Identification of hESC-mediated molecular mechanism that positively regulates the regenerative capacity of post-natal tissues

Grant Award Details

Identification of hESC-mediated molecular mechanism that positively regulates the regenerative capacity of post-natal tissues

Grant Type: New Faculty I

Grant Number: RN1-00532

Project Objective: The objective of this project is to identify hESC-derived factors (proteins) that may positively regulate the regenerative capacity of adult tissues and rejuvenate old tissues, with particular emphasis on muscle.

Investigator:

Name:	Irina Conboy
Institution:	University of California, Berkeley
Type:	PI

Disease Focus: Aging, Muscular Dystrophy, Pediatrics, Skeletal/Smooth Muscle disorders, Trauma

Human Stem Cell Use: Embryonic Stem Cell

Award Value: $2,246,020

Status: Closed

Progress Reports

Reporting Period: Year 2 & 3

View Report

Reporting Period: Year 4

View Report

Reporting Period: Year 5

View Report

Reporting Period: NCE

View Report

Grant Application Details

Application Title: Identification of hESC-mediated molecular mechanism that positively regulates the regenerative capacity of post-natal tissues

Public Abstract: The tissue regenerative capacity deteriorates with age in animals and in humans, leading to the loss of organ function, which is well exemplified in skeletal muscle, but is poorly understood in molecular terms. Our recent work uncovered that factors produced by human embryonic stem cells have a unique ability to enhance the regenerative responses of organ stem cells, dedicated for tissue maintenance and repair, be they young or old and located in young or old organism. This proposal seeks to understand the molecular mechanism of this novel phenomenon, which is two-fold important: in expanding our knowledge of the stem cell biology and in developing entirely novel embryonic stem cell-based therapeutic applications that do not have the side-effects associated with immune rejection. Importantly, this uncovered enhancement of tissue repair is conserved between mice and humans , which allows use of an animal model for identifying these therapeutically-relevant human factors and greatly facilitates the pre-clinical data collection, interpretation and translation to clinic.

The main goals of this Proposal are to identify the embryonic pro-regenerative factors, to understand their mode of action and to validate their efficiency for enhancing and rejuvenating repair of injured and pathological tissues in an animal model. Notably, using the infrastructure of [REDACTED] the data generated by this work will be quickly disseminated to [REDACTED] clinicians and will be applied through Clinical Affiliates Program for clinical studies and human trials.

Identifying these embryonic stem cell-produced pro-regenerative factors will help counter the loss of tissue maintenance and repair in the old, generally and not just in skeletal muscle, and will be of immediate therapeutic value without a need for “humanization” and without the risk of immune rejection. Additionally, for muscle wasting caused by diabetes and immobility, and in Duchenne/Becker and Limb-Girdle myopathies, these factors will boost the performance of satellite cells struggling to repair continuous myofiber deterioration, thus countering degeneration and improving organ function.

Statement of Benefit to California:	Degenerative diseases in which the bodies capacity to regenerate new tissue can no longer keep up with tissue death is a major problem for society in general and for State of California in particular. The lack of tissue repair that eventually leads to the loss of organ function is undeniable and devastating trait of aging that causes many degenerative disorders, exemplified by Parkinson's, Alzheimer's and muscle atrophy. Therefore, Californians with life-long skills, expertise and invaluable knowledge can no longer contribute to society and do not enjoy life fully. In recent years biologists and clinicians realized that practical therapies would only emerge when the balance between the regenerative and the degenerative processes were properly understood in biomedical terms. Comprehensively, the proposed research seeks to uncover novel evolutionary conserved molecular regulation that is mediated by human embryonic stem cells and promotes regenerative capacity of postnatal stem cells (likely, generally and not just in skeletal muscle). Qualified scientists from underrepresented minorities will be involved with this academic and translational stem cell project, hence allowing expand the representation of all Californians in the cutting-edge biomedical research. This proposal describes steps to rejuvenate stem cell responses in the old and to rescue tissue repair in people suffering from debilitating degenerative diseases. The outcomes of this work will insure that the health prognosis is significantly improved for older Californians, especially those afflicted with degenerative disorders, and that the results of these studies are translated as rapidly as possible to the clinical setting where their practical benefit can be fully utilized. Thus this work seeks not only to improve the quality of life for our older citizens, but also to reduce the health-cost associated with treating currently incurable degenerative diseases. The developing therapies will be immediately applicable for all Californians irregardless of their ethnic background, gender or age.