The generation and expansion of tissue-engineered small intestine from human stem/ progenitor cells: a preclinical study of functional translation

Grant Award Details

The generation and expansion of tissue-engineered small intestine from human stem/ progenitor cells: a preclinical study of functional translation

Grant Type: New Faculty Physician Scientist

Grant Number: RN3-06425

Project Objective: To complete the preclinical steps required to file an IND for tissue-engineered small intestine (TESI) as a functional replacement for patients with short bowel syndrome (SBS).

Investigator:

Name:	Tracy Grikscheit
Institution:	Children's Hospital of Los Angeles
Type:	PI

Disease Focus: Intestinal Disease, Metabolic Disorders

Human Stem Cell Use: Adult Stem Cell

Cell Line Generation: Adult Stem Cell

Award Value: $3,146,160

Status: Active

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Grant Application Details

Application Title: The generation and expansion of tissue-engineered small intestine from human stem/ progenitor cells: a preclinical study of functional translation

Public Abstract:

This proposal aims to complete the preclinical steps to develop tissue-engineered intestine (TESI) as a functional replacement of the small intestine to treat short bowel syndrome (SBS). Common birth conditions especially those associated with prematurity result in SBS wherein 50-75% of the small intestine is gone. SBS children cannot get adequate nutrition and supportive medical care is morbid with liver failure a common problem. Small bowel transplants, the only current salvage therapy have many problems including poor graft survival, rejection, limited donor supply, surgical morbidity, and lifelong immunosuppression. We hypothesize that TESI from the patient's own cells offers a potential, durable human progenitor-cell based treatment option for SBS.

We have shown that TESI forms when autologous cells are implanted on a polymer scaffold, and that TESI exactly recapitulates native intestine: all four differentiated epithelial cell types in conjunction with the key supporting structure such as nerves, and muscle, grow from the transplanted OU. Importantly, Lewis rats recover from massive small bowel resection with TESI. Other regions of the gut can also reengineered via this approach.

Our goal is to translate TESI from rodents to an autologous human cell based therapy. Patients who needed emergency surgery for their intestine, which might leave the remaining amount of intestine too short to absorb enough nutrition could potentially be treated with TESI.

Statement of Benefit to California:

In the pediatric population, the incidence of SBS is estimated to be 24.5 per 100,000 live births and associated with a 30% 5-year mortality. To put this in perspective, the NCI reports the cumulative incidence of all invasive childhood cancers is 14.5 per 100,000. In addition, cancer, inflammatory bowel disease and mesenteric ischemia put the adult population at risk. In fact, the incidence of SBS is increasing with a striking 30% 5-year mortality. Annual cost per patient in Europe ranges from $100,000 – 150,000 and is double that in the US [1]. SBS is an unsolved problem with unacceptable human and financial cost. An autologous engineered tissue approach would surpass current therapies. Usable engineered intestine would be far less expensive, more durable, and require less maintenance than any current therapy. California would benefit from this research in many ways- we have a large population and improved and less expensive medical care with less suffering for patients would be the most important benefit to the state and to the people of California. In addition, being at the leading edge of this translational approach will make our state and our institutions experts in the translation of stem cell research, a focus point for attracting scientists and innovators to the state and opening up future therapies building on these results. Finally, this approach will generate intellectual property that can be protected and will also benefit the state and its economy.

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