Energy metabolism and aging pathways in human stem cell reprogramming and differentiation

Grant Award Details

Energy metabolism and aging pathways in human stem cell reprogramming and differentiation

Grant Type: Basic Biology IV

Grant Number: RB4-06087

Project Objective: The goal of the proposal is to test the hypothesis that mechanisms that regulate metabolism and aging are important for stem cell function and could potentially be harnessed to enhance the function of stem cells from aged individuals. Specific plans are to elucidate the mechanism of action of the AMPK pathway, a central player in energy metabolism. Studies will be conducted in iPSCs from young and old individuals. Human and some murine studies are proposed.

Investigator:

Name:	Anne Brunet
Institution:	Stanford University
Type:	PI

Human Stem Cell Use: iPS Cell

Award Value: $1,414,044

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Reporting Period: Year 3

View Report

Grant Application Details

Application Title:	Energy metabolism and aging pathways in human stem cell reprogramming and differentiation
Public Abstract:	The discovery that human skin cells can be reprogrammed into stem cells holds great promise for therapies for degenerative diseases. As many patients in need of regenerative medicine therapies are middle-aged or older, identifying strategies to improve the reprogramming efficiency and quality of cells from aging donors will be crucial in harnessing the full potential of stem cells for therapies. Our idea is that mechanisms that regulate aging, particularly those related to energy metabolism, can be used to enhance stem cell function, particularly when cells come from older individuals. To test this idea, we will analyze the importance of a central energy metabolism gauge in cells termed AMPK in the reprogramming of human skin cells into stem cells. Systematic analysis of metabolic pathways in stem cells and their progeny will give fundamental clues into the mechanisms connecting energy metabolism, aging, and stem cell function. This knowledge will help overcome road-blocks in reprogramming and differentiation into specific lineages, a crucial step in achieving therapeutic tissue replacement. These studies will also increase the pool of drug-targetable molecules that can be used to improve the quality of stem cells for therapies.
Statement of Benefit to California:	Embryonic stem cells hold the promise of treatments and cures for human diseases and conditions that affect millions of people. In particular, neurodegenerative diseases linked with age are affecting increasing number of patients. Thus, one strategy would be to replace degenerating cells in patients with stem cells. However, these approaches will only be possible when the mechanisms controlling the generation of these stem cells and their capacity to produce their functional progeny are better understood in young and old patients. We propose to study the mode of action of metabolism and aging regulators in human cell reprogramming. The AMPK pathway plays major role in metabolism and aging. Metabolic pathways are a major target for the development of therapeutic strategies that may benefit a wide range of patients. However, the mechanisms by which metabolic pathways regulate stem cells are still poorly understood, hampering the development of such strategies. We believe that the results of our experiments will be ultimately translated into novel strategies to cure age-dependent diseases such as neurodegenerative diseases, stroke, diabetes and heart diseases in aging patients.