Influence of systemic immune inflammation upon the tauopathy phenotype in mouse models

https://neurodegenerationresearch.eu/survey/influence-of-systemic-immune-inflammation-upon-the-tauopathy-phenotype-in-mouse-models/

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Country

USA

Title of project or programme

Influence of systemic immune inflammation upon the tauopathy phenotype in mouse models

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 3,198,256.88

Start date of award

01/08/2016

Total duration of award in years

1

The project/programme is most relevant to:

Alzheimer's disease & other dementias

Keywords

Acquired Cognitive Impairment... Aging... Alzheimer's Disease... Alzheimer's Disease including Alzheimer's Disease Related Dementias (AD/ADRD)... Biotechnology... Brain Disorders... Dementia... Genetics... Immune System... Infectious Disease and Bioterrorism... Infectious

Diseases... Neurodegenerative... Neurosciences

Research Abstract

? DESCRIPTION (provided by applicant): This project is in response to RFA “”Immune and Inflammatory Mechanisms in AD””. A consortium of investigators with expertise in mouse models, behavior, surgery, histopathology, neurochemistry, immunology, brain aging and Alzheimer’s disease have been assembled to approach the problem of systemic immune system influences on the development of AD pathology, specifically tau deposition. Two major questions are addressed. The first question regards the role of physiological aging in the nervous system, the cellular/humoral circulation or both in regulating the accumulation of tau pathology or modulating its impact upon the CNS. We plan to discern the relative contribution of CNS versus systemic influences by attempting to rejuvenate or senesce the systemic circulation and monitor the impact upon the tau phenotype in the brain of young and old mice. Our preliminary data indicate that even by middle age mice have enhanced sensitivity to tau over-expression, with accumulation of pathology when tauopathy is initiated at 11 mo, but not at 4 mo. The second question regards the influence of immunostimulants as sterile mimetics of different types of infections. Lipopolysaccharide will be used as a prototype, but immunostimulants mimicking viral and fungal infections will also be examined. An extensive human literature indicates that infections or trauma resulting in delirium increase risk of AD and accelerate the course of cognitive decline. We further expect these immunostimulants will exacerbate the tau pathology, and synergize with the age of the mice. Finally, we will seek to counter the impacts of age or innate immunostimulants by reversing the effects of aging on specific proteins in the circulation. This is based on recent work by others that indicate the rejuvenating effects of parabiosis can be replicated by supplementation with a single protein shown to decline during aging. Other work shows the senescing effects of parabiosis can be replicated by another individual protein that increases with age. We will discover additional candidate proteins through proteomic analysis of plasma protein responses to age and immunostimulant treatment. Success in these aims will provide candidate targets to be explored for intervention in individuals with delirium to make the cognitive decline reversible, as in younger individuals, rather than contributing to the onset or progression of dementia.

Lay Summary

PUBLIC HEALTH RELEVANCE: This project will seek to identify blood-based proteins that may be manipulated in order to benefit individuals with delirium. Studies demonstrate older adults with delirium have increased risk for dementia and/or accelerated decline in cognitive function. This project will seek to identify proteins that in the context of aging influence the brin environment to become susceptible to Alzheimer’s disease pathology. Modifying the levels of these proteins may decrease this susceptibility.

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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