyr Lys
1   5

<210> 261
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 261

His Gly Ala Glu Ile Val Tyr Lys
1   5

<210> 262
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 262

Gly Ala Glu Ile Val Tyr Lys
1   5

<210> 263
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 263

Ala Glu Ile Val Tyr Lys
1 5

<210> 264
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 264

Glu Ile Val Tyr Lys
1 5

<210> 265
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 265

Ile Val Tyr Lys
1

<210> 266
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 266

Asp His Gly Ala Glu Ile Val Tyr Lys Ser
1 5 10

<210> 267
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 267

His Gly Ala Glu Ile Val Tyr Lys Ser
1   5

<210> 268
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 268

Gly Ala Glu Ile Val Tyr Lys Ser
1   5

<210> 269
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 269

Ala Glu Ile Val Tyr Lys Ser
1   5

<210> 270
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 270

Glu Ile Val Tyr Lys Ser
1   5

<210> 271
<211> 5
<212> PRT

<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 271

Ile Val Tyr Lys Ser
1 5

<210> 272
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 272

Val Tyr Lys Ser
1

<210> 273
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 273

Tyr Lys Ser
1

<210> 274
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 274

His Gly Ala Glu Ile Val Tyr Lys Ser Pro
1 5 10

<210> 275

<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 275

Gly Ala Glu Ile Val Tyr Lys Ser Pro
1   5

<210> 276
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 276

Ala Glu Ile Val Tyr Lys Ser Pro
1   5

<210> 277
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 277

Glu Ile Val Tyr Lys Ser Pro
1   5

<210> 278
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 278

Ile Val Tyr Lys Ser Pro
1   5

<210> 279
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 279

Val Tyr Lys Ser Pro
1   5

<210> 280
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 280

Tyr Lys Ser Pro
1

<210> 281
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 281

Lys Ser Pro
1

<210> 282
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 282

Gly Ala Glu Ile Val Tyr Lys Ser Pro Val

1 5 10

<210> 283
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 283

Ala Glu Ile Val Tyr Lys Ser Pro Val
1 5

<210> 284
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 284

Glu Ile Val Tyr Lys Ser Pro Val
1 5

<210> 285
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 285

Ile Val Tyr Lys Ser Pro Val
1 5

<210> 286
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 286

Val Tyr Lys Ser Pro Val
1   5

<210> 287
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 287

Tyr Lys Ser Pro Val
1   5

<210> 288
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 288

Lys Ser Pro Val
1

<210> 289
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 289

Ser Pro Val
1

<210> 290
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 290

Ala Glu Ile Val Tyr Lys Ser Pro Val Val
1 5 10

<210> 291
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 291

Glu Ile Val Tyr Lys Ser Pro Val Val
1 5

<210> 292
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 292

Ile Val Tyr Lys Ser Pro Val Val
1 5

<210> 293
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 293

Val Tyr Lys Ser Pro Val Val
1 5

<210> 294
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 294

Tyr Lys Ser Pro Val Val
1   5

<210> 295
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 295

Lys Ser Pro Val Val
1   5

<210> 296
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 296

Ser Pro Val Val
1

<210> 297
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 297

Pro Val Val
1

<210> 298
<211> 10
<212> PRT

<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 298

Glu Ile Val Tyr Lys Ser Pro Val Val Ser
1 5 10

<210> 299
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 299

Ile Val Tyr Lys Ser Pro Val Val Ser
1 5

<210> 300
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 300

Val Tyr Lys Ser Pro Val Val Ser
1 5

<210> 301
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 301

Tyr Lys Ser Pro Val Val Ser
1 5

<210> 302

<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 302

Lys Ser Pro Val Val Ser
1   5

<210> 303
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 303

Ser Pro Val Val Ser
1   5

<210> 304
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 304

Pro Val Val Ser
1

<210> 305
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 305

Val Val Ser
1

<210> 306
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 306

Ile Val Tyr Lys Ser Pro Val Val Ser Gly
1   5   10

<210> 307
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 307

Val Tyr Lys Ser Pro Val Val Ser Gly
1   5

<210> 308
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 308

Tyr Lys Ser Pro Val Val Ser Gly
1   5

<210> 309
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 309

Lys Ser Pro Val Val Ser Gly

1 5

<210> 310
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 310

Ser Pro Val Val Ser Gly
1 5

<210> 311
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 311

Pro Val Val Ser Gly
1 5

<210> 312
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 312

Val Val Ser Gly
1

<210> 313
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 313

Val Ser Gly
1

<210> 314
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 314

Val Tyr Lys Ser Pro Val Val Ser Gly Asp
1 5 10

<210> 315
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 315

Tyr Lys Ser Pro Val Val Ser Gly Asp
1 5

<210> 316
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 316

Lys Ser Pro Val Val Ser Gly Asp
1 5

<210> 317
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 317

Ser Pro Val Val Ser Gly Asp
1   5

<210> 318
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 318

Pro Val Val Ser Gly Asp
1   5

<210> 319
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 319

Val Val Ser Gly Asp
1   5

<210> 320
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 320

Val Ser Gly Asp
1

<210> 321
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 321

Ser Gly Asp
1

<210> 322
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 322

Tyr Lys Ser Pro Val Val Ser Gly Asp Thr
1   5   10

<210> 323
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 323

Lys Ser Pro Val Val Ser Gly Asp Thr
1   5

<210> 324
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 324

Ser Pro Val Val Ser Gly Asp Thr
1   5

<210> 325
<211> 7
<212> PRT

<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 325

Pro Val Val Ser Gly Asp Thr
1   5

<210> 326
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 326

Val Val Ser Gly Asp Thr
1   5

<210> 327
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 327

Val Ser Gly Asp Thr
1   5

<210> 328
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 328

Ser Gly Asp Thr
1

<210> 329

<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 329

Gly Asp Thr
1

<210> 330
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 330

Lys Ser Pro Val Val Ser Gly Asp Thr Ser
1   5   10

<210> 331
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 331

Ser Pro Val Val Ser Gly Asp Thr Ser
1   5

<210> 332
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 332

Pro Val Val Ser Gly Asp Thr Ser
1   5

<210> 333
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 333

Val Val Ser Gly Asp Thr Ser
1   5

<210> 334
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 334

Val Ser Gly Asp Thr Ser
1   5

<210> 335
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 335

Ser Gly Asp Thr Ser
1   5

<210> 336
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 336

Gly Asp Thr Ser

1

<210> 337
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 337

Asp Thr Ser
1

<210> 338
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 338

Ser Pro Val Val Ser Gly Asp Thr Ser Pro
1   5   10

<210> 339
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 339

Pro Val Val Ser Gly Asp Thr Ser Pro
1   5

<210> 340
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 340

Val Val Ser Gly Asp Thr Ser Pro
1   5

<210> 341
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 341

Val Ser Gly Asp Thr Ser Pro
1   5

<210> 342
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 342

Ser Gly Asp Thr Ser Pro
1   5

<210> 343
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 343

Gly Asp Thr Ser Pro
1   5

<210> 344
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 344

Asp Thr Ser Pro
1

<210> 345
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 345

Thr Ser Pro
1

<210> 346
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 346

Pro Val Val Ser Gly Asp Thr Ser Pro Arg
1 5 10

<210> 347
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 347

Val Val Ser Gly Asp Thr Ser Pro Arg
1 5

<210> 348
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 348

Val Ser Gly Asp Thr Ser Pro Arg
1   5

<210> 349
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 349

Ser Gly Asp Thr Ser Pro Arg
1   5

<210> 350
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 350

Gly Asp Thr Ser Pro Arg
1   5

<210> 351
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 351

Asp Thr Ser Pro Arg
1   5

<210> 352
<211> 4
<212> PRT

<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 352

Thr Ser Pro Arg
1

<210> 353
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 353

Ser Pro Arg
1

<210> 354
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 354

His Gln Pro Gly Gly Gly Lys Val Gln Ile
1 5 10

<210> 355
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 355

Gln Pro Gly Gly Gly Lys Val Gln Ile
1 5

<210> 356

<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 356

Pro Gly Gly Gly Lys Val Gln Ile
1 5

<210> 357
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 357

Gly Gly Gly Lys Val Gln Ile
1 5

<210> 358
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 358

Gly Gly Lys Val Gln Ile
1 5

<210> 359
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 359

Gly Lys Val Gln Ile
1 5

<210> 360
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 360

Lys Val Gln Ile
1

<210> 361
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 361

Val Gln Ile
1

<210> 362
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 362

Gln Pro Gly Gly Gly Lys Val Gln Ile Ile
1   5   10

<210> 363
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 363

Pro Gly Gly Gly Lys Val Gln Ile Ile

1 5

<210> 364
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 364

Ser Val Asp Leu Ser Lys
1 5

<210> 365
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 365

Gly Gly Gly Lys Val Gln Ile Ile
1 5

<210> 366
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 366

Gly Gly Lys Val Gln Ile Ile
1 5

<210> 367
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 367

