

CLAIMS

1. Use of a liposomal vaccine composition comprising:

(a) a β -amyloid (A β)-derived peptide antigen displayed on the surface of the liposome that comprises, consists essentially of or consists of amino acids 1-15 of A β ;

5 (b) a peptide comprising a universal T-cell epitope; and

(c) an adjuvant comprising monophosphoryl lipid A (MPLA);

in the preparation of a medicament for inducing an anti-A β immune response in a human subject without inducing a serious adverse event, in which the β -amyloid (A β)-derived peptide antigen is to be administered in an amount of 300-2000 μ g, preferably
10 300-1600 μ g, 300-1000 μ g or 300-900 μ g.

2. Use according to Claim 1, in which the peptide comprising a universal T-cell epitope:

(a) is, at least partially, encapsulated in the liposome;

(b) comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, and SEQ ID NO: 12, or an
15 analogue thereof;

(c) comprises at least two universal T-cell epitopes, each having an amino acid sequence selected from the group consisting of SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11 or SEQ ID NO: 12, in which the universal T-cell epitopes are joined by one or more linkers, and in which the one or more linker(s) comprise, consist
20 essentially of, or consist of the amino acids VVR, TVGLR, KVSVR, PMGAP or PMGLP, preferably VVR; and/or

(d) comprises, consists essentially of or consists of an amino acid sequence selected from the group consisting of SEQ ID NO: 5 (SAT44), SEQ ID NO: 6 (SAT47), SEQ ID NO: 7 (SAT 58), SEQ ID NO: 3 (SAT42), and SEQ ID NO: 4 (SAT43), or an analogue
25 thereof, preferably in which the peptide comprising a universal T-cell epitope comprises, consists essentially of or consists of the amino acid sequence of SEQ ID NO: 7 (SAT 58), or an analogue thereof.

3. Use according to any preceding claim, in which the β -amyloid (A β)-derived peptide antigen is:

- (a) to be administered in an amount of 300 µg, optionally in which the peptide comprising a universal T-cell epitope is to be administered in an amount of between 90 and 120 µg and the MPLA adjuvant is to be administered in an amount of between 65 and 90 µg;
- 5 (b) to be administered in an amount of 900 µg, optionally in which the peptide comprising a universal T-cell epitope is to be administered in an amount of between 270 and 360 µg and the MPLA is to be administered in an amount of between 200 and 270 µg; or
- 10 (c) to be administered in an amount of 1600 µg, optionally in which the β-amyloid (Aβ)-derived peptide antigen is to be administered in an amount of 1600 µg, the peptide comprising a universal T-cell epitope is to be administered in an amount of between 470 and 650 µg and the MPLA is to be administered in an amount of between 360 and 480 µg.
4. Use according to Claim 1, 2 or 3, in which:
- 15 (a) the β-amyloid (Aβ)-derived peptide antigen is lipidated and/or tetrapalmitoylated;
- (b) the adjuvant forms part of the outer layer of the liposome, optionally in which the adjuvant is, at least in part, displayed on the surface of the liposome;
- (c) the monophosphoryl lipid A (MPLA) comprises synthetic monophosphoryl lipid A (MPLA);
- 20 (d) the monophosphoryl lipid A (MPLA) comprises monophosphoryl Hexa-acyl Lipid A, 3-Deacyl (Synthetic) (3D-(6-acyl) PHAD®) and/or Phosphorylated HexaAcyl Disaccharide (PHAD®);
- (e) the liposome comprises phospholipids, optionally in which the phospholipids comprise dimyristoylphosphatidyl-choline (DMPC) and dimyristoylphosphatidyl-glycerol (DMPG); and/or
- 25 (f) the liposome comprises cholesterol, preferably in which the molar ratio of dimyristoylphosphatidyl-choline (DMPC): dimyristoylphosphatidyl-glycerol (DMPG): cholesterol is 9:1:7, optionally in which the molar ratio of dimyristoylphosphatidyl-choline (DMPC): dimyristoylphosphatidyl-glycerol (DMPG): cholesterol: MPLA is
- 30 9:1:7:0.05.

