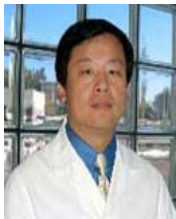


ISCC Research Project Abstracts



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INTESTINAL STEM CELL CULTURE AND ENTERO-ENDOCRINE LINEAGE DEVELOPMENT

The molecular basis of intestinal stem cell biology in both humans and mice is a subject of active research. The goal of this application is to identify the mediators that influence the interaction of human intestinal stem cells with intestinal myofibroblasts in order to enhance the regeneration of human small bowel epithelium. This is a necessary step toward the development of novel cellular therapies for disorders associated with intestinal failure in children. To bring such therapies to the clinic, it will be essential to recapitulate the in situ characteristics of the intestinal epithelium. We will focus on assessing the mechanism by which human intestinal stem cells undergo self-renewal and differentiation. Specifically, we will assess the role of R-Spondin and WNT5a in maintaining stemness of these cells. We will also assess

the mechanism by which Hedgehog signaling and the stress induced by alterations of oxygen tension and pH modulate the interaction between intestinal stem cells and myofibroblasts. Lastly, we will assess whether specific laminin and integrin isotypes alter intestinal stem cell growth and differentiation, and whether they affect cellular engraftment in recipient animal models. At the completion of this study, we anticipate that we will be able to define the mediators that control these stem cell characteristics, which will lead to novel cellular therapies.