
Regulatory T cell induced tolerance to ESC transplantation

Grant Award Details

Regulatory T cell induced tolerance to ESC transplantation

Grant Type: Transplantation Immunology

Grant Number: RM1-01725

Project Objective: Regulatory T cell induced tolerance to ESC transplantation

Investigator:

Name:	Robert Negrin
Institution:	Stanford University
Type:	PI

Award Value: \$1,382,658

Status: Closed

Progress Reports

Reporting Period: Year 1

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Reporting Period: Year 3

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Reporting Period: NCE

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Grant Application Details

Application Title: Regulatory T cell induced tolerance to ESC transplantation

Public Abstract: The goals of this proposal are to utilize cell populations known to control immune reactions termed regulatory T cells and study their ability to protect embryonic stem cells (ESC) from immune rejection. Much has been learned about the control of immune reactions where it has been found that a variety of different factors control excessive and at times harmful immune reactions. Clearly the localization of immune responses, blood flow and both pro-inflammatory and anti-inflammatory cytokines or proteins play a major role in the control of immune reactions. More recently has been the discovery that there are specific populations of T cells, termed regulatory T cells, that have the capability of suppressing immune reactions which have enormous potential in clinical medicine. In this grant proposal, two distinct research groups with complementary expertise will come together to study this important problem. The laboratory of [REDACTED] has studied regulatory T cell biology in the setting of bone marrow transplantation and translated key findings to the clinic. The laboratory of [REDACTED] has studied ESC biology and has demonstrated that ESCs will be rejected in animal models. The goals of this research are to explore the biological activity of two distinct regulatory T cell populations in controlling ESC rejection and to develop strategies that could be directly translated to the clinic that are capable of enhancing survival of the ESCs and mature cells derived from ESCs in living animals. These studies will be performed largely in animals due to the complexity of studying immune reactions and the need to study these complex biological reactions in living animals but could be directly applied to humans. [REDACTED] has already established principles for translating regulatory T cell concepts into the clinic and have several ongoing clinical trials in the setting of bone marrow transplantation to explore the biological function of highly purified regulatory T cells. Therefore, results obtained from studies proposed in this application are intended to demonstrate the biological activity of immune regulatory mechanisms on the rejection of ESCs as well as mature progeny derived from ESC populations and develop strategies that are directly applicable to the human condition.

Statement of Benefit to California: This research will directly benefit the residents of California but like all research also extend to individuals and corporations beyond the State. The goal of this research is to develop clinically applicable strategies to enhance the engraftment and survival of transplanted embryonic stem cells and mature differentiated cell populations derived from these critically important immature cell populations. The studies proposed here will provide important insights into developing clinical trials that will overcome the major problem of rejection of these cell populations which must be solved before this critically important research can reap clinical gains. Insights gained here could be of critical value when ESC based translational strategies are ready for clinical exploration. The studies proposed in this grant application utilize principles that are at the forefront of immunological research and also are directly applicable to the clinic. Importantly, the strategies that will be employed in these studies are being explored in clinical trials of bone marrow transplantation in an effort to reduce the risk of graft-versus-host disease and also to induce tolerance to organ transplantation. These clinical trials are being performed at [REDACTED] located in [REDACTED] which serves as a rich resource for advanced medical care in [REDACTED] and beyond. Therefore, many of the concepts developed in the studies proposed in this grant application will be directly applied to enhancing the biological activity and survival of transplanted embryonic stem cell populations and derived cells and tissues to enhance their function in clinical situations. These studies will be performed eventually in hospitals in the State of California which will be of direct value to the residents of this state, and also could attract other individuals to California for proposed treatments which would enhance the reputations, revenue and overall health of California residents, as well as individuals beyond. Further, many of the reagents, tools and equipment to be utilized in these studies and eventually in the translation of these concepts are under development by companies located in the state of California.