The molecular basis underlying adult neurogenesis during regeneration and tissue renewal

Grant Award Details

The molecular basis underlying adult neurogenesis during regeneration and tissue renewal

Grant Type: New Faculty II

Grant Number: RN2-00940

Project Objective: To develop tools and use planarians as a model for identifying factors that contribute to neural differentiation as it relates to regeneration, tissue homeostasis and stem cell biology.

Investigator:

Name:	Ricardo Zayas
Institution:	San Diego State University Foundation
Type:	PI

Award Value: $1,712,225

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Reporting Period: Year 3

View Report

Reporting Period: Year 4

View Report

Reporting Period: Year 5

View Report

Reporting Period: NCE (Year 6)

View Report

Grant Application Details

Application Title: The molecular basis underlying adult neurogenesis during regeneration and tissue renewal

Public Abstract: Regeneration of lost body parts has long fascinated humans, yet regeneration remains one of the great mysteries in biology. Forty years ago, studies on the mammalian brain provided evidence that new neurons are generated throughout life. It is now widely accepted that neurons are born (neurogenesis) in a wide range of animals, including humans, from neural stem cells maintained in the adult brain. Neural stem cells, however, do not readily compensate for lost neurons after injury or due to diseases of the nervous system, such as Parkinson's or Alzheimer's disease. The existence of neural stem cells has raised hopes that in the future we may be able to manipulate or promote stem cells in living organisms to divide, acquire the fate of specific cell types, migrate to the proper location and replenish lost neurons. Alternatively, another source of stem cells for tissue replacement could be stem cells derived from adult, embryonic, or cells re-programmed to acquire a stem cell-like state. All of these prospects will require that we fully understand how stem cells can be signaled to divide, acquire the desired cell fate and integrate into a functional nervous system. Our understanding of how repair of the nervous system can be achieved could benefit from studies of organisms that, in contrast to humans, are capable of regenerating the nervous system. For more than a century, scientists have been intrigued by freshwater planarians (flatworms); these animals, when cut into small pieces, have the remarkable ability to regenerate complete organisms from small body pieces. This ability to regenerate missing parts originates from a population of adult stem cells planarians maintain throughout life. Thus planarians are an excellent system in which to examine how stem cells are signaled to divide and to become all the different cell types during regeneration. It is now possible to apply advanced scientific methods to study planarians; we can visualize the stem cells, label the different organ types and inhibit the expression of specific genes. One of the truly amazing properties of planarians is their capability for rapid repair and regeneration of the central nervous system, a capacity that is limited in most animal models currently studied. In this study, we will use planarians to identify and analyze the function of genes implicated in neurogenesis during regeneration and normal cell turnover. Successful identification of novel genes would help to fill gaps in our knowledge of conserved biological mechanisms that stimulate proliferation and differentiation of stem cells in the central nervous system. This information has the potential to contribute to our ability to induce human embryonic or adult stem cells to divide and acquire neuronal fates, which would be valuable for transplantation therapies to treat nervous system injuries or neurodegenerative disorders.

Statement of Benefit to California:	The inability to recover from loss of neuronal function afflicts a large number of people: in the U.S. alone, 4 million people have been diagnosed with Alzheimer's disease, 1.5 million have Parkinson's disease, and 0.25 million suffer from spinal cord injuries. The aim of this proposal is to establish a model of regeneration to study how stem cells can be directed to replace lost neurons after injury. Invertebrate organisms have provided powerful venues to investigate biological conserved mechanisms, and their study has led to discoveries of biomedical relevance. Our research on planarian stem cells and neural regeneration has the potential to make contributions to our knowledge of genetic pathways that control neuronal determination of stem cells or, if disrupted, could lead to neurological disorders. These studies provide a unique opportunity to examine how regeneration of the nervous system can be achieved at the molecular and cellular levels and have implications for the development of neural stem cells in regenerative medicine.
