

Gen 3 -2019 ISCC Research Project Abstract



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CHARACTERIZATION OF CELLULAR AND MOLECULAR COMPONENTS OF INTESTINAL NICHE

Characterized by rapid and continual turnover, the intestine provides an elegant system for the study of cells which self-renew and regenerate, and thus hold great promise for regenerative medicine. Studies have provided important insight regarding the capacity of intestinal stem cells for self-repair or healing as well as ongoing maintenance and differentiation into all the various intestinal cell types. However, considerable research is needed to better understand how to treat intestinal disorders.

Many intestinal disorders are due to defects in the stem cells or progenitor cells (which are more specific than stem cells) or to misdirected signals provided by the niche, the microenvironment which helps to regulate stem and progenitor cell behavior. Defining the essential cellular niche components and the associated key signals that direct stem and progenitor cells to proliferate and differentiate will be an innovative and important step toward treating intestinal disorders with regenerative medicine.

The overall mission of the Intestinal Stem Cell Consortium (ISCC) is to characterize the niche components that support intestinal stem cells in health and disease, using an integrated, multidisciplinary team science approach, with the vision of developing novel therapies targeting intestinal stem cells and supportive niche to regenerate and rebuild the human intestine.

To achieve the ultimate goals of pre-clinical development of both humoral and tissue therapy, the research project proposed herein will contribute with the following specific aims: to characterize cellular components and molecular signals of the intestinal niche network under both homeostasis and stress conditions, and to define these in the mouse model to provide an insight into human organoid growth. Methods to be used include bulk and single cell RNA-seq analyses, RNA-scope, 3D immunofluorescent imaging, and 3D organoid culture.

Project Narrative

More than 70 million Americans are impacted by a wide range of digestive diseases, including intestinal disorders, that have an extensive toll on quality of life and capacity of living, and have an astronomical cost exceeding \$142 billion. Evidence indicates that intestinal disorders are due to defective intestinal stem cells or misdirected signals that regulate stem cell behavior. This research employs a collaborative, multidisciplinary team science approach that will advance understanding of intestinal stem cell biology and how that knowledge can best be applied to develop therapies, improve patient outcomes, and ultimately, reduce the public health burden of intestinal disorders.