

Gen 3-2019 ISCC Research Project Abstract



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THE ROLES OF REGIONAL SPECIALIZATION, MECHANICAL FORCES AND EPIGENETIC MEMORY AFTER PERTURBATION AND INJURY OF THE INTESTINAL STEM CELL MICROENVIRONMENT

The epithelium of the small intestine renews every 2 to 5 days, making it one of the most rapidly renewing tissues in the mammalian body. This highly regenerative tissue faces a multitude of insults and injuries on a daily basis. While much has been learned over the past few years about the intestinal stem cells (ISCs) that fuel homeostatic renewal, the mechanisms by which the epithelium senses and responds to damage are poorly described. Understanding how the intestine reacts to insults and how homeostasis is reestablished are important basic science questions as well as essential starting points for translational approaches in regenerative medicine. In the previous round of the ISC Consortium (ISCC), we identified critical signals that regulate ISCs and discovered that injury leads to remodeling of the ISC microenvironment. In this application, we will work toward the ISCC goal of characterizing the minimal, required factors that support ISCs in health and disease. In the Specific Aims, we propose to determine how regional specialization, epigenetic memory and local forces shape responses to perturbation and injury in the crypt microenvironment.

Public Health Relevance Statement:

Stem cells are required for the renewal of the intestinal epithelium. While much has been learned over the past few years about how intestinal stem cells fuel normal renewal, the mechanisms by which the epithelium senses and responds to damage are poorly described. Because many diseases, including inflammatory bowel diseases, metabolic disorders and cancer, have a stem cell component, in this application we will determine how responses to perturbation and injury of the intestine are regulated by the stem cells and their microenvironment.