Reprogramming of human somatic cells back to pluripotent embryonic stem cells

Grant Award Details

Reprogramming of human somatic cells back to pluripotent embryonic stem cells

Grant Type: New Faculty I

Grant Number: RN1-00536-B

Project Objective: The goal of this project is to identify small molecules that enhance reprogramming of fibroblasts to iPSC in the presence of OCT4.

Investigator:

Name:	Sheng Ding
Institution:	Gladstone Institutes, J. David
Type:	PI

Human Stem Cell Use: Embryonic Stem Cell, iPS Cell

Cell Line Generation: iPS Cell

Award Value: $1,320,101

Status: Closed

Progress Reports

Reporting Period: Year 3

View Report

Reporting Period: Year 4

View Report

Reporting Period: Year 5 (5/1/12 - 4/30/13)

View Report

Grant Application Details

Application Title:	Reprogramming of human somatic cells back to pluripotent embryonic stem cells
Public Abstract:	The ability to dedifferentiate or reverse lineage-committed cells to pluripotent/multipotent cells might overcome many of the obstacles (e.g. cell sources, immunocompatibility and bioethical concerns) associated with using other ES and adult stem cells in clinical applications. With an efficient dedifferentiation process, it is conceivable that healthy, abundant and easily accessible somatic cells could be reprogrammed to generate different types of functional cells for the repair of damaged tissues and organs. However, the cellular processes involved in dedifferentiation remain poorly understood, and methods for the control and study of dedifferentiation to pluripotency in human somatic cells are lacking. Reprogramming of murine somatic cells in embryonic and adult fibroblast cultures to pluripotent ESC-like cells has recently been achieved by simultaneous viral transduction of four transcription factors together. With such proof-of-principle demonstration, next critical steps would be to "translate" such reprogramming methods into human somatic cells and identify small molecules that would allow temporal reversible treatment to induce/enhance reprogramming without risks of genetic manipulations. Here we propose to develop homogenous human somatic cell systems to examine reprogramming to pluripotency, and implement a high throughput screen of large and diverse chemical librariesy to identify small molecules that can induce/enhance programming of human somatic cells back to pluripotent hESC-like cells. We will further examine their effects/activities via various in-depth cellular/biochemical assays, and characterize their mechanism of action by integrated chemical and functional genomic approaches. Collectively, the studies described in this proposal will provide novel chemical tools for producing unlimited amount of (autologous) pluripotent cells from differentiated/lineage-restricted cells for various applications as well as studying the underlying molecular mechanisms of pluripotency and epigenetic regulations, and may ultimately facilitate development of small molecule therapeutics to stimulate tissue/organ regeneration in vivo.
Statement of Benefit to California:	Historically, small molecules have been more useful than genetic approaches in the treatment of human disease. However, much of our ability to control reprogramming of somatic cells to pluripotent cells currently involves either genetic manipulation of these cells or complex mixtures of protein factors. The demonstration that one can systematically identify, optimize and characterize the mechanism of action of small drug-like molecules that selectively control cell fate and reprogramming will: (1) provide important tools to manipulate cell fate in the lab; (2) provide new insights into the complex biology that regulates (stem) cell fate; and (3) provide an important first step which may ultimately lead to drugs that facilitate the clinical application of stem cells.