Development of novel inhibitors of C1q for the treatment of Neurodegenerative diseases

https://www.neurodegenerationresearch.eu/survey/development-of-novel-inhibitors-of-c1q-for-the-treatment-of-neurodegenerative-diseases/

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Contact information of lead PI
Country

USA

Title of project or programme

Development of novel inhibitors of C1q for the treatment of Neurodegenerative diseases

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 1,113,683.49

Start date of award

15/08/2016

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... Neurodegenerative... Neurosciences... Prevention... Translational Research

Research Abstract

? DESCRIPTION (provided by applicant): Alzheimer’s disease (AD) is the most common cause of dementia in the aging population and is a serious unmet medical, social and economic problem worldwide. Current therapies provide only modest symptomatic relief, highlighting the need for better, disease-modifying treatments. The goal is to advance a novel therapeutic agent, ANX005, toward the clinic as a potential treatment for AD. ANX005 inhibits C1q, the initiating molecule of the classical complement cascade. C1q has a critical role in the physical pruning of synapses during development. In addition, C1q accumulates on synapses during normal aging – at levels 300-fold higher than those in younger animals. Abnormal accumulation of C1q may put synapses at risk of damage in a variety of neurodegenerative diseases, leading to synapse loss and a decline in neurologic function. It may also help to explain why age is the most important risk factor for neurodegenerative disease. This work will seek to establish proof of concept that inhibition of C1q will both protect against synapse loss and prevent functional decline in animal models of AD. We will establish appropriate dosing regimens with ANX005 for chronic efficacy testing in mice, as well as dose selection for safety evaluation in both rats and primates. In order to achieve these goals over the course of studies, ANX005 will be dosed in the range of 10-100 mg/Kg, parenterally, once weekly for durations of 1 to 6 months in a mouse models of AD. Efficacy in behavioral endpoints that measure learning and memory, such as the Morris water maze, will be evaluated at the end of the dosing period. Serum, CSF and brain samples will be collected for biochemical and histological evaluation, and levels of ANX005 in serum and CSF will be determined. Target engagement of ANX005 will be evaluated by measuring C1q levels in CSF and in hippocampal and cortical brain regions. Efficacy will be evaluated by quantitative histology of pre and post synaptic markers to demonstrate impact on synapse protection and microglial and astrocytic activation. Successful outcome of this work will allow advancement of ANX005 into early phase clinical studies within the next two years. In addition to demonstration of efficacy in AD mouse models, these preclinical studies will test, on a fundamental level, the hypothesis that preventing synapse loss can slow the progression of neurodegenerative disease, and provide novel insights into the process of neurodegeneration.

Lay Summary

PUBLIC HEALTH RELEVANCE: Loss of synaptic connections in the brain during normal aging and in neurodegenerative disorders is associated with memory loss. In this project, we will test the efficacy and safety of an antibody that we hypothesize may block synapse loss in a mouse model of Alzheimer’s disease. These studies will provide the critical in vivo proof of concept required to advance the antibody into human clinical trials.

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