Compositionally and Functionally Distinct Gut Microbiomes Exist Within Ulcerative Colitis Patients and Differentially Associate with Disease Severity

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**Background:** Many studies have described gastrointestinal dysbiosis associated with Ulcerative Colitis (UC) yet no study to date has explained the observed variation in microbiome composition amongst UC patients\(^1\)\(^\text{, 2}\). UC is commonly managed with variable efficacy by treatment plans that have both direct and indirect impact on the microbiome. We hypothesized UC dysbiosis can be classified into a small number of microbiobly discrete bacterial communities, each encoding distinct metabolic capacities that contribute to disease severity.

**Methods:** We profiled the bacterial community of stool obtained from 30 UC patients via sequencing. PICRUSt was used to examine the predicted functional capacity of communities\(^3\). Broad range metabolite profiling was performed to assess variation in the fecal metabolome amongst patients.

**Results:** Fecal microbiota clustered significantly into four groups when classified based on dominant bacterial family present: Prevotellaceae, Bacteroidaceae, Ruminococcaceae/Lachnospiraceae, and Other. This was also observed in data obtained from two recently published studies profiling UC dysbiosis\(^2\)\(^\text{, 4}\). After removing sequence reads mapping to the dominant bacterial family of each sample, clustering was still observed in all studies, indicating dominant families associate with distinct, lower abundance organisms. Moreover, the metagenome of each UC enterotype had significantly distinct predicted functional capacities and were variably enriched for bacteria-host signaling, amino acid and fatty acid metabolism pathways. Fecal metabolite profiling revealed concentrations of numerous amino acids and fatty acids that significantly differentiated UC enterotypes. Simple Clinical Colitis Activity was found to be significantly different between UC enterotypes, indicating the activity of specific UC enterotypes may differentially influence UC.

**Conclusions:** These observations imply UC patients stratify into distinct GI enterotypes, each engaged in functions that may differentially impact disease. Future work investigating the immunogenic potential of these dysbiotic communities and associated metabolites will provide insight into mechanisms behind UC dysbiosis and its relationship to disease outcome.