Characterization of Mucus Barrier Properties:

Understanding Changes in The Presence Of Natural Stimuli and Onset of Disease

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Environmental pathogens and toxins are continually introduced to the body, challenging the host, and often result in gastrointestinal diseases. In many disease states, foreign entities (i.e. microbes and particulates) must overcome a physical barrier, the mucus layer, and make contact with the epithelial surface before the host is affected (e.g., Cholera, Shigellosis, *H. Pylori* infection, and necrotizing enterocolitis (NEC)). Mucus is a mesh-like structure that uses size and interaction filtration to selectively deter foreign entities from invading the epithelium. In disease, mucus is reported to have altered production, quantity, and composition. These changes may potentially alter the mucus structure, and in turn, foreign entities' transport through mucus. It is currently unclear if these changes cause the disease onset or occur during disease progression. Thus, it is critical to elucidate the changes occurring in mucus structure and foreign entity transport through mucus during disease progression. Previous work has demonstrated that exposure of the mucus barrier to lipids significantly strengthens the barrier properties. By understanding the altered mechanism of particulate diffusion and microbe transport in the mucus layer, and exploring other stimuli that may impact the mucus barrier (e.g., calcium, exogenous mucins, proteins, and oligosaccharides) it may be possible to develop strategies to modulate the barrier properties before disease onset or disease progression.

This work will explore potential differences in mucus structure and barrier properties between healthy and disease states, primarily in NEC and Hirschsprung's Disease animal models, to provide potential links between altered mucus properties and enterocolitis in these disease states. In addition, changes in mucus structure and barrier properties after the addition of external stimuli (ES) will be analyzed. Changes in mucus properties will be analyzed by multiple particle tracking, electron microscopy, and confocal imaging. Preliminary experimentation has shown transport properties are altered with disease and by exposure to ES. Ultimately, observed differences in barrier properties due to disease and ES will motivate the development of therapeutic options to modulate mucus barrier properties and prevent the onset of NEC and other disease states.