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 an antigenic peptide fragment derived from amyloid protein or amyloid-like protein for use in the treatment and/or alleviation and/or prevention of memory and/or cognitive impairments or abnormalities in subjects with Down's syndrome.

**[0007b]** In another aspect, there is provided a composition comprising the antigenic peptide as described herein in a therapeutically effective amount together with a pharmaceutically acceptable carrier and/or excipient for use in the treatment and/or alleviation and/or prevention of memory and/or cognitive impairments or abnormalities in subjects with Down's syndrome.

**[0007c]** In yet another aspect, there is provided 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]** In yet another aspect, there is provided 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]** In yet another aspect, there is provided 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]** In yet another aspect, there is provided 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 an antigenic peptide or a composition as described herein in the manufacture of a medicament for inducing an immune response against amyloid protein or amyloid-like protein in a subject with Down's syndrome.

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

**[0007i]** In yet another aspect, there is provided an antibody or an antibody mixture obtainable from an animal immunized with the vaccine obtained by the method of the present disclosure.

**[0007j]** In yet another aspect, there is provided an antibody or an antibody mixture obtainable from an animal immunized with the antigenic peptide according to the present disclosure.

**[0007k]** In yet another aspect, there is provided an antibody produced by immunization of a subject with the antigenic peptide of the present disclosure.

**[0007l]** In yet another aspect, there is provided 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

35. The antigenic peptide of any of the preceding claims, wherein said antigenic peptide is derived from the N-terminal part of the Aβ peptide, particularly said antigenic peptide consists of all or part of amino acid residues Aβ1-15, Aβ1-16, Aβ1-17, Aβ1-18, Aβ1-19, Aβ1-20, Aβ1-22, or Aβ1-23.

36. The antigenic peptide of any of the preceding claims, wherein said antigenic peptide is derived from the N-terminal part of the Aβ peptide, particularly said antigenic peptide consists of all or part of amino acid residues.

37. The antigenic peptide of any of the preceding claims, wherein said antigenic peptide consists of residues Aβ1-15.

38. The antigenic peptide of any of the preceding claims, wherein said antigenic peptide is derived from the C-terminal part of the Aβ peptide, particularly said antigenic peptide consists of all or part of amino acid residues Aβ20-36, Aβ20-40, Aβ20-42, Aβ21-36, Aβ21-40, Aβ21-42, Aβ22-36, Aβ22-40 or Aβ22-42.

39. The antigenic peptide of any of the preceding claims, wherein said antigenic peptide consists of residues Aβ22-35.

40. ~~A method for treating and/or alleviating and/or preventing memory and/or cognitive impairments or abnormalities in a subject with Down's syndrome comprising administering to said subject~~ Use of an antigenic peptide or a composition according to any of the preceding claims 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.

41. The ~~method~~ use of claim 40, wherein said impairment or abnormality originates in the hippocampus and/or the prefrontal cortex and/or the entorhinal cortex of the brain.

42. The ~~method~~ use of claims 40 and 41, wherein said impairment or abnormality concerns 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 other neurological signs including pyramidal and extrapyramidal findings as well as myoclonus or seizures.

43. The ~~method~~ use of any of ~~the preceding~~ claims 40 to 42, wherein said antigenic peptide for use in ~~a method of~~ enhancing or restoring recognition memory in subjects with Down's syndrome is derived from the N-terminal part of the Aβ peptide, particularly said antigenic peptide consists of all or part of amino acid residues Aβ1-15, Aβ1-16, Aβ1-17, Aβ1-18, Aβ1-19, Aβ1-20, Aβ1-22, or Aβ1-23.

44. The ~~method~~ use of any of ~~the preceding~~ claims 40 to 43, wherein said antigenic peptide for use in ~~a method of~~ enhancing or restoring recognition memory in subjects with Down's syndrome is derived from the N-terminal part of the Aβ peptide, particularly said antigenic peptide consists of all or part of amino acid residues.

45. The ~~method~~ use of any of ~~the preceding~~ claims 40 to 44, wherein said antigenic peptide consists of amino acid residues Aβ1-15.

46. The ~~method~~ use of any of ~~the preceding~~ claims 40 to 45, wherein said antigenic peptide for use in ~~a method of~~ enhancing or restoring contextual associative memory in subjects with Down's syndrome is derived from the N-terminal part of the Aβ peptide, particularly said antigenic peptide consists of all or part of amino acid residues Aβ1-15, Aβ1-16, Aβ1-17, Aβ1-18, Aβ1-19, Aβ1-20, Aβ1-22, or Aβ1-23.

