**Lay Summary**

**BRAIN UK Ref: 14/002**

**Age-modified forms of amyloid-β in a Drosophila model of neurodegeneration and in the brain of Aβ immunised Alzheimer's disease patients**

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Alzheimer Disease (AD) is the commonest form of dementia, with ageing as the main risk factor. There are currently over 6 million people with dementia in the European Union (EU). The increasingly ageing population makes AD an economic and social burden for our society, thus investigating the pathological mechanisms of AD and the characterization of the pharmacological targets are research priorities. Deposition of amyloid-Beta (Aβ) is considered a driving force in AD pathogenesis, and the major target for vaccination.

During ageing in humans, the molecules of AD pathogenesis undergo ageing processes resulting in biological modifications that influence protein formation and function. Specially, pyroglutamate-modified Aβ (pEAβ) seems to be a key participant in AD pathology. Accordingly, the identification of markers of protein ageing is important to comprehend AD pathogenesis with relevance in therapies. Indeed, Aβ immunotherapy did not prevent dementia in the treated patients, potentially due to the absence of elimination of aged-modified Aβ implicated in the disease. We propose to take advantage of the unique cohort of human unimmunized and immunized AD brains at UoS to study if pEAβ formation and its interaction with tau, the other deposited molecule in AD, has been modified by Aβ vaccination. The results will expand the Aβ characterization as a pharmacological target, and support the rational design of a second generation of “Aβ vaccination”.