Patient Motor Neuron Assay System for ALS Drug Discovery

https://www.neurodegenerationresearch.eu/survey/patient-motor-neuron-assay-system-for-als-drug-discovery/

Principal Investigators

DU, ZHONGWEI

Institution

BRAINXELL, INC.

Contact information of lead PI
Country

USA

Title of project or programme

Patient Motor Neuron Assay System for ALS Drug Discovery

Source of funding information

NIH (NINDS)

Total sum awarded (Euro)

185575.2294

Start date of award

01/09/2016

Total duration of award in years

1

Keywords

Neurofilament-L, Amyotrophic Lateral Sclerosis, Motor Neurons, neurofilament, drug discovery

Research Abstract

Project Summary/Abstract Amyotrophic lateral sclerosis (ALS), also known as Lou Gehrig's disease, is a devastating neurological disorder with patients typically surviving just three to five years after diagnosis. Approximately 30,000 Americans live with ALS and another 5,600 are diagnosed each year (ALS Association). Despite identification of over 70 candidate drugs from studies with model animals and immortalized human cell lines over the past two decades, only a single FDA-approved drug, riluzole (Rilutek), is available to treat the disease, increasing survival

of patients by two to three months. This sobering status highlights an urgent need of novel pharmaceutical therapies, perhaps via a new drug discovery platform. BrainXell Inc. seeks to create a naturalistic in vitro screening platform to identify promising ALS drug leads for further development. By generating induced pluripotent stem cells (iPSCs) from ALS patients, we discovered that the iPSC-derived motor neurons (MN) exhibit neurofilament (NF) aggregation followed by axonal degeneration and finally MN death, reminiscent of the cardinal pathology seen in ALS patients. We further found that a subunit of NF, NF light chain (NF-L) was decreased, and if NF-L level was restored, NF aggregation and neurite degeneration were mitigated, even in the presence of disease mutations. Thus, NF misregulation is a critical cause of NF aggregation and MN degeneration, and hence a potential therapeutic target. The company has recently engineered ALS patient iPSCs with a reporter gene, nanoluciferase (100 times more sensitive than the traditional luciferase), fused to NF-L to allow for a simple, robust readout of NF-L protein level. It has recently developed a technology to generate large quantities of motor neurons (billions in one batch) from patient iPSCs, making high-throughput screening (HTS) possible. This proposal will build upon these technologies and determine the feasibility of establishing an HTS platform for ALS drug discovery using patient MNs. This effort likely represents the first ever patient cell-based HTS platform. It will provide an opportunity to screen compound libraries in a biological system that more closely resembles the disease as it exists in man.

Further information available at:

Types:
Investments < €500k

Member States:
United States of America

Diseases:
N/A

Years:
2016

Database Categories:
N/A

Database Tags:
N/A