5. Use according to any preceding claim, in which the liposomal vaccine composition is to be administered by injection, optionally in which the liposomal vaccine composition is to be administered intramuscularly or subcutaneously.
6. Use according to any preceding claim, in which the liposomal vaccine composition is to be administered at a first time and is to be administered at a second time 1 to 4 weeks later.
7. Use according to any of Claims 1 to 5, in which the liposomal vaccine composition is to be administered every 4-12 weeks for a period of at least 48 weeks or at least 74 weeks; or in which the liposomal vaccine composition is to be administered at a first time and is to be administered at a second time 2 to 6 weeks later, preferably in which the second administration is 4 weeks after the first administration.
8. Use according to any preceding claim, in which the induced anti-A β immune response is obtained following two administrations of the liposomal vaccine.
9. Use according to Claim 6, 7 or 8, in which the liposomal vaccine composition is to be administered at a third time 6-10 weeks after the second administration of the vaccine composition, preferably in which the third administration is 8 weeks after the second administration, optionally further comprising a booster administration at a subsequent time point.
10. Use according to any preceding claim, in which administration of the liposomal vaccine composition results in a reduction in the amount of A β associated plaques in the brain of the subject.
11. Use according to any preceding claim, in which the induced anti-A β immune response is for treatment, prevention, induction of a protective immune response against or alleviating the symptoms associated with an amyloid-beta associated disease or condition in the human subject, preferably in which the amyloid-beta associated disease or condition is selected from Alzheimer's Disease, mild cognitive impairment (MCI), Down syndrome (DS), including Down syndrome-related Alzheimer's disease, cardiac amyloidosis, cerebral amyloid angiopathy (CAA), multiple sclerosis, Parkinson's disease, Lewy body dementia, ALS (amyotrophic lateral sclerosis), Adult Onset Diabetes, inclusion body myositis (IBM), ocular amyloidosis, glaucoma, macular degeneration, lattice dystrophy and optic neuritis, preferably in which:

(a) the Alzheimer's Disease is early Alzheimer's Disease, optionally in which the early Alzheimer's Disease includes prodromal Alzheimer's Disease, mild cognitive impairment due to Alzheimer's Disease and mild Alzheimer's Disease;

(b) the Alzheimer's Disease is prodromal Alzheimer's Disease, mild Alzheimer's Disease, mild-to-moderate Alzheimer's Disease, moderate Alzheimer's Disease or not severe Alzheimer's Disease; or

(c) the amyloid-beta associated disease or condition is Down Syndrome or Down syndrome-related Alzheimer's disease.

12. Use according to any preceding claim, in which the human subject, prior to treatment, displays cognitive function consistent with a Mini Mental State Examination (MMSE) score of at least 18, such as 18-28, or at least 20, such as 20-28, and/or in which the human subject is receiving at least one additional therapy selected from an acetylcholinesterase inhibitor (ACHEI) and/or memantine.

13. Use according to any preceding claim, in which the β -amyloid ($A\beta$)-derived peptide antigen is tetrapalmitoylated Abeta 1-15 as set forth in SEQ ID NO: 1.

14. Use of a liposomal vaccine composition comprising:

(a) a β -amyloid ($A\beta$)-derived peptide antigen displayed on the surface of the liposome that comprises, consists essentially of or consists of amino acids 1-15 of $A\beta$; in which the β -amyloid ($A\beta$)-derived peptide antigen is tetrapalmitoylated Abeta 1-15 as set forth in SEQ ID NO: 1;

(b) a peptide comprising a universal T-cell epitope comprising, consisting of, or essentially consisting of the amino acid sequence of SEQ ID NO: 7 (SAT 58), or an analogue thereof; and

(c) an adjuvant comprising monophosphoryl lipid A (MPLA), preferably 3D-(6-acyl) PHAD®;

in the preparation of a medicament for inducing an anti- $A\beta$ immune response in a human subject without inducing a serious adverse event, in which the β -amyloid ($A\beta$)-derived peptide antigen is to be administered in an amount of 300-2000 μ g, preferably in an amount of 300-1600 μ g, preferably in an amount of 300 μ g, 900 μ g or 1600 μ g.

15. A liposomal vaccine composition comprising:

(a) a β -amyloid ($A\beta$)-derived peptide antigen displayed on the surface of the liposome that comprises, consists essentially of or consists of amino acids 1-15 of $A\beta$, in which the β -amyloid ($A\beta$)-derived peptide antigen is tetrapalmitoylated Abeta 1-15 as set forth in SEQ ID NO: 1;

5 (b) a peptide comprising a universal T-cell epitope comprising, consisting of, or essentially consisting of the amino acid sequence of SEQ ID NO: 7 (SAT 58), or an analogue thereof;

(c) an adjuvant comprising monophosphoryl lipid A (MPLA), preferably 3D-(6-acyl) PHAD®;

10 preferably in which the vaccine composition comprises the β -amyloid ($A\beta$)-derived peptide antigen in an amount of 300 μ g, the peptide comprising a universal T-cell epitope in an amount of between 90 and 120 μ g, and the MPLA adjuvant in an amount of between 65 and 90 μ g; alternatively, in which the vaccine composition comprises the β -amyloid ($A\beta$)-derived peptide antigen in an amount of 900 μ g, the peptide comprising
15 a universal T-cell epitope in an amount of between 270 and 360 μ g, and the MPLA in an amount of between 200 and 270 μ g; alternatively, in which the vaccine composition comprises the β -amyloid ($A\beta$)-derived peptide antigen in an amount of 1600 μ g, the peptide comprising a universal T-cell epitope in an amount of between 470 and 650 μ g, and the MPLA in an amount of between 360 and 480 μ g.