Autologous cardiac-derived cells for advanced ischemic cardiomyopathy

Grant Award Details

Autologous cardiac-derived cells for advanced ischemic cardiomyopathy

Grant Type: Disease Team Research I
Grant Number: DR1-01461
Investigator:

<table>
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<tr>
<th>Name</th>
<th>Eduardo Marbán</th>
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<td>Institution</td>
<td>Cedars-Sinai Medical Center</td>
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<td>Type</td>
<td>PI</td>
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Disease Focus: Heart Disease
Human Stem Cell Use: Adult Stem Cell
Cell Line Generation: Adult Stem Cell
Award Value: $5,560,232
Status: Closed

Progress Reports

Reporting Period: Year 1
View Report

Reporting Period: Year 2
View Report

Grant Application Details

Application Title: Autologous cardiac-derived cells for advanced ischemic cardiomyopathy
Public Abstract:
The adult human heart contains small numbers of cardiac stem cells that are able to partially repair the heart following a heart attack or throughout the course of progressive heart failure. We have developed a method to isolate these cells and grow them to large numbers in the lab. Isolation begins with a minimally-invasive biopsy taken from a patient’s heart. Our method can be used to then generate clusters of cells (termed “cardiospheres [CSps]”) or individual cells (termed “cardiosphere-derived cells [CDCs]”), each with their own advantages and disadvantages. When delivered to animals after a heart attack or in the midst of heart failure, these cells can better repair the heart, form new heart muscle and new blood vessels. CDCs are currently being given to patients after a recent heart attack, using a catheter to deliver the single cells into a blood vessel supplying the heart, as part of an ongoing clinical trial. The proposed research aims to test both CSps and CDCs in large animals in the midst of heart failure, using a catheter to deliver the cells directly into the heart muscle, in preparation for another clinical trial. Preliminary data shows that CSps may be a more potent cell therapeutic when compared to their single cell counterparts. Direct injection into the muscle not only allows for safe delivery of the cell clusters, but also increases the effective dose of the cells. Patients with heart failure also stand to benefit more from such a cell-based therapeutic when compared to those victims of a recent heart attack. As such, this research will involve not only animal studies, but also cell manufacturing studies, and the preparation and filing of an IND in order to begin a clinical trial. The first study will test both cell products along with the direct-injection catheter in a large scale animal model in order to determine the optimum cell dose. The second study will determine the optimum number of injections to perform during the procedure. These results will be available by the end of the first year, and will allow for a final pivotal study to be conducted during the course of the second year. This pivotal study will examine both the safety and efficacy of cell delivery in the large scale animal model, utilizing a group of control animals, and will serve as key preclinical data when filing an IND. During the course of the first two years, cell manufacturing studies will be conducted in parallel. These studies will enable us to develop procedures to reproducibly generate, store, ship, and deliver the cell therapeutic in the manner that will be adopted during the clinical trial. During the third year, the preclinical and manufacturing data will be combined with a clinical protocol formulated during the course of the pivotal animal study, to constitute the bulk of an IND. Following pre-IND discussions and IND review, we will begin conducting a clinical trial in patients with heart failure in the hope of halting disease progression for these individuals.

Statement of Benefit to California:
Few families in California are not impacted by heart disease. Cardiovascular disease remains the leading cause of death and disability in Americans- on average, cardiovascular disease kills one American every 37 seconds. The death toll from cardiovascular disease is greater than that for cancer, chronic respiratory diseases, accidents, and diabetes combined. Death rates have improved, but new treatments are urgently needed. Aside from the human costs, cardiovascular disease exacts a tremendous fiscal toll: the American Heart Association estimates that the total costs of cardiovascular disease in the United States approached one-half trillion dollars in 2008. All taxpayers must bear the economic burden of resulting death and disability. Clearly, virtually all Californians stand to benefit, directly or indirectly, from the development of more effective treatments of cardiovascular disease. Heart disease is a particularly good target not just because of the magnitude of the public health problem, but also because heart muscle does not ordinarily regenerate once it has been destroyed by heart attacks and other types of damage. We seek to tap into the innate repair mechanisms of the heart by harvesting adult cardiac stem cells. The present work seeks to provide the scientific basis for regulatory filings that would allow us to reintroduce cardiac stem cells into patients with advanced heart failure. The treatment would be “autologous”, in that cells from any given patient would be used to treat that same patient. Thus, the cells are a perfect genetic match, obviating the risk of rejection. If our studies are successful, we may offer a cost-effective way to reduce the tremendous damage to Californians inflicted by major types of cardiovascular disease. This in turn may also reduce the economic burden presently borne by taxpayers who support the health care systems in California. In addition to the public health benefits, spinoff technology developed by this disease team will benefit existing California-based biotechnology companies, leading to fuller employment and an enhanced tax base.