

# The Effect of IL-22 Stimulation on Paneth Cell Granule Morphology and Epithelial Cell Proliferation

Mehta, Neil (School: Ward Melville High School)

Interleukin-22 (IL-22) is a regulatory cytokine in the IL-10 family. Numerous intestinal cell types including absorptive and secretory cells express IL-22RA1, the IL-22 receptor. Intestinal IL-22 promotes mucosal wound healing, mucus secretion, and antimicrobial peptide (AMP) production. However, heightened IL-22 levels have also been observed in diseases including inflammatory bowel disease (IBD) where it may induce protective or detrimental effects. The pivotal roles of IL-22 in mediating intestinal functions and inflammatory responses have made it a promising target for therapeutic applications. IL-22 specifically acts on Paneth cells, a lineage of small intestinal secretory cells that secrete AMPs. Paneth cells package AMPs in granules stored in vesicles. IL-22 orchestrates the release of Paneth cell-derived AMPs, which protect against microbial pathogens and have been suggested to support the intestinal stem cell niche. I observe that IL-22 signaling via Paneth cells promotes intestinal host defense. Using novel *Il22ra1<sup>fl/fl</sup>;Defa6-cre* (Paneth cell-specific IL-22RA1 knockout) mice, I demonstrate that IL-22 signaling via Paneth cell-specific IL-22RA1 receptors promotes organoid growth *ex vivo*. I observe that Paneth cell counts do not vary between *Il22ra1<sup>fl/fl</sup>;Defa6-cre<sup>+</sup>* and *cre-* littermate controls. Furthermore, I determine that Paneth cells of *Il22ra1<sup>fl/fl</sup>;Defa6-cre<sup>+</sup>* and *cre-* mice display no difference in vesicle counts. These results suggest that IL-22 signaling via Paneth cell IL-22RA1 promotes epithelial proliferation *ex vivo*, though it does not directly modify Paneth cell morphology. These findings characterize a previously unclear role of IL-22 in Paneth cell-mediated intestinal defense, contextualizing potential therapeutic applications of IL-22.

## Awards Won:

Third Award of \$1,000