

Genome-wide analysis of tau neurotoxicity

<https://www.neurodegenerationresearch.eu/survey/genome-wide-analysis-of-tau-neurotoxicity/>

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Country

USA

Title of project or programme

Genome-wide analysis of tau neurotoxicity

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NIH (NIA)

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€ 1,834,225.69

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15/09/2012

Total duration of award in years

5

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)... Biotechnology... Brain Disorders... Dementia... Frontotemporal Dementia (FTD)... Genetics... Human Genome... Neurodegenerative... Neurosciences

Research Abstract

DESCRIPTION (provided by applicant): Alzheimer's disease is the most common neurodegenerative disorder and is characterized pathologically by the intraneuronal deposition

of abnormally phosphorylated and aggregated tau protein and by the formation of extracellular amyloid plaques. Abnormal deposition of tau into neurofibrillary tangles is also the primary pathologic feature of a group of less common disorders, collectively termed the “tauopathies.” To define the molecular mechanisms controlling tau-induced neurodegeneration we and others have modeled tauopathies in the simple and powerful genetic model organism *Drosophila*. Genetic, biochemical and cell biological experiments in *Drosophila* have provided important clues regarding the pathogenesis of tauopathies. However, the unbiased forward genetic screens providing the bases for these studies, while valuable, have to date remained incomplete. Here we propose to use newly created and powerful whole-genome transgenic RNAi collections to perform comprehensive genetic analysis of tau neurotoxicity in vivo. We will complement these studies by with a state of the art transcriptomics in human Alzheimer’s disease neurons. These studies will for the first time provide a comprehensive analysis of mechanisms controlling tau toxicity to postmitotic neurons and should identify many new high-value therapeutic targets. Our studies will be particularly important as more and more data emerges from genome wide associated studies showing genetic influences on Alzheimer’s disease and related tauopathies, but with little clear evidence as to the mechanism of action of these newly identified gene products in neurodegenerative disease pathogenesis.

Lay Summary

The proposed studies will combine the strengths of fruit flies as a fast, cheap model system to identify causal factors in tau neurotoxicity with state-of-the-art molecular analysis of tissue from patients with Alzheimer’s disease to outline mechanisms controlling cell dysfunction and death in neurodegeneration. These studies will help us design better therapies for Alzheimer’s disease and related neurodegenerative disorders.

Further information available at:

Types:

Investments > €500k

Member States:

United States of America

Diseases:

Alzheimer's disease & other dementias

Years:

2016

Database Categories:

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