Gly Lys Val Gln Ile Ile
1   5

<210> 368
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 368

Lys Val Gln Ile Ile
1   5

<210> 369
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 369

Val Gln Ile Ile
1

<210> 370
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 370

Gln Ile Ile
1

<210> 371
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 371

Pro Gly Gly Gly Lys Val Gln Ile Ile Asn
1 5 10

<210> 372
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 372

Gly Gly Gly Lys Val Gln Ile Ile Asn
1 5

<210> 373
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 373

Gly Gly Lys Val Gln Ile Ile Asn
1 5

<210> 374
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 374

Gly Lys Val Gln Ile Ile Asn
1 5

<210> 375
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 375

Lys Val Gln Ile Ile Asn
1   5

<210> 376
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 376

Val Gln Ile Ile Asn
1   5

<210> 377
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 377

Gln Ile Ile Asn
1

<210> 378
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 378

Ile Ile Asn
1

<210> 379
<211> 10
<212> PRT

<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 379

Gly Gly Gly Lys Val Gln Ile Ile Asn Lys
1 5 10

<210> 380
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 380

Gly Gly Lys Val Gln Ile Ile Asn Lys
1 5

<210> 381
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 381

Gly Lys Val Gln Ile Ile Asn Lys
1 5

<210> 382
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 382

Lys Val Gln Ile Ile Asn Lys
1 5

<210> 383

<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 383

Ile Ile Asn Lys
1

<210> 384
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 384

Ile Asn Lys
1

<210> 385
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 385

Gly Gly Lys Val Gln Ile Ile Asn Lys Lys
1   5   10

<210> 386
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 386

Gly Lys Val Gln Ile Ile Asn Lys Lys
1   5

<210> 387
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 387

Lys Val Gln Ile Ile Asn Lys Lys
1   5

<210> 388
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 388

Ile Ile Asn Lys Lys
1   5

<210> 389
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 389

Ile Asn Lys Lys
1

<210> 390
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 390

Asn Lys Lys

1

<210> 391
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 391

Gly Lys Val Gln Ile Ile Asn Lys Lys Leu
1 5 10

<210> 392
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 392

Lys Val Gln Ile Ile Asn Lys Lys Leu
1 5

<210> 393
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 393

Ile Ile Asn Lys Lys Leu
1 5

<210> 394
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 394

Ile Asn Lys Lys Leu
1   5

<210> 395
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 395

Asn Lys Lys Leu
1

<210> 396
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 396

Lys Lys Leu
1

<210> 397
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 397

Lys Val Gln Ile Ile Asn Lys Lys Leu Asp
1   5   10

<210> 398
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 398

Val Gln Ile Ile Asn Lys Lys Leu Asp
1 5

<210> 399
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 399

Gln Ile Ile Asn Lys Lys Leu Asp
1 5

<210> 400
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 400

Ile Ile Asn Lys Lys Leu Asp
1 5

<210> 401
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 401

Ile Asn Lys Lys Leu Asp
1 5

<210> 402
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 402

Asn Lys Lys Leu Asp
1   5

<210> 403
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 403

Lys Lys Leu Asp
1

<210> 404
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 404

Lys Leu Asp
1

<210> 405
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 405

Val Gln Ile Ile Asn Lys Lys Leu Asp Leu
1   5   10

<210> 406
<211> 9
<212> PRT

<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 406

Gln Ile Ile Asn Lys Lys Leu Asp Leu
1 5

<210> 407
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 407

Ile Ile Asn Lys Lys Leu Asp Leu
1 5

<210> 408
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 408

Ile Asn Lys Lys Leu Asp Leu
1 5

<210> 409
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 409

Asn Lys Lys Leu Asp Leu
1 5

<210> 410

<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 410

Lys Lys Leu Asp Leu
1 5

<210> 411
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 411

Lys Leu Asp Leu
1

<210> 412
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 412

Leu Asp Leu
1

<210> 413
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 413

Gln Ile Ile Asn Lys Lys Leu Asp Leu Ser
1 5 10

<210> 414
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 414

Ile Ile Asn Lys Lys Leu Asp Leu Ser
1   5

<210> 415
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 415

Ile Asn Lys Lys Leu Asp Leu Ser
1   5

<210> 416
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 416

Asn Lys Lys Leu Asp Leu Ser
1   5

<210> 417
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 417

Lys Lys Leu Asp Leu Ser

1 5

<210> 418
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 418

Lys Leu Asp Leu Ser
1 5

<210> 419
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 419

Leu Asp Leu Ser
1

<210> 420
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 420

Ile Ile Asn Lys Lys Leu Asp Leu Ser Asn
1 5 10

<210> 421
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 421

Ile Asn Lys Lys Leu Asp Leu Ser Asn
1   5

<210> 422
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 422

Asn Lys Lys Leu Asp Leu Ser Asn
1   5

<210> 423
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 423

Lys Lys Leu Asp Leu Ser Asn
1   5

<210> 424
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 424

Lys Leu Asp Leu Ser Asn
1   5

<210> 425
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 425

Leu Asp Leu Ser Asn
1 5

<210> 426
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 426

Asp Leu Ser Asn
1

<210> 427
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 427

Leu Ser Asn
1

<210> 428
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 428

Ile Asn Lys Lys Leu Asp Leu Ser Asn Val
1 5 10

<210> 429
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 429

Asn Lys Lys Leu Asp Leu Ser Asn Val
1   5

<210> 430
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 430

Lys Lys Leu Asp Leu Ser Asn Val
1   5

<210> 431
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 431

Lys Leu Asp Leu Ser Asn Val
1   5

<210> 432
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 432

Leu Asp Leu Ser Asn Val
1   5

<210> 433
<211> 5
<212> PRT

<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 433

Asp Leu Ser Asn Val
1 5

<210> 434
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 434

Leu Ser Asn Val
1

<210> 435
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 435

Ser Asn Val
1

<210> 436
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 436

Asn Lys Lys Leu Asp Leu Ser Asn Val Gln
1 5 10

<210> 437

<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 437

Lys Lys Leu Asp Leu Ser Asn Val Gln
1 5

<210> 438
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 438

Lys Leu Asp Leu Ser Asn Val Gln
1 5

<210> 439
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 439

Leu Asp Leu Ser Asn Val Gln
1 5

<210> 440
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 440

Asp Leu Ser Asn Val Gln
1 5

<210> 441
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 441

Leu Ser Asn Val Gln
1   5

<210> 442
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 442

Ser Asn Val Gln
1

<210> 443
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 443

Asn Val Gln
1

<210> 444
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 444

Lys Lys Leu Asp Leu Ser Asn Val Gln Ser

1 5 10

<210> 445
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 445

Lys Leu Asp Leu Ser Asn Val Gln Ser
1 5

<210> 446
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 446

Leu Asp Leu Ser Asn Val Gln Ser
1 5

<210> 447
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 447

Asp Leu Ser Asn Val Gln Ser
1 5

<210> 448
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 448

Leu Ser Asn Val Gln Ser
1   5

<210> 449
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 449

Ser Asn Val Gln Ser
1   5

<210> 450
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 450

Asn Val Gln Ser
1

<210> 451
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 451

Val Gln Ser
1

<210> 452
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 452

Ser Lys Cys Gly Ser Lys Asp Asn Ile Lys
1 5 10

<210> 453
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 453

Lys Cys Gly Ser Lys Asp Asn Ile Lys
1 5

<210> 454
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 454

Cys Gly Ser Lys Asp Asn Ile Lys
1 5

<210> 455
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 455

Gly Ser Lys Asp Asn Ile Lys
1 5

<210> 456
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 456

Ser Lys Asp Asn Ile Lys
1   5

<210> 457
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 457

Lys Asp Asn Ile Lys
1   5

<210> 458
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 458

Asp Asn Ile Lys
1

<210> 459
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 459

Asn Ile Lys
1

<210> 460
<211> 10
<212> PRT

<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 460

Lys Cys Gly Ser Lys Asp Asn Ile Lys His
1 5 10

<210> 461
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 461

Cys Gly Ser Lys Asp Asn Ile Lys His
1 5

<210> 462
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 462

Gly Ser Lys Asp Asn Ile Lys His
1 5

<210> 463
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 463

Ser Lys Asp Asn Ile Lys His
1 5

<210> 464

<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 464

Lys Asp Asn Ile Lys His
1   5

<210> 465
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 465

Asp Asn Ile Lys His
1   5

<210> 466
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 466

Asn Ile Lys His
1

<210> 467
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 467

Ile Lys His
1

<210> 468
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 468

Cys Gly Ser Lys Asp Asn Ile Lys His Val
1   5   10

<210> 469
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 469

Gly Ser Lys Asp Asn Ile Lys His Val
1   5

<210> 470
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 470

Ser Lys Asp Asn Ile Lys His Val
1   5

<210> 471
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 471

Lys Asp Asn Ile Lys His Val

1 5

<210> 472
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 472

Asp Asn Ile Lys His Val
1 5

<210> 473
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 473

Asn Ile Lys His Val
1 5

<210> 474
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 474

