# Stem Cell Therapy for Duchenne Muscular Dystrophy

## Grant Award Details

Stem Cell Therapy for Duchenne Muscular Dystrophy

**Grant Type:** Early Translational II

**Grant Number:** TR2-01756

**Project Objective:** Demonstrate proof of concept for hiPSC derived satellite cell therapy for Duchenne muscular dystrophy (using the PIs phic32 integrase iPSC generation and correction technologies at safe harbor site).

**Investigator:**

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| **Name:** | Michele Calos |
| **Institution:** | Stanford University |
| **Type:** | PI |

**Disease Focus:** Muscular Dystrophy, Pediatrics, Skeletal/Smooth Muscle disorders

**Human Stem Cell Use:** iPS Cell

**Cell Line Generation:** iPS Cell

**Award Value:** $2,267,261

**Status:** Closed

## Progress Reports

**Reporting Period:** Year 1

**View Report**

**Reporting Period:** Year 2

**View Report**

**Reporting Period:** Year 3 + NCE

**View Report**

## Grant Application Details

**Application Title:** Stem Cell Therapy for Duchenne Muscular Dystrophy

**Public Abstract:**

Duchenne muscular dystrophy (DMD) is the most common and serious form of muscular dystrophy. One out of every 3500 boys is born with the disorder, and it is invariably fatal. Until recently, there was little hope that the widespread muscle degeneration that accompanies this disease could be combated.

However, stem cell therapy now offers that hope. Like other degenerative disorders, DMD is the result of loss of cells that are needed for correct functioning of the body. In the case of DMD, a vital muscle protein is mutated, and its absence leads to progressive degeneration of essentially all the muscles in the body.

To begin to approach a therapy for this condition, we must provide a new supply of stem cells that carry the missing protein that is lacking in DMD. These cells must be delivered to the body in such a way that they will engraft in the muscles and produce new, healthy muscle tissue on an ongoing basis.

We now possess methods whereby we can generate stem cells that can become muscle cells out of adult cells from skin or fat by a process known as “reprogramming”. Reprogramming is the addition of genes to a cell that can dial the cell back to becoming a stem cell. By reprogramming adult cells, together with addition to them of a correct copy of the gene that is missing in DMD, we can potentially create stem cells that have the ability to create new, healthy muscle cells in the body of a DMD patient. This is essentially the strategy that we are developing in this proposal.

We start with mice that have a mutation in the same gene that is affected in DMD, so they have a disease similar to DMD. We reprogram some of their adult cells, add the correct gene, and grow the cells in incubators in a manner that will produce muscle stem cells. The muscle stem cells can be identified and purified by using an instrument that detects characteristic proteins that muscles make.

The corrected muscle stem cells are transplanted into mice with DMD, and the ability of the cells to generate healthy new muscle tissue is evaluated. Using the mouse results as a guide, a similar strategy will then be pursued with human cells, utilizing cells from patients with DMD. The cells will be reprogrammed, the correct gene added, and the cells grown into muscle stem cells. The ability of these cells to make healthy muscle will be tested by injection into mice with DMD that are immune-deficient, so they will accept a graft of human cells.

In order to make this process into something that could be used in the clinic, we will develop standard procedures for making and testing the cells, to ensure that they are effective and safe. In this way, this project could lead to a new stem cell therapy that could improve the clinical condition of DMD patients. If we have success with DMD, similar methods could be used to treat other degenerative disorders, and perhaps even some of the degeneration that occurs during normal aging

**Statement of Benefit to California:**

The proposed research could lead to a stem cell therapy for Duchenne muscular dystrophy (DMD). This outcome would deliver a variety of benefits to the state of California.

First, there would be a profound personal impact on patients and their families if the current inevitable decline of DMD patients could be halted or reversed. This would bring great happiness and satisfaction to the thousands of Californians affected directly or indirectly by DMD.

Progress toward a cure for DMD is also likely to accelerate the development of treatments for other degenerative disorders. The most obvious targets would be other forms of muscular dystrophy and neuromuscular disorders. However, the impact would likely also stimulate medical progress on a variety of conditions in which a stem cell therapy could be beneficial. These conditions may even extend to some of the normal processes of aging, which can be traced to depletion of stem cells.

An effective stem cell therapy for DMD would also bring economic benefits to the state. Currently, there is a huge burden of costs associated with the care of patients with long-term degenerative disorders like DMD, which afflict thousands of patients statewide. If the clinical condition of these patients could be improved, the cost of maintenance would be reduced, saving billions in medical costs. Many of these patients would be more able to contribute to the workforce and pay taxes.

Another benefit is the effect of novel, cutting-edge technologies developed in California on the business economy of the state. Such technologies can have a profound effect on the competitiveness of California through the formation of new manufacturing and health care delivery facilities that would employ California citizens and bring new sources of revenue to the state.

Therefore, this project has the potential to bring health and economic benefits to California that are highly desirable for the state.

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