Technology for hESC-Derived Cardiomyocyte Differentiation and Optimization of Graft-Host Integration in Adult Myocardium

Grant Award Details

Technology for hESC-Derived Cardiomyocyte Differentiation and Optimization of Graft-Host Integration in Adult Myocardium

Grant Type: SEED Grant

Grant Number: RS1-00242

Investigator:

Name:	Krishna Shenoy
Institution:	Stanford University
Type:	PI

Disease Focus: Heart Disease

Human Stem Cell Use: Embryonic Stem Cell

Award Value: $572,891

Status: Closed

Progress Reports

Reporting Period: Year 2

View Report

Grant Application Details

Application Title: Technology for hESC-Derived Cardiomyocyte Differentiation and Optimization of Graft-Host Integration in Adult Myocardium

Public Abstract:

Stem cells therapies hold great promise in the treatment of cardiac diseases such as coronary heart disease or congestive heart failure. Thanks to their ability to transform into almost any kind of tissue, engrafted stem cells can potentially replace damaged heart tissues with healthy tissues, effectively restoring the heart's original functions. While initial studies demonstrated the potential benefits of stem cell injection for repairing heart damage, they told researchers little about exactly how improvements were made to the heart and how the improvement might be enhanced. Also, there is concern that the stem cells could negatively impact some aspects of heart function and lead to disturbances of heart rhythm and future attacks.

In light of this, we propose to develop a model to study the detailed interaction of stem cells and healthy heart tissue in the laboratory, where events within the cells and between the cells can be measured accurately and many experiments can be done to increase our understanding, without the use of human subjects. Specifically, we plan to focus on two main goals.

The first goal is to develop a platform to better understand the gradual transition that stem cell lines make as they mature into heart cells, process known as differentiation. We will record the electrical activity arising from newly formed heart cells to determine when exactly they form and how the behave in response to electrical stimuli or drugs as they mature. This will tell us more about the behavior of the cells that could be injected into the heart so that we know how they will respond when they merge with the heart and when is the best time to introduce them.

The second goal, building on the first one, is to observe how the stem cells make contact with the heart cells, including how they grow together mechanically and how they begin to communicate electrically as a repaired tissue. This will be carried out by growing the stem cells and heart cells separately and then allowing them to grow together, just as they would in the heart. Simultaneous recording of electrical activity at numerous locations in the culture will let us map the activity across the culture and evaluate the communication between heart cells (host) and stem cells (graft).

Understanding the microscopic nature of integration of stem cells into healthy tissue will lead to a greater knowledge of what can happen when stem cells are injected into the heart and begin to replace the non-functional tissue and connect to healthy tissue. Insights gained with such model should lead to a better understanding of the repair process and highlight strategies for making stem cell-based therapies safer and more effective. This model will also allow testing and development of chemical or electrical manipulations that would increase the yield and reliability of the differentiation process, paving the way for the ultimate scale-up of stem cell therapies for clinical use.

Statement of Benefit to California:	There is currently no cure for heart damage caused by heart attack, and stem cells offer a very promising solution to this problem that affects millions of Americans. We feel that addressing possible solutions to this pervasive problem is a very constructive and meaningful way to utilize some of the financial resources allocated for stem cell research in California. Within (and outside) the CIRM community, we also have the important goal of making currently unavailable electronic, microfabrication and signal processing technologies available in the form our proposed research platforms. With our planned outreach efforts, we will freely share our methods and equipment, hopefully enhancing the work of many other research groups. By using CIRM funds, we could make such systems available for use with non-registered (as well as registered) cell lines. The outcome of this research stands to impact not only citizens of California, but also the nation and the world. We aim to make considerable progress with research paid for by the citizens of California, demonstrating the degree to which we, as a people, are committed to solving problems in medicine and health care and improving the lives of others. This work will also benefit our State and taxpayers through the training of post-doctoral and graduate students with a clear mindset of leadership, creativity and compassion. Through publication and presentations at local, national and international forums, we hope to disseminate the knowledge gained and encourage further advances.

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