# Optimization of Human Embryonic Stem Cell Derivation Techniques and Production/Distribution of GMP-Grade Lines

## Grant Award Details

Optimization of Human Embryonic Stem Cell Derivation Techniques and Production/Distribution of GMP-Grade Lines

**Grant Type:** New Cell Lines

**Grant Number:** RL1-00648

**Project Objective:** To generate new hESC lines from embryos and blastomeres.

**Investigator:**

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| **Name:** | Susan Fisher |
| **Institution:** | University of California, San Francisco |
| **Type:** | PI |

**Human Stem Cell Use:** Embryonic Stem Cell

**Cell Line Generation:** Embryonic Stem Cell

**Award Value:** $1,383,419

**Status:** Closed

## Progress Reports

**Reporting Period:** Year 1

**View Report**

**Reporting Period:** Year 2

**View Report**

**Reporting Period:** Year 3

**View Report**

**Reporting Period:** Year 4 (NCE)

**View Report**

## Grant Application Details

**Application Title:** Optimization of Human Embryonic Stem Cell Derivation Techniques and Production/Distribution of GMP-Grade Lines

**Public Abstract:** The government has strict rules for producing cells that will be transplanted into patients. For example, these regulations discourage the use of animal products that could transmit diseases to humans. In this context, the high-quality and tightly regulated procedures that govern other cell-based therapies, e.g., bone marrow transplants, will be applied to regenerative-type clinical applications that employ human embryonic stem cells (hESCs). We need to produce these cells now so that they will be ready to use when research findings are translated into patient therapies. Our goal is to supply researchers in California and outside the state with the highest-quality hESCs. To achieve this goal, we will build on our previous work, published in the scientific literature, which includes deriving hESCs from intact embryos and their single-cell components. We also study the basic properties of embryos and hESCs so that we can formulate theories about how to improve the derivation process, which we then test in our laboratory. For example, adult humans need very precise levels of oxygen. Our work shows that the same is true for embryos and hESCs. We have also developed novel culture conditions that use defined components such as those that are required by the governmental agencies that set the standards for the production of cells used in therapeutic applications. Accordingly, we propose a two-phase approach. During the first two years, guided by advances made by our group and others, we will derive hESCs from embryos in a biologically relevant oxygen environment using defined, high-quality materials. We will also derive hESCs from single cells removed by biopsy from embryos at specific stages of development and/or from particular regions. We think that these lines might have more predictable properties than hESCs that arise randomly, the current practice. Thus, at the end of the first phase we will have produced and banked the next generation of lines, which will be derived under defined conditions that more closely comply with government regulations regarding the production of clinical-grade cells. In the second phase, year 3 of the project, we will use the conditions that best support hESC derivation/propagation to produce lines that can be transplanted into patients. Our efforts will benefit greatly from the infrastructure of our institution, which includes a government-approved facility for doing this work, and from colleagues with the requisite specialized expertise. With the resources provided, we think that we can generate and bank 12 to 20 cell lines; one-third will be produced in a manner that complies with government regulations pertaining to cell-based therapies. All will be widely distributed, as we believe that the pace of translational and clinical research depends on the availability of the highest-quality hESCs and on the important information about their fundamental properties that will emerge from this work.

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| **Statement of Benefit to California:** | California citizens were overwhelmingly in favor of proposition 71, due in large part to the public's belief that laboratory scientists working together with their clinical colleagues could develop therapeutic approaches that utilize human embryonic stem cells and their derivatives in regenerative medicine applications. The research teams are equally excited about cell replacement strategies for treating a variety of medical conditions, as in many cases a cure might be feasible. However, we know from the collective experience of the biotechnology industry that filling the pipeline that leads from basic research to clinical applications inevitably takes time. How do we start this process and shorten the timelines for delivering cell-based therapies to patients? Much of the work in the individual pipelines that focus on specific diseases/conditions can happen in a nonlinear fashion. For example, we need not wait until safe and robust strategies are devised for differentiating human embryonic stem cells into specific cell types to develop the lines that meet government regulations regarding the production of cells for transplantation into patients. There are many reasons that deriving these human embryonic stem cell lines now is crucial. For example, it is likely that production of the cells that will eventually be used in clinical applications will be an iterative process. That is, we will continue to make key discoveries about the fundamental properties of human embryonic stem cells, about which basic information is still needed to improve conditions for growing and deriving lines. This is particularly relevant to the production of clinical-grade cells, as it will be much easier to meet Food and Drug Administration requirements if cells are produced using defined materials that contain only human and recombinant components. It will also be important to know if clinical-grade cells, which for regulatory reasons must be derived under streamlined conditions, have the same properties as other human embryonic cell lines that are used for research purposes. Thus, extensive preclinical testing will be required before these cells are approved by the Food and Drug Administration for use in humans. Thus, accomplishing the major goals set forth in this application will be of enormous benefit to California's citizens. We envision that production of the next generation of human embryonic stem cells that can be used in clinical applications will speed the delivery of therapeutic applications to patients. Along the way these cells will have many other valuable applications. For example, they can be used to screen pharmacologically active compounds for both beneficial and detrimental effects. They will also be valuable tools for understanding the molecular etiology of disease processes. Accordingly, accomplishing the goals of this project will greatly benefit the people's health and California's economy. |