Aβ deposits to eventually solubilize or inhibit the growth of the pre-plaques. The Aβ oligomers are today considered as the most toxic Aβ species, which impairs most cognitive functions in DS people (Teller et al., 1996).

[0006] There is therefore a need for a prevention therapy which aims at preventing or slowing down the development of clinical symptoms associated with amyloid-related pathology in subjects with Down's syndrome (DS), such as, particularly, memory and/or cognitive impairments or abnormalities.

[0007] In particular, there is a need for a treatment of clinical symptoms associated with amyloid-related pathology in subjects with Down's syndrome (DS), which leads to an improvement in learning capabilities in subjects with Down's syndrome (DS) and/or improvement or restoration of memory and/or cognitive capacities.

Summary

[0007a] In one aspect, there is provided use of the M-terminal Aβ1-15 antigenic peptide fragment derived from the amyloid-β protein, in the manufacture of a medicament for the treatment and/or alleviation of memory and/or cognitive impairments or abnormalities in subjects with Down's syndrome, wherein the antigenic peptide is modified by lipophilic or hydrophobic moiety and reconstituted in a liposome and said subjects with Down's syndrome have not yet developed amyloid protein-associated plaques in the brain.

[0007b] In another aspect, there is provided use of a composition comprising the antigenic peptide as defined herein in a therapeutically effective amount together with a pharmaceutically acceptable carrier and/or excipient in the preparation of a medicament for the treatment and/or alleviation of memory and/or cognitive impairments or abnormalities in subjects with Down's syndrome, wherein said subjects with Down's syndrome have not yet developed amyloid protein-associated plaques in the brain.

[0007c] Also disclosed is use of an antigenic peptide or a composition as described herein in the manufacture of a medicament for treating and/or alleviating and/or preventing memory and/or cognitive impairments or abnormalities in a subject with Down's syndrome, wherein said medicament is to be administered to said subject.

[0007d] Also disclosed is the use of an antigenic peptide or a composition as described herein in the manufacture of a medicament for increasing retention of or completely restoring cognitive capacity in a subject with Down's syndrome, wherein said medicament is to be administered to said subject.

[0007e] Also disclosed is the use of an antigenic peptide or a composition as described herein in the manufacture of a medicament for preventing memory impairments or abnormalities in a subject with Down's syndrome, wherein the medicament is to be administered into said subject.

[0007f] Also disclosed is the use of an antigenic peptide or a composition as described herein in the manufacture of a medicament for reducing plaques in the brain in a subject with Down's syndrome, wherein said medicament is to be administered to said subject.

[0007g] In yet another aspect, there is provided use of the antigenic peptide as defined herein or the composition as defined herein in the preparation of a medicament for inducing an immune response against amyloid protein or amyloid-like protein in a subject with Down's syndrome wherein said subject with Down's syndrome has not yet developed amyloid protein-associated plaques in the brain.

[0007h] In yet another aspect, there is provided a method for producing a vaccine comprising formulating the antigenic peptide as defined herein or the composition as defined herein with a pharmacologically acceptable carrier and/or excipient and/or an adjuvant.

[0007i] Also disclosed is an antibody or an antibody mixture obtainable from an animal immunized with the antigenic peptide according to the present disclosure.

[0007j] Also disclosed is an antibody produced by immunization of a subject with the antigenic peptide of the present disclosure.

[0007k] Also disclosed is an antibody produced by immunization of a subject with the composition of the present disclosure.

Detailed Description

[0008] Within the scope of the present invention the measures and means are provided which help to meet this need. In particular, the present invention provides antigenic peptides for use in prevention therapy and in the treatment of AD-like cognitive impairments in children and in young to middle-aged subjects with Down's syndrome.

[0009] In a first embodiment, the present invention provides an antigenic peptide fragment derived from amyloid protein or amyloid-like protein, particularly an antigenic peptide fragment derived from amyloid-beta protein, or a composition comprising said antigenic peptide, for use in the treatment and/or alleviation and/or prevention of memory and/or cognitive impairments or abnormalities, particularly of AD-like memory and/or cognitive impairments or abnormalities, particularly impairments and abnormalities originating in the hippocampus and/or the prefrontal cortex and/or the entorhinal cortex of the brain, in young to middle-aged subjects with Down's syndrome, in particular in young subjects with Down's syndrome, who have not yet developed amyloid protein- or amyloid-like protein-associated plaques, particularly Aβ-associated plaques, in the brain.