47. The ~~method~~ use of any of ~~the preceding~~ claims 40 to 46, wherein said antigenic peptide for use in ~~a method of~~ enhancing or restoring associative learning in subjects with Down's syndrome is derived from the N-terminal part of the Aβ peptide, particularly said antigenic peptide consists of all or part of amino acid residues Aβ1-15, Aβ1-16, Aβ1-17, Aβ1-18, Aβ1-19, Aβ1-20, Aβ1-22, or Aβ1-23.

48. The ~~method~~ use of any of ~~the preceding~~ claims 40 to 47, wherein said antigenic peptide for use in ~~a method of~~ enhancing or restoring associative learning in subjects with Down's syndrome is derived from the C-terminal part of the Aβ peptide, particularly said antigenic peptide consists of all or part of amino acid residues Aβ20-36, Aβ20-40, Aβ20-42, Aβ21-36, Aβ21-40, Aβ21-42, Aβ22-36, Aβ22-40 or Aβ22-42.

49. The ~~method~~ use of any of ~~the preceding~~ claims 40 to 48, wherein said antigenic peptide consists of amino acid residues Aβ22-35.

50. ~~A method according to any one of the preceding claims for increasing retention of or completely restoring cognitive capacity in a subject with Down's syndrome comprising administering to said subject~~ Use of an antigenic peptide or a composition according to any of the preceding claims 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.

51. The antigenic peptide, composition or ~~method~~ use according to any one of the preceding claims, wherein said subject has not yet developed Aβ-associated plaques in the brain.

52. The ~~method~~ antigenic peptide, composition or use according to any one of the preceding claims, wherein said subject has developed Aβ-associated plaques in the brain.

53. The ~~method~~ antigenic peptide, composition or use according to any one of the preceding claims, wherein said subject with Down's syndrome is a young to middle-aged subject.

54. The ~~method~~ antigenic peptide, composition or use according to any one of the preceding claims, wherein said subject with Down's syndrome is a middle-aged subject.

55. The ~~method~~ antigenic peptide, composition or use according to any one of the preceding claims, wherein said subject with Down's syndrome is a young-aged subject.

56. The ~~method~~ antigenic peptide, composition or use according to any one of the preceding claims, wherein said subject with Down's syndrome is a children-aged subject.

57. The ~~method~~ antigenic peptide, composition or use according to any one of the preceding claims, 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.

58. ~~A method for preventing memory and/or cognitive impairments or abnormalities in a subject with Down's syndrome comprising administering to said subject~~ Use of an antigenic peptide or a composition according to ~~any of the preceding~~ claims 1-39 in the manufacture of a medicament for preventing memory and/or cognitive impairments or abnormalities in a subject with Down's syndrome, wherein the medicament is to be administered to said subject.

59. ~~A method for preventing memory impairments or abnormalities in a subject with Down's syndrome comprising administering to said subject~~ Use of an antigenic peptide or a composition according to ~~any of the preceding~~ claims 1-39 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.

60. ~~A method of reducing plaques in the brain in a subject with Down's syndrome comprising administering to said subject~~ Use of an antigenic peptide or a composition according to any of the preceding claims 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.

61. The ~~method~~ use of claim 60 wherein the antigenic peptide or a composition according to any of the preceding claims reduces plaques in the hippocampus and/or the prefrontal cortex and/or the entorhinal cortex of the brain.

62. The ~~method~~ use of claims 60 and 61 wherein said reduction of plaques leads to the alleviation and/or prevention of impairment or abnormality concerning the 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 other neurological signs including pyramidal and extrapyramidal findings as well as myoclonus or seizures.

63. The antigenic peptide, the composition and/or the ~~method~~ use of any of the preceding claims, wherein said antigenic peptide, composition and/or ~~method~~ use is ~~used~~ for prevention of neurodegeneration.

64. Use of an antigenic peptide or a composition according to claims 1 to 39 in the manufacture of a medicament for ~~A method~~ for inducing an immune response against amyloid protein or amyloid-like protein in a subject with Down's syndrome.

65. An *in vitro* method for producing a vaccine comprising formulating the antigenic peptide or composition of any of the preceding claims with a pharmacologically acceptable carrier or excipient and/or an adjuvant. .

66. An antibody **or an antibody mixture** obtainable from an animal immunized with the vaccine obtained by the method of claim 65.

67. An antibody **or an antibody mixture** obtainable from an animal immunized with the antigenic peptide according to any one of the preceding claims.

68. An antibody produced by immunization of a subject with the antigenic peptide of any of the preceding claims.

69. An antibody produced by immunization of a subject with the composition of any of the preceding claims.