There is an unmet need for passive and/or active immunotherapies that work to counteract the pathological protein conformers that are known - or presumed - to cause neurodegenerative disorders, such as amyloid pathology in AD caused, for example, by intra-neuronal aggregates of hyper-phosphorylated protein tau that are as typical for AD as amyloid.

This unmet need could be met within the scope of the present invention by providing passive and active immunization methods using liposome-based vaccines (Nicolau et al., 2002; Muhs et al., 2007) and mAbs based on phospho-peptides mimicking major pathological phospho-epitopes of protein tau. These combined actions generate novel specific mAbs against linear and conformational, simple and complex phospho-epitopes on protein tau that are thought to be responsible for synapto- and neuro-toxicity in tauopathies, including AD.

Summary

In one aspect, there is provided an antigenic construct comprising an antigenic peptide corresponding to a sequence within the tau protein comprising a phospho-epitope, which peptide is (a) modified through linkage to a lipophilic or hydrophobic moiety that facilitates insertion into the lipid bilayer of a liposome and (b) reconstituted in a liposome such that the peptide is presented on the surface of the liposome.

In another aspect, there is provided the antigenic construct as defined herein, or a combination thereof, for use in the treatment of neurodegenerative disorders such as tauopathies.

In another aspect, there is provided the antigenic construct as defined herein for use in the treatment of Alzheimer's Disease.

In another aspect, there is provided a pharmaceutical composition comprising the antigenic construct as defined herein or a combination thereof.

In another aspect, there is provided a pharmaceutical composition comprising an antigenic peptide of SEQ ID NO: 5, which peptide is modified by palmitic acid covalently bound to each of the termini of the peptide, and further comprising a pharmaceutically acceptable carrier and/or a pharmaceutically acceptable adjuvant and/or an immunomodulator and/or a diluent and/or an excipient.

In another aspect, there is provided a pharmaceutical composition comprising an antigenic peptide of SEQ ID NO: 3, which peptide is modified by palmitic acid covalently bound to each of the termini of the peptide, and further comprising a pharmaceutically acceptable carrier and/or a pharmaceutically acceptable adjuvant and/or an immunomodulator and/or a diluent and/or an excipient.

In another aspect, there is provided a pharmaceutical composition comprising an antigenic peptide of SEQ ID NO: 3 and SEQ ID NO: 4, which peptides are modified by palmitic acid covalently bound to each of the termini of the peptides, and further comprising a pharmaceutically acceptable carrier and/or a pharmaceutically acceptable adjuvant and/or an immunomodulator and/or a diluent and/or an excipient.

In another aspect, there is provided a pharmaceutical composition as defined herein for use in the treatment of a neurodegenerative disorder such as tauopathy.

In another aspect, there is provided the use of a therapeutic pharmaceutical composition as defined herein in the manufacture of a medicament for the treatment of a neurodegenerative disease or disorder such as tauopathy in an animal, particularly in a mammal, but especially in a human.

In another aspect, there is provided the use of an antigenic peptide or a therapeutic composition as defined herein in the manufacture of a medicament for inducing an immune response in an animal, particularly a mammal or a human, suffering from a neurodegenerative disorder such as tauopathy.

Description

The present invention provides novel methods and antigenic peptides according to the invention and as described herein and functional fragments thereof including compositions comprising said antigenic peptides or fragments thereof for eliciting a highly specific, particularly a conformation specific, immune response in an organism, but particularly within an animal, particularly a mammal or a human, which is highly effective and capable of preventing or alleviating tauopathies, or the symptoms associated with tauopathies, a group of diseases and disorders associated with the formation of neurofibrillary lesions, the predominant brain pathology in this group of neurodegenerative disorders.

The present invention also relates to the antibodies, particularly monoclonal antibodies, including functional parts thereof, and pharmaceutical compositions comprising said antibodies, which are resulting from the highly specific, particularly the conformation specific, immune response in an organism upon administration of the antigenic peptide according to the invention and as described herein or a functional fragment thereof and the composition comprising said antigenic peptide or fragment thereof for preventing or alleviating tauopathies, or the symptoms associated with tauopathies, a group of diseases and disorders associated with the formation of neurofibrillary lesions, the predominant brain pathology in this group of neurodegenerative disorders.

9. The antigenic construct according to any one of the preceding claims, wherein the hydrophobic moiety is palmitic acid.

10. The antigenic construct according to any one of the preceding claims, wherein said hydrophilic or hydrophobic moiety is covalently bound to each of the termini of the peptide or peptide fragment through at least one, particularly one or two amino acids such as, for example, lysine, glutamic acid and cysteine.

11. The antigenic construct according to any one of the preceding claims, wherein said peptide is further modified through linkage to a hydrophilic moiety.

12. The antigenic construct according to claim 11, wherein said hydrophilic moiety is polyethylene glycol.

13. The antigenic construct according to any one of the preceding claims, wherein said tau protein is a human protein.

14. The antigenic construct according to claim 13, wherein said antigenic peptide has an amino acid sequence of:

a. SEQ ID NO: 2 or an amino acid sequence of SEQ ID NO: 2 modified through conservative substitution, deletion or insertion of at least one but not more than 5 amino acids and still has the same antigenic potential as the unmodified sequence;

b. SEQ ID NO: 3 or an amino acid sequence of SEQ ID NO: 3 modified through conservative substitution, deletion or insertion of at least one but not more than 5 amino acids and still has the same antigenic potential as the unmodified sequence;

c. SEQ ID NO: 4 or an amino acid sequence of SEQ ID NO: 4 modified through conservative substitution, deletion or insertion of at least one but not more than 5 amino acids and still has the same or essentially the same antigenic potential as the unmodified sequence;

d. SEQ ID NO: 5 or an amino acid sequence of SEQ ID NO: 5 modified through conservative substitution, deletion or insertion of at least one