

Claims

1. An antibody, wherein the variable part of the light chain of said antibody comprises or consists of an amino acid sequence of:

DVVMTQSPSLPVTLGQPASISCKSSQSLLYSDGKTYLNWFQQRPGQSPRRLTYLVSKLDSGVP
DRFSGSGSGTDFTLKISRVEAEDVGVYYCVQGTHFPFTFGGGTKVEIK (SEQ ID NO: 1),

wherein the variable part of heavy chain of said antibody comprises or consists of an amino acid sequence of:

QVQLVQSGAEVVKPGASVKVSCKASGYSFTGHTMNWVRQAPGGLEWMGLINPSDGVTRYNQKF
QGRVTITRDTSTTTVHMELTSLTSEDATYYCTREAKREWDETYWGQGLTVTVSS (SEQ ID
NO: 2);

and wherein said antibody specifically binds to an epitope at the N-terminus of pyroglutamated amyloid beta (A β N3pE) peptide.

2. The antibody according to claim 1, wherein the light chain comprises or consists of the amino acid sequence of:

DVVMTQSPSLPVTLGQPASISCKSSQSLLYSDGKTYLNWFQQRPGQSPRRLTYLVSKLDSGVP
DRFSGSGSGTDFTLKISRVEAEDVGVYYCVQGTHFPFTFGGGTKVEIKRTVAAPSVFIFPPSDE
QLKSGTASVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKSTYLSSTLTLSKADYE
KHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 17).

3. The antibody according to any one of the preceding claims, wherein the heavy chain comprises or consists of the amino acid sequence of:

QVQLVQSGAEVVKPGASVKVSCKASGYSFTGHTMNWVRQAPGGLEWMGLINPSDGVTRYNQKF
QGRVTITRDTSTTTVHMELTSLTSEDATYYCTREAKREWDETYWGQGLTVTVSSASTKGPSVF
PLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPS
SSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMIS
RTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKE
YKCAVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE

SNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSVMSHEALHNHYTQKSLSLSPG
K (SEQ ID NO: 18).

4. The antibody according to any one of the preceding claims,
5 wherein the heavy chain comprises or consists of the amino acid
sequence of:

QVQLVQSGAEVVKPGASVKVSCKASGYSFTGHTMNWVRQAPGGLEWMGLINPSDGVTRYNQKF
QGRVTITRDTSTTTVHMELTSLTSEDATYYCTREAKREWDETYWGQGLTVTVSSASTKGPSVF
10 PLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPS
SSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMIS
RTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE
SNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSVMSHEALHNHYTQKSLSLSPG
15 K (SEQ ID NO: 19).

5. The antibody according to any one of the preceding claims,
wherein said humanized antibody binds specifically to an epitope
selected from the group consisting of

20 pEFRHDSGYEVHHQKLV (SEQ ID NO: 23),
pEFRHDSGYEVHHQKL (SEQ ID NO: 24),
pEFRHDSGYEVHHQK (SEQ ID NO: 25),
pEFRHDSGYEVHHQ (SEQ ID NO: 26),
25 pEFRHDSGYEVHH (SEQ ID NO: 27),
pEFRHDSGYEVH (SEQ ID NO: 28),
pEFRHDSGYEV (SEQ ID NO: 29),
pEFRHDSGYE (SEQ ID NO: 30),
pEFRHDSGY (SEQ ID NO: 31),
30 pEFRHDSG (SEQ ID NO: 32), and
pEFRHDS (SEQ ID NO: 33).

6. The antibody according to any one of claims 1 to 5, wherein
said humanized antibody of the invention binds to an A β N3pE

variant, wherein the A β N3pE variant is defined as pE-A β_{3-x} , wherein x is defined as an integer between 19 and 42.

7. The antibody of claim 6, wherein the A β N3pE variant is selected from:

pE-A β_{3-38} ,

pE-A β_{3-40} ,

pE-A β_{3-42} .

8. A pharmaceutical composition comprising the antibody according to any one of the preceding claims.

9. The pharmaceutical composition of claim 8, further comprising a further biologically active substance and/or a pharmaceutically acceptable carrier and/or a diluent and/or an excipient.

10. The pharmaceutical composition of claim 9, wherein said further biologically active substance is selected from neutron-transmission enhancers, psychotherapeutic drugs, acetylcholine esterase inhibitors, calcium-channel blockers, biogenic amines, benzodiazepine tranquillizers, acetylcholine synthesis, storage or release enhancers, acetylcholine postsynaptic receptor agonists, monoamine oxidase-A or -B inhibitors, N-methyl- D-aspartate glutamate receptor antagonists, non-steroidal anti-inflammatory drugs, antioxidants, and serotonergic receptor antagonists.

11. The pharmaceutical composition of claim 10, wherein said further biologically active substance is selected from the group consisting of compounds effective against oxidative stress, anti-apoptotic compounds, metal chelators, inhibitors of DNA repair such as pirenzepin and metabolites, 3- amino-1-propanesulfonic acid (3 APS), 1,3-propanedisulfonate (1,3PDS), α -secretase activators, β - and γ -secretase inhibitors, tau proteins, neurotransmitter, β -sheet breakers, attractants for amyloid beta clearing / depleting cellular components, inhibitors of N-terminal

truncated amyloid beta including pyroglutamated amyloid beta 3-42, such as inhibitors of glutaminy cyclase, anti-inflammatory molecules, or cholinesterase inhibitors (ChEIs) such as tacrine, rivastigmine, donepezil, and/or galantamine, M1 agonists and other drugs including any amyloid or tau modifying drugs and nutritive supplements, cholinesterase inhibitors (ChEIs), memantine or glutaminy cyclase inhibitors.

12. Use of the antibody according to any one of claims 1 to 7 or the pharmaceutical composition according to any one of claims 8 to 11 in the manufacture of a medicament for the treatment of a neurodegenerative disease selected from the group consisting of mild cognitive impairment (MCI), Alzheimer's disease (AD), like for instance sporadic Alzheimer's disease (SAD) or Familial Alzheimer's dementias (FAD) like Familial British Dementia (FBD) and Familial Danish Dementia (FDD), neurodegeneration in Down Syndrome and clinical or pre-clinical cerebral amyloid angiopathy; and/or the treatment of a condition selected from prodromal AD, mild AD, moderate AD and severe AD and/or the slowing of cognitive decline in a patient diagnosed with a condition selected from clinical or pre-clinical Alzheimer's disease, Down's syndrome, and clinical or pre-clinical cerebral amyloid angiopathy.

13. The use according to claim 12, wherein the administration of said antibody or said pharmaceutical composition leads to the reversion of cognitive decline, improvement of cognition or the prevention of cognitive decline in a subject diagnosed with mild cognitive impairment (MCI), Alzheimer's disease (AD), like for instance sporadic Alzheimer's disease (SAD) or Familial Alzheimer's dementias (FAD) like Familial British Dementia (FBD) and Familial Danish Dementia (FDD), neurodegeneration in Down Syndrome and clinical or pre-clinical cerebral amyloid angiopathy

and/or of a condition selected from prodromal AD, mild AD, moderate AD and severe AD; or

5 wherein the administration of said antibody or said pharmaceutical composition leads to the clearance or removal of A β N3pE from plaques or other biological complexes; or

10 wherein the administration of said antibody or said pharmaceutical composition leads to the reduction of the plaque load and/or the removal of complete plaques from the affected tissue, such as brain tissue.