A Translational Program of BDNF Gene Delivery in Alzheimers Disease

https://www.neurodegenerationresearch.eu/survey/a-translational-program-of-bdnf-gene-delivery-in-alzheimers-disease/

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Country

USA

Title of project or programme

A Translational Program of BDNF Gene Delivery in Alzheimers Disease

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 3,741,080.73

Start date of award

15/06/2014

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... Dementia... Diagnostic Radiology... Gene Therapy... Genetics... Neurodegenerative... Neurosciences... Translational Research

Research Abstract

DESCRIPTION (provided by applicant): Alzheimer’s disease (AD) is the most common neurodegenerative disorder, afflicting 5 million people in the U.S. alone. This U grant application will support studies leading to the filing of an Investigational New Drug (IND) application to the FDA for Brain-Derived Neurotrophic Factor (BDNF) gene delivery in AD. We have completed proof-of-concept studies in mice, rats and non-human primates, demonstrating that BDNF prevents entorhinal cortical neuronal cell loss, enhances synaptic markers, reverses molecular and biochemical features associated with AD, and improves learning and memory. These effects extend into the hippocampus, thereby treating key memory circuitry of the brain. Importantly, this approach provides a much-needed alternative to amyloid-modifying therapeutics currently under development, providing future possibilities for combined therapies if both prove to be partly effective. We propose gene delivery of BDNF because of the need to administer this protein directly into the brain and sustain its delivery over time. In the proposed work plan, we will manufacture adeno-associated virus serotype 2 (AAV2) vectors expressing human BDNF at a GMP facility, then use this clinical-grade material to perform IND-enabling studies in two species (rat and primates). In addition, we will generate expertise in accurately targeting and delivering AAV2-BDNF to the primate entorhinal cortex using real-time, MR-guided imaging. The following aims will be performed: Aim 1: Produce AAV2-BDNF for IND-enabling safety/toxicity/dosing studies. Aim 2: Optimize AAV2-BDNF gene delivery to the entorhinal cortex in non-human primates using convection-enhanced delivery and real-time MR guidance. Aim 3: Safety/toxicity/dosing/biodistribution studies in rodents and non-human primates. Aim 4: Draft and Submit an IND Application. Relevance: Successful completion of this work will lead to clinical translation of a new approach to prevent cell loss and stimulate neural function in a common, severe and disabling neurodegenerative disorder.

Lay Summary

PUBLIC HEALTH RELEVANCE: Project Narrative Alzheimer’s disease is the most common neurodegenerative disease, afflicting over 5 million people in the United States, and costs of treatment exceed $170 billion annually: accordingly, new and effective therapies are needed to slow this disorder and improve cognitive function. Studies have shown that the nervous system growth factor Brain-Derived Neurotrophic Factor (BDNF) can prevent neuronal death and stimulate function. Work proposed in this study will perform dosing and safety studies that, if successful, will lead to the filing of an application to test BDNF gene delivery in patients with Alzheimer’s disease.

Further information available at:

Types:
Investments > €500k

Member States:
United States of America

Diseases:
Alzheimer's disease & other dementias

Years:
2016

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