Gene regulatory mechanisms that control spinal neuron differentiation from hES cells.

Grant Award Details

Gene regulatory mechanisms that control spinal neuron differentiation from hES cells.

Grant Type: SEED Grant

Grant Number: RS1-00288

Investigator:

Name:	Samuel Pfaff
Institution:	Salk Institute for Biological Studies
Type:	PI

Disease Focus: Amyotrophic Lateral Sclerosis, Neurological Disorders, Spinal Muscular Atrophy

Human Stem Cell Use: Embryonic Stem Cell

Award Value: $704,543

Status: Closed

Progress Reports

Reporting Period: Year 2

View Report

Grant Application Details

Application Title: Gene regulatory mechanisms that control spinal neuron differentiation from hES cells.

Public Abstract:

More than 600 disorders afflict the nervous system. Common disorders such as stroke, epilepsy, Parkinson's disease and autism are well-known. Many other neurological disorders are rare, known only to the patients and families affected, their doctors and scientists who look to rare disorders for clues to a general understanding of the brain as well as for treatments for specific diseases. Neurological disorders strike an estimated 50 million Americans each year, exacting an incalculable personal toll and an annual economic cost of hundreds of billions of dollars in medical expenses and lost productivity. There are many potential applications for using human embryonic stem (hES) cells to treat neurological diseases and injuries; however, a critical barrier to progress in the field is the ability to efficiently and reliably control neuronal differentiation from these cells. The main goal of this proposal is to define the gene regulatory mechanisms that control the acquisition of neuronal fate from hES cells. Longer term, we plan to produce small compounds (drugs) that greatly facilitate this process. Drugs that enhance neuron formation are likely to improve scientists' ability to manipulate hES cells and create in vitro models for studying neurological diseases. Most importantly, drugs of this type may stimulate endogenous stem cells within adults to self-repair damaged areas of the brain. Because so little is known about how hES cells differentiate into neurons at the molecular level, this grant will focus on understanding how a single neuronal subtype is generated – motor neurons. Why motor neurons? Motor neuron diseases are a group of progressive neurological disorders that destroy cells that control essential muscle activity such as speaking, walking, breathing and swallowing. Eventually, the ability to control voluntary movement can be lost. Motor neuron diseases may be inherited or acquired, and they occur in all age groups. In adults, symptoms often appear after age 40. In children, particularly in inherited or familial forms of the disease, symptoms can be present at birth or appear before the child learns to walk. Is there a treatment? There is no cure or standard treatment for motor neuron diseases. Prognosis varies depending on the type of motor neuron disease and the age of onset; however, many types such as ALS and some forms of spinal muscular atrophy are typically fatal.The experiments in this proposal seek to understand mechanisms that will be directly applicable to hES cells and their use for treating motor neuron diseases. Moreover, the mechanisms controlly motor neuron formation are also likely to be relevant to many other neuronal subtypes. Therefore, these studies should provide essential and general insight into medically deploying strategies for converting hES cells into specific neuronal subtypes and thereby serve as a platform for treating a wide range of neurological diseases.

Statement of Benefit to California:

The long term goal of this research grant proposal is to understand and treat diseases and injuries of the nervous system using hES cells. Neurological disorders such as stroke, epilepsy, Parkinson's disease and autism strike an estimated 5 million Californians each year, exacting an incalculable personal toll and an annual economic cost of billions of dollars in medical expenses and lost productivity. Thus, one benefit that will be derived from this area of research is the generation of specific tools and methods for reducing medical costs and increasing the quality of life and level of productivity of afflicted Californians. A second key benefit derived from this research grant proposal is the training of new scientists to serve as educators and researchers for the future, many in the burgeoning area of stem cell biology for which the State of California has emerged as a world's leader. Finally, the discoveries derived from innovative and multidisciplinary research on hES cells described in this proposal, including the use of chemistry to create drug leads for regulating stem cell differentiation, are likely to lead to important new areas of intellectual property that are essential for creating high quality jobs in the biotechnology and pharmaceutical industries in California.
