Volume 12

Washington University
Undergraduate Research Digest

Spring 2017

Epimorphin Regulates the Mouse Intestinal Stem Cell Nice via the Stromal Microenvironment

Courtney Vishy
Washington University in St. Louis

Epimorphin Regulates the Mouse Intestinal Stem Cell Niche via the Stromal Microenvironment

Courtney Vishy

Mentor: Deborah C. Rubin

Intestinal resection for disorders such as Crohn's disease may result in short bowel syndrome, with nutrient malabsorption and parenteral nutrition dependence. There are few effective treatments. Stem cell therapies represent a novel therapeutic approach. Epimorphin (Epim) regulates growth factor secretion from intestinal subepithelial myofibroblasts. Although Epim is not expressed in epithelial cells, we previously showed that primary cultures of *Epim*$^{-/-}$ enteroids have increased surface area and budding compared to wild type (WT) enteroids. Our aims are to understand the mechanisms for this increase and determine whether this reflects stromal environmental effects on the stem cell niche.

Crypts were isolated from WT and *Epim*$^{-/-}$ mouse small intestines and cultured *in vitro*. Enteroids were imaged after 6 days and analyzed for surface area, budding, and epithelial differentiation by staining. Enteroids were then passaged two more times, reimaged, and harvested for RNA. RNAseq was performed to determine the effect on global epithelial gene expression.

In primary crypt stem cell cultures, *Epim*$^{-/-}$ enteroids had significantly larger surface area and more buds vs. WTs ($p<0.001$). At the second passage, enteroid area and budding in *Epim*$^{-/-}$ vs. WT enteroids were no longer significantly different (p=NS). The percentage of goblet and Paneth cells per enteroid was significantly increased in *Epim*$^{-/-}$ enteroids ($p=0.01$). Stem cell marker expression was significantly increased in *Epim*$^{-/-}$ vs WT enteroids by qRT-PCR ($p<0.05$). RNAseq analysis revealed significant differences in 86 genes. We conclude that Epim regulates mouse intestinal epithelial and stem cell proliferation and gene expression via stromal contributions to the niche microenvironment.