Ile Lys His Val
1

<210> 475
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 475

Lys His Val
1

<210> 476
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 476

Gly Ser Lys Asp Asn Ile Lys His Val Pro
1 5 10

<210> 477
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 477

Ser Lys Asp Asn Ile Lys His Val Pro
1 5

<210> 478
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 478

Lys Asp Asn Ile Lys His Val Pro
1 5

<210> 479
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 479

Asp Asn Ile Lys His Val Pro
1 5

<210> 480
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 480

Ile Lys His Val Pro
1 5

<210> 481
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 481

Lys His Val Pro
1

<210> 482
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 482

His Val Pro
1

<210> 483
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 483

Ser Lys Asp Asn Ile Lys His Val Pro Gly
1   5   10

<210> 484
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 484

Lys Asp Asn Ile Lys His Val Pro Gly
1   5

<210> 485
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 485

Asp Asn Ile Lys His Val Pro Gly
1   5

<210> 486
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 486

Asn Ile Lys His Val Pro Gly
1   5

<210> 487
<211> 6
<212> PRT

<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 487

Ile Lys His Val Pro Gly
1 5

<210> 488
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 488

Lys His Val Pro Gly
1 5

<210> 489
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 489

His Val Pro Gly
1

<210> 490
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 490

Val Pro Gly
1

<210> 491

<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 491

Lys Asp Asn Ile Lys His Val Pro Gly Gly
1 5 10

<210> 492
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 492

Asp Asn Ile Lys His Val Pro Gly Gly
1 5

<210> 493
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 493

Asn Ile Lys His Val Pro Gly Gly
1 5

<210> 494
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 494

Ile Lys His Val Pro Gly Gly
1 5

<210> 495
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 495

Lys His Val Pro Gly Gly
1   5

<210> 496
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 496

Val Pro Gly Gly
1

<210> 497
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 497

Pro Gly Gly
1

<210> 498
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 498

Asp Asn Ile Lys His Val Pro Gly Gly Gly

1 5 10

<210> 499
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 499

Asn Ile Lys His Val Pro Gly Gly Gly
1 5

<210> 500
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 500

Ile Lys His Val Pro Gly Gly Gly
1 5

<210> 501
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 501

Val Pro Gly Gly Gly
1 5

<210> 502
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 502

Pro Gly Gly Gly
1

<210> 503
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 503

Gly Gly Gly
1

<210> 504
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 504

Asn Ile Lys His Val Pro Gly Gly Gly Ser
1   5   10

<210> 505
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 505

Ile Lys His Val Pro Gly Gly Gly Ser
1   5

<210> 506
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 506

Lys His Val Pro Gly Gly Gly Ser
1 5

<210> 507
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 507

His Val Pro Gly Gly Gly Ser
1 5

<210> 508
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 508

Val Pro Gly Gly Gly Ser
1 5

<210> 509
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 509

Pro Gly Gly Gly Ser
1 5

<210> 510
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 510

Gly Gly Gly Ser
1

<210> 511
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 511

Gly Gly Ser
1

<210> 512
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 512

Ile Lys His Val Pro Gly Gly Gly Ser Val
1   5   10

<210> 513
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 513

Lys His Val Pro Gly Gly Gly Ser Val
1   5

<210> 514
<211> 8
<212> PRT

<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 514

His Val Pro Gly Gly Gly Ser Val
1 5

<210> 515
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 515

Val Pro Gly Gly Gly Ser Val
1 5

<210> 516
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 516

Pro Gly Gly Gly Ser Val
1 5

<210> 517
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 517

Gly Gly Gly Ser Val
1 5

<210> 518

<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 518

Gly Gly Ser Val
1

<210> 519
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 519

Gly Ser Val
1

<210> 520
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 520

Lys His Val Pro Gly Gly Gly Ser Val Gln
1 5 10

<210> 521
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 521

His Val Pro Gly Gly Gly Ser Val Gln
1 5

<210> 522
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 522

Val Pro Gly Gly Gly Ser Val Gln
1   5

<210> 523
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 523

Pro Gly Gly Gly Ser Val Gln
1   5

<210> 524
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 524

Gly Gly Gly Ser Val Gln
1   5

<210> 525
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 525

Gly Gly Ser Val Gln

1 5

<210> 526
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 526

Gly Ser Val Gln
1

<210> 527
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 527

Ser Val Gln
1

<210> 528
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 528

His Val Pro Gly Gly Gly Ser Val Gln Ile
1 5 10

<210> 529
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 529

Val Pro Gly Gly Gly Ser Val Gln Ile
1   5

<210> 530
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 530

Pro Gly Gly Gly Ser Val Gln Ile
1   5

<210> 531
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 531

Gly Gly Gly Ser Val Gln Ile
1   5

<210> 532
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 532

Gly Gly Ser Val Gln Ile
1   5

<210> 533
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 533

Gly Ser Val Gln Ile
1 5

<210> 534
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 534

Ser Val Gln Ile
1

<210> 535
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 535

Gly Gly Ser Val Gln Ile Val Tyr Lys Ser
1 5 10

<210> 536
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 536

Gly Ser Val Gln Ile Val Tyr Lys Ser
1 5

<210> 537
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 537

Ser Val Gln Ile Val Tyr Lys Ser
1   5

<210> 538
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 538

Val Gln Ile Val Tyr Lys Ser
1   5

<210> 539
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 539

Gln Ile Val Tyr Lys Ser
1   5

<210> 540
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 540

Ile Val Tyr Lys Ser
1   5

<210> 541
<211> 4
<212> PRT

<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 541

Val Tyr Lys Ser
1

<210> 542
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 542

Tyr Lys Ser
1

<210> 543
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 543

Gly Ser Val Gln Ile Val Tyr Lys Ser Val
1   5   10

<210> 544
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 544

Ser Val Gln Ile Val Tyr Lys Ser Val
1   5

<210> 545

<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 545

Val Gln Ile Val Tyr Lys Ser Val
1 5

<210> 546
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 546

Gln Ile Val Tyr Lys Ser Val
1 5

<210> 547
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 547

Ile Val Tyr Lys Ser Val
1 5

<210> 548
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 548

Val Tyr Lys Ser Val
1 5

<210> 549
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 549

Tyr Lys Ser Val
1

<210> 550
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 550

Ser Val Gln Ile Val Tyr Lys Ser Val Asp
1   5   10

<210> 551
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 551

Val Gln Ile Val Tyr Lys Ser Val Asp
1   5

<210> 552
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 552

Gln Ile Val Tyr Lys Ser Val Asp

1 5

<210> 553
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 553

Ile Val Tyr Lys Ser Val Asp
1 5

<210> 554
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 554

Val Tyr Lys Ser Val Asp
1 5

<210> 555
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 555

Tyr Lys Ser Val Asp
1 5

<210> 556
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 556

Lys Ser Val Asp
1

<210> 557
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 557

Ser Val Asp
1

<210> 558
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 558

Val Gln Ile Val Tyr Lys Ser Val Asp Leu
1 5 10

<210> 559
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 559

Gln Ile Val Tyr Lys Ser Val Asp Leu
1 5

<210> 560
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 560

Ile Val Tyr Lys Ser Val Asp Leu
1 5

<210> 561
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 561

Val Tyr Lys Ser Val Asp Leu
1 5

<210> 562
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 562

Tyr Lys Ser Val Asp Leu
1 5

<210> 563
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 563

Lys Ser Val Asp Leu
1 5

<210> 564
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 564

Ser Val Asp Leu
1

<210> 565
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 565

Gln Ile Val Tyr Lys Ser Val Asp Leu Ser
1   5   10

<210> 566
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 566

Ile Val Tyr Lys Ser Val Asp Leu Ser
1   5

<210> 567
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 567

Val Tyr Lys Ser Val Asp Leu Ser
1   5

<210> 568
<211> 7
<212> PRT

<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 568

Tyr Lys Ser Val Asp Leu Ser
1 5

<210> 569
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 569

Lys Ser Val Asp Leu Ser
1 5

<210> 570
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 570

Ser Val Asp Leu Ser
1 5

<210> 571
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 571

Ile Val Tyr Lys Ser Val Asp Leu Ser Lys
1 5 10

<210> 572

<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 572

Val Tyr Lys Ser Val Asp Leu Ser Lys
1 5

<210> 573
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 573

Tyr Lys Ser Val Asp Leu Ser Lys
1 5

<210> 574
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 574

Lys Ser Val Asp Leu Ser Lys
1 5

<210> 575
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 575

Val Tyr Lys Ser Val Asp Leu Ser Lys Val
1 5 10

<210> 576
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 576

Tyr Lys Ser Val Asp Leu Ser Lys Val
1   5

<210> 577
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 577

Lys Ser Val Asp Leu Ser Lys Val
1   5

<210> 578
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 578

Ser Val Asp Leu Ser Lys Val
1   5

<210> 579
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 579

Tyr Lys Ser Val Asp Leu Ser Lys Val Thr

1 5 10

<210> 580
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 580

