Asymmetric stem cell division oriented by a local self-renewing signal

Grant Award Details

Asymmetric stem cell division oriented by a local self-renewing signal

Grant Type: Basic Biology IV

Grant Number: RB4-05825

Project Objective: The goal is to move experiments the lab did in mESC, showing that Wnt protein causes asymmetric division, into hESC and human epidermal stem cells (EpSC), and to study the mechanism by which Wnt controls asymmetric divisions.

Investigator:

Name:	Roel Nusse
Institution:	Stanford University
Type:	PI

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

Award Value: $1,038,600

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/NCE

View Report

Grant Application Details

Application Title: Asymmetric stem cell division oriented by a local self-renewing signal

Public Abstract: When stem cells divide, the two daughter cells have a choice. Commonly, one of the daughter cells becomes a new stem cell while the other one will be more specialized (or differentiated). This property -- the ability to generate more stem cells (self-renewal) while making differentiated cells simultaneously -- defines a stem cell. Stem cells have the unique ability to divide asymmetrically but how this happens is poorly understood. Moreover, there is little knowledge on the mechanisms by which external signals control asymmetric division of stem cells. In tissues, it is also essential that the orientation of stem cell division is properly regulated. At the most fundamental level, asymmetry and the orientation of cell division are at the heart of stem cell biology.

We have found that we can instruct stem cells to divide in an asymmetric way by applying an external signaling molecule (called Wnt) to stem cells in a spatially controlled way. We found that the proximal daughter cell will become another stem cell while the distal cell is differentiated. We propose to examine the organization of human stem cells as they divide asymmetrically. Using live imaging microscopy and other tools, we intend to follow how critical determinants segregate over the two daughter cells. We expect that the new mechanistic insights into asymmetric stem cell division will ultimately lead to a better understanding of the possible use of stem cells for therapy.

Statement of Benefit to California: This research proposal aims at understanding asymmetric divisions of stem cells, a fundamental biological property. The research will initially increase our insights into the basic biology of stem cells. In the longer term however, this work will also lead to better methods to manipulate stem cells for therapeutic purposes, as it will be essential to understand the ways that stem cells divide and differentiate.

Our work will also lead to technological advances that will be of use to stem cell researchers and stem cell-based applications. In fact, we have already made several advances in designing methods to direct the growth of stem cells, including the use of artificial niches and the use of specific growth factors that influence stem cells.