Investigating the Role of the Histone Demethylase LSD1/KDMI in Neurodegeneration

https://neurodegenerationresearch.eu/survey/investigating-the-role-of-the-histone-demethylase-lsd1-kdmi-in-neurodegeneration/

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Country

USA

Title of project or programme

Investigating the Role of the Histone Demethylase LSD1/KDMI in Neurodegeneration

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 1,706,461.47

Start date of award

01/03/2015

Total duration of award in years

2

The project/programme is most relevant to:

Alzheimer's disease & other dementias

Keywords

histone demethylase, Frontotemporal Dementia, Nerve Degeneration, neuron loss, Alzheimer's Disease

Research Abstract
? DESCRIPTION (provided by applicant): Alzheimer’s disease (AD) and the related

Frontotemporal Dementia (FTD) together affect ~5.4 million Americans and result in nearly $200 billion annually in healthcare and long-term patient care costs. Yet despite this massive health problem, large gaps remain in our understanding of these diseases. We have uncovered a novel epigenetic mechanism in mice that functions in the maintenance of differentiated hippocampus neurons, and we have linked this mechanism to AD and FTD. We hypothesize that this epigenetic mechanism is inhibited by pathological protein aggregates in aging adults, resulting in inappropriate transcription (including reactivation of stem cell transcription) and neuronal cell death. In this proposal, we will investigate this new epigenetic pathway in our mouse model as well as in human patient's samples. In addition, because (unlike other dementia models) our mouse model exhibits massive hippocampus neuronal cell death, we will combine our mouse model with other mouse models to identify common mechanisms of neuronal cell death, as occur in neurodegeneration. This proposal is significant in that it mechanistically bridges the gap between pathological aggregates observed in AD and FTD cases and the neuronal cell death that underlies these dementias. Based on these studies, it may be possible to therapeutically target this new pathway in AD and FTD patients. These studies will also investigate common mechanisms of neuronal cell death that could serve as additional potential therapeutic targets. As a result, this proposal is directly responsive to the National Plan to Address Alzheimer's Disease priority; to investigate new pathways that can be targeted for treatment. In addition, this proposal is innovative because it links a novel epigeneti mechanism that is required to maintain differentiated cell fates to AD and FTD. As a result, these studies will also significantly impact our understanding of basic developmental biology and stem cell biology.

Lay Summary

PUBLIC HEALTH RELEVANCE: This proposal investigates a novel epigenetic mechanism that we have linked to the mechanism of Alzheimer's Disease and Frontotemporal dementia. In addition, this proposal aims to define new therapeutic targets by using our novel mouse model to identify common mechanisms of neuronal cell death, as occur in neurodegeneration. As a result, this proposal is directly responsive to the National Alzheimer's Disease plan priority; to investigate new pathways that can be targeted for treatment.

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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