DEVELOPMENT OF NOVEL THERAPEUTIC ANTI-TAU ANTIBODIES

https://www.neurodegenerationresearch.eu/survey/development-of-novel-therapeutic-anti-tau-antibodies/

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Country

USA

Title of project or programme

DEVELOPMENT OF NOVEL THERAPEUTIC ANTI-TAU ANTIBODIES

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 2,877,568.81

Start date of award

01/08/2015

Total duration of award in years

2

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)... Immunization... Neurodegenerative... Neurosciences... Translational Research

Research Abstract

? DESCRIPTION (provided by applicant): The tauopathies are neurodegenerative disorders defined by the accumulation of the microtubule associated protein tau in insoluble amyloid aggregates. All are relentlessly progressive. Emerging research suggests that progression is based on trans-cellular propagation of aggregates in a prion-like manner, in which a fibrillar aggregate forms in one cell, is released into the extracellular space, and enters a nearby cell to corrupt natively folded protein. This hypothesis suggests that it might be possible to target extracellular species with appropriate antibodies. Indeed, recent work from our laboratories suggests that it is possible to use cellular models of aggregate seeding to select antibodies with potent activity in vivo. This proposal seeks to develop a sophisticated understanding of antibody mechanisms, and to develop the next generation of therapeutic anti-tau antibodies, and to test the most promising candidates in vivo. The two PIs involved in this work have a history of highly productive collaboration to develop and assess therapeutic antibodies in vivo. The Specific Aims of the project are 1: Characterize existing anti-tau antibodies in vitro. We will use a variety of ell and in vitro assays to prioritize monoclonal antibodies already produced. 2: Purify seeding activity from tauopathy brains for characterization and novel antibody production. Prior antibodies have been directed against preconceived epitopes that may or may not be relevant for trans-cellular propagation. We will use our ability to purify seeding activity from brain tissus to create monoclonal antibodies directed against seeds derived from human tauopathy brains. 3: Test mechanisms and efficacy of antibodies in vivo. We will use established laboratory methods to evaluate the effect of candidate antibodies on uptake of tau aggregates into neurons and glia, interstitial tau levels, and tau aggregate clearance. Further, we will determine their therapeutic efficacy in P301S mouse models of tauopathy. The work proposed in this grant is of great significance to the health of the U.S. population, because it seeks to develop novel antibody-based therapies for neurodegenerative diseases due to tau accumulation. Success in this effort will bear directly on the use of similar strategies to develop therapies for neurodegenerative diseases caused by other protein amyloids.

Lay Summary

PUBLIC HEALTH RELEVANCE: Neurodegenerative diseases account for an enormous cost to our society, in excess of $200B per year, and have an enormous human and social toll as well. This grant seeks to develop therapies for a group of neurodegenerative disorders that together account for the vast majority of cases of neurodegeneration. It is thus of enormous potential importance to human health.

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