A Novel Small molecule TNF-alpha inhibitor as a disease-modifying AD drug treatment.

https://neurodegenerationresearch.eu/survey/a-novel-small-molecule-tnf-alpha-inhibitor-as-a-disease-modifying-ad-drug-treatment/

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Contact information of lead PI
Country

USA

Title of project or programme

A Novel Small molecule TNF-alpha inhibitor as a disease-modifying AD drug treatment.

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 1,366,874.31

Start date of award

01/09/2015

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)... Brain Disorders... Dementia... Neurodegenerative... Neurosciences... Translational Research

Research Abstract

? DESCRIPTION (provided by applicant): The goal of this proposal is to develop tumor necrosis factor a (TNFa)-inhibiting compounds as neuroprotectant drugs for treating Alzheimer's disease (AD). Current FDA-approved AD interventions are symptomatic treatments with limited efficacy which do not affect AD etiology or modify the course of disease progression. Thus, a critical need exists for a novel AD treatment directed towards AD pathophysiology. Recent studies implicate the neuroinflammatory cytokine TNF-a as a key mediator in AD- associated neurodegenerative pathology. Multiple preclinical and clinical studies indicate that TNFa is a ""druggable"" molecular target to modify the course of AD progression. Preliminary Studies demonstrate that our lead compound, IDT, shows potent TNFa inhibition in vitro. Our Phase 1 SBIR studies demonstrate that a low dose of IDT administered orally every day for 10 months significantly improved cognitive function in the triple-transgenic (3xTg) AD mouse model. IDT also modulated brain TNFa protein levels and halted the progress of AD- associated neuropathology including Aß plaques and neurofibrally tangles as assessed by immunohistological staining. No morbidity, mortality or any obvious side effects were observed despite the long-term oral daily treatment regimen with IDT. Taken together, these data strongly suggest that our lead compound is an excellent anti-AD drug candidate. The proposed Phase 2 SBIR studies are designed to achieve two goals. First, we want to conduct the FDA safety and toxicology studies required for submission of IDT as an Investigational New Drug (IND) application which would allow its use in humans when approved (Aims 1-4). Second, our efficacy data suggests IDT may be more effective at an even lower dose. Aim 5 will optimize IDT dose-efficacy response at lower doses in 3xTgAD mice. Aim 1: Assess IDT genotoxicity. Aim 2: Assess IDT absorption, distribution, metabolism and excretion (ADME) Aim 3: Assess oral IDT safety pharmacology in three studies: Aim 4: Assess repeated IDT dose toxicity in rats. Aim 5: Assess lower IDT doses in 3xTg AD mice.

Lay Summary

PUBLIC HEALTH RELEVANCE: Alzheimer's Disease (AD) is a significant neurological problem affecting 4.5 million of our senior U.S. citizens. The present research aims to develop a compound that targets the underlying neuroinflammation in AD to modify disease progression and improve cognitive function.

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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