Molecular Mechanisms of Reprogramming towards Pluripotency

Grant Award Details

Molecular Mechanisms of Reprogramming towards Pluripotency

Grant Type: Basic Biology I

Grant Number: RB1-01292

Project Objective: to uncover mechanisms of nuclear reprogramming of human cells through the study of a cell fusion (heterokaryon; HK) assay system

Investigator:

Name:	Helen Blau
Institution:	Stanford University
Type:	PI

Human Stem Cell Use: iPS Cell

Award Value: $1,408,332

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: Molecular Mechanisms of Reprogramming towards Pluripotency

Public Abstract:

Stem cell biology and its applications to cell-based therapies, since its inception 30 years ago, has been hindered by the immunological considerations of rejection of non-autologous cells in patients, as well as by ethical concerns. The generation of pluripotent cells from a patient's own somatic cells has therefore been the holy grail of regenerative medicine. A variety of techniques have been used to attempt nuclear 'reprogramming' including transfer of somatic nuclei into oocytes (SCNT) that led to cloning of the sheep 'Dolly'. A recent breakthrough was the demonstration by Yamanaka and colleagues that the introduction of only four molecular factors into skin fibroblasts could generate induced pluripotent cells (iPS cells), with potential similar to ES cells in their ability to generate all of the germ layers. iPS cells have an unparalled potential for cell based therapies as they overcome the immunological and ethical concerns as well as provide a means to obtain cellular disease models from patients as invaluable tools for disease characterization and drug screening. However, before their clinical applications can be realized, it is of utmost importance (a) to characterize reprogramming of iPS cells at a molecular level and (b) to use this information to increase the efficiency of iPS cell generation. Our proposed studies take advantage of a novel cell-fusion based system that we have developed, in which reprogramming is initiated rapidly and efficiently. Such studies are of fundamental importance in increasing our understanding of how to direct and maintain cell fate. In addition, they will benefit the production of iPS cells and advance the entire field of regenerative medicine.

Statement of Benefit to California:

The state of California is the front-runner in stem cell research, having gathered not only private investments, as demonstrated by the numerous biotechnology companies that are developing innovative tools, but also extensive public funds via Prop 71, that allows the state, through CIRM to sponsor stem cell research in public and private institutions. In order to preserve its leadership position and encourage research on stem cells, the CIRM is calling for research proposals that could lead to significant breakthroughs or the development of technologies useful for studying stem cells in order to improve human health. We propose here to develop a platform that will enhance our understanding of the basic biology of stem cells and establish a molecular understanding of the phenomenon of iPS cell generation, a breakthrough that has taken the stem cell world by storm in the last few years. California is fortunate to be the home for the laboratory of Shinya Yamanaka, who pioneered this technique. Yet, the study of pluripotency is a field in its infancy and a better understanding of iPS cell biology, especially of the molecular events that allow a skin cell from any human being to be turned into an iPS cell (akin to an embryonic stem cell in its potential) is greatly needed before the potential of iPS cells can be fully realized. Our proposed studies are based on an innovative use of cell fusion to study reprogramming as a complimentary approach to iPS cells with the aim of enhancing our understanding of the process of nuclear reprogramming to iPS cells and making their derivation much more efficient. These studies will contribute substantially to all types of stem cell research, including human embryonic stem cells and induced pluripotent stem cells advancing the entire field of regenerative medicine.
