
In Vivo Molecular Magnetic Resonance Imaging of Human Embryonic Stem Cells in Murine Model of Myocardial Infarction

Grant Award Details

In Vivo Molecular Magnetic Resonance Imaging of Human Embryonic Stem Cells in Murine Model of Myocardial Infarction

Grant Type: SEED Grant

Grant Number: RS1-00326

Investigator:

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|---------------------|---------------------|
| Name: | Phillip Yang |
| Institution: | Stanford University |
| Type: | PI |

Disease Focus: Heart Disease

Human Stem Cell Use: Embryonic Stem Cell

Award Value: \$629,952

Status: Closed

Progress Reports

Reporting Period: Year 2

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Reporting Period: NCE

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Grant Application Details

Application Title: In Vivo Molecular Magnetic Resonance Imaging of Human Embryonic Stem Cells in Murine Model of Myocardial Infarction

Public Abstract: Magnetic resonance imaging (MRI) has emerged as one of the predominant modalities to evaluate the effects of stem cells in restoring the injured myocardium. However, MRI does not enable assessment of a fundamental issue in cell therapy, survival of the transplanted cells. The transplanted human embryonic cells (hESC) must at the very least survive to restore the injured myocardium. This research proposal will address this specific challenge to image non-invasively both the survival of the transplanted hESC and the resultant restoration of the myocardium through sensitive detection of the molecular events indicating hESC survival and rapid imaging of myocardial function. In order to achieve this dual capability, there are 2 primary considerations: 1) amplification of molecular signals and 2) high spatial and temporal resolution imaging of the myocardium.

No single imaging modality will fulfill all needs of non-invasive molecular imaging in the heart. Only an imaging modality that optimizes the 2 technical specifications will provide physiologically relevant meaning of the molecular signal of the transplanted hESC. The molecular signal will be useful if some correlation between hESC survival and functional restoration can be established. In order to address these critical issues, this proposal will describe efforts to implement molecular MRI to image both the survival of transplanted hESC and restoration of cardiac function using mouse model of myocardial infarction.

This research proposes an integrated, multidisciplinary approach to converge innovative approaches in MRI and stem cell biology to address a fundamental yet very critical issue in cardiac restoration: survival of hESC following transplantation into the injured myocardium. This proposal combines novel molecular techniques with the high resolution capabilities of MRI. Upon conclusion of this research, an integrated MRI platform will be developed to allow dual evaluation of the survival of transplanted hESC and their effects on myocardial function. Maturation of this imaging technology will ultimately enable accurate assessment of the survival of hESC and restoration of recipient tissue in all human organs.

Statement of Benefit to California: Coronary artery disease (CAD) continues to be the leading cause of death in the United States. Recent advances in cardiovascular therapy have improved immediate survival following an acute myocardial infarction (MI). The persistence of high overall mortality of CAD despite improved treatment is due to a shift in the disease process. Studies have demonstrated a critical role of the infarcted myocardium in the development of congestive heart failure (CHF). The incidence of CHF is now reaching epidemic proportions. Today, there is higher number of deaths from patients developing CHF rather than those sustaining acute MI. CHF is the leading cause of hospital admissions resulting in approximately 300,000 deaths annually. There are nearly 5 million Americans who are suffering from this illness with 550,000 new cases reported each year. Over the last several decades, advances in biomedical technology provided significant improvement in morbidity and mortality. However, the average 5-year survival today still remains around a dismal 50%, creating a major public health concern. Heart transplantation is an established treatment for end-stage CHF. Yet, this definitive therapy is limited to only 2000 donor hearts per year. Thus, a strong mandate exists for an alternative therapeutic option. Human embryonic stem cells (hESC) have demonstrated the ability to differentiate into cardiac cells, representing a potential application of cell therapy to restore the injured myocardium.

The public health impact of CHF in California is representative of the emerging trend seen across the United States. As the most populous State in the nation, CHF has resulted in equivalent burden to California's health care cost, morbidity and mortality. The State of California stands to benefit tremendously with accurate MRI-guided monitoring of the therapeutic efficacy of hESC in an effort to advance the treatment for CHF.