Detection and Clearance of AD Lesions

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Country

USA

Title of project or programme

Detection and Clearance of AD Lesions

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 1,249,762.39

Start date of award

01/02/2002

Total duration of award in years

15

The project/programme is most relevant to:

Alzheimer's disease & other dementias

Keywords

Acquired Cognitive Impairment... Aging... Alzheimer's Disease... Alzheimer's Disease Related Dementias (ADRD)... Alzheimer's Disease including Alzheimer's Disease Related Dementias (AD/ADRD)... Brain Disorders... Cerebrovascular... Dementia... Immune System... Immunization... Neurodegenerative... Neurosciences... Prevention... Vaccine Related... Vascular Cognitive Impairment/Dementia

Research Abstract

DESCRIPTION (provided by applicant): The extracellular accumulations of amyloid ¿ (A¿)

peptides as plaques and cerebral amyloid angiopathy (CAA), as well as intracellular neurofibrillary tangles (NFTs) are pathological hallmarks of Alzheimer’s disease (AD). Treatments for AD available currently provide largely symptomatic relief with only minor effects on the course of the disease; hence, there is an urgent need for better therapeutic interventions. An intervention that is hoped to have a significant impact on disease progression in the near future is active or passive immunization with numerous past and on-going clinical trials. However, results so far indicate that despite successfully reducing plaque amyloid, the clinical benefits to patients are very limited. Major difficulties identified with the current approaches is that they specifically only target plaque amyloid, while having limited effect on CAA or may increase CAA and associated microhemorrhages and also limited or no effect on tau related pathology. The central hypothesis we plan to test in our proposal is that it is essential to develo and test therapeutic interventions which are effective against both amyloid plaques and CAA, as well as reducing tau related pathology. In this proposal we will further develop and test two approaches which we have already shown to be able to clear plaque amyloid, in the prior funded period of this grant. We hypothesize that these therapeutic approaches can also ameliorate both CAA and tau related pathology. We have previously shown that stimulation of innate immunity with the TLR9 agonist CpG ODN administration in Tg2576 AD model mice led to a remarkable reduction of the plaque amyloid burden which was associated with significant cognitive improvement, in the absence of any toxicity. We have preliminary data that TLR9 stimulation is also effective at reducing tau related pathology in 3xTg mice with both plaque and tau pathology. We have also shown that modulating the binding between A¿ and apolipoprotein (apo) E can diminish amyloid plaques using A¿12-28P (an inhibitor of A¿ and apoE binding) and dramatically reduce CAA in a vascular amyloid mouse model TgSwDI. In this proposal we will further test these two approaches in models of extensive CAA and in tau AD models for efficacy and safety. We will also test whether the treatment effect on the reduction of the CAA burden can be followed longitudinally in vivo using USPIO amyloid binding particles for mMRI on a subset of Tg mice in aims 1 and 2, using a modification of methods we have recently published. We believe our planned studies of these innovative methods to clear and detect AD pathology will have a significant impact on the field.

Lay Summary

The central hypothesis we plan to test in our proposal is that to effectively treat Alzheimer’s disease, it is essential to develop and test therapeutic interventions, such as the two methods we plan to use, which are effective against both amyloid plaques and congophilic amyloid angiopathy, as well as reducing tau related pathology. We will test stimulation of the innate immune system via TLR9 agonists and blocking the interaction between apolipoprotein E and amyloid ?, as therapeutic interventions where we plan to follow the treatment effect with our novel mMRI approach.

Further information available at:

Types:
Investments > €500k

Member States:
United States of America

Diseases:
Alzheimer's disease & other dementias

Years:
2016

Database Categories:
N/A

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