
Elucidating Molecular Basis of Hypertrophic Cardiomyopathy with Human Induced Pluripotent Stem Cells

Grant Award Details

Elucidating Molecular Basis of Hypertrophic Cardiomyopathy with Human Induced Pluripotent Stem Cells

Grant Type: Basic Biology III

Grant Number: RB3-05129

Project Objective: The project objective is to derive iPSC from patients with hypertrophic cardiomyopathy with known mutations, as well as unaffected controls, to characterize the disease phenotype, and to correct the mutation to determine if this corrects the disease phenotypes.

Investigator:

Name:	Sean Wu
Institution:	Stanford University
Type:	PI

Disease Focus: Heart Disease

Human Stem Cell Use: iPS Cell

Cell Line Generation: iPS Cell

Award Value: \$1,260,537

Status: Closed

Progress Reports

Reporting Period: Year 1

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Reporting Period: Year 3

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Grant Application Details

Application Title: Elucidating Molecular Basis of Hypertrophic Cardiomyopathy with Human Induced Pluripotent Stem Cells

Public Abstract: Familial hypertrophic cardiomyopathy (HCM) is the leading cause of sudden cardiac death in young people, including trained athletes, and is the most common inherited heart defect. Until now, studies in humans with HCM have been limited by a variety of factors, including variable environmental stimuli which may differ between individuals (e.g., diet, exercise, and lifestyle), the relative difficulty in obtaining human cardiac samples, and inadequate methods of maintaining human heart tissue in cell culture systems. Cellular reprogramming methods that enable derivation of human induced pluripotent stem cells (hiPSCs) from adult cells, which can then be differentiated into cardiomyocytes (hiPSC-CMs), are a revolutionary tool for creating disease-specific cell lines that may lead to effective targeted therapies.

In this proposal, we will derive hiPSC-CMs from patients with HCM and healthy controls, then perform a battery of functional and molecular tests to determine the presence of cardiomyopathic disease and associated abnormal molecular programs. With these preliminary studies, we believe hiPSC-CMs with HCM phenotype will dramatically enhance the ability to perform future high-throughput drug screens, evaluate gene and cell therapies, and assess novel electrophysiologic interventions for potential new therapies of HCM. Because HCM is not a rare disease but rather the leading cause of inherited heart defects, we believe the findings here should have broad clinical and scientific impact toward understanding the molecular and cellular basis of HCM.

Statement of Benefit to California: Familial hypertrophic cardiomyopathy (HCM) is the leading cause of sudden cardiac death in young people and is the most common inherited heart defect. In this study, we will generate hiPSC-derived cardiomyocytes from patients with HCM, then perform a number of functional, molecular, bioinformatic, and imaging analyses to determine the extent and nature of cardiomyopathic disease. We believe hiPSC-CMs with HCM phenotype will dramatically enhance the ability to perform future high-throughput drug screens, evaluate gene and cell therapies, and assess electrophysiologic interventions for potential novel therapies of HCM. The experiments outlined are pertinent and central to the overall mission of CIRM, which seeks to explore the use of stem cell platforms to yield novel mechanistic insights into the molecular and cellular basis of disease. Because HCM is not an orphan disease, but rather the leading cause of sudden cardiac death in young people, we believe the research findings will benefit the state of California and its citizens.

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