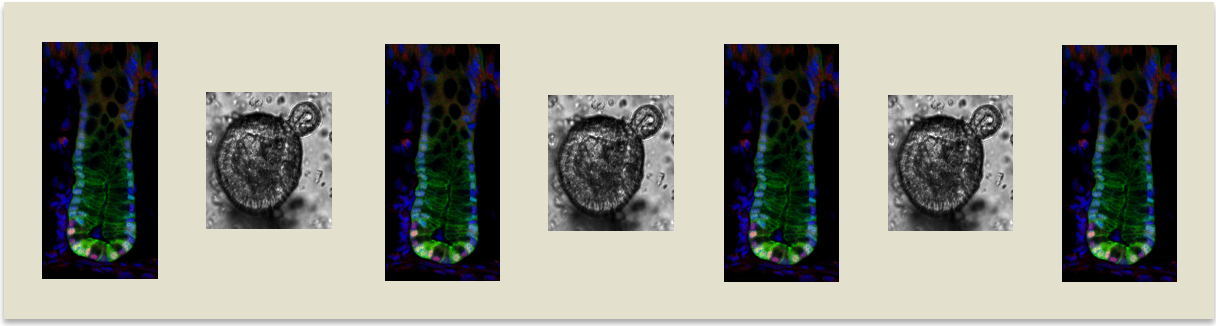

Intestinal Stem Cells

New concepts and methods

Toulouse, November 21st 2013

CHU Purpan

Scott MAGNESS (University of North Carolina, Chapel Hill, USA)

Intestinal Stem Cell Culture: A new era for in vitro discovery

Recent discoveries in biomarker identification and culture methods have fueled a rapid expansion in our understanding of how intestinal stem cells (ISCs) behave in physiology and disease. Our work focuses on describing how the Sox (Sry-Box) family of transcription factors contribute to intestinal stem cell identify and also how these factors influence differentiation and epithelial regeneration. Development of a Sox9EGFP mouse model has enabled the differential isolation of *bone fide* stem cells that are consistent with 'active' and 'reserve' states. Single 'active' ISCs marked by low levels of Sox9EGFP are able to generate self-sustaining spherical units in long-term 3-dimensional culture conditions. These epithelial structures are termed enteroids (small intestine) or colonoids (colon) and recapitulate the ISC, progenitor and differentiated cellular compartments found *in vivo*. During post-irradiation regeneration, high-expressing Sox9 cells function as an ISC pool, re-entering cell cycle and adopting ISC-like gene expression and function. Results from these murine studies have also facilitated isolation of human ISCs. A remaining and significant challenge in the field is efficient and quantitative use of culture methods to answer detailed mechanistic questions. In collaboration with biomedical engineers, we have developed novel micro-scale devices to study single ISCs or enteroids/colonoids in long-term culture. These platforms combined with mouse and human intestinal epithelial culture will serve as an *in vitro* foundation to study a broad range of conditions including cancers, inflammatory bowel disease, congenital birth defects, and ischemic injury.