Use of iPS cells (iPSCs) to develop novels tools for the treatment of spinal muscular atrophy.

Grant Award Details

Use of iPS cells (iPSCs) to develop novels tools for the treatment of spinal muscular atrophy.

Grant Type: Tools and Technologies II

Grant Number: RT2-02040

Project Objective: To produce new non-integrating iPSC lines from Type I, II and III SMA patients as tools to develop and validate drug screens
To develop high content screening assays on SMA iPSC-derived motor neurons
To perform HCS screens to discover novel therapeutic compounds for SMA

Investigator:

Name:	Clive Svendsen
Institution:	Cedars-Sinai Medical Center
Type:	PI

Disease Focus: Neurological Disorders, Pediatrics, Spinal Muscular Atrophy

Human Stem Cell Use: iPS Cell

Cell Line Generation: Adult Stem Cell

Award Value: $1,933,022

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Reporting Period: Year 3

View Report

Reporting Period: Year 4/NCE

View Report

Grant Application Details

Application Title: Use of iPS cells (iPSCs) to develop novels tools for the treatment of spinal muscular atrophy.

Public Abstract:

Spinal Muscular Atrophy (SMA) is one of the most common lethal genetic diseases in children. One in thirty five people carry a mutation in a gene called survival of motor neurons 1 (SMN1) which is responsible for this disease. If two carriers have children together they have a one in four chance of having a child with SMA. Children with Type I SMA seem fine until around 6 months of age, at which time they begin to show lack of muscular development and slowly develop a "floppy" syndrome over the next 6 months. Following this period, SMA children become less able to move and are eventually paralyzed by the disease by 3 years of age or earlier. We know that this mutation causes the death of motor neurons - which are important for making muscle cells work. Interestingly, there is a second gene which can lessen the severity of the disease process (SMN2). Children with more copies of this modifying gene have less severe symptoms and can live for longer periods of time (designated Type II, III and IV and living longer periods respectively).

There is no therapy for SMA at the current time. One of the roadblocks is that there are no human models for this disorder as it is very difficult to make the motor neurons that die in the disease in the laboratory. The researchers in the current proposal have recently created pluripotent stem cells from a patient with Type I SMA (the most severe) and shown that motor neurons grown out from the pluripotent stem cells also die in the culture dish just like they do in children. This is an important model for SMA.

The proposed research takes this model of SMA and extends it to Type II and Type III children in order to have a wider range of disease severity in the culture dish (Type IV is very rare and difficult to get samples from). It then develops new technologies to produce very large numbers of motor neurons and perform large scale analysis of their survival profiles. Finally, it will explore whether novel compounds can slow down the degeneration of motor neurons in this model which should lead to the discovery of dew drugs that then may be used to treat the disease.

Statement of Benefit to California:

The aim of this research is to develop novel drugs to treat a lethal childhood disease - SMA. There would be three immediate benefits to the state of California and its citizens.

1. Children in California would have access to novel drugs to slow or prevent their disease.
2. SMA is a world wide disease. The institutions involved with the research would be able to generate income from any new drugs developed and the profit from this would come back to California.
3. The project will employ a number of research staff in Californian institutions