Lys Ser Val Asp Leu Ser Lys Val Thr
1 5

<210> 581
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 581

Ser Val Asp Leu Ser Lys Val Thr
1 5

<210> 582
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 582

Asp Leu Ser Lys Val Thr
1 5

<210> 583
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 583

Leu Ser Lys Val Thr
1 5

<210> 584
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 584

Ser Lys Val Thr
1

<210> 585
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 585

Lys Val Thr
1

<210> 586
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 586

His Gly Ala Glu Ile Val Tyr Lys Ser Val
1 5 10

<210> 587
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 587

Gly Ala Glu Ile Val Tyr Lys Ser Val
1 5

<210> 588
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 588

Ala Glu Ile Val Tyr Lys Ser Val
1 5

<210> 589
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 589

Gly Ala Glu Ile Val Tyr Lys Ser Val Val
1 5 10

<210> 590
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 590

Ala Glu Ile Val Tyr Lys Ser Val Val
1 5

<210> 591
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 591

Glu Ile Val Tyr Lys Ser Val Val
1   5

<210> 592
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 592

Ile Val Tyr Lys Ser Val Val
1   5

<210> 593
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 593

Val Tyr Lys Ser Val Val
1   5

<210> 594
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 594

Tyr Lys Ser Val Val
1   5

<210> 595
<211> 4
<212> PRT

<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 595

Lys Ser Val Val
1

<210> 596
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 596

Ser Val Val
1

<210> 597
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 597

Ala Glu Ile Val Tyr Lys Ser Val Val Ser
1 5 10

<210> 598
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 598

Glu Ile Val Tyr Lys Ser Val Val Ser
1 5

<210> 599

<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 599

Ile Val Tyr Lys Ser Val Val Ser
1   5

<210> 600
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 600

Val Tyr Lys Ser Val Val Ser
1   5

<210> 601
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 601

Tyr Lys Ser Val Val Ser
1   5

<210> 602
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 602

Lys Ser Val Val Ser
1   5

<210> 603
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 603

Ser Val Val Ser
1

<210> 604
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 604

Glu Ile Val Tyr Lys Ser Val Val Ser Gly
1 5 10

<210> 605
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 605

Ile Val Tyr Lys Ser Val Val Ser Gly
1 5

<210> 606
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 606

Val Tyr Lys Ser Val Val Ser Gly

1 5

<210> 607
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 607

Tyr Lys Ser Val Val Ser Gly
1 5

<210> 608
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 608

Lys Ser Val Val Ser Gly
1 5

<210> 609
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 609

Ser Val Val Ser Gly
1 5

<210> 610
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 610

Val Val Ser Gly
1

<210> 611
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 611

Val Ser Gly
1

<210> 612
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 612

Ile Val Tyr Lys Ser Val Val Ser Gly Asp
1 5 10

<210> 613
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 613

Val Tyr Lys Ser Val Val Ser Gly Asp
1 5

<210> 614
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 614

Tyr Lys Ser Val Val Ser Gly Asp
1 5

<210> 615
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 615

Lys Ser Val Val Ser Gly Asp
1 5

<210> 616
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 616

Ser Val Val Ser Gly Asp
1 5

<210> 617
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 617

Val Val Ser Gly Asp
1 5

<210> 618
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 618

Val Tyr Lys Ser Val Val Ser Gly Asp Thr
1   5   10

<210> 619
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 619

Tyr Lys Ser Val Val Ser Gly Asp Thr
1   5

<210> 620
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 620

Lys Ser Val Val Ser Gly Asp Thr
1   5

<210> 621
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 621

Ser Val Val Ser Gly Asp Thr
1   5

<210> 622
<211> 10
<212> PRT

<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 622

Tyr Lys Ser Val Val Ser Gly Asp Thr Ser
1 5 10

<210> 623
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 623

Lys Ser Val Val Ser Gly Asp Thr Ser
1 5

<210> 624
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 624

Ser Val Val Ser Gly Asp Thr Ser
1 5

<210> 625
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 625

Tyr Lys Ser Val Val Ser Gly Asp Thr Ser
1 5 10

<210> 626

<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 626

Lys Ser Val Val Ser Gly Asp Thr Ser
1 5

<210> 627
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 627

Ser Val Val Ser Gly Asp Thr Ser
1 5

<210> 628
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 628

Val Val Ser Gly Asp Thr Ser
1 5

<210> 629
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 629

Lys Ser Val Val Ser Gly Asp Thr Ser Pro
1 5 10

<210> 630
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 630

Ser Val Val Ser Gly Asp Thr Ser Pro
1   5

<210> 631
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 631

Ser Val Val Ser Gly Asp Thr Ser Pro Arg
1   5   10

<210> 632
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 632

Asp His Gly Ala Glu Ile Val Tyr Lys Pro
1   5   10

<210> 633
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 633

His Gly Ala Glu Ile Val Tyr Lys Pro

1 5

<210> 634
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 634

Gly Ala Glu Ile Val Tyr Lys Pro
1 5

<210> 635
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 635

Ala Glu Ile Val Tyr Lys Pro
1 5

<210> 636
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 636

His Gly Ala Glu Ile Val Tyr Lys Pro Val
1 5 10

<210> 637
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 637

Gly Ala Glu Ile Val Tyr Lys Pro Val
1   5

<210> 638
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 638

Ala Glu Ile Val Tyr Lys Pro Val
1   5

<210> 639
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 639

Gly Ala Glu Ile Val Tyr Lys Pro Val Val
1   5   10

<210> 640
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 640

Ala Glu Ile Val Tyr Lys Pro Val Val
1   5

<210> 641
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 641

Glu Ile Val Tyr Lys Pro Val Val
1 5

<210> 642
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 642

Ile Val Tyr Lys Pro Val Val
1 5

<210> 643
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 643

Val Tyr Lys Pro Val Val
1 5

<210> 644
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 644

Tyr Lys Pro Val Val
1 5

<210> 645
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 645

Lys Pro Val Val
1

<210> 646
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 646

Ala Glu Ile Val Tyr Lys Pro Val Val Ser
1   5   10

<210> 647
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 647

Glu Ile Val Tyr Lys Pro Val Val Ser
1   5

<210> 648
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 648

Ile Val Tyr Lys Pro Val Val Ser
1   5

<210> 649
<211> 7
<212> PRT

<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 649

Val Tyr Lys Pro Val Val Ser
1 5

<210> 650
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 650

Tyr Lys Pro Val Val Ser
1 5

<210> 651
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 651

Lys Pro Val Val Ser
1 5

<210> 652
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 652

Glu Ile Val Tyr Lys Pro Val Val Ser Gly
1 5 10

<210> 653

<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 653

Ile Val Tyr Lys Pro Val Val Ser Gly
1   5

<210> 654
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 654

Val Tyr Lys Pro Val Val Ser Gly
1   5

<210> 655
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 655

Tyr Lys Pro Val Val Ser Gly
1   5

<210> 656
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 656

Lys Pro Val Val Ser Gly
1   5

<210> 657
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 657

Ile Val Tyr Lys Pro Val Val Ser Gly Asp
1   5   10

<210> 658
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 658

Val Tyr Lys Pro Val Val Ser Gly Asp
1   5

<210> 659
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 659

Tyr Lys Pro Val Val Ser Gly Asp
1   5

<210> 660
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 660

Lys Pro Val Val Ser Gly Asp

1 5

<210> 661
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 661

Val Tyr Lys Pro Val Val Ser Gly Asp Thr
1 5 10

<210> 662
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 662

Tyr Lys Pro Val Val Ser Gly Asp Thr
1 5

<210> 663
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 663

Lys Pro Val Val Ser Gly Asp Thr
1 5

<210> 664
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 664

Tyr Lys Pro Val Val Ser Gly Asp Thr Ser
1   5   10

<210> 665
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 665

Lys Pro Val Val Ser Gly Asp Thr Ser
1   5

<210> 666
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 666

Pro Val Val Ser Gly Asp Thr Ser
1   5

<210> 667
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 667

Val Val Ser Gly Asp Thr Ser
1   5

<210> 668
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 668

Lys Pro Val Val Ser Gly Asp Thr Ser Pro
1 5 10

<210> 669
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 669

Cys Asn Ile Lys
1

<210> 670
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 670

Cys Asn Ile Lys His
1 5

<210> 671
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 671

Cys Asn Ile Lys His Val
1 5

<210> 672
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 672

Cys Asn Ile Lys His Val Pro Gly Gly
1   5

<210> 673
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 673

Cys Asn Ile Lys His Val Pro Gly Gly Gly
1   5   10

<210> 674
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 674

Cys Asn Ile Lys His Val Pro Gly Gly Gly Ser
1   5   10

<210> 675
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 675

Glu Asn Leu Lys His Gln Pro Gly Gly Gly
1   5   10

<210> 676
<211> 9
<212> PRT

<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 676

Asn Leu Lys His Gln Pro Gly Gly Gly
1 5

<210> 677
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 677

Leu Lys His Gln Pro Gly Gly Gly
1 5

<210> 678
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 678

Lys His Gln Pro Gly Gly Gly
1 5

<210> 679
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 679

His Gln Pro Gly Gly Gly
1 5

<210> 680

<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 680

Gln Pro Gly Gly Gly
1   5

<210> 681
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 681

Thr Glu Asn Leu Lys His Gln Pro Gly Gly
1   5   10

<210> 682