[0010] In one embodiment, the present invention provides an antigenic peptide fragment derived from amyloid protein or amyloid-like protein, particularly an antigenic peptide fragment derived from amyloid beta protein, or a composition

CLAIMS

1. Use of the N-terminal Aβ1-15 antigenic peptide fragment derived from the amyloid-β protein, in the manufacture of a medicament for the treatment and/or alleviation of memory and/or cognitive impairments or abnormalities in subjects with Down's syndrome, wherein the antigenic peptide is modified by lipophilic or hydrophobic moiety and reconstituted in a liposome and said subjects with Down's syndrome have not yet developed amyloid protein-associated plaques in the brain.

2. The use of claim 1, wherein said memory and/or cognitive impairments originate in the hippocampus and/or the prefrontal cortex and/or the entorhinal cortex of the brain.

3. The use of claim 1 or claim 2, wherein said memory and/or cognitive impairments are impairments of recognition memory and/or impairments of the contextual associative memory and/or impairments of the associative learning and/or impairments of the declarative memory for facts and events and/or episodic memory impairments and/or language dysfunction such as aphasia and/or visuospatial impairments, such as misplacement of items and difficulty navigating in unfamiliar and familiar terrain and/or decreased executive functions, such as apathy, disinhibition, social isolation, poor judgment, difficulties with planning and/or poor abstract reasoning and/or personality changes and/or emotional changes such as apathy, agitation and psychosis and/or apraxia and/or impairments of performing learned motor tasks and/or pyramidal and extrapyramidal findings as well as myoclonus or seizures.

4. The use of any one of claims 1 to 3, wherein said memory and/or cognitive impairments or abnormalities in subjects with Down's syndrome are AD-like memory and/or cognitive impairments or abnormalities.

5. The use of any one of claims 1 to 4, wherein said subject with Down's syndrome is

    a) a middle-aged subject; or
    b) a young-aged subject; or

c) a children-aged subject.

6. The use of any one of claims 1 to 5, wherein said subject is below age 65, particularly below 60, particularly below 55, particularly below 50, particularly below 45, particularly below 40, particularly below 35, particularly below 30, particularly below 25, particularly below 20, particularly below 15, particularly below 10 particularly below 5, particularly below 3.

7. The use of any one of claims1 to 6, wherein said treatment leads to

a. an amelioration, and/or enhancing and/or restoration of memory; and/or

b. an increase in the retention or a restoration of cognitive capacity in the treated subject.

8. The use of any of the claims 1 to 6, wherein said treatment leads to

a. enhancing or restoring recognition memory; and/or
b. enhancing or restoring contextual associative memory; and/or
c. enhancing or restoring associative learning.

9. The use of any one of claims 1 to 8, wherein said treatment does not induce unwanted side effects such as meningoencephalitis and microhemorrhage.

10. The use of any one of claims 1 to 9,wherein the Aβ peptide antigen is modified by one or more palmitic acids bound to the N- and/or C-terminus of the peptide.

11. The use of claim 10, wherein the Aβ peptide antigen is modified by

a. four palmitic acids bound to the N- and/or C-terminus of the peptide; or

b. two palmitic acids bound to the N- and/or C-terminus of the peptide.

12. Use of a composition comprising the antigenic peptide as defined in any one of claims 1 to 11 in a therapeutically effective amount together with a pharmaceutically acceptable carrier and/or excipient in the preparation of a medicament for the treatment and/or alleviation of memory and/or

cognitive impairments or abnormalities in subjects with Down's syndrome, wherein said subjects with Down's syndrome have not yet developed amyloid protein-associated plaques in the brain.

13. The use of claim 12, wherein the composition comprises an adjuvant.

14. The use of claim 12 or claim 13 for the treatment and/or alleviation of a disease or impairment as defined in any one of claims 2 to 9.

15. Use of the antigenic peptide as defined in any one of claims 1 to 11 or the composition as defined in any one of claims 12 to 14 in the preparation of a medicament for inducing an immune response against amyloid protein or amyloid-like protein in a subject with Down's syndrome, wherein said subject with Down's syndrome has not yet developed amyloid protein-associated plaques in the brain.

16. A method for producing a vaccine comprising formulating the antigenic peptide as defined in any one of claims 1 to 11 or the composition as defined in claims 12 with a pharmacologically acceptable carrier and/or excipient and/or an adjuvant.