
Modeling Human Embryonic Development with Human Embryonic Stem Cells

Grant Award Details

Modeling Human Embryonic Development with Human Embryonic Stem Cells

Grant Type: SEED Grant

Grant Number: RS1-00259

Project Objective: To use hESC to study the process by which embryonic ectoderm bifurcates down two lineages of seemingly distinct cell types, namely neural and epidermal.

Investigator:

Name:	William Lowry
Institution:	University of California, Los Angeles
Type:	PI

Human Stem Cell Use: Embryonic Stem Cell, iPS Cell

Award Value: \$528,096

Status: Closed

Progress Reports

Reporting Period: Year 2

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Grant Application Details

Application Title: Modeling Human Embryonic Development with Human Embryonic Stem Cells

Public Abstract:

Stem cells have entered the public consciousness as “cells that can do anything” and have been hailed as a panacea in the fight against disease, aging and cancer. Unfortunately, we have only scratched the surface in understanding these cells. Some of the things we think we know are that: embryonic stem cells hold great promise because they do seem to be “cells that can do anything”, but still cannot be isolated from consenting adults, and that adult stem cells, while isolatable, are much more limited in their ability to replenish tissue beyond their organ of origin. In addition, we know very little about human embryonic development for the simple fact that experiments on human embryos has proven to be nearly impossible due to ethical and technical obstacles. Clearly, if we gained a deep understanding about human embryos and human embryonic stem cells, we could not only develop useful clinical opportunities, but also potentially detect and treat errors made during human development. This proposal suggests that in fact we could learn a great deal about not only the therapeutic potential of hESCs, but also human development by exploiting cell culture. We propose to model human embryonic development in order to understand how a particular portion of the embryo undergoes a transformation to become either the brain or the skin. The fact that seemingly one cell type early on in the embryo can form either the complete nervous system or the skin has intrigued scientists for decades, we now hope to understand how this process works and in the process we hope to challenge existing theories of the potential of adult stem cells as well. With a deeper understanding of what makes a neuron a neuron as opposed to a skin cell, we will in fact be able to impart a neural code on a skin cell, and perhaps turn a skin cell into a neuron. If this becomes possible, we could: take a skin biopsy from a patient with parkinson's disease (a degenerative disorder where dopaminergic neurons are lost), use already established mechanisms for expanding those skin cells in culture, turn on the “neural code” to turn them into dopaminergic neurons, and then transplant them back into the same donor patient. This kind of self-transplant obviates the need for either immuno-suppression therapy which is toxic and sometimes deadly, or for patient-specific stem cells which are, for now, impossible to derive.

Statement of Benefit to California:

The people and the state of California stands to gain both scientifically and economically from the work proposed here. We propose a plan to augment our working knowledge of a process that, without hESC, we have no other method to address. We are developing a model to describe a fundamental process that occurs during human embryonic development. Obviously, we cannot perform experiments on human embryos, so we are taking advantage of the primitive nature of hESCs in order to model this process in vitro. Clearly, a working knowledge of human embryonic development would be of enormous significance to not only the scientific community, but the world at large. Mistakes during development lead to tragic consequences such as mental retardation, spina bifida, and perinatal mortality. Another benefit of the development of this model system is that currently the process by which hESC differentiate down different cells lines is somewhat of a black box. We know that hESCs can make many different cell types, some of which might be useful clinically for degenerative disorders, but we really do not know anything about how these different cell types come about. If we could gain some insight into how cell fate decisions are made, then we might be able to coerce not only hESCs, but other cell types as well, down a particular lineage. For instance, if we can understand the genetic program makes a primitive cell become a dopaminergic neuron, we could apply this program to another cell type such as a skin cell. Then, we could isolate skin cells from a patient with Parkinson's disease, a debilitating disease where dopaminergic neurons are destroyed, and turn these cells into dopaminergic neurons and put these neurons back into the patient with the disease. This kind of protocol would obviate the need for immunosuppressive therapy or patient specific stem cells.

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