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 682

Glu Asn Leu Lys His Gln Pro Gly Gly
1   5

<210> 683
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 683

Asn Leu Lys His Gln Pro Gly Gly
1   5

<210> 684
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 684

Leu Lys His Gln Pro Gly Gly
1   5

<210> 685
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 685

Lys His Gln Pro Gly Gly
1   5

<210> 686
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 686

His Gln Pro Gly Gly
1   5

<210> 687
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 687

Gln Pro Gly Gly

1

<210> 688
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 688

Thr Glu Asn Leu Lys His Gln Pro Gly
1 5

<210> 689
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 689

Glu Asn Leu Lys His Gln Pro Gly
1 5

<210> 690
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 690

Asn Leu Lys His Gln Pro Gly
1 5

<210> 691
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 691

Leu Lys His Gln Pro Gly
1   5

<210> 692
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 692

Lys His Gln Pro Gly
1   5

<210> 693
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 693

His Gln Pro Gly
1

<210> 694
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 694

Gln Pro Gly
1

<210> 695
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 695

Thr Glu Asn Leu Lys His Gln Pro
1 5

<210> 696
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 696

Glu Asn Leu Lys His Gln Pro
1 5

<210> 697
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 697

Asn Leu Lys His Gln Pro
1 5

<210> 698
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 698

Leu Lys His Gln Pro
1 5

<210> 699
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 699

Lys His Gln Pro
1

<210> 700
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 700

His Gln Pro
1

<210> 701
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 701

Thr Glu Asn Leu Lys His Gln
1   5

<210> 702
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 702

Glu Asn Leu Lys His Gln
1   5

<210> 703
<211> 5
<212> PRT

<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 703

Asn Leu Lys His Gln
1 5

<210> 704
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 704

Leu Lys His Gln
1

<210> 705
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 705

Lys His Gln
1

<210> 706
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 706

Thr Glu Asn Leu Lys His
1 5

<210> 707

<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 707

Glu Asn Leu Lys His
1   5

<210> 708
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 708

Asn Leu Lys His
1

<210> 709
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 709

Leu Lys His
1

<210> 710
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 710

Thr Glu Asn Leu Lys
1   5

<210> 711
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 711

Glu Asn Leu Lys
1

<210> 712
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 712

Asn Leu Lys
1

<210> 713
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 713

Thr Glu Asn Leu
1

<210> 714
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 714

Glu Asn Leu

1

<210> 715
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 715

Thr Glu Asn
1

<210> 716
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 716

Lys Asp Asn Ile Lys His Val Pro Gly Gly Gly
1 5 10

<210> 717
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 717

Lys Asp Asn Ile
1

<210> 718
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 718

Lys Asp Asn
1

<210> 719
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 719

Ile Lys His Val Gly Gly Gly
1 5

<210> 720
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 720

Ile Lys His Val Gly Gly
1 5

<210> 721
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 721

Ile Lys His Val Gly
1 5

<210> 722
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 722

Lys His Val Gly Gly Gly
1 5

<210> 723
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 723

Lys His Val Gly Gly
1 5

<210> 724
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 724

Lys His Val Gly
1

<210> 725
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 725

Leu Gly Asn Ile His His Lys Pro Gly Gly Gly
1 5 10

<210> 726
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 726

Gly Asn Ile His His Lys Pro Gly Gly Gly
1   5   10

<210> 727
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 727

Asn Ile His His Lys Pro Gly Gly Gly
1   5

<210> 728
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 728

Ile His His Lys Pro Gly Gly Gly
1   5

<210> 729
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 729

His His Lys Pro Gly Gly Gly
1   5

<210> 730
<211> 5
<212> PRT

<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 730

Lys Pro Gly Gly Gly
1 5

<210> 731
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 731

Leu Gly Asn Ile His His Lys Pro Gly Gly
1 5 10

<210> 732
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 732

Gly Asn Ile His His Lys Pro Gly Gly
1 5

<210> 733
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 733

Asn Ile His His Lys Pro Gly Gly
1 5

<210> 734

<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 734

Ile His His Lys Pro Gly Gly
1 5

<210> 735
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 735

His His Lys Pro Gly Gly
1 5

<210> 736
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 736

Lys Pro Gly Gly
1

<210> 737
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 737

Leu Gly Asn Ile His His Lys Pro Gly
1 5

<210> 738
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 738

Gly Asn Ile His His Lys Pro Gly
1   5

<210> 739
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 739

Asn Ile His His Lys Pro Gly
1   5

<210> 740
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 740

Ile His His Lys Pro Gly
1   5

<210> 741
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 741

His His Lys Pro Gly

1 5

<210> 742
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 742

His Lys Pro Gly
1

<210> 743
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 743

Lys Pro Gly
1

<210> 744
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 744

Leu Gly Asn Ile His His Lys Pro
1 5

<210> 745
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 745

Gly Asn Ile His His Lys Pro
1   5

<210> 746
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 746

Asn Ile His His Lys Pro
1   5

<210> 747
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 747

Ile His His Lys Pro
1   5

<210> 748
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 748

His His Lys Pro
1

<210> 749
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 749

His Lys Pro
1

<210> 750
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 750

Leu Gly Asn Ile His His Lys
1 5

<210> 751
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 751

Gly Asn Ile His His Lys
1 5

<210> 752
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 752

Asn Ile His His Lys
1 5

<210> 753
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 753

Ile His His Lys
1

<210> 754
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 754

His His Lys
1

<210> 755
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 755

Leu Gly Asn Ile His His
1   5

<210> 756
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 756

Gly Asn Ile His His
1   5

<210> 757
<211> 4
<212> PRT

<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 757

Asn Ile His His
1

<210> 758
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 758

Ile His His
1

<210> 759
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 759

Leu Gly Asn Ile His
1   5

<210> 760
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 760

Gly Asn Ile His
1

<210> 761

<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 761

Asn Ile His
1

<210> 762
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 762

Leu Gly Asn Ile
1

<210> 763
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 763

Gly Asn Ile
1

<210> 764
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 764

Leu Gly Asn
1

<210> 765
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 765

Leu Asp Asn Ile Thr His Val Pro Gly Gly Gly
1   5   10

<210> 766
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 766

Asp Asn Ile Thr His Val Pro Gly Gly Gly
1   5   10

<210> 767
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 767

Asn Ile Thr His Val Pro Gly Gly Gly
1   5

<210> 768
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 768

Ile Thr His Val Pro Gly Gly Gly

1 5

<210> 769
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 769

Thr His Val Pro Gly Gly Gly
1 5

<210> 770
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 770

Leu Asp Asn Ile Thr His Val Pro Gly Gly
1 5 10

<210> 771
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 771

Asp Asn Ile Thr His Val Pro Gly Gly
1 5

<210> 772
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 772

Asn Ile Thr His Val Pro Gly Gly
1   5

<210> 773
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 773

Ile Thr His Val Pro Gly Gly
1   5

<210> 774
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 774

Thr His Val Pro Gly Gly
1   5

<210> 775
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 775

Leu Asp Asn Ile Thr His Val Pro Gly
1   5

<210> 776
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 776

Asp Asn Ile Thr His Val Pro Gly
1 5

<210> 777
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 777

Asn Ile Thr His Val Pro Gly
1 5

<210> 778
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 778

Ile Thr His Val Pro Gly
1 5

<210> 779
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 779

Thr His Val Pro Gly
1 5

<210> 780
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 780

Leu Asp Asn Ile Thr His Val Pro
1   5

<210> 781
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 781

Asp Asn Ile Thr His Val Pro
1   5

<210> 782
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 782

Asn Ile Thr His Val Pro
1   5

<210> 783
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 783

Ile Thr His Val Pro
1   5

<210> 784
<211> 4
<212> PRT

<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 784

Thr His Val Pro
1

<210> 785
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 785

Leu Asp Asn Ile Thr His Val
1 5

<210> 786
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 786

Asp Asn Ile Thr His Val
1 5

<210> 787
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 787

Asn Ile Thr His Val
1 5

<210> 788

<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 788

Ile Thr His Val
1

<210> 789
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 789

Thr His Val
1

<210> 790
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 790

Leu Asp Asn Ile Thr His
1   5

<210> 791
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 791

Asp Asn Ile Thr His
1   5

<210> 792
