Developing a method for rapid identification of high-quality disease specific hIPSC lines

Grant Award Details

Developing a method for rapid identification of high-quality disease specific hIPSC lines

Grant Type: Tools and Technologies II

Grant Number: RT2-01927

Project Objective: To develop a pipeline of methods for rapid identification of high quality disease-specific hiPSC lines, and to demonstrate/evaluate success and cost-effectiveness of this pipeline by generating 6 lines from each of 50 Alzheimer's Disease patients.

Investigator:

Name:	Lawrence Goldstein
Institution:	University of California, San Diego
Type:	PI

Disease Focus: Alzheimer's Disease, Neurological Disorders

Human Stem Cell Use: iPS Cell

Cell Line Generation: iPS Cell

Award Value: $1,692,334

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Reporting Period: Year 3

View Report

Grant Application Details

Application Title: Developing a method for rapid identification of high-quality disease specific hIPSC lines

Public Abstract:

Elucidating how genetic variation contributes to disease susceptibility and drug response requires human Induced Pluripotent Stem Cell (hIPSC) lines from many human patients. Yet, current methods of hIPSC generation are labor-intensive and expensive. Thus, a cost-effective, non-labor intensive set of methods for hIPSC generation and characterization is essential to bring the translational potential of hIPSC to disease modeling, drug discovery, genomic analysis, etc.

Our project combines technology development and scaling methods to increase throughput and reduce cost of hiPSC generation at least 10-fold, enabling the demonstration, and criterion for success, that we can generate 300 useful hiPSC lines (6 independent lines each for 50 individuals) by the end of this project. Thus, we propose to develop an efficient, cost effective, and minimally labor-intensive pipeline of methods for hIPSC identification and characterization that will enable routine generation of tens to hundreds of independent hIPSC lines from human patients. We will achieve this goal by adapting two simple and high throughput methods to enable analysis of many candidate hIPSC lines in large pools. These methods are already working in our labs and are called "fluorescence cell barcoding" (FCB) and expression cell barcoding (ECB).

To reach a goal of generating 6 high quality hIPSC lines from one patient, as many as 60 candidate hIPSC colonies must be expanded and evaluated individually using labor and cost intensive methods. By improving culturing protocols, and implementing suitable pooled analysis strategies, we propose to increase throughput at least 10-fold with a substantial drop in cost. In outline, the pipeline we propose to develop will begin with the generation of 60 candidate hIPSC lines per patient directly in 96 well plates. All 60 will be analyzed for diagnostic hIPSC markers by FCB in 1 pooled sample. The 10 best candidates per patient will then be picked for expression and multilineage differentiation analyses with the goal of finding the best 6 from each patient for digital karyotype analyses. Success at 10-fold scaleup as proposed here may be the first step towards further scaleup once these methods are fully developed.

Aim 1: To develop a cost-effective and minimally labor-intensive set of methods/pipeline for the generation and characterization high quality hIPSC lines from large numbers of human patients. We will test suitability/develop a set of methods that allow inexpensive and rapid characterization of 60 candidate hIPSC lines per patient at a time.

Aim 2: To demonstrate/test/evaluate the success and cost-effectiveness of our pipeline by generating 6 high quality hIPSC lines from each of 50 human patients from [REDACTED]. We will obtain skin biopsies and expand fibroblasts from 50 patients, and generate and analyze a total of 6 independent hIPSC lines from each using the methods developed in Aim 1.

Statement of Benefit to California:

Many Californians suffer from diseases whose origin is poorly understood, and which are not treatable in an effective or economically advantageous manner. Part of solving this problem relies upon elucidating how genetic variation contributes to disease susceptibility and drug response and better understanding disease mechanism. Achieving these goals can be accelerated through the use of human Induced Pluripotent Stem Cell (hIPSC) lines from many human patients. Yet, current methods of hIPSC generation are labor-intensive and expensive. Thus, a cost-effective, non-labor intensive set of methods for hIPSC generation and characterization is essential to bring the translational potential of hIPSC to disease modeling, drug discovery, genomic analysis, etc.

If successful, our project will lead to breakthroughs in understanding of disease, development of better therapies, and economic development in California as businesses that use our methods are launched. In addition, new therapies will bring cost-savings in healthcare to Californians, stimulate employment since Californians will be employed in businesses that develop and sell these therapies, and relieve much suffering from the burdens of chronic disease.

Source URL: https://www.cirm.ca.gov/our-progress/awards/developing-method-rapid-identification-high-quality-disease-specific-hipsc-lines