
Scaffold for dermal regeneration containing pre-conditioned mesenchymal stem cells to heal chronic diabetic wounds

Grant Award Details

Scaffold for dermal regeneration containing pre-conditioned mesenchymal stem cells to heal chronic diabetic wounds

Grant Type: Preclinical Development Awards

Grant Number: PC1-08118

Project Objective: The objective of this award is to hold a successful Type C pre-IND meeting with the FDA about plans to develop a combination of a collagen-based wound-healing scaffold for dermal regeneration (SDR, Integra) seeded with preconditioned MSC for treatment of non-healing diabetic foot ulcers.

Investigator:

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Institution:	University of California, Davis
Type:	PI

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Institution:	University of California, Davis
Type:	Co-PI

Disease Focus: Diabetes, Diabetic Wounds, Metabolic Disorders, Skin Disease

Human Stem Cell Use: Adult Stem Cell

Award Value: \$4,620,144

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Grant Application Details

Application Title: Scaffold for dermal regeneration containing pre-conditioned mesenchymal stem cells to heal chronic diabetic wounds

Public Abstract: The goal of our CIRM-funded Early Translational (ETA) grant was to engineer a product to improve healing in diabetic foot ulcers, a devastating consequence of diabetes that occurs in about 25% of all diabetic patients and is responsible for most leg or foot amputations. More than 6 million people in the US and up to 91 million people worldwide have diabetic foot ulcers (DFU). There is a clear medical need. There are products on the market that can improve wound healing for some, but not all patients. This causes a large financial burden for the health care system, and great suffering for the patients who live with open wounds, often infected, that progress to amputations. Therefore there is a clear medical need for advanced therapies to heal diabetic ulcers faster.

We proposed to create a combination product consisting of a scaffold for dermal regeneration (SDR) populated with human allogeneic mesenchymal stem cells (MSC) that have been pre-conditioned for optimized reparative function. We formed a team of established wound and stem cell/matrix experts, and this team has indeed successfully engineered and demonstrated efficacy of the preconditioned MSC-SDR in two animal models, and is now ready to progress to further dose-finding and initial biosafety studies in support of our very promising Development Candidate.

During the Early Translational grant, we developed a product that consists of an FDA-approved scaffold for dermal regeneration (SDR) filled with human bone marrow-derived Mesenchymal Stem Cells (MSC). These are then pre-incubated for 2 days in hypoxia and in the presence of a beta adrenergic antagonist. We have completed studies that demonstrate that this "next generation" stem cell product is highly efficacious in healing diabetic skin wounds, using mouse skin wound models in diabetic mice that have impaired and delayed healing and a porcine model.

In the PreClinical Development award period we propose to bring this product closer to clinical use for human patients. We propose dose finding studies to achieve the optimal dose with the largest safety margin. We will use a large animal wound model where skin wounds more closely resemble those in humans, to carry out these efficacy and early safety studies. We will use this time to create a Master Cell Bank of pure and effective human MSCs and to generate standard operating procedures to move us into the clinical arena. Finally, we will prepare a package for presentation to the FDA for moving the preclinical product forward toward a Phase I/II clinical trial that will demonstrate efficacy and safety of the product in affected patients.

Statement of Benefit to California: While the number of individuals with all forms of chronic wounds is increasing in the general population, particularly with the rise of diabetes and aging of the population, the number of individuals affected by diabetic foot ulcers (DFU), the target disease for the development candidate in this proposal, is increasing in California at an alarming rate. That is because the prevalence of type 2 diabetes is now increasing within the state of California to epidemic proportions. In 2002, over one million California adults age 45 and older were diagnosed with diabetes, and by 2011 that number had risen to 2.3 million: 8.4% of the California population (1).

For reasons that are not all that clear, there are marked differences in the prevalence of diabetes in different Californian ethnic and racial groups. Among Californians 65 and older, diabetes is significantly more common in African Americans (25.6%) , and Latinos (24.4%) as compared to Caucasians (12.2%). (1) The diabetes brings with it devastating health impacts: it is the sixth most common cause of death in the United States. Among the morbidities associated with diabetes, DFU is one of the most debilitating. Approximately 15-25 percent of patients with diabetes will develop DFU, and of those, six percent will be hospitalized due to infection or other ulcer-related complications. According to a recent census, DFU is the leading cause of lower limb amputation and greater than 85% of amputations are preceded by an active foot ulcer.

Sadly for our state, we lead others in the US in the prevalence of DFU: "Of the 45 areas (44 states and DC) that reported information to the Behavioral Risk Factor Surveillance System, the world's largest, on-going telephone health survey system, the BRFSS diabetes module shows that Indiana (16.3%), California (16.2%), and Nevada (16.2%) had the highest age-adjusted prevalence of a history of foot ulcer among persons with diabetes, and Colorado (7.4%), Wisconsin (8.8%), and Hawaii (8.9%) had the lowest " (2).

Treatments for curing DFU are very far from optimal. Current standard of care can cure only about 30% of DFU and even the most advanced therapies, cell-based devices containing skin derived keratinocytes and fibroblasts, boosts the cure rate only to about 50%, leaving a tremendous unmet need for new effective cures for DFU, particularly in California. We anticipate that the development candidate that we propose, a stem cell-based "biological bandage", will bring a new and effective cure to our citizens who are suffering from diabetic foot ulcers.

Sources: 1) California Health Care Survey, UCLA, <http://www.chis.ucla.edu/>

2) CDC reports Morbidity and Mortality Weekly Report (MMWR), <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5245a3.htm>

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