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 792

Asn Ile Thr His
1

<210> 793
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 793

Ile Thr His
1

<210> 794
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 794

Leu Asp Asn Ile Thr
1   5

<210> 795
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 795

Asp Asn Ile Thr

1

<210> 796
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 796

Asn Ile Thr
1

<210> 797
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 797

Leu Asp Asn Ile
1

<210> 798
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 798

Leu Asp Asn
1

<210> 799
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 799

Lys Asn Val Lys Ser Lys Ile Gly Ser Thr
1   5   10

<210> 800
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 800

Asn Val Lys Ser Lys Ile Gly Ser Thr
1   5

<210> 801
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 801

Val Lys Ser Lys Ile Gly Ser Thr
1   5

<210> 802
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 802

Lys Ser Lys Ile Gly Ser Thr
1   5

<210> 803
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 803

Ser Lys Ile Gly Ser Thr
1 5

<210> 804
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 804

Lys Ile Gly Ser Thr
1 5

<210> 805
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 805

Ile Gly Ser Thr
1

<210> 806
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 806

Gly Ser Thr
1

<210> 807
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 807

Asn Val Lys Ser Lys Ile Gly Ser Thr Glu
1   5   10

<210> 808
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 808

Val Lys Ser Lys Ile Gly Ser Thr Glu
1   5

<210> 809
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 809

Lys Ser Lys Ile Gly Ser Thr Glu
1   5

<210> 810
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 810

Ser Lys Ile Gly Ser Thr Glu
1   5

<210> 811
<211> 6
<212> PRT

<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 811

Lys Ile Gly Ser Thr Glu
1 5

<210> 812
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 812

Ile Gly Ser Thr Glu
1 5

<210> 813
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 813

Gly Ser Thr Glu
1

<210> 814
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 814

Ser Thr Glu
1

<210> 815

<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 815

Val Lys Ser Lys Ile Gly Ser Thr Glu Asn
1 5 10

<210> 816
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 816

Lys Ser Lys Ile Gly Ser Thr Glu Asn
1 5

<210> 817
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 817

Ser Lys Ile Gly Ser Thr Glu Asn
1 5

<210> 818
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 818

Lys Ile Gly Ser Thr Glu Asn
1 5

<210> 819
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 819

Ile Gly Ser Thr Glu Asn
1   5

<210> 820
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 820

Gly Ser Thr Glu Asn
1   5

<210> 821
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 821

Ser Thr Glu Asn
1

<210> 822
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 822

Lys Ser Lys Ile Gly Ser Thr Glu Asn Leu

1 5 10

<210> 823
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 823

Ser Lys Ile Gly Ser Thr Glu Asn Leu
1 5

<210> 824
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 824

Lys Ile Gly Ser Thr Glu Asn Leu
1 5

<210> 825
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 825

Ile Gly Ser Thr Glu Asn Leu
1 5

<210> 826
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 826

Gly Ser Thr Glu Asn Leu
1 5

<210> 827
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 827

Ser Thr Glu Asn Leu
1 5

<210> 828
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 828

Ser Lys Ile Gly Ser Thr Glu Asn Leu Lys
1 5 10

<210> 829
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 829

Lys Ile Gly Ser Thr Glu Asn Leu Lys
1 5

<210> 830
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 830

Ile Gly Ser Thr Glu Asn Leu Lys
1 5

<210> 831
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 831

Gly Ser Thr Glu Asn Leu Lys
1 5

<210> 832
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 832

Ser Thr Glu Asn Leu Lys
1 5

<210> 833
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 833

Lys Ile Gly Ser Thr Glu Asn Leu Lys His
1 5 10

<210> 834
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 834

Ile Gly Ser Thr Glu Asn Leu Lys His
1   5

<210> 835
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 835

Gly Ser Thr Glu Asn Leu Lys His
1   5

<210> 836
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 836

Ser Thr Glu Asn Leu Lys His
1   5

<210> 837
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 837

Ile Gly Ser Thr Glu Asn Leu Lys His Gln
1   5   10

<210> 838
<211> 9
<212> PRT

<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 838

Gly Ser Thr Glu Asn Leu Lys His Gln
1 5

<210> 839
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 839

Ser Thr Glu Asn Leu Lys His Gln
1 5

<210> 840
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 840

Gly Ser Thr Glu Asn Leu Lys His Gln Pro
1 5 10

<210> 841
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 841

Ser Thr Glu Asn Leu Lys His Gln Pro
1 5

<210> 842

<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 842

Ser Thr Glu Asn Leu Lys His Gln Pro Gly
1   5   10

<210> 843
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 843

Ser Asn Val Gln Ser Lys Cys Gly Ser Lys
1   5   10

<210> 844
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 844

Asn Val Gln Ser Lys Cys Gly Ser Lys
1   5

<210> 845
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 845

Val Gln Ser Lys Cys Gly Ser Lys
1   5

<210> 846
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 846

Gln Ser Lys Cys Gly Ser Lys
1 5

<210> 847
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 847

Ser Lys Cys Gly Ser Lys
1 5

<210> 848
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 848

Lys Cys Gly Ser Lys
1 5

<210> 849
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 849

Cys Gly Ser Lys

1

<210> 850
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 850

Gly Ser Lys
1

<210> 851
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 851

Asn Val Gln Ser Lys Cys Gly Ser Lys Asp
1 5 10

<210> 852
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 852

Val Gln Ser Lys Cys Gly Ser Lys Asp
1 5

<210> 853
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 853

Gln Ser Lys Cys Gly Ser Lys Asp
1   5

<210> 854
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 854

Ser Lys Cys Gly Ser Lys Asp
1   5

<210> 855
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 855

Lys Cys Gly Ser Lys Asp
1   5

<210> 856
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 856

Cys Gly Ser Lys Asp
1   5

<210> 857
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 857

Gly Ser Lys Asp
1

<210> 858
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 858

Ser Lys Asp
1

<210> 859
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 859

Val Gln Ser Lys Cys Gly Ser Lys Asp Asn
1 5 10

<210> 860
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 860

Gln Ser Lys Cys Gly Ser Lys Asp Asn
1 5

<210> 861
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 861

Ser Lys Cys Gly Ser Lys Asp Asn
1   5

<210> 862
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 862

Lys Cys Gly Ser Lys Asp Asn
1   5

<210> 863
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 863

Cys Gly Ser Lys Asp Asn
1   5

<210> 864
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 864

Gly Ser Lys Asp Asn
1   5

<210> 865
<211> 4
<212> PRT

<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 865

Ser Lys Asp Asn
1

<210> 866
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 866

Gln Ser Lys Cys Gly Ser Lys Asp Asn Ile
1 5 10

<210> 867
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 867

Ser Lys Cys Gly Ser Lys Asp Asn Ile
1 5

<210> 868
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 868

Lys Cys Gly Ser Lys Asp Asn Ile
1 5

<210> 869

<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 869

Cys Gly Ser Lys Asp Asn Ile
1 5

<210> 870
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 870

Gly Ser Lys Asp Asn Ile
1 5

<210> 871
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 871

Ser Lys Asp Asn Ile
1 5

<210> 872
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 872

Ser Lys Val Thr Ser Lys Cys Gly Ser Leu
1 5 10

<210> 873
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 873

Lys Val Thr Ser Lys Cys Gly Ser Leu
1   5

<210> 874
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 874

Val Thr Ser Lys Cys Gly Ser Leu
1   5

<210> 875
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 875

Thr Ser Lys Cys Gly Ser Leu
1   5

<210> 876
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 876

Ser Lys Cys Gly Ser Leu

1 5

<210> 877
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 877

Lys Cys Gly Ser Leu
1 5

<210> 878
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 878

Cys Gly Ser Leu
1

<210> 879
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 879

Gly Ser Leu
1

<210> 880
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 880

Lys Val Thr Ser Lys Cys Gly Ser Leu Gly
1 5 10

<210> 881
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 881

Val Thr Ser Lys Cys Gly Ser Leu Gly
1 5

<210> 882
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 882

Thr Ser Lys Cys Gly Ser Leu Gly
1 5

<210> 883
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 883

Ser Lys Cys Gly Ser Leu Gly
1 5

<210> 884
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 884

Lys Cys Gly Ser Leu Gly
1 5

<210> 885
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 885

Cys Gly Ser Leu Gly
1 5

<210> 886
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 886

Gly Ser Leu Gly
1

<210> 887
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 887

Ser Leu Gly
1

<210> 888
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 888

Val Thr Ser Lys Cys Gly Ser Leu Gly Asn
1   5   10

<210> 889
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 889

Thr Ser Lys Cys Gly Ser Leu Gly Asn
1   5

<210> 890
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 890

Ser Lys Cys Gly Ser Leu Gly Asn
1   5

<210> 891
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 891

Lys Cys Gly Ser Leu Gly Asn
1   5

<210> 892
<211> 6
<212> PRT

<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 892

Cys Gly Ser Leu Gly Asn
1 5

<210> 893
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 893

Gly Ser Leu Gly Asn
1 5

<210> 894
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 894

Ser Leu Gly Asn
1

<210> 895
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 895

Thr Ser Lys Cys Gly Ser Leu Gly Asn Ile
1 5 10

<210> 896

<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 896

Ser Lys Cys Gly Ser Leu Gly Asn Ile
1   5

<210> 897
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 897

