**Intestinal fucose, in sickness and in health**

The surface of all human cells is covered with a dense coating of glycosylated molecules that dictates the interactions of the cells with their environment. Nowhere is this more true than within the gastrointestinal tract, where the epithelial surface is coated with a mucus layer that is a critical mediator of communication with the diverse community of microorganisms that form the gut microbiome. The intestinal epithelial mucus layer is composed primarily of heavily O-glycosylated glycoproteins, called mucins, along with additional N-linked glycoproteins and glycolipids. A defining characteristic of the mucus layer is the presence of the fucose monosaccharide. Fucosylation of the intestinal epithelial occurs in a interleukin 22 (IL-22)-dependent manner in response to colonization with certain species of commensal bacteria, and fucose serves as nutrient for many gut microbes. However, pathogens also take advantage of intestinal fucosylation, and use recognition of fucosylated epitopes as a means to attack host cells. In my seminar, I will discuss roles for intestinal fucose in both normal physiology and in infectious disease. First, we examined the host cell receptors for cholera toxin, the secreted protein toxin that causes the symptoms of cholera. While cholera toxin has long been known to bind to the glycolipid GM1 with high affinity, we found little GM1 present in human intestinal epithelial cells. Rather, an important factor in binding of cholera toxin to human cells appears to be recognition of fucosylated structures, which bind to the toxin in a secondary glycan binding site. We also found that fucosylated molecules present in high abundance in human milk can competitively inhibit cholera toxin binding to intestinal epithelial cells. Current efforts focus on identifying the fucosylated glycoconjugates present in human intestinal epithelia and delineating the relative contributions of GM1 and fucosylated molecules to host cell intoxication. In a second project, we examined the effects of the cytokine IL-22 on glycosylation of human intestinal epithelia cells grown in culture. We observed an increase in fucosylation, with the majority of the fucose found on mucin-type glycoproteins. This increase in fucosylation was not accompanied by changes in the transcript level of any fucose-related genes. Rather, our data suggest that changes in the expression of other glycosyltransferases may alter the mucin glycoprotein structure to allow for increased fucosylation. Current efforts focus on defining the mechanism underlying the IL-22-dependent change in fucosylation, and investigating the impact on susceptibility to gut pathogens and on the ability of the mucus layer to promote a healthy microbiome.