# Molecular Characterization of hESC and hIPSC-Derived Spinal Motor Neurons

## Grant Award Details

Molecular Characterization of hESC and hIPSC-Derived Spinal Motor Neurons

**Grant Type:** Basic Biology I

**Grant Number:** RB1-01367

**Project Objective:** 1)
Determine the molecular, genetic, and physiological
similarities of hESC- and hIPSC-derived MNs in comparison to human embryonic
MNs
2) Determine the innervation capacity of hESC- and hIPSCderived
MNs.

**Investigator:**

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| **Name:** | Bennett Novitch |
| **Institution:** | University of California, Los Angeles |
| **Type:** | PI |

**Disease Focus:** Amyotrophic Lateral Sclerosis, Genetic Disorder, Neurological Disorders, Pediatrics, Spinal Cord Injury, Spinal Muscular Atrophy

**Human Stem Cell Use:** Embryonic Stem Cell, iPS Cell

**Award Value:** $1,229,922

**Status:** Closed

## Progress Reports

**Reporting Period:** Year 1

**View Report**

**Reporting Period:** Year 2

**View Report**

**Reporting Period:** Year 3

**View Report**

**Reporting Period:** NCE

**View Report**

## Grant Application Details

**Application Title:** Molecular Characterization of hESC and hIPSC-Derived Spinal Motor Neurons

**Public Abstract:** One of the main objectives of stem cell biology is to create physiologically relevant cell types that can be used to either facilitate the study of or directly treat human disease. Tremendous progress towards these goals has been made in the area of motor neuron disease and spinal cord injury through the findings that motor neurons can be generated from human embryonic stem cells and induced pluripotent stem cells. These advances have made possible the creation of motor neurons from patients afflicted with neurodegenerative diseases such as amyotrophic lateral sclerosis and spinal muscular atrophy that can be studied in the laboratory to determine the root causes of these diseases. In addition, stem cell-derived motor neurons could potentially serve as replacement cells that could be introduced into the spinal cord to recover motor functions in these patients, as well as those suffering from spinal cord injuries. A major assumption, however, is that human embryonic and induced pluripotent cell-derived motor neurons are identical to their normal counterparts. Despite its relevance, few studies of human motor neuron development have been carried out, and little information on the genetic and functional similarities between stem cell- and embryo-derived motor neurons has been obtained. The proposed research will provide important new insights into the profile of human motor neurons that must be recapitulated by stem cell studies. This approach is critical given that most of our knowledge on human motor neuron development is based on animal models. In addition, work with mouse embryonic stem cell-derived motor neurons has revealed limitations in the motor neuron subtypes that can be generated in culture, something others and we have also observed in human embryonic and induced pluripotent stem cell-derived motor neurons. The differences between embryo and stem cell-derived motor neurons are currently unknown, though our preliminary studies suggest that this deficiency may result from the inability of stem cell-derived motor neurons to express key regulators of motor neuron development. We will directly test this hypothesis by examining whether artificially expressing some of these important motor neuron fate determinants can alter the classes of motor neurons formed in culture and thereby broaden their innervation potential. Since most motor neuron diseases tend to affect certain motor neuron populations more than others, and that the pattern of motor innervation is highly specific to the type of cells formed, these studies will significantly advance our understanding of how the full repertoire of motor neuron subtypes may be created from stem cells to build disease models and generate therapeutically beneficial cells.

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| **Statement of Benefit to California:** | Neurological diseases are among the most debilitating medical conditions that affect millions of Californians each year, and many more worldwide. Few effective treatments for these diseases currently exist, in part because we know very little about the mechanisms underlying these conditions. Through the use of human embryonic stem cell and induced pluripotent stem cell technologies, it is now possible to create neurons from patients suffering from a variety of neurological disorders that can serve as the basis for cell culture-based models to study disease pathologies in an experimentally accessible setting. Our proposed research seeks to develop the means to form different classes of neurons, confirm their physiological identities, and establish a system for studying their neurological activity in a cell culture setting. The generation of these models will constitute an important step towards understanding the basis of neurological illnesses and developing a platform for the discovery of drugs that can alter disease progression and improve the productivity and quality of life for many Californians. Moreover, progress in this field will help solidify the leadership role of California in bringing stem cell research to the clinic, and stimulate the future growth of the biotechnology and pharmaceutical industries within the state. |