Lys Cys Gly Ser Leu Gly Asn Ile
1   5

<210> 898
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 898

Cys Gly Ser Leu Gly Asn Ile
1   5

<210> 899
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 899

Gly Ser Leu Gly Asn Ile
1   5

<210> 900
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 900

Ser Leu Gly Asn Ile
1   5

<210> 901
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 901

Ser Lys Cys Gly Ser Leu Gly Asn Ile His
1   5   10

<210> 902
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 902

Lys Cys Gly Ser Leu Gly Asn Ile His
1   5

<210> 903
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 903

Cys Gly Ser Leu Gly Asn Ile His

1 5

<210> 904
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 904

Gly Ser Leu Gly Asn Ile His
1 5

<210> 905
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 905

Ser Leu Gly Asn Ile His
1 5

<210> 906
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 906

Lys Cys Gly Ser Leu Gly Asn Ile His His
1 5 10

<210> 907
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 907

Cys Gly Ser Leu Gly Asn Ile His His
1   5

<210> 908
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 908

Gly Ser Leu Gly Asn Ile His His
1   5

<210> 909
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 909

Ser Leu Gly Asn Ile His His
1   5

<210> 910
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 910

Cys Gly Ser Leu Gly Asn Ile His His Lys
1   5   10

<210> 911
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 911

Gly Ser Leu Gly Asn Ile His His Lys
1 5

<210> 912
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 912

Ser Leu Gly Asn Ile His His Lys
1 5

<210> 913
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 913

Gly Ser Leu Gly Asn Ile His His Lys Pro
1 5 10

<210> 914
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 914

Ser Leu Gly Asn Ile His His Lys Pro
1 5

<210> 915
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 915

Ser Leu Gly Asn Ile His His Lys Pro Gly
1   5   10

<210> 916
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 916

Asp Arg Val Gln Ser Lys Ile Gly Ser Leu
1   5   10

<210> 917
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 917

Arg Val Gln Ser Lys Ile Gly Ser Leu
1   5

<210> 918
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 918

Val Gln Ser Lys Ile Gly Ser Leu
1   5

<210> 919
<211> 7
<212> PRT

<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 919

Gln Ser Lys Ile Gly Ser Leu
1 5

<210> 920
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 920

Ser Lys Ile Gly Ser Leu
1 5

<210> 921
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 921

Lys Ile Gly Ser Leu
1 5

<210> 922
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 922

Ile Gly Ser Leu
1

<210> 923

<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 923

Arg Val Gln Ser Lys Ile Gly Ser Leu Asp
1 5 10

<210> 924
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 924

Val Gln Ser Lys Ile Gly Ser Leu Asp
1 5

<210> 925
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 925

Gln Ser Lys Ile Gly Ser Leu Asp
1 5

<210> 926
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 926

Ser Lys Ile Gly Ser Leu Asp
1 5

<210> 927
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 927

Lys Ile Gly Ser Leu Asp
1   5

<210> 928
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 928

Ile Gly Ser Leu Asp
1   5

<210> 929
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 929

Gly Ser Leu Asp
1

<210> 930
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 930

Ser Leu Asp

1

<210> 931
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 931

Val Gln Ser Lys Ile Gly Ser Leu Asp Asn
1 5 10

<210> 932
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 932

Gln Ser Lys Ile Gly Ser Leu Asp Asn
1 5

<210> 933
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 933

Ser Lys Ile Gly Ser Leu Asp Asn
1 5

<210> 934
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 934

Lys Ile Gly Ser Leu Asp Asn
1   5

<210> 935
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 935

Ile Gly Ser Leu Asp Asn
1   5

<210> 936
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 936

Gly Ser Leu Asp Asn
1   5

<210> 937
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 937

Ser Leu Asp Asn
1

<210> 938
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 938

Gln Ser Lys Ile Gly Ser Leu Asp Asn Ile
1 5 10

<210> 939
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 939

Ser Lys Ile Gly Ser Leu Asp Asn Ile
1 5

<210> 940
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 940

Lys Ile Gly Ser Leu Asp Asn Ile
1 5

<210> 941
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 941

Ile Gly Ser Leu Asp Asn Ile
1 5

<210> 942
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 942

Gly Ser Leu Asp Asn Ile
1   5

<210> 943
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 943

Ser Lys Ile Gly Ser Leu Asp Asn Ile Thr
1   5   10

<210> 944
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 944

Lys Ile Gly Ser Leu Asp Asn Ile Thr
1   5

<210> 945
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 945

Ile Gly Ser Leu Asp Asn Ile Thr
1   5

<210> 946
<211> 7
<212> PRT

<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 946

Gly Ser Leu Asp Asn Ile Thr
1 5

<210> 947
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 947

Ser Leu Asp Asn Ile Thr
1 5

<210> 948
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 948

Lys Ile Gly Ser Leu Asp Asn Ile Thr His
1 5 10

<210> 949
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 949

Ile Gly Ser Leu Asp Asn Ile Thr His
1 5

<210> 950

<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 950

Gly Ser Leu Asp Asn Ile Thr His
1 5

<210> 951
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 951

Ser Leu Asp Asn Ile Thr His
1 5

<210> 952
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 952

Ile Gly Ser Leu Asp Asn Ile Thr His Val
1 5 10

<210> 953
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 953

Gly Ser Leu Asp Asn Ile Thr His Val
1 5

<210> 954
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 954

Ser Leu Asp Asn Ile Thr His Val
1   5

<210> 955
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 955

Gly Ser Leu Asp Asn Ile Thr His Val Pro
1   5   10

<210> 956
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 956

Ser Leu Asp Asn Ile Thr His Val Pro
1   5

<210> 957
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 957

Ser Leu Asp Asn Ile Thr His Val Pro Gly

1 5 10

<210> 958
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 958

Pro Asp Leu Lys Asn Val Lys Ser
1 5

<210> 959
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 959

Asp Leu Lys Asn Val Lys Ser Lys
1 5

<210> 960
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 960

Leu Lys Asn Val Lys Ser Lys Ile
1 5

<210> 961
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 961

Lys Asn Val Lys Ser Lys Ile Gly
1   5

<210> 962
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 962

Asn Val Lys Ser Lys Ile Gly Ser
1   5

<210> 963
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 963

Asp Leu Ser Asn Val Gln Ser Lys
1   5

<210> 964
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 964

Leu Ser Asn Val Gln Ser Lys Cys
1   5

<210> 965
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 965

Ser Asn Val Gln Ser Lys Cys Gly
1 5

<210> 966
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 966

Asn Val Gln Ser Lys Cys Gly Ser
1 5

<210> 967
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 967

Val Asp Leu Ser Lys Val Thr Ser
1 5

<210> 968
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 968

Asp Leu Ser Lys Val Thr Ser Lys
1 5

<210> 969
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 969

Leu Ser Lys Val Thr Ser Lys Cys
1   5

<210> 970
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 970

Ser Lys Val Thr Ser Lys Cys Gly
1   5

<210> 971
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 971

Lys Val Thr Ser Lys Cys Gly Ser
1   5

<210> 972
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 972

Leu Asp Phe Lys Asp Arg Val Gln
1   5

<210> 973
<211> 8
<212> PRT

<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 973

Asp Phe Lys Asp Arg Val Gln Ser
1 5

<210> 974
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 974

Phe Lys Asp Arg Val Gln Ser Lys
1 5

<210> 975
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 975

Lys Asp Arg Val Gln Ser Lys Ile
1 5

<210> 976
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 976

Asp Arg Val Gln Ser Lys Ile Gly
1 5

<210> 977

<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 977

Arg Val Gln Ser Lys Ile Gly Ser
1 5

<210> 978
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 978

Ser Lys Ile Gly Ser Thr Glu Asn Leu Lys His
1 5 10

<210> 979
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 979

Ser Lys Ile Gly Ser Thr Glu Asn Ile Lys His
1 5 10

<210> 980
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 980

Ser Lys Ile Gly Ser Lys Asp Asn Leu Lys His
1 5 10

<210> 981
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 981

Ser Lys Ile Gly Ser Lys Glu Asn Ile Lys His
1   5   10

<210> 982
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 982

Ser Lys Ile Gly Ser Leu Glu Asn Leu Lys His
1   5   10

<210> 983
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 983

Ser Lys Ile Gly Ser Leu Glu Asn Ile Lys His
1   5   10

<210> 984
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 984

Ser Lys Ile Gly Ser Thr Asp Asn Leu Lys His

1 5 10

<210> 985
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 985

Ser Lys Ile Gly Ser Thr Asp Asn Ile Lys His
1 5 10

<210> 986
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 986

Ser Lys Ile Gly Ser Lys Asp Asn Ile Lys His
1 5 10

<210> 987
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 987

Ser Lys Ile Gly Ser Leu Asp Asn Leu Lys His
1 5 10

<210> 988
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 988

Ser Lys Ile Gly Ser Leu Asp Asn Ile Lys His
1   5   10

<210> 989
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 989

Ser Lys Ile Gly Ser Thr Gly Asn Leu Lys His
1   5   10

<210> 990
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 990

Ser Lys Ile Gly Ser Thr Gly Asn Ile Lys His
1   5   10

<210> 991
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 991

Ser Lys Ile Gly Ser Lys Gly Asn Leu Lys His
1   5   10

<210> 992
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 992

Ser Lys Ile Gly Ser Lys Gly Asn Ile Lys His
1 5 10

<210> 993
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 993

Ser Lys Ile Gly Ser Leu Gly Asn Leu Lys His
1 5 10

<210> 994
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 994

Ser Lys Ile Gly Ser Leu Gly Asn Ile Lys His
1 5 10

<210> 995
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<220>
<221> MISC_FEATURE
<222> (2)..(2)
<223> Xaa is I or C

