Monthly research highlight: Dual role for eosinophils in the gastrointestinal tract

Description of the studies

Deliterious role of eosinophils-
Eosinophils have long been associated with remodeling processes in chronic inflammation within other organs, but their role in chronic remodeling of the GI tract is unclear. We determined a role for eosinophils in chronic GI remodeling processes by using anti-eosinophil therapies in a pre-clinical model of Crohn’s disease (Masterson JC et al. American Journal of Pathology 2011). Further studies determined this was mediated in part by eosinophil release of IL-13 in response to IL-33 stimulation (Masterson JC et al. Inflammatory Bowel Diseases 2015). We also determined the relationship between eosinophils and radiologic evidence of chronic colonic disease in clinical investigations (Brandon JL et al. Pediatric Radiology, 2013).

Beneficial role of eosinophils-
However, one perplexing issue is that eosinophils are normal residents of the lower GI tract, but little is known about their role(s) in intestinal immunity. This is a critical factor to understand since a number of treatments may eliminate eosinophils throughout the body. To begin to address this concern, we induced an acute colitis in mice that was characterized by rich eosinophilic infiltrate and then induced this model in eosinophil-null mice. Results of these studies determined that mice with no eosinophils fared far worse than those with eosinophils, an observation that appeared to occur secondary to lack of expression of a pro-resolving lipid mediator named Protectin D1 (Masterson JC et al. Gut 2015; Video Abstract online at publisher’s website). These results implicate intestinal eosinophils in the production of Protectin D1 and set the stage for further studies examining the potential for the use of Protectin in inflammatory gastrointestinal diseases.

What the study/science means to patients and the field

Our research suggests that eosinophils may, in chronic intestinal inflammatory situations, contribute to tissue dysfunction via remodeling and fibrosis, making them a good target for therapies in chronic intestinal inflammation.

The potential impact of our findings has relevance for both eosinophils as well as the molecule Protectin. From a scientific standpoint our results suggest that eosinophils may in fact participate in host health during acute intestinal inflammation. From a clinical standpoint the molecule Protectin may in fact be a molecule that can be used in clinical studies to improve mucosal integrity and help to heal inflammatory processes.

Scientific investigator’s profile

Joanne Masterson, PhD, Assistant Professor, Department of Pediatrics, University of Colorado School of Medicine.

Education: BSc and PhD, National University of Ireland Maynooth; Postdoctoral Fellowship, University of Colorado School of Medicine.

Background: Dr. Masterson has a long-standing interest in defining novel mechanisms of mucosal inflammation, specifically related to the eosinophils contribution to epithelial cell biology and eosinophilic gastrointestinal diseases (EGIDs). Her studies have identified novel mechanisms through which eosinophils participate in EGIDs and Inflammatory Bowel Diseases impacting intestinal barrier
function and remodeling. In 2008, Dr. Masterson began working with Glenn T. Furuta, MD and Sean P. Colgan, PhD within the frameworks of the Gastrointestinal Eosinophilic Diseases Program, Children’s Hospital Colorado and the Mucosal Inflammation Program at University of Colorado School of Medicine (CUSOM). During her postdoctoral training Dr. Masterson refined and fostered her expertise as a translational-basic science investigator in the field of gastrointestinal epithelial cell biology. During this time she was funded for both a Fellowship and a Career Development Award, in addition by other foundation and industry partnership grants. Dr. Masterson is currently funded by an NIH-NIDDK K01 to examine the relationship between eosinophils and epithelial barrier dysfunction in Eosinophilic Esophagitis (EoE). The overall goal of her studies is to identify novel strategies to prevent, treat, and cure intestinal diseases. Dr. Masterson is a member of the American Gastroenterology Association; North American Society for Pediatric Gastroenterology, Hepatology and Nutrition; the Crohn’s and Colitis Foundation of America; and the International Eosinophil Society.

Summary research figure

Figure 1: Proposed dual roles for eosinophils within the intestinal mucosa. Based on basic, translational and clinical studies derived from other organs and the gastrointestinal tract, this figure presents complex and dynamic potential mechanisms for eosinophils to interact with resident intestinal cells. A number of lines of evidence support both potential beneficial and deleterious roles for eosinophils in the gut. (Woodruff et al. Journal of Pediatric Gastroenterology & Nutrition 2011)