

## ISCC Research Project Abstracts



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### CELLULAR, MOLECULAR, AND FUNCTIONAL CHARACTERIZATION OF QUIESCENT/ACTIVE INTESTIN

Characterized by continual turnover, the intestine provides an elegant system for the study of adult stem cells - 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 (ISCs) 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 the different states and functions of subpopulations of ISCs and how these are regulated. In other tissues, such as hair and blood, the quiescent stem cell subpopulation is known to be critical, especially for long-term maintenance of the stem cell pool and for regeneration in response to stress or injury. However, in intestine, it is a matter of debate whether bona fide quiescent ISCs exist and/or where they reside. This research proposes that bona fide quiescent ISCs coexist with active ISCs. The active subpopulation accounts for generation and regeneration of intestinal epithelial lineages, and the quiescent subpopulation functions as a 'reserve' pool to replenish lost active ISCs and damaged tissues. The goal of this research is to further investigate quiescent ISCs, in particular, and to determine potential molecular regulation of quiescent and active ISC subpopulations. Methods to be used will include: surface markers and in vitro culture and in vivo lineage tracing assays to identify and characterize quiescent ISCs under stable and stressed conditions; RNA sequencing to determine how and where certain factors (Frizzled5 and/or 7) mediate signaling (noncanonical and/or canonical Wnt) that govern ISC maintenance, activation, self-renewal and location; and genetic mouse models to study the effect of protein inactivation on quiescent and active ISCs. Understanding signaling regulation of the state and fate of quiescent and active ISCs can uncover potential therapeutic targets for treating intestinal disorders, including cancer. If this goal can be achieved, it will open avenues not only for advancing the study of ISC behavior, but also for treating intestinal disorders in which ISC-driven tissue regeneration is essential and for screening drugs to target cancer stem cells. The ability to identify and isolate and characterize ISCs is critical for therapeutic advancements, especially tissue replacement, and for enhanced understanding of the development, prevention, and cure of intestinal disease.