Differentiation of Human Hematopoietic Stem Cells into iNKT Cells

Grant Award Details

Differentiation of Human Hematopoietic Stem Cells into iNKT Cells

Grant Type: Basic Biology V

Grant Number: RB5-07089

Project Objective: The project objective is to study the differentiation of human hematopoietic stem cells (HSCs) into invariant natural killer T (iNKT) cells using a novel iNKT T cell receptor (TCR) transgenic approach in humanized mice. In so doing, they will test their hypothesis that the fate of resulting iNKT cells is programmed by the relevant TCR.

Investigator:

Name:	Lili Yang
Institution:	University of California, Los Angeles
Type:	PI

Disease Focus: Blood Disorders

Award Value: $614,400

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Grant Application Details

Application Title: Differentiation of Human Hematopoietic Stem Cells into iNKT Cells

Public Abstract:

Blood stem cells living in the bone marrow of adult humans give rise to all of the cells in our blood, including the red blood cells that carry oxygen to supply our body, and the white blood cells such as T and B lymphocytes that fight infections and keep us healthy. Among the T lymphocytes there is a small population called invariant natural killer T (iNKT) cells. Despite their low frequency in humans (~0.001-1% in blood), iNKT cells have the remarkable capacity to mount immediate and potent responses when stimulated, and have been suggested to play important roles in regulating multiple human diseases including infections, allergies, cancer, and autoimmunity (such as Type I diabetes and multiple sclerosis). However, successful clinical interventions with iNKT cells have been greatly hindered by our limited knowledge on how these cells are produced by blood stem cells, largely due to the lack of tools to track these cells in humans. We therefore propose a novel model system to overcome this research bottleneck by transplanting human blood stem cells into a mouse and genetically programming these cells to develop into iNKT cells. This “humanized” mouse model will allow us to directly track the differentiation of human blood stem cells into iNKT cells in a living animal. From this study, we will address some critical unanswered questions for iNKT cell development, and shed light on developing stem-cell based iNKT cell therapies.

Statement of Benefit to California:

Allergies, cancer and autoimmunity are leading health hazards in California. These diseases affect millions of Californians, impairing their life quality and creating huge economic burdens for the State of California. This proposal intends to study invariant natural killer (iNKT) T cells, a special population of T lymphocytes that have been suggested to play important roles in regulating these diseases. To date, clinical applications of iNKT cells have been greatly limited by their low frequency in humans and their high variability between individuals (~0.001-1% in blood). Thus, an improved understanding of how these cells are naturally generated is important for their use clinically. Like all other cells in blood, iNKT cells are descendants of the blood stem cells that live in the bone marrow of adult humans. Our goal is to study how human blood stem cells give rise to iNKT cells. If successful, our results can be exploited to develop stem cell-based iNKT cell therapies to treat allergies, cancer and autoimmunity, and therefore may benefit the millions of Californians currently suffering from these diseases. In addition, the knowledge and reagents generated from this proposed study will be shared freely with non-profit and academic organizations in California, and any new intellectual property derived from this study will be developed under the guidance of CIRM to benefit the State of California.

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