<220>
<221> MISC_FEATURE
<222> (3)..(3)
<223> Xaa is G

<220>
<221> MISC_FEATURE
<222> (5)..(5)
<223> Xaa is T or K or L

<220>
<221> MISC_FEATURE
<222> (6)..(6)
<223> Xaa is E or D or G

<220>
<221> MISC_FEATURE
<222> (8)..(8)
<223> Xaa is L or I

<220>
<221> MISC_FEATURE
<222> (9)..(9)
<223> Xaa is K or H or T

<400> 995

Lys Xaa Xaa Ser Xaa Xaa Asn Xaa Xaa His
1   5   10

<210> 996
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa can be Q or E

<220>
<221> MISC_FEATURE
<222> (6)..(6)
<223> Xaa can be S or P

<400> 996

Xaa Ile Val Tyr Lys Xaa
1   5

<210> 997
<211> 20
<212> PRT

<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 997

Asp Ala Glu Phe Arg His Asp Arg Arg Val Lys Ser Lys Ile Gly Ser
1 5 10 15

Thr Gly Gly Cys
20

<210> 998
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 998

Asp Ala Glu Phe Arg His Asp Arg Arg Ser Lys Ile Gly Ser Thr Glu
1 5 10 15

Asn Gly Gly Cys
20

<210> 999
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 999

Asp Ala Glu Phe Arg His Asp Arg Arg Thr Glu Asn Leu Lys His Gln
1 5 10 15

Pro Gly Gly Cys
20

<210> 1000
<211> 20
<212> PRT

<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1000

Asp Ala Glu Phe Arg His Asp Arg Arg Glu Asn Leu Lys His Gln Pro
1 5 10 15

Gly Gly Gly Cys
20

<210> 1001
<211> 23
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1001

Asp Ala Glu Phe Arg His Asp Arg Arg Ser Lys Ile Gly Ser Lys Asp
1 5 10 15

Asn Ile Lys His Gly Gly Cys
20

<210> 1002
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1002

Val His His Gln Lys Leu Val Phe Phe Ala
1 5 10

<210> 1003
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1003

Val His His Gln Lys Leu Val Phe Phe
1 5

<210> 1004
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1004

Val His His Gln Lys Leu Val Phe
1 5

<210> 1005
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1005

Val His His Gln Lys Leu Val
1 5

<210> 1006
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1006

Val His His Gln Lys Leu
1 5

<210> 1007
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1007

His His Gln Lys Leu Val Phe Phe Ala Glu
1   5   10

<210> 1008
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1008

His His Gln Lys Leu Val Phe Phe Ala
1   5

<210> 1009
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1009

His His Gln Lys Leu Val Phe Phe
1   5

<210> 1010
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1010

His His Gln Lys Leu Val Phe
1   5

<210> 1011
<211> 6
<212> PRT

<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1011

His His Gln Lys Leu Val
1 5

<210> 1012
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1012

His His Gln Lys Leu
1 5

<210> 1013
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1013

His Gln Lys Leu Val Phe Phe Ala Glu Asp
1 5 10

<210> 1014
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1014

His Gln Lys Leu Val Phe Phe Ala Glu
1 5

<210> 1015

<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1015

His Gln Lys Leu Val Phe Phe Ala
1   5

<210> 1016
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1016

His Gln Lys Leu Val Phe Phe
1   5

<210> 1017
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1017

His Gln Lys Leu Val Phe
1   5

<210> 1018
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1018

His Gln Lys Leu Val
1   5

<210> 1019
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1019

His Gln Lys Leu
1

<210> 1020
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1020

Gln Lys Leu Val Phe Phe Ala Glu Asp Val
1 5 10

<210> 1021
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1021

Gln Lys Leu Val Phe Phe Ala Glu Asp
1 5

<210> 1022
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1022

Gln Lys Leu Val Phe Phe Ala Glu

1 5

<210> 1023
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1023

Gln Lys Leu Val Phe Phe Ala
1 5

<210> 1024
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1024

Gln Lys Leu Val Phe Phe
1 5

<210> 1025
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1025

Gln Lys Leu Val Phe
1 5

<210> 1026
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1026

Gln Lys Leu Val
1

<210> 1027
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1027

Gln Lys Leu
1

<210> 1028
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1028

Lys Leu Val Phe Phe Ala Glu Asp Val Gly
1 5 10

<210> 1029
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1029

Lys Leu Val Phe Phe Ala Glu Asp Val
1 5

<210> 1030
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1030

Lys Leu Val Phe Phe Ala Glu Asp
1 5

<210> 1031
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1031

Lys Leu Val Phe Phe Ala Glu
1 5

<210> 1032
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1032

Lys Leu Val Phe Phe Ala
1 5

<210> 1033
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1033

Lys Leu Val Phe Phe
1 5

<210> 1034
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1034

Lys Leu Val Phe
1

<210> 1035
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1035

Lys Leu Val Phe
1

<210> 1036
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1036

Leu Val Phe Phe Ala Glu Asp Val Gly
1   5

<210> 1037
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1037

Leu Val Phe Phe Ala Glu Asp Val
1   5

<210> 1038
<211> 7
<212> PRT

<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1038

Leu Val Phe Phe Ala Glu Asp
1   5

<210> 1039
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1039

Leu Val Phe Phe Ala Glu
1   5

<210> 1040
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1040

Leu Val Phe Phe Ala
1   5

<210> 1041
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1041

Leu Val Phe Phe
1

<210> 1042

<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1042

Leu Val Phe
1

<210> 1043
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1043

Val Phe Phe Ala Glu Asp Val Gly
1   5

<210> 1044
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1044

Val Phe Phe Ala Glu Asp Val
1   5

<210> 1045
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1045

Val Phe Phe Ala Glu Asp
1   5

<210> 1046
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1046

Val Phe Phe Ala Glu
1   5

<210> 1047
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1047

Val Phe Phe Ala
1

<210> 1048
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1048

Val Phe Phe
1

<210> 1049
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1049

Phe Phe Ala Glu Asp Val Gly

1 5

<210> 1050
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1050

Phe Phe Ala Glu Asp Val
1 5

<210> 1051
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1051

Phe Phe Ala Glu Asp
1 5

<210> 1052
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1052

Phe Phe Ala Glu
1

<210> 1053
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1053

Phe Phe Ala
1

<210> 1054
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1054

Phe Ala Glu Asp Val Gly
1 5

<210> 1055
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1055

Phe Ala Glu Asp Val
1 5

<210> 1056
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1056

Phe Ala Glu Asp
1

<210> 1057
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1057

Phe Ala Glu
1

<210> 1058
<211> 31
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1058

Gln Thr Ala Pro Val Pro Met Pro Asp Leu Lys Asn Val Lys Ser Lys
1 5 10 15

Ile Gly Ser Thr Glu Asn Leu Lys His Gln Pro Gly Gly Gly Lys
20 25 30

<210> 1059
<211> 31
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1059

Val Gln Ile Ile Asn Lys Lys Leu Asp Leu Ser Asn Val Gln Ser Lys
1 5 10 15

Cys Gly Ser Lys Asp Asn Ile Lys His Val Pro Gly Gly Gly Ser
20 25 30

<210> 1060
<211> 31
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1060

Val Gln Ile Val Tyr Lys Pro Val Asp Leu Ser Lys Val Thr Ser Lys

1 5 10 15

Cys Gly Ser Leu Gly Asn Ile His His Lys Pro Gly Gly Gly Gln
20 25 30

<210> 1061
<211> 32
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 1061

Val Glu Val Lys Ser Glu Lys Leu Asp Phe Lys Asp Arg Val Gln Ser
1 5 10 15

Lys Ile Gly Ser Leu Asp Asn Ile Thr His Val Pro Gly Gly Gly Asn
20 25 30

<210> 1062
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> linker

<400> 1062

Gly Gly Gly Ser
1

<210> 1063
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> linker

<400> 1063

Gly Gly Gly Gly Ser
1 5