Gen 3- 2019 ISCC Research Project Abstract

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DEFINING THE INTESTINAL STEM CELL NICHE DURING ORGANOID DEVELOPMENT INTO A FUNCTIONAL HUMAN INTESTINE

This proposal capitalizes on our recently developed *in vitro* methods to culture human pluripotent stem cell derived intestinal and colonic organoids (HIO/HCO), combined with our unique organoid transplantation models to identify specific mesenchymal and endodermal niche cell types that support the small and large intestine. The clinical relevance of this work done within the Intestinal Stem Cell Consortium (ISCC) is that it will contribute to our groups effort to identify optimal ISC niche components that will enable both transplantation of functional human regionalized intestine and inform therapies required to regenerate damage intestine. Our preliminary data demonstrates the successful development of reporter tools and recombination assays to localize specific mesenchymal and endodermal populations with cutting edge molecular approaches to identify specific signal pathways supporting the human ISC and in vivo human intestinal models to study regeneration following systemic administration of chemotherapy.

Public Health Relevance Statement:

The proposed work utilizes cutting edge pluripotent stem cell technology to derive human intestinal organoids to study the development of the ISC niche. This work will identify temporally and spatially the cellular and molecular human ISC niche contributing to methods developed by the Intestinal Stem Cell Consortium that will enable intestinal tissue transplantation supporting building and regeneration of a functional human intestine.