DECIPHERING THE INSTRUCTIONS FOR VERTEBRATE HSC SPECIFICATION AND AMPLIFICATION.

Grant Award Details

DECIPHERING THE INSTRUCTIONS FOR VERTEBRATE HSC SPECIFICATION AND AMPLIFICATION.

Grant Type: Basic Biology IV

Grant Number: RB4-06158

Project Objective: The overall goal is to unravel the environmental cues governing emergence and amplification of HSCs during development, ultimately to inform generation and amplification of HSCs ex vivo. The project makes use of zebrafish, mouse, chicken, and human cell systems, and involves work with a partner PI from France (CFP = ANR).

Investigator:

Name:	David Traver
Institution:	University of California, San Diego
Type:	PI

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Name:	Thierry Jaffredo
Institution:	Centre National de la Recherche Scientifique
Type:	Partner-PI

Collaborative Funder: France

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

Award Value: $1,363,698

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Reporting Period: Year 3

View Report

Grant Application Details

Application Title: DECIPHERING THE INSTRUCTIONS FOR VERTEBRATE HSC SPECIFICATION AND AMPLIFICATION.

Public Abstract: Hematopoietic stem cells (HSCs) are an important population of cells that continuously produce and replace blood and immune cells over the course of our lifetimes. These rare, self-renewing cells are the key element of bone marrow transplants, which are used to treat a variety of conditions including many forms of leukemia and solid tumors. Understanding how hematopoietic stem cells are made during embryonic development is important because it could teach us how to make such cells in the laboratory, and possibly allow circumvention of immune compatibility issues between donor and host. In this research we will perform genetic comparisons of how HSCs are generated in a diverse array of vertebrate embryos to determine the conserved core components of the hematopoietic niche. These results will be validated functionally, then translated to human pluripotent stem cells where we will use our new knowledge to instruct HSCs in vitro, something which is not currently possible.

Statement of Benefit to California: Understanding how hematopoietic stem cells (HSCs) are made during embryonic development is important because it could teach us how to make and amplify such cells in the laboratory. We will perform genetic comparisons of how HSCs are generated in a diverse array of vertebrate embryos to determine the conserved core components of the hematopoietic niche. These results will be translated to human stem cell populations where we will use our new knowledge to instruct and amplify HSCs in vitro, feats which are not currently possible.

The creation of human induced pluripotent stem cells (hiPSCs) holds great promise for new cell-based therapies, including bone marrow transplants (BMTs). These cells have the potential to generate any tissue type, and can be generated in a patient-specific manner. Thus, hiPSCs hold the promise of cellular replacement therapies without the risk of immune rejection. For use in BMTs, however, hiPSCs must be coaxed to differentiate into hematopoietic stem cells (HSCs), the rare cells responsible for the long-term, curative effects of BMT. This is currently not possible, due to a lack of understanding of the cues required to generate HSCs in vivo.

Insight into the factors needed to instruct and amplify HSCs will be used to provide similar factors at similar timepoints to differentiate hiPSCs into HSCs. Our research will thus lead to great improvements in stem cell therapies to better meet the needs of patients in California.