Laying the groundwork for building a tooth: analysis of dental epithelial stem cells

Grant Award Details

Laying the groundwork for building a tooth: analysis of dental epithelial stem cells

Grant Type: New Faculty II

Grant Number: RN2-00933

Project Objective: the PI has examined the basis of epithelial stem cells for tooth regeneration.

Investigator:

Name:	Ophir Klein
Institution:	University of California, San Francisco
Type:	PI

Human Stem Cell Use: Adult Stem Cell, Embryonic Stem Cell

Award Value: $3,075,251

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

Grant Application Details

Application Title: Laying the groundwork for building a tooth: analysis of dental epithelial stem cells

Public Abstract: To fix a broken car, the mechanic either repairs or replaces the defective part. Similarly, one of the most promising approaches physicians foresee for treating human disease and ameliorating the aging process is regenerative medicine. A major aim of this field is to restore function by repairing or replacing damaged organs. Scientists envision a day when people with heart failure can be cured with hearts grown from their own cells, and a future in which dialysis machines are not needed because patients with damaged kidneys can be furnished with new ones. However, organ engineering is highly complex, and the field of regenerative biology is still in its early stages. Therefore, it is important to provide proof of principle and lay the foundation for creation of new organs by first using as simple a system as possible, and teeth provide an excellent model system for organ replacement. Their physiology is less complex than many other organs, but their development has much in common with that of other organs. This means that much of the information obtained from studying tooth regeneration will be generally applicable for building other organs. Teeth are a relatively safe prototype for organ regeneration, and there is a significant need for replacement teeth, as those born without teeth due to genetic defects, as well as elderly patients, patients with caries and periodontal disease, and victims of physical trauma all need new teeth. Our ultimate goal is to take advantage of basic biological principles in order to develop new therapeutic approaches. As such, we seek to help lay the groundwork for the formation of new teeth that can replace missing teeth, in the same way that permanent teeth replace the primary teeth formed in early childhood. This ambitious goal must be built on the proper foundation if it is to succeed. Therefore, we will first concentrate on a more readily achievable objective, which is to understand a naturally occurring version of regeneration by studying the continuous growth of the mouse incisor. This unusual tooth depends on the presence of adult stem cells to constantly produce all the cell types of the mature organ. Toward this end, we propose in this application to first analyze the biological processes that regulate the stem cells in this remarkable tooth. We will develop tools to grow the mouse stem cells outside of the animal in order to better understand them. Subsequently, we propose to translate what we have learned from the mouse model into human cells by learning how to induce human embryonic stem cells, fetal cells, or adult cells to become tooth progenitor cells. This last step will help lay the necessary groundwork for growing human teeth and blaze the trail for regeneration of larger organs.

Statement of Benefit to California:	The promise of stem cell biology for regenerative medicine lies in the ability of these remarkable cells to give rise to more differentiated cell types that, individually or as part of a bioengineered organ, can replace structures that have been damaged by disease or aging. We propose to help lay the groundwork for organ regeneration by focusing on the tooth as a prototype organ. In addition to addressing the health issues posed by dental decay and tooth loss, which require prosthetic replacements that are functionally inferior to natural teeth, our project will help to pave the way for safe clinical applications of human embryonic stem cells in regeneration of larger organs, such as hearts or lungs. We anticipate that our research will be a significant step towards making the promise of regenerative medicine from adult stem cells and human embryonic stem cells a reality. Our studies will provide a much-needed model system that will allow us to study the basic mechanisms underlying guided development of organs from stem cells, which will be central to fulfilling the therapeutic potential of stem cell-based organ regeneration. Eventually, stem cell-based therapies will reduce health care costs for Californians by improving treatment for diseases for which we currently do not have effective therapies. Our work could provide economic benefits to the state by helping to lay the groundwork for commercial efforts to regenerate teeth as well as other solid organs, such as the heart and pancreas. Such developments would be of great benefit to California by making the state a leader in a field that is poised to become economically important in the future. The State of California will also stand to benefit from the intellectual property generated by this research, as generalizable principles regarding the use of stem cells, in vitro differentiation of cells, scaffolding materials, and organ bioengineering may be patentable.