# Distinct Mucin Profiles are Associated with Inflammation in Ulcerative Colitis Patients

Alyssa Gutierrez[1], Anna Tingler[1], Amy Engevik[1], Melinda A. Engevik[1,2]

Medical University of South Carolina
[1]Department of Regenerative Medicine & Cell Biology

[2]Department of Microbiology & Immunology

**Background**: All intestinal epithelial cells have mucins anchored to their apical membrane, while goblet cells additionally synthesize secretory mucins. Both mucin types contribute to a mucosal barrier that is crucial for gut homeostasis. Mucin dysfunction leads to increased risks for infection, inflammation, and may contribute to inflammatory bowel disease (IBD). Prior studies indicate that ulcerative colitis (UC) patients have reduced goblet cell counts, altered mucin glycosylation, and more permeable mucus compared to healthy individuals. The objective of this study was to investigate the relationship between mucin profiles and inflammation in UC. **Methods & Results**: We analyzed RNAseq data from rectal biopsies of 206 control non-IBD individuals and new-onset UC patients (GSE109142). Patients were categorized by inflammation levels determined by calprotectin levels and histological scores from diagnostic colonoscopy. RNAseq revealed that UC patients had increased adherent mucins MUC1, MUC4, and MUC13, and levels were positively correlated with histological severity. Contrarily, MUC3A and MUC20 levels were negatively correlated with inflammation severity. No changes were observed in other adherent mucins. As for secreted mucins, we found that histological severity scores of 2 and 3 were associated with increased MUC2, MUC5B, and MUC5AC. We confirmed differences in MUC5B and MUC5AC protein levels by immunostaining colonic tissue from healthy individuals and UC patients. To determine if host-derived cytokines affect mucin profiles, we examined the mucin profiles of intestinal organoids derived from healthy individuals and UC patients. Interestingly, only MUC4 was significantly elevated in UC organoids, suggesting that other components absent in the cultures likely drive mucin alterations. To identify involved cytokines, we assessed mucin profiles in organoids treated with INF-y, IL-17A, IL-22 or TNF. IL-22, but not the others, increased MUC1, MUC4, MUC13, and MUC5B levels. Finally, we found decreased levels of glycosyltransferases GALNT3, GALNT5, GALNT7, GALNT12, B4GALT4, B4GALT5, B3GNT2, B3GNT3, B3GALT5, B3GNT7, B3GNT8, and ST6GALNAC1, and increased levels of ST3GAL1 and ST3GAL2 in UC patients, suggesting that mucins in UC may also be abnormally glycosylated. **Conclusions**: Inflammatory cytokines may contribute to UC by altering mucin profiles, such as increasing mucin expression and abnormal glycosylation.