Misfolded protein-clearance enhancers for Alzheimers therapy

https://www.neurodegenerationresearch.eu/survey/misfolded-protein-clearance-enhancers-for-alzheimers-therapy-2/

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Contact information of lead PI
Country

USA

Title of project or programme

Misfolded protein-clearance enhancers for Alzheimers therapy

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 1,492,681.65

Start date of award

15/09/2015

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 including Alzheimer's Disease Related Dementias (AD/ADRD)... Brain Disorders... Dementia... Neurodegenerative... Neurosciences... Prevention... Translational Research

Research Abstract

? DESCRIPTION (provided by applicant): Alzheimer’s disease (AD) is a proteinopathy characterized by deficient proteostasis of amyloid ß-protein and tau. Therefore, enhancement of clearance of the misfolded proteins involved in AD is a promising therapeutic strategy for preventing and treating the disease. We have been developing “”molecular tweezers”” (MTs) which act as Misfolded-Proteins Clearance Enhancers (MPCEs) using a unique mechanism. MTs bind to amyloidogenic proteins and remodel their abnormal self-assembly into non-toxic and non-amyloidogenic structures that can be efficiently degraded by the natural cellular clearance mechanisms. Our current lead compound, CLR01, has been found to be effective in multiple in vitro and in vivo systems, including prevention of Aß self-assembly and toxicity, inhibition of tau aggregation, and reduction of both amyloid plaques and neurofibrillary tangles in transgenic mouse brain. In addition, CLR01 was shown to have a high safety margin. However, the pharmacological characteristics of CLR01 need to be optimized, its effect on tau needs to be explored further, and certain questions about its mechanism of action and therapeutic potential are yet to be answered. In this project we will use a multi-prong approach to optimizing CLR01’s pharmacokinetics, expand the characterization of its effect on tau, study CLR01’s binding to amyloid plaques and neurofibrillary tangles in the brain, and characterize the capability of different doses and treatment durations of CLR01 treatment to remove toxic Aß and tau oligomers, reduce synaptotoxicity, and improve learning and memory deficits in a mouse model of AD. The study is expected to address currently unanswered questions and provide strong support for future formal development of MTs towards prevention and disease-modifying treatment of AD.

Lay Summary

PUBLIC HEALTH RELEVANCE: This project addresses the urgent public health need to develop disease-modifying therapy for Alzheimer’s disease (AD). This is a particularly pressing goal in view of the rapid aging of the American population and the fast increasing costs of care for AD patients. We address this urgent need by developing novel compounds that enhance the clearance of toxic proteins from the brain as potential drugs for AD.

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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