Transmembrane mucins: barrier and signaling function at the intestinal host-microbe interface

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In the healthy gut, intestinal bacteria are separated from the epithelium by a thick mucus barrier. A thin or permeable mucus layer leads to increased host-microbe interactions and inflammation, as occurs during inflammatory bowel disease (IBD). At the host-microbe interface, epithelial cells express transmembrane mucins (MUC proteins) with barrier and signaling function that regulate cell differentiation and inflammatory pathways. During invasive bacterial infection, the extracellular domain of transmembrane mucins can be shed which activates signaling of the cytoplasmic tail. MUC cytoplasmic tails are involved in regulation of the epithelial NF-kB response and integrity of tight junctions. For MUC1 it has been shown that the cytoplasmic tail can also be cleaved and translocate to the nucleus where it impacts transcription of genes involved in immune responses. Our goals are to identify intestinal bacteria that interact with and activate transmembrane mucins MUC1 and MUC13 and characterize MUC-associated signaling pathways. Using CRISPR/Cas9 genome editing, we generated MUC1 and MUC13 intestinal epithelial knockout cell lines. With invasion assays and confocal microscopy, we found that both MUC1 and MUC13 pose barrier function during *Salmonella enteritidis* but not *Campylobacter jejuni* invasion. MUC13 plays a central role in epithelial cell proliferation and apoptosis. In addition to enteropathogenic bacteria, we are screening IBD-associated commensal bacteria for interactions with transmembrane mucins. Characterization of bacteria-mucin interactions in the intestinal tract will advance our understanding of the factors that contribute to IBD.