An In Vitro Model of Stem Cell Innervation of Myotubes

https://neurodegenerationresearch.eu/survey/an-in-vitro-model-of-stem-cell-innervation-of-myotubes/

Principal Investigators

HICKMAN, JAMES J

Institution

UNIVERSITY OF CENTRAL FLORIDA

Contact information of lead PI
Country

USA

Title of project or programme

An In Vitro Model of Stem Cell Innervation of Myotubes

Source of funding information

NIH (NINDS)

Total sum awarded (Euro)

€ 2,209,073.39

Start date of award

23/09/2005

Total duration of award in years

5

The project/programme is most relevant to:

Motor neurone diseases

Keywords

nerve supply, Muscle Fibers, in vitro Model, Reflex action, Amyotrophic Lateral Sclerosis

Research Abstract

Project Description: A long-term goal of the research in our laboratory is to re-create the components and compartments of mammalian systems, and in particular human systems, to engineer functional hybrid models. The previous grant period for this Bioengineering Research

Grant (BRG) was to investigate the formation of a model system of the reflex arc with rat then human stem cells. During this funding period we have made the following breakthroughs with this model system that move us closer to the goal of creating a functional in vitro model of the complete reflex arc for applications as a phenotypic drug screening system: 1) A functional human to human NMJ system that can be stimulated by both chemical and electrical means that exhibit dose response measurement capabilities to selected compounds that modulate the NMJ. 2) Demonstrated differentiation of Type II, Type Ia and nociceptive sensory neurons from human stem cells and shown functional, mature electrophysiological properties. 3) Derived human intrafusal fibers from stem cells and demonstrated functional human sensory to human intrafusal fiber innervation. 4) Demonstrated sensory neuron to motoneuron innervation with functional synapse formation. 5) Demonstrated human ?-motoneuron innervation of human intrafusal fibers. The previous grant has led to the publication of 26 manuscripts, 3 submitted and another 6 are in preparation, as well as the submission of 12 patents. Six of the articles are in Biomaterials, which has an impact factor of 8.557, and is the leading journal in the field of Biomedical Engineering. This renewal BRG application seeks to complete the development of the complete reflex arc in vitro using cells derived from human stem cells in Aim 1 and then apply aspects of the system to investigation of Amyotrophic Lateral Sclerosis (ALS) in Aims 2 and 3, respectively. The major innovation of this interdisciplinary proposal is the creation of physiologically realistic human in vitro functional units of the CNS and PNS with the proper cell types, cellular interactions and connectivity for application to enable phenotypic screening systems. This technology integration is necessary as we believe these systems are crucial to the creation of the next generation high-content screening platforms. Our idea is that we can create functional in vitro models of the reflex arc or its components, with cells derived from human stem cells, to then recreate phenotypic disease models. The continuation of the grant will enable 1) A functional human cell based reflex arc in a defined, serum-free environment and 2) application of the motoneuron to muscle segment to understand mechanisms in ALS by investigating combinations of WT and mutant cells from patients and 3) to validate the systems. Our expertise in surface chemistry, Micro- ElectroMechanical Systems (MEMS) fabrication and developmental/cellular/molecular biology enables the construction of complex functional neuronal systems in vitro. Our team possesses the necessary expertise in all aspects of this project, as well as the facilities to effectively and successfully perform the research.

Lay Summary

Project Narrative The goal of this project is to engineer a system to model one of the most fundamental motor circuits in the human body, the spinal reflex arc and apply it to the neurological disease Amyotrophic Lateral Sclerosis (ALS). We will use nanotechnology and microelectronics in combination with biomedical engineering techniques to build this hybrid biological/non-biological system. Other potential benefits include prevention, diagnosis, and treatment of developmental abnormalities in the spinal cord, rehabilitation of chronic neurological/muscle disorders and accompanying pain, and new strategies for prosthetic and orthotic design and evaluation.

Further information available at:

Types:

Investments > €500k

Member States:

United States of America

Diseases:
Motor neurone diseases

Years:
2016

Database Categories:
N/A

Database Tags:
N/A