Epigenetic regulation of human cardiac differentiation

Grant Award Details

Epigenetic regulation of human cardiac differentiation

Grant Type: Basic Biology IV

Grant Number: RB4-05901

Project Objective: The objective of this project is to define the epigenetic blueprint of differentiating human cardiac myocytes derived from hESC and hiPSC.
This will be done by:
Aim 1: Mapping histone modifications associated with active or inactive chromatin, as well as RNA Pol II binding and DNA methylation, for four stages of differentiation. These maps will be compared to the known transcriptome.
Aim 2: Mapping gene expression and epigenetic landscapes for the first and second heart fields at the precursor and differentiated stages.
Aim 3: Use iPSC from patients with congenital heart disease (Holt-Oram syndrome) caused by TBX5 hapolinsufficiency to uncover epigenetic changes that accompany dysregulated gene expression in CHD.

Investigator:

Name:	Benoit Bruneau
Institution:	Gladstone Institutes, J. David
Type:	PI

Disease Focus: Heart Disease

Human Stem Cell Use: Embryonic Stem Cell, iPS Cell

Award Value: $1,568,148

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: Epigenetic regulation of human cardiac differentiation

Public Abstract: Each cell type in our body has its own identity. This identity allows a heart cell to contract repetitively, and a brain cell to conduct nerve impulses. Each cell type gains its identity by turning on or off thousands of genes that together give the cell its identity. Understanding how these sets of genes are regulated together as a cell gains its identity is important to be able to generate new cells in disease. For example, after a heart attack, heart muscle dies, leaving scar tissue and a poorly functioning heart. It would be very useful to be able to make new heart muscle by introducing the right set of instructions into other cells in the heart, and turn them into new heart muscle cells. One way that many genes are turned on or off together is by a cellular mechanism called epigenetic regulation. This global regulation coordinates thousands of genes. We plan to understand the epigenetic regulatory mechanisms that give a human heart muscle cell its identity. Understanding their epigenetic blueprint of cardiac muscle cells will help develop strategies for cardiac regeneration, and for a deeper understanding of how cells in our body acquire their individual identities and function.

Statement of Benefit to California: This research will benefit the state of California and its citizens by helping develop new approaches to cardiac regeneration that will be more efficient than current approaches, and amenable to drug-based approaches. In addition, the knowledge acquired in these studies will be important not only for heart disease, but for any other disease where reprogramming to regenerate new cells is desirable. The mechanisms revealed by this research will also lead to new understanding of the basis for congenital heart defects, which affect several thousand Californian children every year, and for which we understand very little.