

Human induced neuronal stem cell models of familial Alzheimers disease

<https://www.neurodegenerationresearch.eu/survey/human-induced-neuronal-stem-cell-models-of-familial-alzheimers-disease/>

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Country

USA

Title of project or programme

Human induced neuronal stem cell models of familial Alzheimers disease

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 2,247,792.66

Start date of award

01/08/2012

Total duration of award in years

5

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... Genetics... Neurodegenerative... Neurosciences... Stem Cell Research... Stem Cell Research - Induced Pluripotent Stem Cell... Stem Cell Research - Induced Pluripotent Stem Cell - Human

Research Abstract

DESCRIPTION (provided by applicant): We recently described the directed conversion of human skin fibroblasts from unaffected individuals and Alzheimer's disease (AD) patients to a CNS neuron phenotype, termed human induced neuronal cells (hiN) 1. Herein we propose to further develop hiN cells as tools for AD modeling, and subsequently to validate the approach in a more detailed analysis of cellular mechanisms of AD. The focus of the proposed studies is on familial AD (FAD)-associated disease with defined genetic lesions in presenilin-1 (PSEN1) or presenilin-2 (PSEN2). A clear advantage of such an analysis of FAD with defined mutations is that this facilitates genetic 'rescue' studies, as well as genetic dissection of function. Yet ultimately, perhaps the most exciting aspect of the hiN cell technology is that it may permit a cellular analysis of 'sporadic' disease. The overarching hypotheses to be tested in this work are that cellular aspects of FAD pathophysiology are: (1) Cell-autonomous to neurons and maintained through epigenetic reprogramming, and therefore amenable to hiN cell modeling. (2) Include altered intracellular vesicular trafficking at the soma and the synapse. The proposed deliverables for this proposed work are: (1) Novel human neuronal cell models for dissection of AD mechanisms and drug screening. (2) Directed reprogramming tools that may be broadly applied to the study of neurological disease.

Lay Summary

We describe a novel approach to the generation of human neurons by the directed conversion of human skin cells. Such neurons, when derived from patients with familial forms of Alzheimer's, show pathological changes that typify the disease. Here we propose to investigate the mechanism by which human Alzheimer patient neurons develop cellular and molecular deficits.

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