Animal Models for Studying Human Frontotemporal Dementia

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Country

USA

Title of project or programme

Animal Models for Studying Human Frontotemporal Dementia

Source of funding information

NIH (NINDS)

Total sum awarded (Euro)

€ 1,606,419.27

Start date of award

01/12/2006

Total duration of award in years

2

The project/programme is most relevant to:

Alzheimer's disease & other dementias

Keywords

Frontotemporal Lobar Degenerations, Frontotemporal Dementia, ubiquilin, valosin-containing protein, C9orf72

Research Abstract

DESCRIPTION (provided by applicant): Defects in the endosomal-lysosomal pathway have been implicated in several neurodegenerative diseases but the detailed underlying molecular

mechanisms remain largely unknown. Frontotemporal lobar degeneration (FTLD) is a progressive neurodegenerative condition associated with focal atrophy of the frontal and/or temporal lobes. FTLD is one of the most common forms of presenile dementia. Increasing clinical and molecular evidence indicates that FTLD and amyotrophic lateral sclerosis share many common pathogenic mechanisms. Indeed, several genes, including CHMP2B, VCP, TDP-43, FUS, Ubiquilin 2, and C9ORF72, have been implicated in the molecular pathogenesis of both diseases. During the first funding cycle of this R01 grant, we established a neuronal cell model and a Drosophila model of mutant CHMP2B toxicity and investigated the roles of ESCRTs and autophagy in neurodegeneration. To more closely model human disease, we established a novel transgenic mouse model that exhibits several key features of FTLD-associated neurodegeneration. In this renewal application, we propose to carry out molecular, cellular, genetic, and behavioral analyses to further characterize this novel mouse model of FTLD, with the goal of gaining mechanistic insights into pathogenic events in vivo. The proposed studies will significantly enhance our understanding of disease mechanisms in FTLD and may reveal novel targets for therapeutic interventions.

Lay Summary

PUBLIC HEALTH RELEVANCE: In this proposal, we will perform a number of experiments to examine a novel mouse model of neurodegeneration. These studies will offer novel mechanistic insights into the neurotoxicity of mutant CHMP2B, which will likely enhance our understanding of molecular pathogenic mechanisms of frontotemporal dementia and amyotrophic lateral sclerosis.

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

Database Tags:
N/A