A small molecule tool for reducing the malignant potential in reprogramming human iPSCs and ESCs

Grant Award Details

A small molecule tool for reducing the malignant potential in reprogramming human iPSCs and ESCs

Grant Type: Tools and Technologies III

Grant Number: RT3-07678

Project Objective: To characterize the specificity of MitoBloCK-6 (MB6) to selectively kill hESCs and hiPSCs, and not differentiated lineages and to explore its mechanism of action.

Investigator:

Name:	Carla Koehler
Institution:	University of California, Los Angeles
Type:	PI

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Name:	Michael Teitell
Institution:	University of California, Los Angeles
Type:	Co-PI

Disease Focus: Other

Human Stem Cell Use: Embryonic Stem Cell, iPS Cell

Award Value: $1,283,900

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 3

View Report

Reporting Period: Year 4 (NCE 6-mo)

View Report

Grant Application Details

Application Title: A small molecule tool for reducing the malignant potential in reprogramming human iPSCs and ESCs

Public Abstract: This research project aims to solve a key bottleneck in the use of differentiated human embryonic stem cells and induced pluripotent stem cells for the regeneration and replacement of diseased or damaged tissues. This bottleneck is the potential of unintended transplants containing failed-to-differentiate stem cells developing into benign growths called teratomas, or worse, malignant teratocarcinomas. It is essential to overcome this safety concern before stem cell-derived therapies can become acceptable for human use. Stem cells and cancer cells have many common properties. Both can replenish themselves indefinitely, and can potentially grow in different parts of the body. Before they are administered to patients, stem cells must be forced in the laboratory to turn into more mature cells that are programmed to become neurons, heart cells, beta cells of the pancreas, and other differentiated cell types. The mature cells, unlike the stem cells, do not grow indefinitely, but rather can replace a specific function that is defective in disease. We have identified a specific small molecule tool that selectively kills pluripotent stem cells but does not damage differentiated lineage cells. We will investigate the mechanism of action of the tool and test the tool for specificity in a variety of pluripotent stem cells and their differentiated lineages. The end goal is to develop a technology that will minimize the potential of developing unexpected tumors from stem cell therapies.

Statement of Benefit to California: Our proposal benefits California by adding new essential knowledge on mitochondrial mechanisms that control human pluripotent stem cell (hPSC) function to support the taxpayers' commitment to personalized cell therapies. This work builds on highly successful CIRM Seed & Basic Biology I awards. CIRM funds to date resulted in 20+ publications and training of 14 individuals including post-docs, graduate students, undergraduates, and CIRM Bridges to Stem Cell Biology program trainees, some of whom have entered the California workforce. Here we have identified a small molecule modulator of a mitochondrial redox protein that selectively kills pluripotent stem cells but not their differentiated lineages. Because contamination by hPSCs in transplanted donor cell pools is a key concern for regenerative cell therapies, there is a critical need to develop methods for reproducibly eliminating potentially cancerous cells. Our small molecule is an exciting candidate tool and will be characterized extensively. Our ongoing work underpins therapy development in California's major academic centers and will provide data for many of California's biotechnology companies in the growing stem cell industry, whose success will propel hiring and increased economic prosperity for the state. With success, tangible health and economic impact on California, its academic institutions and companies, and the rest of the nation will be achieved as California leads the way forward with personalized medicine.