Generation and characterization of corticospinal neurons from human embryonic stem cells

Grant Award Details

Generation and characterization of corticospinal neurons from human embryonic stem cells

Grant Type: Basic Biology III

Grant Number: RB3-02143

Project Objective: In the last reporting period (1st year), PI has established the basic differentiation scheme to obtain Fezf2-YFP positive neural progenitors and neurons from hESCs. basic marker analysis was performed and developed FACS purification of Fezf2-YFP positive cells. results obtained were that Fezf2 was expressed in an early neural stem/progenitor stage. PI has now started to conduct in vivo transplantation studies.

Investigator:

Name:	Binhai Zheng
Institution:	University of California, San Diego
Type:	PI

Disease Focus: Neurological Disorders

Human Stem Cell Use: Embryonic Stem Cell

Cell Line Generation: iPS Cell

Award Value: $1,355,063

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Reporting Period: Year 3 + NCE

View Report

Grant Application Details

Application Title: Generation and characterization of corticospinal neurons from human embryonic stem cells

Public Abstract: A major goal of stem cell research is to generate various functional human cell types that can be used to better understand how these cells work and to use them directly in therapies. There are currently no effective treatments, let alone a cure, for many neurological conditions. Two particular devastating neurological conditions, spinal cord injury and amyotrophic lateral sclerosis (ALS, or Lou Gehrig's disease) share a common element. That is, in both conditions, the corticospinal motor neurons that control skilled voluntary movement are severely damaged, leading to significant loss of motor control. There has been extensive research on spinal cord injury and ALS in recent years. In the field of spinal cord injury, much effort has been devoted to repairing the damaged nerve paths, but this has turned out to be extremely challenging. The work on ALS, on the other hand, has mostly focused on the spinal motor neurons (often referred to as the lower motor neurons in the context of ALS). Our proposed study focuses on the corticospinal motor neurons (or the upper motor neurons) and, more broadly, the subcerebral projection neurons. Taking clues from studies in mice, we aim to understand how the subcerebral projection neurons including the corticospinal motor neurons can be made from human embryonic stem cells. We will focus on the later steps in differentiation that are not well understood, which gave rise to different types of neurons in the cerebral cortex. To aid in this process, we have engineered a fluorescent reporter in human embryonic stem cells, which, when the stem cells are turned into corticospinal motor neurons and related subcerebral projection neurons, will light up – literally. We will probe the molecular control of this process and determine if corticospinal motor neurons made in a culture dish, when introduced back into an organism, can send projections to the spinal cord, as they would normally do during development. Most of our knowledge about the development of corticospinal motor neurons comes from studies with mouse models. As there are likely to be important differences between humans and mice, we will pay special attention to the similarities and differences between mouse and human corticospinal motor neurons. Knowledge gained from this study will pave the way to make better disease-models-in-a-dish for neurological conditions such as ALS and to develop therapies for ALS, spinal cord injury, traumatic brain injury, stroke and other neurological conditions when corticospinal motor neurons are damaged.

Statement of Benefit to California: Neurological conditions affect millions of Californians each year. Spinal cord injury is one particularly debilitating neurological condition. The disability, loss of earning power, and loss of personal freedom associated with spinal cord injury is devastating for the injured individual, and creates a financial burden of an estimated $400 million annually for the state of California. Research is the only solution as currently there is no cure for spinal cord injury. A major functional deficit for patients of spinal cord injury is the loss of motor control. Corticospinal motor neurons mediate skilled, voluntary movement in humans and damage to these neurons leads to severe disability. Our proposed study focuses on the understanding of how corticospinal motor neurons and, more broadly, subcerebral projection neurons can be made from human embryonic stem cells under culture conditions, and how they can be introduced back to central nervous system. Understanding this process will allow scientists to design ways to use these cells for transplantation therapies not only for spinal cord injury, but also for other neurological conditions such as amyotrophic lateral sclerosis (ALS, or Lou Gehrig's disease). Effective treatments promoting functional repair will significantly increase personal independence for people with spinal cord injury and decrease the financial burden for the State of California. More importantly, treatments that enhance functional recovery will improve the quality of life for those who are directly or indirectly affected by spinal cord injury, ALS and other neurological conditions.