In Utero Embryonic Stem Cell Transplantation to Treat Congenital Anomalies

Grant Award Details

In Utero Embryonic Stem Cell Transplantation to Treat Congenital Anomalies

Grant Type: New Faculty Physician Scientist

Grant Number: RN3-06532

Project Objective: To achieve donor-specfic tolerance to stem cell-derived / differentiated hematopoietic cells by in utero transplantation into the host fetus recipient. The Aims relate to derivation of the proper cell for transplantation, modulation of the host hematopoietic niche to allow engraftment and differentiation of the hematopoietic stem cells and to do so in the proper animal model.

Investigator:

Name:	Tippi MacKenzie
Institution:	University of California, San Francisco
Type:	PI

Disease Focus: Blood Disorders, Pediatrics

Human Stem Cell Use: Embryonic Stem Cell

Award Value: $2,661,742

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Reporting Period: Year 3

View Report

Reporting Period: Year 4

View Report

Reporting Period: Year 6/NCE

View Report

Grant Application Details

Application Title: In Utero Embryonic Stem Cell Transplantation to Treat Congenital Anomalies

Public Abstract: Many fetuses with congenital blood stem cell disorders such as sickle cell disease or thalassemia are prenatally diagnosed early enough in pregnancy to be treated with stem cell transplantation. The main benefit to treating these diseases before birth is that the immature fetal immune system may accept transplanted cells without needing to use immunosuppressant drugs to prevent rejection. Moreover, transplanting stem cells into the fetus—in which many stem cell types are actively multiplying and migrating—can promote similar growth and differentiation of the transplanted cells. Although this strategy works well in animal models, when applied clinically, the number of surviving cells in the blood ("engraftment") has been too low to achieve a reliable cure.

Our lab studies ways to improve engraftment, with the long-term goal of applying these strategies to treat fetuses with congenital blood disorders. In this application, we will use novel embryonic stem cells that may be better suited to differentiate into blood cells in the fetal environment. We will also test various approaches to improve the survival advantage of these stem cells in fetal organs that make blood cells. Finally, we will study the fetal immune system to determine how fetuses become tolerant to the transplanted cells. The experiments in this proposal will give us important information to design clinical trials to treat fetuses with common, currently incurable stem cell disorders.

Statement of Benefit to California: The long-term goal of our project is to develop safe and effective ways to perform prenatal stem cell transplantation to treat fetuses with congenital blood disorders, such as thalassemia and hemoglobin disorders. These diseases affect many California citizens. For example, hemoglobin disorders are so common that they are routinely screened for at birth (and prenatal screening is performed if there is a family history). Thalassemias are found more commonly in persons of Mediterranean or Asian descent and are therefore prevalent in our state's population. Prenatal screening is routinely offered, especially to patients with a family history or those with an ethnic predisposition. Fetal stem cell transplantation would also benefit children with sickle cell disease, 2000 of which are born each year in the United States, and inborn errors of metabolism, which occur in 1 in 4000 births. Thus, once we develop reliable techniques to treat these disorders before birth, there will be an enormous potential to make a difference.

Fetal surgery was pioneered in California and is performed only in select centers across the country. Therefore, once we have developed safe and effective therapies for fetuses with stem cell disorders, we also expect increased referrals of such patients to California. The convergence of our expertise in fetal therapies with those in stem cell biology carries great promise for finally realizing the promise of fetal stem cell transplantation.