Modulation of microRNA pathways by gemfibrozil in predementia Alzheimer disease

https://www.neurodegenerationresearch.eu/survey/modulation-of-microrna-pathways-by-gemfibrozil-in-predementia-alzheimer-disease/

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Country

USA

Title of project or programme

Modulation of microRNA pathways by gemfibrozil in predementia Alzheimer disease

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 1,438,365.14

Start date of award

15/07/2013

Total duration of award in years

3

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... Clinical Research... Clinical Research - Extramural... Clinical Trials and Supportive Activities... Dementia... Neurodegenerative... Neurosciences... Prevention... Translational Research

Research Abstract

DESCRIPTION (provided by applicant): Our preliminary data indicate that miR-107 plays an important role in AD pathogenesis. Fibrates (PPAR agonists) increase miR-107 expression, and down-regulated BACE1 protein, an essential enzyme contributing to AD, in cultured H4 cells. We plan to test our hypotheses and evaluate a potential therapy for Alzheimer’s disease (AD) based on this novel microRNA (miRNA) pathway. Preclinical work in this area using animal models of AD has been thwarted by the species-specific hepatotoxicity not seen in humans. Thus, human clinical trials are necessary to test this important hypothesis on the disease modifying properties of fibrates in AD. Specifically, we propose an evaluation of the safety and efficacy of gemfibrozil administration on micro-RNA modulation of AD mechanisms in a parallel-design, double- blind, placebo-controlled study. We will evaluate both safety and target engagement of miR- 107 by gemfibrozil as well as alterations in relevant AD biomarkers. Gemfibrozil is a safe, orally- administered, FDA-approved drug for treatment of hyperlipidemia in aged individuals. The FDA has indicated IND exemption status for these studies. This study is designed to provide the foundation for future large-scale Phase II & III studies of fibrates in AD and AD prevention trials and represents the first attempt we are aware of designed to modulate disease progression in AD through influences on novel micro-RNA pathways. As such the proposed study represents a cutting-edge, data-driven, exploration of a novel disease relevant pathway that may hold promise for our global efforts targeting this major health priority among developing and developed nations.

Lay Summary

PUBLIC HEALTH RELEVANCE: Widespread recognition of the current and projected impact of the AD epidemic has spurred research into novel drug discovery efforts. This proposal seeks to further progress in this area, investigating the novel actions of PPAR agonists as a disease modifying therapy in AD through their modulation of novel miRNA pathways that influence A production, repurposing an existing drug therapy. As such, the proposed study represents a cutting-edge, data-driven, low-cost, exploration of a novel disease relevant pathway that may hold promise for our global efforts targeting this major health priority among developing and developed nations.

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