

De novo induction of amyloid- β deposition in vivo

Alzheimer's disease (AD), the most common type of senile dementia, is associated to the buildup of misfolded amyloid- β (A β) in the brain. Although compelling evidences indicate that the misfolding and oligomerization of A β is the triggering event in AD, the mechanisms responsible for the initiation of A β accumulation are unknown. In this study, we show that A β deposition can be induced by injection of AD brain extracts into animals, which, without exposure to this material, will never develop these alterations. The accumulation of A β deposits increased progressively with the time after inoculation, and the A β lesions were observed in brain areas far from the injection site. Our results suggest that some of the typical brain abnormalities associated with AD can be induced by a prion-like mechanism of disease transmission through propagation of protein misfolding. These findings may have broad implications for understanding the molecular mechanisms responsible for the initiation of AD, and may contribute to the development of new strategies for disease prevention and intervention.

Link: <http://www.ncbi.nlm.nih.gov/pubmed/21968933>

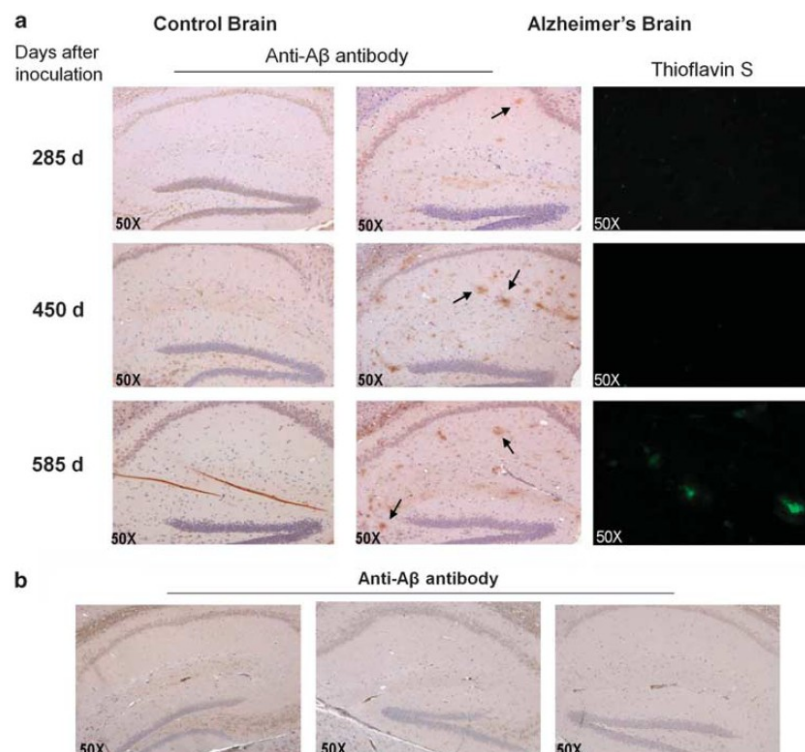


Figure. Human wild-type amyloid precursor protein (APP) gene (HuAPPwt) mice inoculated with Alzheimer's disease (AD) brain extracts develop cerebral amyloid- β (A β) deposits. (a) HuAPPwt mice injected with brain homogenates from a healthy individual (left panel) or an AD patient (middle and right panels) were killed at different times after injection. Brain slides were stained with anti-A β (4G8) antibody (left and middle panels) or Thioflavin S (ThioS; right panels). Pictures correspond to

representative slides of all animals analyzed. Arrows point to A β deposits typically observed in the inoculated mice. (b) Representative slides of the hippocampus of three different mice killed 30 days-post injection (dpi), where no A β deposits were detected by immunohistochemistry (4G8). Similar results were obtained in animals killed 90 dpi (data not shown). Picture magnification is indicated in the bottom-left corner.