Screening for Oncogenic Epigenetic Alterations in Human ES Cells

Grant Award Details

Screening for Oncogenic Epigenetic Alterations in Human ES Cells

Grant Type: SEED Grant

Grant Number: RS1-00408

Investigator:

Name:	Peter Laird
Institution:	University of Southern California
Type:	PI

Disease Focus: Cancer

Human Stem Cell Use: Embryonic Stem Cell

Award Value: $647,431

Status: Closed

Progress Reports

Reporting Period: Year 2

View Report

Reporting Period: NCE

View Report

Grant Application Details

Application Title: Screening for Oncogenic Epigenetic Alterations in Human ES Cells

Public Abstract:

Embryonic stem cell-based therapies hold great promise for the treatment of many human diseases. These therapeutic strategies involve the culture and manipulation of embryonic stem cells grown outside the human body. Culture conditions outside the human body can encourage the development of changes to the cells that facilitate rapid and sustained cell growth. Some of these changes can resemble abnormal changes that occur in cancer cells. These include “epigenetic” changes, which are changes in the structure of the packaging of the DNA, as opposed to “genetic” changes, which are changes in the DNA sequence.

Cancer cells frequently have abnormalities in one type of epigenetic change, called “DNA methylation”. We have found that cultured embryonic stem cells may be particularly prone to develop the type of DNA methylation abnormalities seen in cancer cells. A single rogue cell with DNA methylation abnormalities predisposing the cell to malignancy can jeopardize the life of the recipient of stem cell therapy. We have developed highly sensitive and accurate technology to detect DNA methylation abnormalities in a single cell hidden among 10,000 normal cells.

In this seed grant, we propose to screen DNA methylation abnormalities at a large number of genes in different embryonic stem cells and compare their DNA methylation profiles to normal and cancer cells. This will allows us to identify the dangerous DNA methylation abnormalities most likely to occur in cultured embryonic stem cells. We will then develop highly sensitive assays to detect these DNA methylation abnormalities, using our technology. We will then use these assays to determine ES cell culture conditions and differentiation protocols most likely to cause these DNA methylation abnormalities to arise in cultured ES cells.

The long-term benefits of this project include 1) an increased understanding of the epigenetics of human embryonic stem cells, 2) insight into culture conditions to avoid the occurrence of epigenetic abnormalities, and 3) a technology to monitor for epigenetic abnormalities in ES cells intended for introduction into stem cell therapy patients.

Statement of Benefit to California:

The successful implementation of human embryonic stem cell therapy will require rigorous quality control measures to assure the safety of these therapies. Cells cultured outside the human body are known to be at risk of developing abnormalities similar to those found in cancer cells. Since a single rogue cell hidden among thousands of normal cells could cause cancer in an embryonic stem cell therapy recipient, it will be essential to have highly sensitive and accurate assays to detect these abnormalities in cultured embryonic stem cells before they are introduced into the patient. The goal of this proposal is to develop such sensitive and accurate assays. The citizens of the State of California will benefit from the availability of such assay technology to help assure the safety of human embryonic stem cell therapies.
