Macaca mulatta as advanced model for predictive preclinical testing of engineered cardiac autografts and allografts

Grant Award Details

Macaca mulatta as advanced model for predictive preclinical testing of engineered cardiac autografts and allografts

Grant Type: Tools and Technologies III

Grant Number: RT3-07798

Project Objective: Development of a large animal (macaca mulatta) model for predictive preclinical testing of engineered cardiac autografts and allografts.

Investigator:

Name:	Joseph Wu
Institution:	Stanford University
Type:	PI

Disease Focus: Heart Disease

Human Stem Cell Use: iPS Cell

Award Value: $1,689,744

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 3

View Report

Grant Application Details

Application Title: Advanced animal model for predictive preclinical testing of engineered cardiac autografts and allografts

Public Abstract:

Heart disease is the number one cause of death in the US. Heart muscle injured during a heart attack does not regenerate, and the resulting damage leads to heart failure, which inflicts almost 6 million people in the US alone. Recently, several studies have shown that direct injection of stem cell-derived heart cells may offer regenerative potential in the damaged heart. However, injected heart cells often lack the spatial and temporal organization required to create uniform tissue with synchronized beating, while rapid donor cell death poses another key limitation. For these reasons, we propose to transplant engineered heart muscle (EHM) that is spatially and temporally organized into a relevant large animal model. Our proposal addresses unique translational challenges pertaining to tissue engineered heart repair by scaling our established human induced pluripotent stem cell (iPSC) differentiation protocol to create one billion human and large animal model cardiomyocytes for each EHM, in order to meet clinical demands by: (1) adopting our established human EHM tissue engineering process to the large animal model; (2) defining conditions for EHM implantation; and (3) performing a pivotal feasibility, safety, and efficacy study in the large animal model with chronic heart failure. Our studies will establish long-term safety and efficacy of iPSC-EHM therapies in a clinically relevant large animal model, which will overcome a major unresolved bottleneck to the translation of stem cell therapies to humans.

Statement of Benefit to California:

Cardiovascular disease (CVD) affects more than 1.7 million Californians. The societal and financial costs are tremendous, with CVD accounting annually for an estimated $8 billion in California health care costs alone. Following a heart attack, the endogenous regenerative process is not sufficient to compensate for heart tissue death. Thus, using regenerative therapies with human stem cells to form engineered heart tissue is emerging as a promising therapeutic avenue. Engineered tissues are already being used in patients needing artificial blood vessels, bladders, and tracheas. Our multidisciplinary team proposes to create human engineered heart tissue (EHT) for treatment of post-attack heart failure in a clinically-enabling large animal model, and we are confident we will be able to move our potential therapy into preclinical human trials. Development of therapies for diseases such as CVD could potentially improve the California health care system by reducing the long-term health care cost burden on California. In addition, our research may provide an opportunity for California to benefit from royalties, patents, and licensing fees, which will create cutting-edge projects, attractive jobs, and innovative therapies that will generate millions of dollars in new tax revenues and opportunities in our state. Finally, our research could further advance the flourishing biotech industry in California, serving as a crucial engine to power California's economic future.
