

Project Number: U01DK85525-01

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Awardee Organization: Oregon Health and Science University

Title: Characterization of Intestinal Stem Cells (Research Project)

Abstract Text:

DESCRIPTION (provided by applicant): The existence of intestinal stem cells residing in an interactive niche has been well-accepted as the source of continual self-renewal of the intestinal epithelium. However, while other organ systems have appreciated substantial progress in identifying stem populations and exploiting this knowledge for therapeutic treatment of disease, advances in the intestinal stem cell field have been hampered by the inability to definitively identify, isolate, and grow the stem cell population. Recent identification of a number of putative intestinal stem cell markers displaying distinct expression patterns within the stem cell niche suggests that multiple progenitor pools co-exist. Intriguingly, these intestinal progenitor populations may belong to a stem cell hierarchy analogous to that in the well-characterized hematopoietic system. Defining a similar hierarchy within the intestinal stem cell niche will allow us to prospectively isolate discrete populations, thereby extending our knowledge of intestinal stem cell dynamics. Our long-range research goal is to understand the mechanisms regulating intestinal stem cell behavior in homeostasis and in disease. The studies proposed for this Research Project for the Intestinal Stem Cell Consortium are designed to test the hypothesis that discrete populations of intestinal stem or progenitor cells exist within a hierarchy in both normal tissue, and among cancer stem cells in intestinal cancer. Studies to address these goals are designed to define progenitor populations using protein expression patterns by immunohistochemical analyses and 3-dimensional intestinal crypt reconstruction along with profiling of cell surface antigen expression by fluorescence-activated cell sorting. Further, novel monoclonal antibodies against undifferentiated cells within the crypt will be generated to expand the available resources for effective isolation of intestinal progenitor and stem cells. The ability to isolate discrete pools of intestinal stem cells is critical for advancing our understanding of intestinal biology, which is paramount for understanding, classifying and treating intestinal disease.

PUBLIC HEALTH RELEVANCE: The key to unlocking intestinal biology and harnessing this knowledge for treatment of intestinal disease lies in the ability to identify and isolate the adult intestinal stem cell. This project, designed to understand how this cell functions, will provide insight into diseases where these stem cells do not function properly, such as in intestinal cancer. These studies have the potential for improving diagnoses, informing directed treatment, and designing new therapies for intestinal disease.