Generation of functional cells and organs from iPSCs

Grant Award Details

Generation of functional cells and organs from iPSCs

Grant Type: Research Leadership

Grant Number: LA1-06917

Project Objective: To develop therapeutically useful cells from hiPSCS, including antigen-specific T cells for adoptive immunotherapy, HSCs for bone marrow transplants, and whole organs (pancreas, liver).

Investigator:

Name:	Hiromitsu Nakauchi
Institution:	Stanford University
Type:	PI

Disease Focus: Blood Disorders

Human Stem Cell Use: iPS Cell

Award Value: $5,426,135

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Reporting Period: Year 6

View Report

Grant Application Details

Application Title: Generation of functional cells and organs from iPSCs

Public Abstract: The development of induced pluripotent stem cell (iPSC) technology may be the most important advance in stem cell biology for the future of medicine. This technology allows one to generate a patient's own pluripotent stem cells (PSCs) from skin or blood cells. iPSCs can then be reprogrammed to multiply and produce high quality mature cells for cell therapy. Because iPSCs are derived from a patient's own cells, therapies that use them will not stimulate unwanted immune reactions or necessitate lifelong immunosuppression. If organs can be generated from iPSCs, many patients with organ failure awaiting transplants will be helped. The goal of this project is to further develop iPSC technology to bring about personalized regenerative medicine for treating intractable diseases such as cancers, viral infections, genetic blood disorders, and organ failure. Specifically, we would like to establish three major core programs for generating from iPSCs: personalized immune cells; an unlimited supply of blood stem cells; and functional organs.

First, we will generate iPSC-derived immune cells that kill viruses and cancer cells. Current immunotherapy uses immune cells that are exhausted (have limited ability to function and proliferate) after they multiply in a test tube. To supply active nonexhausted immune cells, iPSCs will be generated from a patient's immune cells that target tumor cells and infections and then redifferentiated to mature immune cells with the same targets.

Second, we aim to develop iPSC technology to generate blood stem cells that replenish all blood cells throughout life. Harvesting blood stem cells from a leukemia patient for transplantation back to the patient after chemotherapy and radiation has been challenging because few blood stem cells can be harvested and may be contaminated with cancer cells. Alternatively, transplanting blood stem cells from cord blood or another person requires genetic matching to prevent immune reactions. However, generating blood stem cells from a patient's iPSCs may avoid contamination with cancer cells, immune reactions, and the need to find a matched donor. Furthermore, we aim to generate iPSCs from a patient with a genetic blood disease, correct the genetic defect in the iPSCs, and generate from these corrected iPSCs healthy blood stem cells that may be curative when transplanted back into the patient.

Lastly, we will try to generate from iPSCs not just mature cells, but organs for transplantation, to potentially address the tremendous shortage of donated organs. In a preliminary study, we generated preclinical models that could not develop pancreases. When we injected stem cells into these models, they developed functional pancreases derived from the injected cells and survived to adulthood. We hope that within 10 years, we will be able to provide a needed organ to a patient by growing it from the patient's own PSCs in a compatible animal.

Statement of Benefit to California:

Cancer is the second leading cause of death, accounting for 24% of all deaths in the U.S. Nearly 55,000 people will die of the disease--about 150 people each day or one of every four deaths in California. In 2012, nearly 144,800 Californians will be diagnosed with cancer. We need effective treatment to cure cancer.

End-stage organ failure is another difficult disease to treat. Transplantation of kidneys, liver, heart, lungs, pancreas, and small intestine has become an accepted treatment for organ failure. In California, more than 21,000 people are on the waiting lists at transplant centers. However, one in three of these people will die waiting for transplants because of the shortage of donated organs. While end-stage renal failure patients can survive for decades with hemodialysis treatment, they suffer from high morbidity and mortality. In addition, the high medical costs for increasing numbers of dialysis patients is a social issue. We need to find a way to increase organs that can be used for transplantation. In our proposed projects, we aim to use iPSC technology and recent discoveries to develop new methods for treating cancers,
viral infections, and organ failure. More specifically, we will pursue our recent discoveries using iPSCs to: (1) multiply person's T cells that specifically target cancers and viral infections; (2) generate normal blood-forming stem cells that can be transplanted back into a patient to correct a blood disease (3) regenerate tissues and organs from a patient's cells for transplantation back into that patient.

These projects are likely to benefit the state of California in several ways. Many of the methods, cells, and reagents generated by this research will be patentable, forming an intellectual property portfolio shared by the state and the institutions where the research is performed. The funds generated from the licensing of these technologies will provide revenue for the state, will help increase hiring of faculty and staff (many of whom will bring in other, out-of-state funds to support their research), and could be used to ameliorate the costs of clinical trials--the final step in translation of basic science research to clinical use. Most importantly, this research will set the platform for stem cell-based therapies. Because tissue stem cells are capable of lifelong self-renewal, these therapies have the potential to provide a single, curative treatment. Such therapies will address chronic diseases that have no cure and cause considerable disability, leading to substantial medical expenses and loss of work. We expect that California hospitals and health care entities will be first in line for trials and therapies. Thus, California will benefit economically and the project will help advance novel medical care.

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