Generation of regulatory T cells by reprogramming

Grant Award Details

Generation of regulatory T cells by reprogramming

Grant Type: Transplantation Immunology

Grant Number: RM1-01729

Project Objective: Overall objective of the project is to generate regulatory T cells by reprogramming stem cells or immune system cells to induce tolerance to stem cells or stem cell derived tissues

Investigator:

Name:	Anjana Rao
Institution:	La Jolla Institute for Allergy and Immunology
Type:	PI

Disease Focus: Immune Disease

Human Stem Cell Use: Adult Stem Cell

Cell Line Generation: Adult Stem Cell

Award Value: $1,464,446

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: Generation of regulatory T cells by reprogramming

Public Abstract: The goal of our research is to develop efficient methods for making a particular class of immune-system cells known as regulatory T cells (Tregs). Tregs have the potential to be useful in a wide variety of clinical situations. For instance, they could be used to control the harmful immune responses seen in patients with autoimmune diseases such as childhood (Type I) diabetes, rheumatoid arthritis, multiple sclerosis and inflammatory bowel disease; and to suppress rejection of transplanted organs in patients given heart, liver or kidney transplants. These patients are normally treated with toxic immunosuppressive drugs to prevent transplant rejection, but nevertheless tend to lose the organs and need to get on a long waiting list all over again. Treating them with Tregs might preserve the transplant, possibly indefinitely, and is expected to be much less toxic because it would decrease or eliminate the need for the immunosuppressive drugs.

Bone marrow transplants are a special case. Stem cells present in the bone marrow give rise to all types of blood cells, including red blood cells which carry oxygen, platelets which are necessary for blood clotting so that one does not bleed to death from a minor injury, and a large variety of cells which fight off bacterial and viral infection. Aging patients tend to develop bone marrow failure spontaneously, and patients who have been given chemotherapy for cancer also almost invariably lose bone marrow function. When these patients are treated with bone marrow from a different donor, the bone marrow (graft) itself can start attacking the patient (host), in a life-threatening scenario known as graft-versus-host disease. Again, Tregs can help to prevent this disease, thus realizing the promise of transplantation with bone marrow stem cells.

We plan to develop efficient ways to make Tregs from different types of stem cells. For patients receiving transplanted organs, we hope to take their own normal T cells and turn them into Tregs. For patients suffering from autoimmune diseases, it might be more useful to make Tregs artificially from their bone marrow stem cells, whereas for cancer patients who have been given chemotherapy followed by a bone marrow transplant from a different person, it might be possible to make Tregs from the same bone marrow cells that the patient receives, in the hope that these Tregs can suppress graft-versus-host disease. And finally, there are clinical situations in which it might be useful to use the very new technique of induced pluripotent stem cells to make stem cells from a patient's skin, then turn those stem cells into Tregs. We believe that all these approaches are feasible in principle, given recent discoveries from our own and other labs. Although our research will be done mostly in animals (mice), we believe that it will be possible to translate it quickly into humans, and that if successful, it will address a pressing clinical need.

Statement of Benefit to California:	In this application we propose to develop efficient methods for making cells of the immune system known as regulatory T cells (Tregs). As described in the proposal, Tregs have the potential to be outstandingly useful to many different types of patients: people receiving solid organ transplants, bone marrow transplants and stem cell transplants, as well as people with autoimmune diseases of various kinds. Our research is therefore aimed at improving the health of the citizens of the State of California and the United States. Any clinical trials that result from the research would be performed in hospitals in California and would be of benefit to patients in the state. Aside from the purely medical importance of our research, however, our project will benefit the State of California from an economic point of view as well. The research institute and the core facilities where the research is to be performed are located in the State of California and will be led by a California-based research team, and all technology licensing will benefit the state directly. We intend to hire and train at least one research technician, two postdoctoral fellows and one Ph.D. graduate student who will all live and work in the State of California and by buying goods and services, will contribute to the economic health of the state. California-based businesses and vendors will be used as suppliers of all needed equipment, services and supplies. Any meetings that involve external speakers and collaborators will be held in California, even though other locations could be chosen. Thus there would be substantial long term employment in the State of California if this research were funded.